THE NEW BORN

e JOURNAL OF NNF KERALA

Theme: 'Journal watch'

From the **Editorial** Desk

Dear Colleagues,

A year has flown by & this editor's desk has been a bevy of frantic activity these past several days

This time round we are coming out with a e-magazine, first attempt of it's kind; what with "Going Green " being the watch word these days!

Our underlying theme is " Journal that made a difference in my Practice" .As you peruse the electronic pages, you will realise that a multitude of different perspectives will indeed whet your appetite for further reading.

I conclude with a big thank you to the entire editorial team with me and hasten to add that all deficiencies are unintentional & solely mine!

Preetha Remesh

Message

Dear Friends,

It's with great pride and happiness I am writing this message for NNF Kerala's journal - The Newborn. Second time in a span of one year. One more highlight for this issue is, this is our first E magazine.

It was an year of renaissance for NNF Kerala and our works along with the works of our very active district branches were appreciated with The Best State branch Award by the central NNF. Getting such an award is the first of its kind in the history of NNF Kerala.

With the support of my team and colleagues all over the state, I am sure NNF Kerala can make a remarkable change in the quality of Newborn Care.

Let me take this opportunity to congratulate Dr Preetha and her editorial team for the wonderful job they have done in coming out with journals of high academic standards which have set a benchmark for any journal editor.

Congratulations,

Best Wishes

Dr.Santosh MK

President-NNF Kerala

Message

Dear Colleagues....

It is indeed another feather in the cap of NNF Kerala to release its first E- Journal that will be uploaded in our website.

Formal release of this will be on 10/2/18 during South Neocon at Palakkad.

2017 was a historical year for our association and our systematic and pathbreaking activities were recognised by the Central NNF and we bagged the best state branch award.

Iassure you that we will continue our relentless efforts to promote neonatal care of our state. I thank you and request your continued support

All the very best

Dr.Jayachandran

Secretary-NNF Kerala

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Evolution of Neonatology

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The formal birth of neonataology appears to be of recent (60 yrs), but its roots extend into the 19th century when systematic and organized care began for groups of premature infants. It has evolved from a state of helplessness to heroic years and now it has reached a phase of experienced years. The practice of neonatology has now reached this years of wisdom and the thrust is on 'intact survival'.

A J Schaffer (1960) wrote " We have been forgiven for coining the words neonatology and neonatologist- the one designates the art and science of diagnosis and treatment of disorders of newborn infant, the other physician whose primary concern lies in this specialty" Many scientists played key roles in developing the basic concepts in the neonatal perinatal medicine .

The health and well being of new born is linked with maternal health. Healthy and well nourished mothers are likely to produce healthy and normal infants. The shamelessly high morality rate and morbidities in developing countries like India is due to poor maternal health and lack of antenatal care and assistance during delivery. Illiteracy, lack of financial independence and empowerment make matters worse. Teenage marriages and frequent pregnancies are also contributing to this.

An analysis of 2.6 million neonatal deaths from 192 countries in 2010 shows direct causes of neonatal death as prematurity (29%), infections (29%), asphyxia (23%), congenital malformations (8%).

Community based interventions without use of complex technology and also counties with low GDP have demonstrated low neonatal mortality. Several low cost interventions like exclusive breast feeding, kangaroo mother care for low birth weight babies, use of antibiotics for infections always brighten their survival. The child survival and safe mother hood programme focussed on reduction of post neonatal deaths by the promotion of universal breast feeding, immunisation, ORS for diarrhea and antibiotics for respiratory infections.

Involving mothers in the care of highrisk newborns helps to bring out a better outcome. Mother is the best primary health worker because of her stronger motivation, concern and commitment. She can provide skin to skin contact or kangaroo mother care which is credited to reduce the risk of nosocomial infections and hypothermia with improved survival of low birth weight babies. In an impressive feat, Kerala has become the first state in the country with a single digit IMR, by adopting these low cost but effective strategies. In order to reduce neonatal mortality essential or basic new born care services should be available at all the health care levels, because they are highly cost effective.

The outcome and survival of preterm babies has improved by use of antenatal steroids, administration of exogenous surfactant and respiratory support (CPAP, assisted ventilation) pharmacological manipulation of ductus arteriosus, support of blood pressure, portable echocardiography, use of inhaled nitric oxide, interventional cardiology, newer modalities of assisted ventilation (PTV, SIMV & high frequency ventilation) and ECMO have revolutionized the cardiopulmonary management of critically sick neonates. A number of therapeutic misadventures or disasters of our good intents, like ROP, pulmonary air leaks, BPD, Kernicterus, gray baby syndrome, pyloric stenosis, intraventricular haemorrhage, cerebral palsy are prevented or recognized early and managed effectively. It is important that we must exercise restraint and caution while introducing newer therapentic interventions while keeping in mind their safety and cost effectiveness.

A large number of newer interventions are in the pipeline to further revolutionize the practice of neonatology. The most important limiting factor is the cost and regionalization of centres with state funding will go a long way in achieving 'intact survival'. ■

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Section -1

Journal watch

- An article that changed my practice

Hip examination of newborn

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Shaw BA, Segal LS. AAP SECTION ON ORTHOPEDICS. Evaluation and referral for development dysplasia of the hip in infants. Pediatrics 2016, 138 (6): e 20163107

Hip dysplasia is the commonest cause of hip replacements in USA. Milder forms of DDH may be self-resolving and require no treatment.

Practices before this paper.

The convention has been to recognize unstable hip joints (Barlow test) and treat early by Pawlik's harness. This practice had limited benefits demonstrated, if fact Barlow himself reported all the mild cases detected by his method to resolve to normal health without active intervention. In contrast, a few authors have reported increased risk of avascular necrosis of hip by applying harness.

These insights have led to the new guidelines, a complete change in practice recommendations.

New Recommendations

1. Perform Ortolani test in newborn, to find dislocated hip (previous practice was Barlow test to find unstable hip that is easy to dislocate)
2. After 4 weeks, look for limited abduction of hip (mostly positive after 3 months age),
3. Responsibility of primary care physician is to diagnose and refer DDH before 6 months age (previously this would amount to delayed diagnosis)
4. X-ray may be useful after 4 months age, it is cheaper, reliable and easier to interpet.
5. Treatment of neonatal CDH is not an emergency and in- hospital initiation of bracing is not required. Orthopaedic consult can be safely obtained within weeks of discharge of a baby with positive Ortolani test. Persistent Barlow test positive (instability) may be evaluated by orthopedician.

We have surely referred many unstable hips (positive Barlow) in the last decade, hurriedly to protect the developing hip joint. A few of them had the harness applied. After, this paper was published, we have changed our practices.

1. The AAP, POSNA, AAOS, and Canadian DDH Task Force recommend newborn and periodic surveillance physical examinations for DDH to include detection of limb length discrepancy, examination for asymmetric thigh or buttock (gluteal) creases, performing the Ortolani test for stability (performed gently and which is usually negative after 3 months of age), and observing for limited abduction (generally positive after 3 months of age). Use of electronic health records can be considered to prompt and record the results of periodic hip examinations. The AAP recommends against universal ultrasonographic screening.
2. Selective hip ultrasonography can be considered between the ages of 6 weeks and 6 months for "high-risk" infants without positive physical findings. High risk is a relative and controversial term, but considerations include male or female breech presentation, a positive family history, parental concern, suspicious but inconclusive periodic examination, history of a previous positive instability physical examination, and history of tight lower-extremity swaddling. Because most DDH occurs in children without risk factors, physical examination remains the primary screening tool.
3. It is important that infantile hip ultrasonography be performed and interpreted per American Institute of Ultrasound in Medicine and the American College of Radiology guidelines by experienced, trained examiners. Developing local criteria for screening imaging and referral based on best resources may promote more uniform and cost-effective treatment. Regional variability of ultrasonographic imaging quality can lead to under- or overtreatment.
4. Most minor hip anomalies observed on ultrasonography at 6 weeks to 4 months of age will resolve spontaneously. These include minor variations in α and β angles and subluxation ("uncoverage") with stress maneuvers. Current levels of evidence do not support recommendations for treatment versus observation in any specific case of minor ultrasonographic variation. Care is, therefore, individualized through a process of shared decision-making in this setting of inadequate information.
5. Radiography (anteroposterior and frog pelvis views) can be considered after 4 months of age for the high-risk infant without physical findings or any child with positive clinical findings. Age 4 to 6 months is a watershed during which either imaging modality may be used; radiography is more readily available, has a lower rate of false-positive results, and is less expensive than ultrasonography but involves a very low dose of radiation.
6. A referral to an orthopedist for DDH does not require ultrasonography or radiography. The primary indication for referral includes an unstable (positive Ortolani test result) or dislocated hip on clinical examination. Any child with limited hip abduction or asymmetric hip abduction after the neonatal period (4 weeks of age) should be referred for evaluation. Relative indications for referral include infants with risk factors for DDH, a questionable examination, and pediatrician or parental concern.
7. Evidence strongly supports screening for and treatment of hip dislocation (positive Ortolani test result) and initially observing milder early forms of dysplasia and instability (positive Barlow test result). Depending on local custom, either the pediatrician or the orthopedist can observe mild forms by periodic examination and possible follow-up imaging, but actu-

al treatment should be performed by an orthopedist.

8. A reasonable goal for the primary care physician should be to diagnose hip subluxation or dislocation by 6 months of age by using the periodic physical examination. Selective ultrasonography or radiography may be used in consultation with a pediatric radiologist and/or orthopedist. No screening program has been shown to completely eliminate the risk of a late presentation of DDH. There is no high-level evidence that milder forms of dysplasia can be prevented by screening and early treatment.
9. Tight swaddling of the lower extremities with the hips adducted and extended should be avoided. The concept of “safe” swaddling, which does not restrict hip motion, minimizes the risk of DDH.
10. Treatment of neonatal DDH is not an emergency, and in-hospital initiation of bracing is not required. Orthopaedic consultation can be safely obtained within several weeks of discharge for an infant with a positive Ortolani test result. Infants with a positive Barlow test results should be reexamined and referred to an orthopedist if they continue to show clinical instability. ■

Hyperglycemia In Hie
— A Predictor For Better Outcome?

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"Hyperglycaemia in infants with hypoxic–ischaemic encephalopathy is associated with improved outcomes after therapeutic hypothermia: a post hoc analysis of the CoolCap Study" - Basu SK, Salemi JL, Gunn AJ, et al. Arch Dis Child Fetal Neonatal Ed 2017;102:F299–F306.

Neonatal encephalopathy occurs in 1 to 3 per 1000 live births in high-income countries, and in up to 20 per 1000 live births in low and middle-income countries. Hypoxic–ischaemic encephalopathy (HIE) is characterised by evolving neurological dysfunction and frequently, systemic multiorgan injury. In the above study, Basu SK, Salemi JL, Gunn AJ, et al has tried to assess whether early glycaemic profile in infants with moderate-to-severe HIE is associated with both the risk of multiorgan dysfunction and the outcome of therapeutic hypothermia.Glucose is the primary energy source for the new born brain and the derangement in glucose homoeostasis may be a biomarker of, or contribute to, neuronal injury and adverse longterm outcomes. Given the central role of glucose homoeostasis in cell metabolism, potentially early glycaemic status could contribute to the risk of multiorgan injury and recovery in HIE. In the above study, the authors examined the hypotheses first, that early glycaemic perturbations (ie, hypoglycaemia and hyperglycaemia) are biomarkers for the severity, chronicity and timing of perinatal hypoxia-ischaemia and hence it may be associated with risk of multiorgan dysfunction, and second, that glycaemic status would be associated with benefit from therapeutic hypothermia

The CoolCap clinical trial was an international multicenter, prospective randomized control study of selective headcooling and mild systemic hypothermia for the treatment of perinatal moderate - severe HIE. The study was conducted from July 1999 through January 2002, and follow-up was completed in September 2003. CoolCap Study cohort was reanalysed using a different statistical approach, exploring the laboratory and clinical characteristics of infants by their early glycaemic profile (hypoglycaemia, hyperglycaemia and normoglycaemia within the first 12 hours after randomisation), to investigate for associations with multiorgan dysfunction. It was evaluated whether glycaemic status was associated with the outcome of therapeutic hypothermia for the primary outcome of death and/or severe disability at 18 months of age.

Plasma glucose levels collected at prespecified time points (0, 4, 8 and 12 hours after randomisation) were used to classifyinfants into three groups based on their glycaemic profile duringthe first 12 hours after randomisation:

(1) hypoglycaemia (≥1glucose level ≤40 mg/dL, ≤2.2 mmol/L)

(2) hyperglycaemia(≥1 glucose level >150 mg/dL, >8.3 mmol/L)and

(3) normoglycaemia(all glucose levels >40 to ≤150 mg/dL, >2.2 to≤8.3 mmol/L)

In this post hoc analysis of the CoolCap Study, it was observed that early postnatal glycaemic profile (during the first 12 hours after randomisation) was associated both with the greater risk of deranged multiorgan function and with the response to induced hypothermia in infants with moderate-to-severe HIE. The rate of death and/or severe neurological disability at 18 months (the primary outcome) was higher for hypoglycaemic (83%) and hyperglycaemic (68%) infants, compared with normoglycaemic (49%) infants. Only among hyperglycaemic infants did hypothermia therapy confer a statistically significant lower risk of the primary adverse outcome & one case of death or severe disability at 18 months was averted for about every five hyperglycaemic infants who were cooled. For the first time, this study showed that hyperglycaemic infants from the Cool Cap Study significantly benefited from hypothermia treatment, whereas hypoglycaemic and normoglycaemic infants showed no apparent benefit.

However, there has been few limitations of this post hoc analysis -

- Glucose values between the prespecified time points or continuous values are not available.
- Glucose infusion rates,treatmentthresholdsandinterventionsusedwerenotstandardised across centres, and variations in practice may have influenced the results.
- Noinformation on the source (arterial, venous or capillary) of all blood samples, laboratory test protocols and monitoring devices, which may affect interpretation of the findings.
- The assessment of subsequent brain injury was limited because continuous EEG and MRI were not systematically done at all the centres.
- Further, there were few hypoglycaemic infants and many of them did not receive hypothermia, and thus the study had limited power toassesstheimpactofhypothermiaonthissubgroup.

This study has shown that early postnatal glycaemic profiles were associated with risk of multiorgan injury and the response to hypothermia treatment. Hypoglycaemic infants had the most severe multiorgan dysfunction, whereas hyperglycaemic infants had relative sparing of systemic organs. It was noted that infants with hyperglycaemia appeared to benefit most from therapeutic hypothermia. It is essential that further prospective studies are needed to investigate the role of early glycaemic patterns and their potential role in predicting response to therapeutic hypothermia, whether these patterns could guide individualised treatment protocols and finally whether controlled euglycaemia could further improve outcomes in infants with moderate-to-severe HIE. ■

Antenatal Magnesium Sulphate for Fetal Neuroprotection

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The department of neonatology at Rajagiri Hospital is mainly involved in the care of extreme preterm babies born in the hospital itself. They are born as the outcome of high risk pregnancies ,a significant number of which are the result of assisted reproductive techniques.In such a scenario, it is imperative upon the department to ensure a level of care which would allow a high rate of survival and at the same time limit the risk of neurodevelopmental problems as much as possible.

With this objective in mind, we along with the doctors in the department of obstetrics decided to enforce a protocol of administering magnesium sulphate to mothers below 32 weeks of pregnancy who are at risk of iminent preterm delivery.

Importance of Preterm Birth

The survival of infants born preterm has improved with interventions such as antenatal corticosteroids and surfactant. However, survival has been associated with substantial risk of medical and neurodevelopmental impairment.

Two identified patterns of injury appear to underlie the central nervous system complications of preterm infants: intraventricular hemorrhage and white matter injury. Severe **intraventricular hemorrhage** (grades 3 and 4) is reliably detected by ultrasound and occurs primarily among babies who are born at or before 28 weeks' gestation. Although the incidence of severe intraventricular hemorrhage is highest at 24 to 25 weeks, severe intraventricular hemorrhage is still a relevant problem up to 28 weeks, because there are more births at 26 to 28 weeks than at 24 to 25 weeks. MRI is required for reliable detection of white matter injury, which has a peak prevalence at 28 weeks. Its severity is associated with adverse motor and cognitive outcomes.[1]

Clinically, the most frequent adverse neurological outcomes associated with preterm birth are cerebral palsy and cognitive impairment. Other adverse outcomes include blindness, deafness, developmental delay, and/or other neurological impairment. More

than 50% of very preterm babies suffer from learning or motor disabilities or school difficulties, compared with about 20% of normal birthweight controls.

Importance of Cerebral Palsy

Cerebral Palsy(CP) can be reliably diagnosed by the age of 2 years. The prevalence of CP is 2 to 2.5 per 1000 live births.[2] The risk of CP is highest at earlier gestational ages.[3] Compared with infants born at term, infants born preterm have a CP risk that is approximately 3-fold higher at 34 to 36 weeks, 8-fold to 14-fold higher at 30 to 33 weeks, 46-fold higher at 28 to 30 weeks, and as high as 30-fold to 80-fold higher at <28 weeks.[4,5] The gestational age-related risk is associated, in part, with very low birth weight (i.e., <1500 g) and intraventricular hemorrhage.[6,7] Multiple gestation babies are also at heightened CP risk. The economic burden associated with CP is enormous. There is no known cure for CP, which makes effective preventive measures of primary importance. To date, no antenatal interventions have been identified that effectively decrease CP risk among preterm infants.

Magnesium Sulphate for Neuroprotection:

In two studies published in the 1980s, preterm infants born to women with preeclampsia had a lower incidence of adverse CNS outcomes than gestational age-matched neonates born to mothers without preeclampsia.[8,9] In 1995, a seminal case-control study was conducted with data derived from the California Cerebral Palsy project.[10] It demonstrated an association between antenatal magnesium sulphate administration prior to preterm birth and fewer cases of CP among infants born <1500g. It has been proposed that use of magnesium sulphate for eclampsia treatment and prophylaxis may underlie the potential association between antenatal administration of magnesium sulphate and CP, but the findings of subsequent observational studies investigating the association have been inconsistent.[10,11] Although the effectiveness of magnesium sulphate for prevention and treatment of maternal eclampsia is well proven, there remains a lack of understanding of how it may act as a neuroprotective agent. Magnesium acts in many intracellular processes, and its actions include cerebral vasodilation, reduction in inflammatory cytokines and/or oxygen free radicals, and/or inhibition of calcium influx into cells.[12] Animal studies have shown a neuroprotective effect.

The most common pathological lesion associated with cerebral palsy in preterm infants is periventricular white matter injury. Oligodendrocytes constitute a major glial population in the white matter. N-methyl-D-aspartic acid (NMDA) receptors on oligodendrocytes are thought to be important in the glial injury process. NMDA receptor antagonists are potent neuroprotective agents in several animal models of perinatal brain injury. Magnesium sulphate may reverse the harmful effects of hypoxic/ischaemic brain injury by blocking NMDA receptors, acting as a calcium antagonist and reducing calcium influx into the cells.Magnesium sulphate is also implicated in tissue protection against free radical activity, has been shown to act as a vasodilator, reduces vascular instability, prevents hypoxic damage,attenuates cytokine or excitatory amino acid induced cell damage and has anti-apoptotic actions. Magnesium complexed with adenosine triphosphate is required for the activity of many functional proteins, including membrane transporters, ion pumps and a broad array of other enzymes.

From 2002 to 2008, 5 randomized controlled trials (6145 babies) studied magnesium sulphate for fetal neuroprotection. In 2009, a milestone was reached with the publication of 3 meta-analyses, all of which concluded that magnesium sulphate for fetal neuroprotection decreases the risk of childhood CP.[13,14,15] Four trials used magnesium sulphate specifically for fetal neuroprotection among women likely to deliver within 24 hours.The fifth trial evaluated the effectiveness of magnesium sulphate for eclampsia prevention in women with preeclampsia. Of the 4 trials with neuroprotective intent, one also included a tocolytic arm. Three of these 4 trials enrolled primarily women with

preterm labour (with or without PPROM), whereas the fourth focused on women with PPROM. Children were followed-up to the age of 2 years for CP assessment, and 3 trials undertook cognitive testing. Study quality was good.[16]

The department has implemented this protocol as a quality improvement initiative in the year 2016.

Policy: Administration of magnesium sulphate to all mothers at ≤ 31+6/7 weeks gestation who are at risk for iminent preterm delivery.

"Imminent preterm birth" is defined as a high likelihood of birth due to one or both of the following conditions :

- Active labour with≥ 4 cm of cervical dilation
- with or without PPROM
- Planned preterm birth for fetal or maternal indications

Dosage and Schedule:

- For women with imminent preterm birth, antenatal magnesium sulphate for fetal neuroprotection should be administered as a 4g IV loading dose, over 30 minutes, followed by a 1g/hr maintenance infusion until birth.
- For planned preterm birth for fetal or maternal indications, magnesium sulphate should be started, ideally within 4 hours before birth, as a 4g IV loading dose, over 30 minutes, followed by a 1g/hr maintenance infusion until birth
- Magnesium sulphate should be discontinued if delivery is no longer imminent or a maximum of 24 hours of therapy has been administered

In the year 2016, we had 27 preterm deliveries where the gestation was below 32 weeks. Of these, there were 2 babies who had Grade 3 IVH.One of these mothers arrived in active labour and delivered within 30 minutes and therefore magnesium sulphate could not be administered.Both these babies were discharged home. In all 26 babies survived. They are on neurodevelopmental follow up.The statistics for the year 2017 is yet to be released.

References:

1. Woodward LJ, Anderson PJ, Austin NC, Howard K, Inder TE. Neonatal MRI to predict neurodevelopmental outcomes in preterm infants. N Engl J Med 2006;355:685–94.
2. Vincer MJ, Allen AC, Joseph KS, Stinson DA, Scott H, Wood E. Increasing prevalence of cerebral palsy among very preterm infants: a population-based study. Pediatrics 2006;118(6):e1621-e1626.
3. Petrini JR, Dias T, McCormick MC, Massolo ML, Green NS, Escobar GJ. Increased risk of adverse neurological development for late preterm infants. J Pediatr 2009;154:169–76.
4. Moster D, Lie RT, Markestad T. Long-term medical and social consequences of preterm birth. N Engl J Med 2008;359:262–73.
5. Stanley FJ. Survival and cerebral palsy in low birthweight infants: implications for perinatal care. Paediatr Perinat Epidemiol 1992;6:298–310.
6. Leviton A, Kuban KC, Pagano M, Brown ER, Krishnamoorthy KS, Allred EN. Maternal toxemia and neonatal germinal matrix hemorrhage in intubated infants less than 1751 g. Obstet Gynecol 1988;72:571-6.
7. Van de B or [Van de Bor M] M, Verloove-Vanhorick SP, Brand R, Keirse MJ, Ruys JH. Incidence and prediction of periventricular-intraventricular hemorrhage in very preterm infants. J Perinat Med 1987;15:333-9.
8. Leviton A, Kuban KC, Pagano M, Brown ER, Krishnamoorthy KS, Allred EN. Maternal toxemia and neonatal germinal matrix hemorrhage in intubated infants less than 1751 g. Obstet Gynecol 1988;72:571-6.
9. Van de B or [Van de Bor M,] M, Verloove-Vanhorick SP, Brand R, Keirse MJ, Ruys JH. Incidence and prediction of periventricular-intraventricular hemorrhage in very preterm infants. J Perinat Med 1987;15:333-9.
10. Nelson KB, Grether JK. Can magnesium sulfate reduce the risk of cerebral palsy in very low birthweight infants? Pediatrics 1995; 95:263–9.
11. O'Shea TM, Klinepeter KL, Dillard RG. Prenatal events and the risk of cerebral palsy in very low birth weight infants. Am J Epidemiol 1998;147:362–9. 25. Schendel DE, Berg CJ, Yeargin-Allsopp M, Boyle CA, Decoufle P. Prenatal magnesium sulfate exposure and the risk for cerebral palsy or mental retardation among very low-birth-weight children aged 3 to 5 years. JAMA 1996;276:1805–10.
12. Gathwala G. Neuronal protection with magnesium. Indian J Pediatr 2001;68:417-9. 29. Nelson KB, Grether JK. Causes of cerebral palsy. Curr Opin Pediatr 1999;11:487-91.
13. Conde-Agudelo A, Romero R. Antenatal magnesium sulfate for the prevention of cerebral palsy in preterm infants less than 34 weeks' gestation: a systematic review and metaanalysis. Am J Obstet Gynecol 2009;200:595–609.
14. Costantine MM, Weiner SJ. Effects of antenatal exposure to magnesium sulfate on neuroprotection and mortality in preterm infants: a metaanalysis. Obstet Gynecol 2009;114(2 Pt 1):354–64.
15. Doyle LW, Crowther CA, Middleton P, Marret S, Rouse D. Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. Cochrane Database Syst Rev 2009;(1):CD004661.
16. Rouse DJ, Hirtz DG, Thom E, Varner MW, Spong CY, Mercer BM, et al. A randomized, controlled trial of magnesium sulfate for the prevention of cerebral palsy. N Engl J Med 2008; 359(9):895–905.

Continuous Positive Airway Pressure

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CPAP helps maintain the functional residual capacity (FRC), which is much similar to "grunting" - the natural physiologic response to low lung complianceand low end-expiratory lung volumes (EELVs).Professor August Ritter voReuss, almost a century ago described bubble CPAPfor use in new borninfants.

In 1970s it wasrediscovered as the "missing link" between supplemental oxygen and mechanical ventilation to treatRDS.

Effects of NCPAP:

1. Reduces tachypnoea,
2. Increase FRC, improve lung compliance and PaO2
3. Decrease intrapulmonaryshunting (optimum FRC keeps the pulmonary vascular resistance minimal)
4. Stabilizationof the highly compliant thoracic cage of newborn particularly a premature baby
5. Decreases thoracoabdominal asynchrony
6. Helps to prevent apnoea of prematurity and more consistently obstructive apnoea by splinting the upper airways

Types of CPAP:

1. Constant flow CPAP
   Flow driven CPAP
   Bubble CPAP
2. Variable flow CPAP

Indications for NCPAP:

1. Stabilisation of Prematureinfants in the deliveryroom.
2. In infantswith increased work of breathing (poorly expanded and/or increased lungopacification in the CXR)
3. apnoea of prematurity.

Determining the optimum NCPAP:

Blood gases(especially pCO2) and chest X-rays(to assess adequacy of inflation) - more objective, but invasive and injurious.

Prudent assessment by pulse oximetry and transcutaneous CO2 along with clinical evaluation (respiratory distress score and vital parameters) s more practical

In practice, oxygen requirement to achieve target saturation of 90 to 94% reflects of adequacyof ventilation. The requirement of high FiO2 suggests possibility of unacceptably high pCO2. The goal is to keep FiO2 below 0.30 to 0.40 by increasing the NCPAP level stepwise up to a maximum of 8 cm H2O.

Patient interface of NCPAP:

Proper airway management is the mostimportant skill in improving outcomes and reducing complicationsof NCPAP.

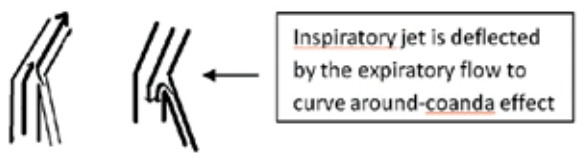
The following points to be noted

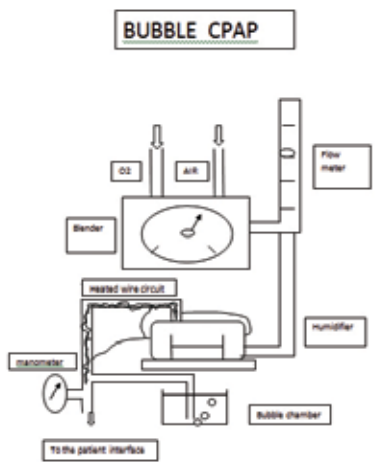
1. properprong size filling the entire nares without blanching
2. secure the prongs well to avoid dislodgment while avoiding injury to the nasal septum.
3. Binasal short prongs remain the most common method of administering NCPAP in neonates. Because infants are generally obligate nose breathers, NCPAP may be facilitated when delivered directly into the nose.
4. Complications like obstruction by secretions and nasal septal injury can be prevented by skin care, nasal suctioning,-frequent saline instillation and use of a protective barrier.
5. Nasal masks may be useful when the infant's nares are too small for nasal prongs. Alternating devices help to minimize the pressure effects of the prongs on the nares.

variable-flow NCPAP:

Reduces thepatient's WOB. NCPAP is generated by varying the flow deliveredto the infant's nares and a specially constructed nosepiece isemployed. These devices use the Bernoulli effect and gas entrainmentvia dual injector jets directed toward each nasal prong tomaintain a constant pressure. when the infant makes a spontaneous expiratorybreathing effort,the outward flow of expired air causes the flow of gas going toward the nares, to flip around (Coandă effect) and leave the generator chamber via the expiratory limb, thus assisting exhalation. Coandă effect is the tendency of a fluid to follow a curved surface.

A residual gas pressure is provided bythe constant gas flow, enabling stable NCPAP delivery at a particularpressure during the entire respiratory cycle. variable-flow devices appear to be able to maintain a more uniformpressure level compared to continuous-flow NCPAP. This may be the reason for the improved lung recruitment seenwith variable-flow NCPAP of this type





ZINC
- A Wonder Micronutrient In Neonates!!!!

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Recently I came across with 3 articles which proved the effectiveness of zinc in reducing the morbidity and mortality in neonates and improve neurological outcomes.

1. **Effect of Zinc Supplementation on Early Outcome of Neonatal Sepsis - A Randomized Controlled Trial, Banupriya Newton et al., The article was published in Indian Journal of Paediatrics, November 2015 edition.** Total of 134 babies with sepsis, who had two screening tests positive (micro ESR, CRP, band cell count) or blood culture positive were recruited for the trial. After exclusion criteria, 88 babies were randomised into treatment and control group. Treatment group received antibiotics and zinc. Control group received only antibiotics. Zinc was given in a dose of 3mg/kg twice a day for 10 days after initial stabilisation with oral feeding. The analysis was done on serum zinc levels, outcome and neurological status. The serum zinc concentration after 10 days of zinc supplementation in the treatment group showed an increasing trend but the difference was not statistically significant. There was not much variation in zinc levels in the control group before and after standard antibiotic treatment. The mortality rate though important clinically, was also not statistically important. The hospital stay in days was also not statistically significant between the two groups. At one month follow up, neurological assessment showed 70% less chance of having abnormalities in the treatment group compared to

controls. To conclude, the trial showed that zinc supplementation reduces the rate of mortality in neonates treated for sepsis, which is clinically relevant, but not statistically significant. However it has a beneficial effect on the neurological status at one month in babies treated for sepsis.

2. **Research paper by NB Mathur and Devendra K Agarwal, published in Indian Paediatrics in November 2015** assessed the effect of zinc supplementation on neuro-development and growth of preterm neonates. The Randomised Control trial studied 100 preterm neonates less than 7 days old. The treatment group received Zinc supplementation at a dose of 2mg/kg/day once daily till 3 month corrected age and the control group didn't receive Zinc. The primary objective was to assess Neuro-development status at 40 weeks post conceptional age and at 3 month corrected age using Amiel-Tison neurologic assessment and secondary objective to measure anthropometry and serum Alkaline phosphatase at 3 months corrected age. The research showed that zinc supplementation in preterm breastfed infants improves alertness and attention pattern and decreases signs of hyper-excitability, and proportion with abnormal reflexes. No adverse event of zinc supplementation was observed.

3. **Hospital based prospective, double blind randomised placebo controlled trial by Gianluca Terrin et al., was published in the American Journal of Clinical Nutrition in December, 2013**. In this trial very-low-birth-weight preterm neonates randomly allocated on the seventh day of life to receive (zinc group) or not receive (control group) oral zinc supplementation. Total prescribed zinc intake ranged from 9.7 to 10.7 mg/d in the zinc group and from 1.3 to 1.4 mg/d in the placebo control group. The main endpoint was the rate of neonates with more than one of the following morbidities: late onset sepsis, necrotizing enterocolitis, bronchopulmonary dysplasia, periventricular leucomalacia, and retinopathy of prematurity. Secondary outcomes were mortality and body growth. 97 neonates were enrolled in the zinc group and 96 in the control group. Morbidities were significantly lower in the zinc group (26.8% compared with 41.7%; P =0.030). The occurrence of NEC was significantly higher in the control group (6.3% compared with 0%; P = 0.014). However the daily weight gain was similar in both the groups.

All these studies show that zinc supplementation may help to reduce the mortality and morbidity seen in preterms and also improves neurological outcome. Zinc supplementation in sepsis also improves the neurological outcome. There is no consensus on the recommended dose and more detailed trials may be needed in this area. As zinc is easily available and has no serious adverse effects, we have included its routine supplementation in our preterm babies.

Apnea of prematurity - A common problem

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Neoreviews, March 2017 volume 18, authored by KalpashriKesavan and Joana Parga.

In this era of information explosion one is bombarded with journal articles from all sides. While searching answers for a clinical question there is every chance that some important articles might be missed.While the debate on superiority of a well conducted RCT versus a metaanalysis continues, some clinicians favour systematic reviews for getting a vantage point view of things.When you talk of a paper that changed your practice ,there are many but I would like to share with you a review paper which gives relevant insights into apnea of prematurity.I will share with the readers points which I gained from the paper in question answer format.

How common is AOP(apnea of prematurity) ?

While we all know that AOP is the rule in <28 weekers,upto 20% of 34 weekers also can get it.So do not let the vigil down just because infant is near 34 weeks.

How will you define an apnea?

1) Cessation of breathing lasting 15 to 20 seconds.
2) Cessation of breathing less than 10 seconds with any of the following
   a) SpO2 fall to 80 to 85%
   b) Bradycardia to 80 /minute or less than two thirds from the baseline heart rate

A note of caution is added by the authors stating that definitions vary across references.

What is the role of neurotransmittors in apnea?

Preterm brain's respiratory centre is more sensitive to inhibitory transmittors likeadenosine,serotonin,prostaglandin,GABA. We all know that caffeine acts by inhibiting adenosine. There may be scope for molecules that modulate other transmittors as well in future.

What is the relation between FiO2 and apnea?

This is an interesting fact to know.Suppose if a preterm gets repeated hypoxic episodes (as seen typically in chronic lung disease of preterms), the sensitivity of its peripheral chemoreceptors get altered in the carotid body. Carotid body gets used to these hypoxic spells to such an extent that it starts thinking of a normal pO2 or higher pO2 as abnormal and paradoxically leads to apnea !. So also inutero carotid body is used to fetal pO2 in 30-35,so post natal with the pO2 surge the carotis body gets silenced. Food for thought here is to remember how sensitive a parameter is fiO2. Increasing fiO2 in an apneic may not be the easy way out but may be counterproductive.

Capnea and apnea

We all know that hypercapnea stimulates respiration. A term infant or a child responds to same by increasing the respiratory rate and tidal volume. The catch in preterms is that they do not behave like this but rather increase expiratory time which leads to less minute volume and uncoordinated movements of the chest wall which leads paradoxically to apnea.

How does a preterm respond to hypocapnea?

Preterms are very sensitive to pCO2.Say for eg a term baby developes apnea when pCO2 falls to 25,whreas a preterm develops the same with a pCO2 of 30. These are not absolute reference numbers given in the article but written for the sake of understanding.

The message is that be it hypercapnea or hypocapnea , a preterm may respond with apnea.Again,its time to respect pCO2 and the need to chase it proactively.

Can GERD lead to apnea?

This association is highly controversial without enough evidential back up. Authors state that GERD or the presence of milk in pharynx can trigger the dreaded laryngeal chemoreflex leading to apnea.GERD treatment is not advocated for treating AOP.

Do you want premies to wake up or just sleep?

AOP is seen more during active REM sleep. Respirations become irregular during this time.Lets hope that in future apnea monitoring will pave the way to monitoring of sleep states and the variation in the pattern of breathing that can preempt an episode.

What are the simple things which can be done to avoid obstructive apnea?

Pharyngeal wall is the most collapsible portion of the upper airway in preterms. Whenever the neck is more flexed it collpses and predisposes to apnea. So pay attention to subtlity in head position.Prone nursing is also advocated in this paper to avoid apnea. Nasal block can lead to apnea. So, Avoid unnecessary and vigorous suctioning of the nose. Do not put higher sized NGT and block the nose. (OGT scores here) If on O2 prefer heated humidified air to avoid nasal crusting.

Sophisticated alarm systems needed?

Apnea monitors, capnography, sats monitoring all can never replace bedside monitoring. SpO2 target suggested is 88 to 94% and heart rate alarm should be set at 100/min,well ahead of the 80 per minute cutoff. A stable thermoneutral environment isalso an important measure to prevent apnea.

Caffeine citrate for all preterms?

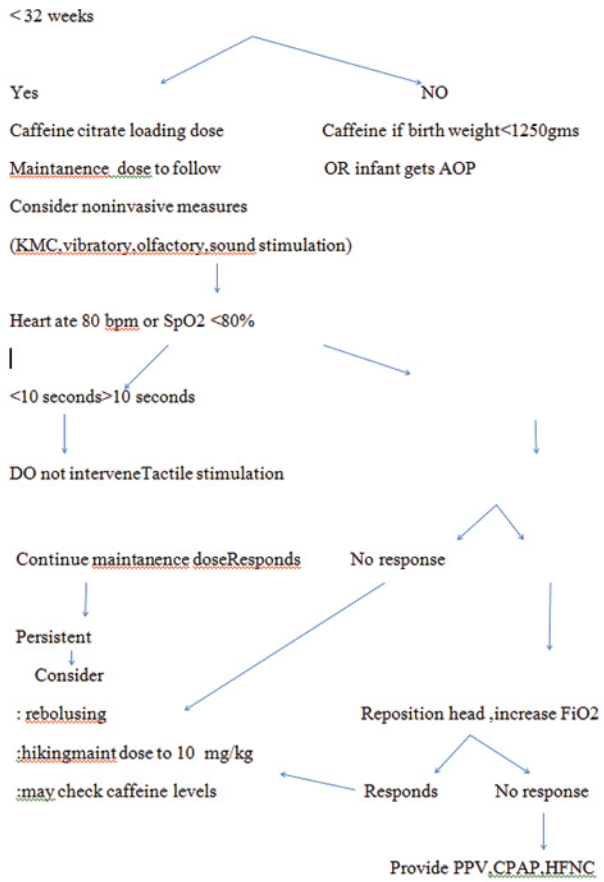
Article suggests caffeine citrate for all premies<28 weeks. Between 29 to 32 weeks it may be given (practice varies across units) Beyond 32 weeks prophylactic caffeine may not be needed routinely. Widely used now a days

,following points are to be remembered,regarding caffeine.

Caffeine citrate can cause feeding intolerance. So also diminished growth in preterms especially when therapeutic ranges exceed. Though it has a wide therapeuticrange,it can be exceeded even at standard doses!, due to fluid imbalances,illnesses that alter itsmetabolism, distribution and excretion.

Caffiene citrate has to be discontinued around 33-34 weeks especially if the infant has been apnea free for 5-7 days.Authors quote a study where it was noted that prolongation of caffieine beyond 34 weeks might predispose to hypoxic events ,of course an issue which has too be looked into by other studies.

This article gives a flow chart which may act as a guideline for managing AOP.



Respiratory strategies recommended include, nasalCPAP, validated synchronizedNIPPV, high or low flow nasal canula.

Future

More RCT's might be needed to look more into noninvasive measures like olfactory-stimulation, soundstimulation,mechanosensory stimulation.

AOP and future risk of SIDS?

There is no direct causal relationship between AOP and SIDS. But, preterms who had AOP have higher baseline heart rate and lower heart rate variability for the first several months after birth.This is a finding which has been reported in infants who had died of SIDS as well. AOP resolves at 44 weeks PMA whereas SIDS typically ocurrs at 47 weeks PMA suggestive of difference in pathology.

Can AOP cause neurodevelopmental impairment?

Authors use chicken or egg idiom to describe this situation.An already compromised brain might have more apneas or is it that recurrent apneas damage the brain?. Need for more vigorous studies is suggested. One fact that is known for sure is that AOP has the potential to trigger inflammatory cascade in the baby mediated by cytokines. Before conluding it has to be reiterated that the article does reinforce the need to screen for secondary causes of apnea especially anemia. ■

A Study which influenced our clinical practice

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'Impact of antibiotic policy on antibiotic consumption in a NICU in India' is a recent study from RDT Hospital,Andrapradesh by DasarathaRamaiahJinka and et al. which came in Indian Pediatrics in September 2017. As we all know, misuse of antibiotics in NICU and current emergence of antibiotic resistant organisms are one of the major challenges faced by the neonatologists worldwide. Though we have lots of studies on the misuse of antibiotics in NICU, nobody has done a good study on the impact of having an antibiotic policy on antibiotic consumption till date in India. That's why this study drew our attention and we decided to have a recent antibiotic audit in our unit also to update our existing antibiotic policy.

Details of study:

This was a retrospective study over a period of two years (between January 2013 and December 2014). The antibiotic policy was implemented in January 2014 and this study was done 1 year before and after that in a single center (30 bedded level 3 unit). The primary outcome was to compare the overall antibiotic consumption in the year before and after the initiation of antibiotic policy using WHO s DDD per 100 patient days. The secondary outcomes were to calculate proportion of admitted newborns on antibiotics, choices of antibiotics, overall mortality and sepsis related mortality.

Review of Article:

This study had a relevant,well framed research question which included the study population,intervention and outcome. The study design was a also acceptable as a randomized controlled study may not be ethically feasible in this scenario. As it was a retrospective study, chance of bias was also less. They had decided their antibiotic policy as per their sensitivity data on the previous year. There was no deviation from the actual protocol. A few limitations noticed were the study duration and lack of analyzing individual case sheets.It was only a one year study from a single centre. Study duration should be prolonged to know the consistency of the results.As individual case sheets were not analyzed, it was not sure whether the proposed empirical antibiotics and duration are used in all the included cases.

Results:

According to their results, the antibiotic consumption decreased from 12.47 to 11.47 DDD/100 patient days before and after implementation of antibiotic policy. But it was not found to be statistically significant. There was a significant drop in the consumption of third generation cephalosporin drugs. The overall proportion of babies on antibiotics decreased significantly. There was a significant rise in the proportion of babies on first line antibiotics. No significant difference in overall mortality. This clearly shows that the results were really promising and we can strongly recommend all the units to have an antibiotic policy according to the local sensitivity pattern.

How did it influence us?

We decided to review our antibiotic policy based on our previous year's data. We did a retrospective audit for 1 year. We calculated total number of cultures taken and total number of positive culture results from that. Out of this, percentage of inborn and out born were calculated. The sensitivity pattern for both inborn and out born were analyzed. According to these reports, we modified our antibiotic choices for both inborn and outborn babies.

Our results:

We had sent total of 816 blood culture samples over 1 year period. Out of this, 569 were from inborn babies and 247 were from out born babies. We got 41 positive cultures from 569 inborn samples and 35 positive cultures from 247 out born samples. The incidence of sepsis was 7.2% in inborn babies (3.3% EOS and 3.9% LOS) and 14.2% in out born babies (7.7% EOS and 6.5% LOS).

The most common gram negative organism among inborn babies were Klebsiella pneumoniae and then Acinetobacter baumannii. They were sensitive to Amikacin/Gentamycin/ Meropenem. Most common gram positive organism among inborn babies was Staphylococcus hemolyticus which was sensitive to Amikacin/ Gentamycin and Vancomycin. The most common gram negative organism among out born babies wereagain Klebsiellapneumoniae and Acinetobacterbaumannii. They were sensitive to Amikacin/Piperazillin-Tazobactam/ Meropenem. Most common gram positive organism among out born babies was again Staphylococcus hemolyticus which was sensitive to Amikacin/ Gentamycin and Vancomycin.

	MCC Gram negative organism (sensitivity)	MCC Gram positive organism (Sensitivity)
Inborn	Klebsiellapneumoniae , AcinetobacterBaumannii (Sensitive to Amikacin/ Gentamycin/Meropenem)	Staphylococcus Hemolyticus (Sensitive to Gentamycin/ Amikacin/ Vancomycin)
Outborn	Klebsiellapneumoniae , AcinetobacterBaumannii (Sensitive to Amikacin/ Piperacillin-Tazobactam/Meropenem)	Staphylococcus Hemolyticus (Sensitive to Gentamycin/ Amikacin/ Vancomycin)

According to the above data, we updated our antibiotic policy.

First line (Inborn)- Gentamycin/ Amikacin (Monotherapy)

Second line (Inborn)-Piperazillin- Tazobactam/ Vancomycin

First line (Outborn)-Amikacin/ Piperazillin-Tazobactam

Second line (Outborn)-Meropenem/ Vancomycin

Discussion:

All newborn units should have an Antibiotic stewardship programme (ASP). ASP means the right antibiotic, to the right patient, in the right dose, through right route,in the right time with minimal harm to the patient. This improves the patient outcome and safety decreasing the cost at the same time. It emphasizes appropriate empirical antimicrobial therapy with early and accurate identification of the pathogen and susceptibility, combination or monotherapy chosen on the basis of the pathogen identified and de-escalation of initial broad spectrum therapy after definitive diagnosis.

Implementation of 'ASP':

1. The first step is to have a policy on optimal antimicrobial use to ensure documentation of doses, duration, and indications for antibiotics; and developing facility specific treatment recommendations in the health facility.
2. Designing and executing policies on antimicrobial "time out": Reassessment of the need and choice of the antibiotics started empirically,usually done after 48 hours.
3. Adhering to the dictum of "Prior authorization": An antibiotic expert who can review and decide the need of antibiotics before the therapy is initiated.
4. Regular changes from intravenous to oral
5. Dose adjustments and dose optimization
6. Automatic alerts to avoid unnecessary duplication of drugs.
7. Time sensitive automatic stop orders for surgical prophylaxis.

Conclusion:

Every NICU should have an antibiotic policy and follow the principles of Antibiotic stewardship programme. Antibiotic of choice should be updated regularly according to the audit results. ■

Vaginal Seeding: An interesting Concept

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Vaginal seeding (also called Microbirthing) is a novel procedure whereby vaginal fluids (and hence vaginal microbes) are applied to a new-born delivered by caesarean section in order to create an equivalent microbiome to a baby delivered vaginally.

Why is restoration of the microbiota of caesarean-born infants via transfer of vaginal microbes an interesting concept?

Ever since the The Human Genome Project was able to sequence and map the genome of homosapiensin April 2003, major sequencing technologies gave us the tools to study the microbiomethat inhabit the human beings. This has generated considerable interest in the study of the microbiota of the human body which is now proposed to have a major role in the pathogenesis of various illnesses in the body.The gut microbiota is essential to human health throughout life, but the acquisition and development of this microbial community during infancy remains poorly understood. The microbiome that colonizes the body of newborns can have a determinant role in educating the immune system of the body.

Meanwhile, there is increasing concern over rising rates of caesarean delivery and insufficient exclusive breastfeeding of infants in most parts of the world.Joseph Neu and colleagues have reported that the infants born by C section have a higher risk of developing both autoimmune diseases and allergic diseases and have proposed the hygiene hypothesis as the aetiology(1). Caesarean section interrupts the natural exposure of newborn infants

to the maternal vaginal microbiota and babies delivered by caesarean section (C-section) acquire a microbiota that is different from that of vaginally delivered infants.

Pilot study:

Pilot study of vaginal seeding was carried out by byMaria G Dominguez-Bello, et al in New York[2].The authors conducted a randomized controlled study of 18 dyads (mother and neonate) in which infants delivered by C-section were swabbed with maternal vaginal fluids at birth (study group) and compared with the control group where no intervention was carried out.

The gut, oral and skin bacterial communities of these infants were studied during the first 30 days of life. A total of 1,519 samples were obtained from anal, oral and skin sites of infants and mothers at six time points during the first month of life (1, 3, 7, 14, 21 and 30 d after birth). Microbiome composition was characterized by sequencing the V4 region of 16S rRNA gene and 1,016 samples were used for analysis after quality filtering.

Authors reported that their results demonstrate that vaginal microbes can be partially restored at birth in C-section–delivered babies by vaginal seeding. The gut, oral and skin bacterial communities of those newborn infants delivered by C-section and swabbed with vaginal fluids was found to be enriched in vaginal bacteriasimilar to vaginally delivered babies and unlike those infants delivered by C-sectionwithout intervention.

A word of caution:

The long-term health consequences of restoring the microbiota of C-section-delivered infants remain unclear in this study. The study had a small number with some heterogeneity in recruitment like reasons for C-section (microbiomes differ depending on emergency versus elective C-section), antibiotic usage in most C-section deliveries and the stress of vaginal delivery vs. C-section delivery (corticosteroid and other hormonal responses).It is also important to recognize that the transfer of some pathogens, which may be asymptomatic in the mother, could result in severe adverse consequences for infants, including group B streptococcus, herpes simplex virus, Chlamydia trachomatis, and Neisseria gonorrhea unless screened thouroughly.However, this study generated enough interest in US in 2016 and there was a huge demand for vaginal seeding to “boost the baby’s health” from mothers undergoing C-Section!

American College of Obstetricians and Gynaecologists (ACOG) Statement[3]:

ACOG brought out the following statement inNov 2017: “The intended purpose of vaginal seeding is to transfer maternal vaginal bacteria to the newborn. As the increase in the frequency of asthma, atopic disease, and immune disorders mirrors the increase in the rate of cesarean delivery, the theory of vaginal seeding is to allow for proper colonization of the fetal gut and, therefore, reduce the subsequent risk of asthma, atopic disease, and immune disor-

ders. At this time, vaginal seeding **should not be performed outside** the context of an institutional review board-approved research protocol until adequate data regarding the safety and benefit of the process become available..”

Final Comments:

The newer trends in epigenetics indicate that microbial flora of the mother’s gut and newborninfant may have an important role in the development of future adult diseases.As of now, vaginal seeding, though an interesting concept should be carried out only under a well designed research setting.

References:

1. Neu, Josef et al, Cesarean Versus Vaginal Delivery: Long-term Infant Outcomes and the Hygiene Hypothesis, Clinics in Perinatology, Volume 38, Issue 2, 321 - 331
2. Maria G Dominguez-Bello, et al, Partial restoration of the microbiota of caesarean-born infants via vaginal microbial transfer, Nature Medicine March 2016, published online 1 February 2016; doi:10.1038/nm.4039
3. Committee Opinion No. 725: Vaginal SeedingObstetrics & Gynecology: November 2017-Volume 130 - Issue 5 - p e274-e278

tal Unit!!

Article that changed my practice
Baby Friendly Neonatal Unit!!

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1. Editorial
   NICU Environment : Can we be Ignorant?
   Col MNG Nair*, Surg Cdr Girish Gupta+, Lt Col SK Jatana# MJAFI 2003; 59 : 93-95
2. Archives of Disease in Childhood, 1987, 62, 987-988 Environmental neonatology
3. **Neonatal Intensive Care Practices Harmful to the Developing Brain**
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   From the Division of Neonatology, Department of Pediatrics, KEM Hospital, Pune 411 011, India.
   Correspondence to: Dr Sudha Chaudhari, Consultant, Department of Pediatrics, KEM Hospital, Pune 411 011, India. kemhrc@vsnl.com
4. **Eight principles for patient-centred and familycentred care for newborns in the neonatal intensive care unit**
   Jean-Michel Roué,1 Pierre Kuhn,2 Maria Lopez Maestro,3 Ragnhild Agnethe Maastrup,4 Delphine Mitanchez,5 Björn Westrup,6 Jacques Sizun7

Survival of premature babies less than 32 weeks of gestation is now more and more common in countries across the world. In India out of 27 million babies born every year (2010 data), 3.5 million babies are born premature.[1] As the rate of survival increases, the rate of complications of these premature babies is also on the rise. Clinicians do give best of their knowledge and efforts for the betterment of the baby. But at the same time, forget or unable to focus on some areas of the newborn care, mainly creating a baby friendly neonatal unit.

Unfortunately, adverse neurodevelopmental outcomes, including cognitive, language, visual-perceptual, sensory, and attention and learning deficits, occur more frequently in preterm infants.2 Exposure to painful experiences and/or stressful environmental stimuli may also be potential sources of altered brain development.3 Environmental neonatology was one term which used to describe non-pharmacological strategies aimed at preventing the detrimental impact of overwhelming sensory input and procedures on the developing newborn brain.[4]

In one of the article, which I came across the discussion was about Eight principles for patient-centred and family-centred care for newborns in the neonatal intensive care unit.[5] In 2005, the ESF European Research Network on Early Developmental Care[6] suggested that eight procedures could be considered 'principles of care'. Now 12 years down the line, we have got significant amount of evidences about these eight principles and most of these can be implemented in our neonatal unit without waiting for further evidences.

1. Free 24*7 parental access:

Most of the parents suffers extreme degree of stress after the birth of their preterm baby. Parental presence in NICU may alleviate some of these stresses from them. Also this helps to develop a bonding between them and their little one and can move as a single family unit. And from the baby's perspective, it has got multiple advantages. The bonding and attachment process is based on the close proximity between mother and child and the mother's adapted reactions to her newborn's cues.[7] Also there are some studies which shows lower prevalence of retinopathy of prematurity and reduced total length of stay and a reduced risk of moderate-to-severe bronchopulmonary dysplasia.[8,9]

2. Psychological support for parents:

New parents eagerly look forward bringing their baby home, so it can be frightening if your newborn is admitted to the neonatal intensive care unit (NICU). It can be due to various factors, which includes the sickness of the baby, hospital stay, thinking about the future, medical bills etc. Understanding the NICU and what goes on there can help ease parents' fears. Lack of good communication and doorstep updates contributes to parents feeling lonely and abandoned. A poor parental psychological well-being seems to be associated with behavioral problems of very low birth weight infants.10 So supporting parents targeting on parenting education and therapeutic developmental support for the infant, is an essential component of early intervention.[11]

3. Pain Management in newborn:

Neonates in the intensive care unit are exposed to painful procedures and stimuli. Smallest and sickest babies are more prone to get exposed to more number of painful procedures in NICU. Neonatal exposure to pain has been identified as being significantly associated with specific changes in brain development in this population.[12] The prevention of pain in neonates should be the goal of all caregivers. Assessment of pain should be using validated scales. Two scales have metric adjustments for prematurity (the PIPP and the N-PASS). Only two scales, EDIN and N-PASS, have demonstrated validity and reliability for prolonged neonatal pain.[13]

There are pharmacologic and non-pharmacologic ways to alleviate pain. Although there are major gaps in our knowledge regarding the most effective way to prevent and relieve pain in neonates, proven and safe therapies are currently underused for routine minor yet painful procedures. According to a recent Cochrane meta-analysis, non-nutritive sucking-related interventions, breast feeding, sucrose and swaddling/facilitated tucking are efficient in reducing pain reactivity during invasive procedures in preterm newborn infants.[14-16] Different pharmacologic treatments includes opiates for endotracheal intubation and mechanical ventilation, paracetamol for post operative pain etc. But the long term consequences of some these drugs are still not known.

4. Supportive environment:

Preterm and high risk infants are exposed to multitude of stimuli from NICU, mostly noxiuos sounds and lights, which is totally different from intrauterine period, during their critical period of brain development. Lasky and Williams demonstrated that extremely low birthweight neonates are exposed to noise levels averaging 56.44 dB and light levels averaging 70.56 lux during their stay from 26 to 42 weeks of postmenstrual age in the NICU.[17] This environment could negatively impact the quality and duration of sleep which could alter brain development.18 So adequate control of the lighting and noise is very essential. Early exposure to the parents' voice seems to be important for the infant's cognitive and language development.[19]

5. Postural support for newborn infants:

This is another essential component for the development of the baby. The position should optimise the infant's ability to breathe independently. Infants with increased respiratory demands may be more stable in prone. Evidence suggests prone position provides improved respiration and greater chest wall synchrony and improved gas exchange. Inappropriate positioning can lead to abnormalities in muscle tone in preterm newborns.[20] Moreover, preterm newborn infants in unsupported extended positions can exhibit increased stress and agitation.[21] Stress should be minimized by positioning the infant to maximize comfort and enable the infant to self soothe e.g. hands to midline, boundaries close enough for the infant to reach with feet. The general goals of positioning the preterm infant in the incubator are to promote flexion, facilitate hand-to-mouth activity, facilitate midline orientation and symmetrical positioning, support posture and movement, optimise skeletal development and alignment, promote a calm state and prevent head deformities and torticollis.[22]

6. Skin to skin contact:

Skin to skin contact can be performed for stable babies at all levels of neonatal care across the globe irrespective of the socioeconomic status. It has got proven benefits which includes developing bonding between the mother and infant, decreased risk of mortality, severe infection/sepsis, hypothermia and hypoglycaemia, shortened the length of hospital stay, and increased infant growth and breast feeding. Skin to skin contact or Kangaroo Mother Care is recommended by WHO and the pediatric societies all over the world.

7. Breast feeding and lactation support:

Breast feeding has proven benefits, both short term and long term. It has impact on the long term neurodevelopment of the baby. Breast feeding from birth has got numerous advantages which include prevention of necrotizing enterocolitis, helps in immunity etc. Clinical practice should adapt the BFHI, which provides evidence-based recommendations on how to protect, promote, and support breast feeding in neonatal units.[23]

8. Sleep protection:

Sleep is essential to human life and involves both physiologic and behaveoral processes. It plays an important role in brain de-

velopment. In neonatal unit, sleep disruption can occur by various factors which includes unadjusted sound and light levels and/or medical and nursing procedures.[24] There are not much studies in relation to sleep deprivation in preterm infants. Research in animal models demonstrated changes in respiratory patterns, altered subsequent learning, and long-term effects on behavior and brain function due to sleep deprivation during the neonatal period.[25] So sleep deprivation in preterm infants may have long term consequences, and we should be giving due attention to give them adequate sleep.

Discussions:

We have an advanced neonatal care which helps in the survival of extreme preterm babies, but the long term outcome in terms of neurodevelopment needs to be studied further. In our current practice, we are trying to follow the above listed principles, but there is a big gap between the evidence and practice. We do give due attention to the clinical management, but not giving adequate importance to some of the things, especially related to infants sleep, creating a friendly environment for the babies and pain management. There are limitations in our setting, especially related to space, lack of adequate staffing, lack of awareness among medical and nursing team.

Encouraging parental participation is one of the key elements for the demedicalisation neonatal unit. They should be given access to the unit 24 hours, involve them in the care, for feeds, nappy changes positioning, and staff should support them. By doing this, they may feel as a part of the health care team for the baby. Allowing free access for the parents may alleviate their anxiety and stress regarding an intensive care unit

In utero, infants are exposed to a sound of 40-60 dB, but it can be around 70-80dB average in a neonatal unit.[26] These intermittent high sounds can lead to startles, bradycardia, apneas,desaturations and alterations in blood pressure which even can lead to intraventricular hemorrhage.[27] The US environment protective agency (EPA) has recommended a sound level of 45dB. It is important to attend the alarms quickly, opening and closing the doors of incubator gently, and to minimize unnecessary conversations inside NICU to avoid the noise. Soft music can be considered as and when appropriate, monitoring the infant's response.

Apart from sound, light is another major stimulus which needs to be regulated. The source can be from general lighting of NICU, spot lights for procedures, phototherapy etc. Things that can be done to minimize the exposure includes placing a blanket over incubator, dimming the lights in NICU, position the neonate to not look directly into a light source, cover the eyes during phototherapy, to cycle the lighting that may help in attaining circadian rhythms, avoiding rapid change in ambient lighting

The unborn infant lives in a warm cushion of fluid with gentle rocking by the movements. So procedures and even care giving can be stressful and intrusive. Gentle handling and avoiding sudden changes in posture helps in promoting tactile and vestibular development. For babies, procedures, caregiving etc can be combined so that infant gets adequate rest time or sleep. Interruptions can be avoided if the infant has reached a stage of deep sleep.[26] Cue based care can be used to facilitate undisturbed rest periods. Some of the non pharmacological practices such as sucrose and breast feeding before a procedure, non-nutritive sucking can be routinely adapted to all NICUs for pain relief. Pharmacological therapies also can be considered in major procedures such as intubation, post operative, ventilated infants.

Many aspects of these principles are practiced in NICUs across the world. The need is to bring down the gap between these theoretical principles and daily practice. Most of them doesn't need any additional cost or facil-

ities, but endeavor of the medical and nursing team can do miracles for the future of these preterm babies. Nowadays, a program called NIDCAP(Newborn Individualized Developmental Care and Assessment Program) is emerging. A key focus of the NIDCAP program is the educational and consultative support and assistance to NICU and special care nursery settings towards effective delivery of intensive and special care in a neurodevelopmentally supportive, individualized, and family-centered framework.[28]

We should aim to reach close to a stage where the neonatal intensive care unit can be considered a surrogate for the maternal womb especially for preterm babies.

References:

1. Preterm birth. https://www.nhp.gov.in/disease/reproductive-system/female-gynaecological-diseases-/preterm-birth
2. Jarjour IT Neurodevelopmental outcome after extreme prematurity: a review of the literature. Pediatr Neurol2015;52:143 52.
3. Smith GC,Gutovich J,Smyser C, et al Neonatal intensive care unit stress is associated with brain development in preterm infants. Ann Neurol 2011;70:541-9
4. Browne JV Developmental care for high-risk newborns: emerging science, clinical application, and continuity from newborn intensive care unit to community. Clin Perinatol 2011;38:719–29
5. Roué JM, Kuhn P, Lopez Maestro M, et al Eight principles for patient-centred and family-centred care for newborns in the neonatal intensive care unit. Arch Dis Child Fetal Neonatal 2017;102(4):364-368
6. Research on Early Developmental Care for Extremely Premature Babies in Neonatal Intensive Care Units (EDC). Secondary Research on Early Developmental Care for Extremely Premature Babies in Neonatal Intensive Care Units (EDC). http://www.esf.org/index.php?id=1514 ■

Breathing a Sigh of Relief: What's New in Apnea of Prematurity?

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Apnoea of prematurity is one of the most common diagnoses in the NICU. It is a very important condition which we come across in newborn ICU because resolution of apnea is a precondition for discharge and adds significant contribution to length of hospital stay for preterm infants. Despite the frequency of apnea of prematurity, it is unknown whether recurrent apnea, bradycardia, and hypoxemia in preterm infants are harmful. Limited data suggest that the total number of days with apnea and resolution of episodes at more than 36 weeks' postmenstrual age (PMA) are associated with worse neurodevelopmental outcome in preterm infants[1, 2]. However, the lack of consistent definitions, monitoring practices, and consensus about clinical significance leads to significant variation in practice.

Eichenwald EC and AAP COMMITTEE ON FETUS AND NEWBORN. Apnea of Prematurity. Pediatrics. 2016;137(1):e20153757 is aclinical report which has reviewed the evidence basis for the definition, epidemiology, and treatment of apnea of prematurity as well as discharge recommendations for preterm infants diagnosed with recurrent apneic events. The full text is an extensive one and is not the matter of discussion in this forum. But the article has highlighted the clinical implications beautifully and clearly into 10 points, which is of great importance for all the clinicians.

CLINICAL IMPLICATIONS

1. Apnea of prematurity reflects immaturity of respiratory control. It generally resolves by 36 to 37 weeks' PMA in infants born at ≥28 weeks' gestation.
2. Infants born at <28 weeks' gestation may have apnea that persists to or beyond term gestation.
3. Individual NICUs are encouraged to develop policies for cardiorespiratory monitoring for infants considered at risk of apnea of prematurity.
4. Initial low heart rate alarms are most commonly set at 100 beats per minute. Lower settings for convalescent preterm infants older than 33 to 34 weeks' PMA may be reasonable.
5. Caffeine citrate is a safe and effective treatment of apnea of prematurity when administered at a 20-mg/kg loading dose and 5 to 10 mg/kg per day maintenance. Monitoring routine serum caffeine levels usually is not contributory to management. A trial off caffeine may be considered when an infant has been free of clinically significant apnea/bradycardia events off positive pressure for 5 to 7 days or at 33 to 34 weeks' PMA, whichever comes first.
6. Evidence suggests that GER is not associated with apnea of prematurity, and treatment of presumed or proven GER solely for the reduction in apnea events is not supported by currently available evidence.
7. Brief, isolated bradycardic episodes that spontaneously resolve and feeding-related events that resolve with interruption of feeding are common in convalescent preterm infants and generally need not delay discharge.
8. Individual units are encouraged to develop policies and procedures for caregiver assessment, intervention, and documentation of apnea/bradycardia/desaturation events as well as the duration of the period of observation before discharge.
9. A clinically significant apnea event–free period before discharge of 5 to 7 days is commonly used, although a longer period may be suitable for infants born at less than 26 weeks' gestation. The specific event-free period may need to be individualized for some infants depending on the gestational age at birth and the nature and severity of recorded events.
10. Interrogation of electronically archived monitoring data may reveal clinically unsuspected events of uncertain significance. Such events do not predict subsequent outcomes, including recurrent clinical apnea or SIDS.

Though most of the things are been practiced in most of the NICUs, this article adds to the clarity when the apnoea usually resolves in different gestational ages and about the monitoring policies. Though caffeine is well known, it was always a question whether to monitor caffeine levels. In this clinical report it is clearly detailed that it is not contributory to management.

Similarly when to stop caffeine was another question and most centers practiced discontinuing at 34 weeks PMA which have added significantly to length of hospital stay. Here it is recommended a trial off caffeine may be considered when an infant has been free of clinically significant apnea/bradycardia events off positive pressure for 5 to 7 days or at 33 to 34 weeks' PMA, whichever comes first, although a longer period may be suitable for infants born at less than 26 weeks' gestation.

GER is always been a topic of discussion along with apnoea. Preterm infants have a hyper reactive laryngeal chemo reflex response that precipitates apnea when stimulated. In addition, almost all preterm infants show some degree of gastro esophageal reflux (GER). These 2 physiologic observations have led to speculation that GER can precipitate apnea in

preterm infants and that pharmacologic treatment of GER might decrease the incidence or severity of apnea. Despite the frequent coexistence of apnea and GER in preterm infants, several studies examining the timing of reflux episodes in relation to apneic events indicate that they are rarely temporally related3, 4. Here the recommendations clearly says there is no evidence to suggest that GER is associated with apnea of prematurity, and treatment of presumed or proven GER solely for the reduction in apnea events is not supported by currently available evidence.

Again brief, isolated bradycardic episodes that spontaneously resolve and feeding-related events that resolve with interruption of feeding are always a concern and had significantly delayed discharge in convalescent preterm. In this clinical report it points out this should not be a concern for delaying discharge.There is no evidence, however, that such events predict the recurrence of clinically significant events on discharge, SIDS, or the need for readmission to the hospital.

Infants born preterm may develop apnea and other signs of respiratory control instability with certain stresses, including general anesthesia and viral illnesses. Additional close monitoring in these situations may be indicated in preterm infants until 44 weeks' PMA, including former preterm infants readmitted for elective surgical procedures, such as hernia repair. In addition, the exacerbation of apnea has been reported in very preterm infants after their initial 2-month immunizations or ophthalmologic examinations, and rarely after the 4-month immunizations, while still in the NICU5.

References

1. Janvier A, Khairy M, Kokkotis A, Cormier C, Messmer D, Barrington KJ. Apnea is associated with neurodevelopmental impairment in very low birth weight infants. J Perinatol. 2004;24(12):763–768
2. Pillekamp F, Hermann C, Keller T, von Gontard A, Kribs A, Roth B. Factors influencing apnea and bradycardia of prematurity—implications for neurodevelopment. Neonatology. 2007;91(3):155–161.
3. Westkamp E, Soditt V, Adrian S, Bohnhorst B, Groneck P, Poets CF. Blood transfusion in anemic infants with apnea of prematurity. Biol Neonate. 2002;82(4):228-232
4. Zagol K, Lake DE, Vergales B, et al. Anemia, apnea of prematurity, and blood transfusions. J Pediatr. 2012;161(3):417-421.
5. Sánchez PJ, Laptook AR, Fisher L, Sumner J, Risser RC, Perlman JM. Apnea after immunization of preterm infants. J Pediatr. 1997;130(5):746–751. ■

Prevention of Hospital Acquired Infection In NICU

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ABSTRACT

Hospital acquired infection is a major cause of morbidity and mortality in neonates. Infants, who are very low birth weight or extreme preterm, are at high risk of nosocomial infection due to their dependency on multiple interventions such as ventilation, central line, antibiotics for survival. These infections are more serious and deadly due to high prevalence of infection by multidrug resistant organism. In this article, evidence based interventions to prevent hospital acquired infection, shall be reviewed. Topics such as hand hygiene, personal protective equipments, prevention of catheter line associated blood stream infection (CLABSI), prevention of ventilator associated pneumonia (VAP), prevention of catheter associated urinary tract infection and vaccination for NICU health care worker (HCW) will be reviewed.

HOSPITAL ACQUIRED INFECTION (HAI)

Nosocomial infection is defined as an infection acquired in the hospital that was neither present nor incubating at the time of hospital admission[1]. Risk factors predisposing to infection include prematurity, central lines, ventilator support, urinary catheters, parenteral nutrition and lipids, exposure to broad spectrum antimicrobials. Prevalence of hospital acquired infection is inversely proportional to the gestational age and birth weight. National Healthcare Safety Network (US) reports that between 2006 and 2008, the prevalence of Central line associated blood stream infection at birth weight 750 g or less is 4.9% [2]. However, all NICUs should maintain

a “zero tolerance unit belief” that all infections are preventable and unacceptable.

HAND HYGIENE PRACTICES

Semmelweis while working in Vienna General Hospital’s Obstetric Clinic, introduced the concept of hand hygiene in 1847, where it was found that doctor’s ward had three times the mortality found in midwive’s wards and that they often conduct deliveries after performing autopsies. Doctors at that time became offended at being told to do hand hygiene. Semmelweis was put to asylum, where he succumbed to custodial torture[3]. The practice of hand hygiene became widely accepted after the works of the microbiologist Louis Pasteur and the surgeon Joseph Lister, who operated using hygienic methods and improved post operative mortality and morbidity.

Hand hygiene is the single most important intervention to prevent nosocomial infection. Meticulous, routine hand hygiene effectively interrupts both direct and indirect contact transmission. Despite the knowledge about the effectiveness of hand hygiene in preventing infection, the compliance among health care workers including doctors is disappointingly suboptimal, with an overall average 40% compliance rate[4].

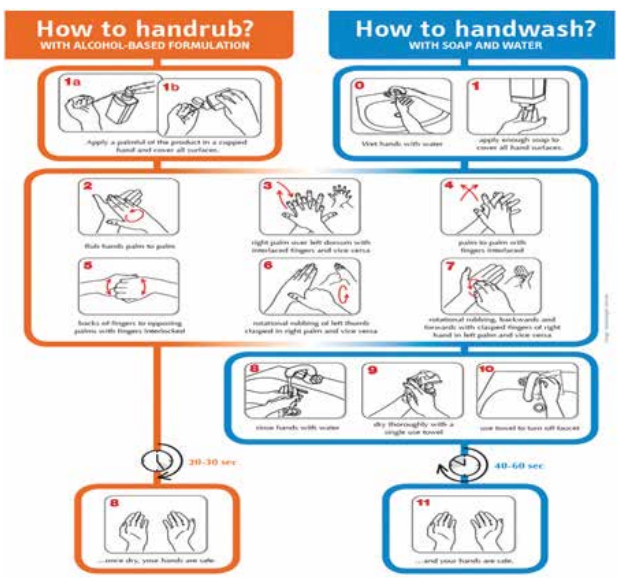

Fig 1. WHO Chart on Hand hygiene

Surgical scrub on unit entry is considered standard of care. Fingernails should be natural, trimmed short, and free of artificial nails or wraps. Artificial finger nails have been associated with Pseudomonas aeroginosa outbreak (5). Rings, bracelets and wrist watches distal to the elbows should be removed because it is associated with contamination by gram-negative organism[6].

Sinks at unit entry should be wide and deep enough to prevent inadvertent contamination of hands while washing and splashing of running water on the hands. Sleeves are rolled 3 inches above the elbow. Surgical scrub involves six steps of hand wash along with washing till the elbows atleast for 2 minutes. While washing till elbows, keep the hands always above the elbow. Once inside the unit, the health care worker (HCW) needs to do hand hygiene procedure at each of the “5 moments for hand hygiene” (Fig. 2) Routine and meticulous hand hygiene needs to be done before and after every patient contact. Sinks and alcohol-based product dispensers should be numerous and conveniently located throughout the unit for easy HCW access. Both soap and water and alcohol-based rubs are effective in reducing the level of pathogens on hands. All the six steps of hand hygiene (except hygiene till elbow) needs to be done for 40-60 sec in case of soap and water and for 20-30 sec in case of alcohol-based (take 3-5ml) hand rub (Fig 1). If gloves are used during care, hand hygiene is required before donning and after removing gloves. Soap and water, meanwhile, are still recommended for visibly soiled hands, Clostridium deficile[7] and Norovirus exposure[8]. Hand hygiene compliance can be increased by motivation, training, secret observers, non-punitive feedbacks, etc. A new concept is “Directly observed Hand hygiene” in which hand hygiene ambassadors are appointed who ensures that all steps of hand hygiene are followed by all HCW at all the 5 moments of hand

hygiene. In a study among hospitalised adult patients at Hong Kong, the compliance of hand hygiene among hospitalised patients were 97% in ambassador-initiated directly observed hand hygiene was 97.3% compared to 37% in patients' self-initiated hand hygiene via a patient education program ($p < .001$)[9].

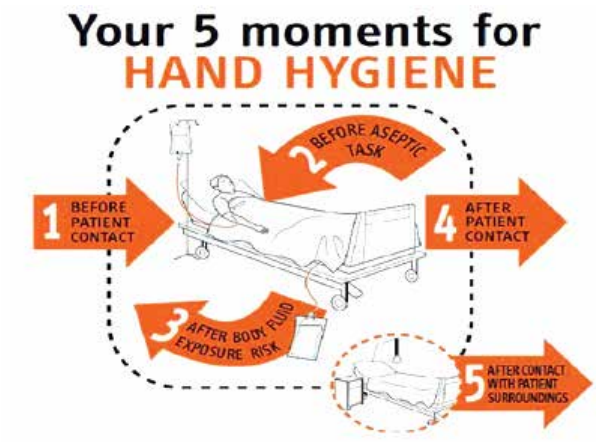

Fig. 2 Five moments for hand hygiene

PERSONAL PROTECTIVE EQUIPMENT

Health care workers should assume that all patients are potentially infected or colonized. Standard precautions should be followed with every single patient encounter. Before each patient encounter, HCW should think about the type of anticipated exposure and the necessary precaution and equipments needed for personal protection. Hand hygiene and disposable gloves with or without gown should be used when transmission by direct or indirect contact is expected, e.g. multidrug resistant organisms[10]. Gloves should be used when:1) anticipating direct contact with mucous membranes, blood or body fluids, or non-intact skin; 2) having direct contact with infants who are infected or colonized with pathogens transmitted by contact route 3) touching visibly soiled or potentially contaminated surfaces or equipment. Non-sterile gloves may be used in procedures where sterility is not an issue. HCWs should follow universal gloving policy in conjunction with routine hand hygiene before and after each patient contact. HCWs may be misled to think that hand hygiene is not required if a universal gloving policy is followed. Because hands may become contaminated during glove manipulation, hand hygiene always is required after glove removal

Hand hygiene and mask along with gloves should be used to prevent transmission by close contact with respiratory secretions within short distance (<3 feet), e.g. Adenovirus bronchiolitis, Pertussis and RSV. Airborne transmission by organisms suspended in air capable of travel over long distance can be prevented by N-95 or powered air-purifying respirator and special airflow room, e.g., Measles, Varicella, Pulmonary tuberculosis[11].

PREVENTION OF CENTRAL LINE–ASSOCIATED BLOOD STREAM INFECTIONS (CLABSI)

Most common type of hospital-acquired infection among infants in the NICU is CLABSI[12]. Most frequently, CLABSIs results from colonization of the catheter hub. Duration is likely the most important risk factor. Median time to onset of infection was 9 days for UVCs and 14 days for PICCs[13]. Biofilm producing organisms such as Coagulase-negative staphylococci, S aureus, and enterococci or gram-negative organisms (Escherichia coli and Klebsiella species) predominate. Candidal infections are also seen less commonly with increased broad-spectrum antibiotic exposures, prolonged periods without enteral feeding, and use of histamine2-blocking medications.

Bundle Approach involves bringing together a number of evidence-based practices that, when applied as a single intervention (i.e., the bundle), may result in improvement that is greater than single evidence-based practices. Bundle approach to prevent CLABSI include:[1] promotion of hand hygiene;[2] optimization of central catheter insertion, use, and removal;[3]

Initiation and advancement of breastmilk/ enteral feeding of VLBW infants; (4) Infection surveillance and communication; (5) antimicrobial stewardship and use of organism specific prevention strategies (such as active surveillance of MRSA colonization and fluconazole prophylaxis against fungal colonization)

Insertion of Central Venous Catheter

There should be dedicated Central venous catheter (CVC) placement set with all necessary supplies. Caregivers who participate in CVC placement should be properly trained, by repeated observation followed by repeated insertion under consultant supervision, before doing independently. There should be atleast two sterile persons who perform the procedure and a non-sterile observer caregiver who ensures that each step of the placement process is done per the insertion checklist, should assist and monitor for any lapse in sterile practice. Insertion checklist includes:

A. Written informed consent of the procedure
B. Time-out to document right patient, right procedure, and right location
C. Hand hygiene, aseptic preparation of insertion site and maximal sterile barrier components (caps, masks, sterile gowns, sterile gloves, and sterile drapes that completely cover the infant)
D. Number of line insertion attempts and outcome of attempts
E. Sterile post-insertion processes: radiographs and line adjustments
F. Names and signatures of all involved (operator, sterile assistant, and/or nonsterile observer)

Povidone iodine or Chlorhexidine gluconate (CHG) may be used for preparing the skin before insertion. Residual antisepsis from 2- 7 days is seen with CHG, which can be inactivated by normal saline. The Food and Drug Administration recommends use of 2% CHG in caution in premature infants <2 months of age. These products may cause irritation or chemical burns. The contact dermatitis associated with CHG-impregnated foam[14], may not be associated with the transient use of CGH for skin antisepsis before central catheter insertion.

Maintenance of Central Venous Catheter

A sterile occlusive dressing should be placed over the entry site. Dressing need not be changed unless it becomes damp, soiled, or loosened. Before changing the iv connections to the hub, “scrub the hub” for 15 sec, followed by time for drying before connecting to the CVC hub. The use of 2 persons for tubing changes or dressing changes, 1 in sterile performer and 1 non-sterile assistant, is needed to maintain sterile precautions. Open systems where hubs are capped with Luer locks or stopcocks must be replaced by closed systems. CDC recommendations include changing tubing no more frequently than every 72-96 hours for most fluids. Tubing must be changed for every infusion of blood product, and lipid-containing lines should be changed every 24 hours. Needleless connectors should be changed at the same time as tubing change.

Removal of Central Venous Catheter

Daily review the need to maintain catheter and remove promptly if not needed as soon as possible. Umbilical arterial and venous catheters should not be retained more than 5 days and 14 days respectively. PICC line may be used as long as required and need not be changed routinely[15] to prevent infection (however it may be prudent to change PICC line once in 15 days). Once the infant is bacteraemic with the organisms, catheter must be removed.

Central Venous Catheter – infection surveillance

Surveillance for HAI must adhere to NHSN standards for CLABSIs, including the need for 2 or more positive cultures drawn on separate occasions to confirm a CLABSI diagnosis with a normal skin flora (including coagulase-neg-

ative staphylococci). NICUs must also have accurate recording for accounting for central line-days. Run charts need to be made plotting monthly CLABSI incidence. Data needs to be reviewed in regular forums, such as infection review meetings

PREVENTION OF VENTILATOR ASSOCIATED PNEUMONIA (VAP)

Ventilator-associated pneumonia (VAP) is defined by CDC as an episode of pneumonia in a patient who requires a device to assist or control respiration through a tracheostomy or endotracheal tube within 48 hours before the onset of the infection. VAP may be responsible for as many as one-third of the health-care–related infections in neonates. Low birthweight, prolonged mechanical ventilation, muscle relaxants, sedation, frequent suctioning and re-intubation, and steroid use have all been noted to be associated with increased risk of VAP. Contaminated oral or gastric secretions of intubated, ventilated patients can pool and leak around the endotracheal tube, and enter the lower respiratory tract. Shortly after intubation, bacteria can coat the surface of endotracheal tubes and become enveloped within a biofilm produced by the microbes. Exogenous source of micro-organisms include hands of health care worker and ventilator circuit. Gram-negative organisms, which often colonize endotracheal tubes, are frequently noted in the flora that colonizes the hands of caregivers. Although the CDC radiographic and clinical criteria of VAP are useful, it is difficult to diagnose VAP using the CDC microbiologic criteria because bronchoalveolar lavage is not done in NICU commonly. Tracheal aspirates from neonates who have suspected VAP may play a role in helping to identify organisms colonizing the airway and aid in the choice of appropriate antibiotic therapy. Tracheal colonization of the airway with Gram-negative bacteria has been associated with adverse outcomes. Sterile tracheal aspirate cultures have a high negative predictive value for VAP.

Ventilator associated pneumonia: CDC CRITERIA <1 YEAR

- Radiographic criteria: New or progressive infiltrate and persistent infiltrate, Consolidation, Cavitation, Pneumatoceles
- Clinical criteria: Worsening gas exchange (e.g. oxygen desaturations, increased oxygen requirements, increased ventilator demand) and three of the following:
  i. Temperature instability
  ii. Leukopenia (<4,000 WBC/mm3) or leukocytosis (>15,000 WBC/mm3) and left shift (>10% band forms)
  iii. New onset of purulent sputum or change in character of sputum, or increased respiratory secretions or increased suctioning requirements
  iv. Apnea, tachypnea, nasal flaring with retraction of chest wall or nasal flaring with grunting
  v. Wheezing, rales, or rhonchi
  vi. Cough
  vii. Bradycardia (<100 beats per minute) or tachycardia (>170 beats per minute)
- Microbiologic criteria: At least one of the following is present:
  i. Positive growth in blood /pleural fluid culture
  ii. Positive quantitative culture from minimally contaminated lower respiratory tract specimen (e.g., BAL, protected specimen brushing)
  iii. > 5% BAL-obtained cells contain intracellular bacteria on direct microscopic examination (e.g., Gram-stain)
  iv. Histopathologic examination shows at least one of the following indications of pneumonia:
    a. Abscess formation or foci of consolidation with intense PMN accumulation in bronchioles and alveoli
    b. Positive quantitative culture of lung parenchyma
    c. Evidence of lung parenchyma invasion by fungal hyphae or pseudohyphae

Prevention of VAP- Bundle approach

Head end elevation of 30° to 45° needs to be maintained to prevent aspiration of contaminated oropharyngeal and gastric fluids. Hand hygiene should be done before and after contact with respiratory equipment should reduce cross-contamination between patients. Oropharynx around the endotracheal tube is suctioned before adjusting it or removing it, in order to reduce risk of aspiration of contaminated oropharyngeal secretions. Separate suctioning equipment should be used for tracheal and oral secretions (comprehensive oral hygiene program). Respiratory tubing should be drained away from ventilated infants to prevent aspiration of potentially contaminated condensate by keeping it below the neck level. Breathing circuits do not need routine changing unless they become visibly soiled or they malfunction. Closed or open suction system, difference was not noted in tracheal colonization patterns between groups, nor were there differences in VAP rates (16). Current data do not support such H2 blocker treatment in ventilated neonates because it is associated with increased risk of late-onset fungal infection and necrotizing enterocolitis among very low birth weight infants. Regarding the weaning from ventilator, assess for extubation readiness on a daily basis. Noninvasive measures such as nasal continuous positive airway pressure and nasal prong ventilation may help to reduce VAP rate by reducing the duration of invasive ventilation. Re-intubation after extubation should be avoided if possible because of the increased risk of VAP associated with re-intubation.

PREVENTION OF CATHETER ASSOCIATED URINARY TRACT INFECTION (CAUTI)- BUNDLE APPROACH

Insert urinary catheter only when necessary. While insertion of urinary catheter, do hand hygiene, follow aseptic technique, allow povidone iodine to dry and use appropriate catheter size. Daily care of indwelling catheter needs to be done. Maintain unobstructed urinary flow (do not flush) and avoid backflow of urine into the bladder. Daily review the need for maintaining urinary catheter and promptly remove when it is not needed.

Prevention of various infections in NICU

Prevention of multidrug resistant organisms such as Staphylococcal infection may be done by mandatory hand-washing, isolation of infants who have MRSA disease. The concept of cohorting infants colonized with S aureus has gained favor in the 1960s after observations of “cloud” of S aureus[17], by air sampling surrounding infants colonized with the organism (the “cloud baby” phenomenon). Annual seasonal influenza employee immunization campaign is a standard practice[18]. In case of Bordetella pertussis outbreak, infection control measures included active screening, testing, and treatment of suspect cases; HCW sick leave; and antibiotic prophylaxis to all infants / HCWs. Vaccine dTaP is recommended routinely for adults who have contact with infants younger than 12 months of age. In addition, education about pertussis vaccination should be provided to NICU parents and other close contacts of these vulnerable patients[19].

Prevention of Varicella Zoster can be done by giving 2 doses of the Varicella vaccine 4 to 8 weeks apart in Health care workers who do not have immunity. Isolation of individuals with suspected or proven VZV infection is done, ideally in negative pressure rooms with airborne and contact precautions[20]. Varicella zoster immunoglobulin (VZIG) should be given to newborns whose mothers have signs and symptoms of VZV infection in the 5 days before delivery or 2 days after delivery and hospitalized preterm infants born before 28 weeks of gestation or with birth weights less than 1,000 g regardless of the mother’s immunity. Dose of VZIG for weight < 2 kg dose is 62.5U (0.6ml) and for weight > 2-10kg dose is 125U (1.2ml). Very low birth weight newborns who acquire CMV during birth or from mother’s milk can have acute illness associated with the onset of infection that is char-

acterized by a sepsis-like picture, worsening of respiratory illness, hematological changes, abnormal liver function, and cholestasis. Wash hands often with soap and water, especially after changing diapers/ feeding/wiping nose or drool/handling toys. Do not share expressed breastmilk, food, drinks, or eating utensils used by young children. Do not put a child's pacifier in one's mouth. Avoid contact with saliva when kissing a child. Clean toys, countertops, and other surfaces that come into contact with children's urine or saliva (21). Prevention of Early Onset Sepsis (GBS) may be done by provide intra-partum antibiotic prophylaxis to women with risk factors: previous infant with Early onset GBS disease (< 7 days), GBS bacteriuria in current pregnancy, maternal fever, preterm labor before 37 wk, premature rupture of membranes >18 hrs[22].

CONCLUSION

Although neonates are at risk of acquiring infection, HCW should regard nosocomial infections as preventable and unacceptable, maintaining a "zero tolerance work culture". Hospital acquired infection is associated with higher mortality and morbidity due to prevalence of multidrug resistant organisms. Infection can be prevented by basic infection control practices, hand hygiene compliance, appropriate use of PPE, bundle approach and routine HCW vaccination.

REFERENCE

1. Siegel JD, Rinehart E, Jackson M, Chiarello L, and the Healthcare Infection Control Practices Advisory Committee. 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings. Atlanta, Ga: Centers for Disease Control and Prevention; 2007. Accessed at: http://www.cdc.gov/hicpac/2007IP/2007isolationPrecautions.html
2. Edwards JR, Peterson KD, Mu Y, et al. National Healthcare Safety Network (NHSN) report: data summary for 2006 through 2008, issued December 2009. Am J Infect Control. 2009;37:783–805
3. Hanninen O.; Farago M.; Monos E. "Ignaz Philipp Semmelweis, the prophet of bacteriology", Infection Control, 1983;4 (5): 367–70, doi:10.1017/S0195941700059762, PMID 6354955
4. Centers for Disease Control and Prevention. Guideline for hand hygiene in health-care settings: recommendations of the healthcare infection control practices advisory committee and theHICPAC/SHEA/APIC/IDSA hand hygiene task force. MMWR. 2002;51(RR-16):22
5. Foca M, Jakob K, Whittier S, et al. Endemic Pseudomonas aeruginosa infection in a neonatal intensive care unit. NEngl J Med. 2000;343:695–700
6. Fagerenes M, Lingaas E. Impact of finger rings on transmission of bacteria during hand contact. Infect Control Hosp Epidemiol. 2009;30:427–32
7. Oughton MT, Loo VG, Dendukuri N, Fenn S, Libman MD. Hand hygiene with soap and water is superior to alcohol rub and antiseptic wipes for removal of Clostridium difficile. Infect Control Hosp Epidemiol. 2009;30(10):939-44. doi: 10.1086/605322.
8. Blaney DD, Daly ER, Kirkland KB, Tongren JE, Kelso PT, Talbot EA. Use of alcohol-based hand sanitizers as a risk factor for norovirus outbreaks in long-term care facilities in northern New England: December 2006 to March 2007. Am J Infect Control. 2011;39(4):296-301. doi: 10.1016/j.ajic.2010.10.010. Epub 2011 Mar 16.
9. Cheng VC, Tai JW, Li WS, Chau PH, So SY, Wong LM, Ching RH, Ng MM, Ho SK, Lee DW, Lee WM, Wong SC, Yuen KY. Implementation of directly observed patient hand hygiene for hospitalized patients by hand hygiene ambassadors in Hong Kong. Am J Infect Control. 2016;44(6):621-4. doi: 10.1016/j.ajic.2015.11.024. Epub 2016 Jan 14.
10. Bearman GM, Marra AR, Sessler CN, et al. A controlled trial of universal gloving versus contact precautions for preventing the transmission of multidrug-resistant organisms. Am J Infect Control. 2007;35:650-655
11. American Academy of Pediatrics. Adenovirus and Pertussis (whooping cough). In: Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. Red Book: 2009 Report of the Committee on Infectious Diseases. 28th ed. Elk Grove Village, Ill: American Academy of Pediatrics; 2009:204–206 and 504–518

Prologue

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European RDS 2016 Guidelines update has yet again come out with some well known, commonly practiced, care of the newborn.

It is now a common practice to provide care as soon as the child is born, i.e maintaining normo-thermia in the delivery suite, inflation breaths (sustained vs normal bagging) followed by ventilation breaths, early initiation of CPAP etc, but without undermining the importance of all that , are we doing enough ?

Piecemeal approach to newborn care leads to suboptimal care and more importantly, waste of previous time and effort from all involved in the care. The guidelines has reiterated the importance of immediate newborn care, including surfactant ,adequate oxygenation ,permissive co2 levels, invasive to non invasive ventilation ,Blood pressure and cardiac status .

It has also confirmed, the importance of team working .

we need to transcend the artificial boundaries of our individual specialities and work as a team with our obstetric colleagues in ensuring optimal care for preterm .Ensuring appropriate antenatally care, i.e progesterone, magnesium sulphate, tocolytics and steroids are some of the steps towards the same. Knowledge available is not translated into clinical practice due to various constraints, but treating physicians mindset, should not be one among them.

What we have often tended to ignore, to our own peril, that the mother is still a useful resource when it comes to caring for preterm. What I mean by this is that ,apart from the emotional support, the extra amount of blood during delivery - Delayed cord clamping /milking, appropriate mode of delivery, prevention of infection and/or antibiotics all contributes to the final outcome.

Learning points are, keep reading a.k.a keep looking for evidence, care involves perinatology care, integrate both the obstetric and the neonatal team practices early on. Ensure that the maternal resources, physical and emotional are used prudently

Article that Brought Change in Practice

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Ho JJ, Henderson-Smart DJ, Davis PG

"Early versus delayed institution of continuous distending pressure for respiratory distress syndrome in preterm infants"

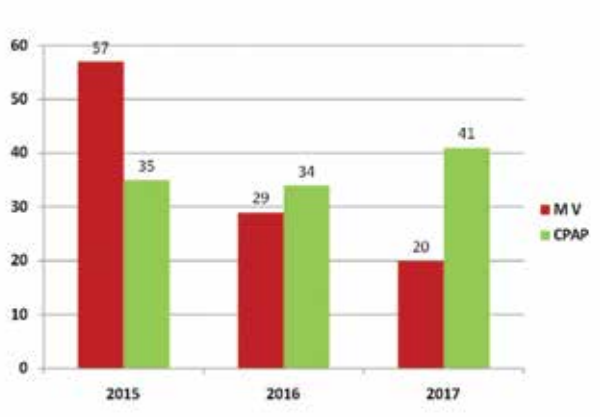
Cochrane Database Syst Rev.2002;(2):CD002975

This article can definitely be identified as one which has changed our practice of Neonatology, with regard to management of RDS in preterm newborns. As rightly described by the authors, the **application of continuous distending pressure (CDP or CPAP) has been shown to have some benefits** in the treatment of pre-term infants with respiratory distress syndrome (RDS). CDP has the potential to reduce lung damage, **particularly if applied early before atelectasis** has occurred. Early application of CPAP may better conserve an infant's own surfactant stores and consequently be more effective than CPAP applied later in the course of RDS.

This systematic review, after analyzing the data, concludes by stating that ***"early application of CDP (CPAP) has a clinical benefit in the treatment of RDS in that it reduces subsequent use of IPPV and thus may be useful in preventing the adverse effects of this treatment."*** Over the last 2 decades, Neonatologists world over have endorsed this and early CPAP ventilation has become first line management of preterm babies with RDS. Early CPAP paved way for other concepts like Labor room CPAP and "INSURE" technique.

Now, it is a genuine doubt that whether this systematic review done in 2002 still holds good or not. Yes, a study on ***"comparison of the effects of invasive ventilation/surfactant therapy and Noninvasive nasal CPAP in preterm newborns"*** (by Celic M et al, J Matern Fetal Neonatal med. 2017: Aug 31) has shown that early nasal CPAP in preterm infants (< 32 weeks) decreases the need for MV and the use of surfactant, but without a significant effect on BPD development. This recent study underlines the fact that early CPAP is here to stay, as far as the management of RDS in preterm babies is concerned.

Though a late starter of CPAP, after the initial learning curve, we too at PVS hospital, Kozhikode developed confidence and started using CPAP more and more frequently with ease and benefit. Whatever small data we have (last 3 years - 2015,2016 & 2017), is plotted in the bar diagram below.



To conclude, early CPAP has to be popularized in Neonatal practice, as it is cost effective, baby friendly and user-friendly. Popularizing its usage in level 2 nurseries (including SNCUs of Govt hospitals) can avoid unnecessary referrals to tertiary centers without any adverse outcome, at the same time, ensuring intact survival. ■

Mitochondrial Disease :- A Thumbnail Sketch

Dr. Preetha Remesh
Aster MIMS Hospital, Kozhikode.

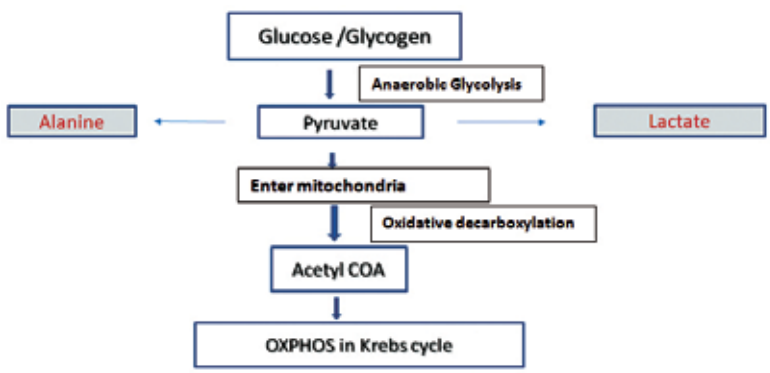
Diagnostic Approach in Infants & Children with Mitochondrial Diseases. Ching-Shiang Chi Pediatrics & Neonatology (2015) 56,7-18

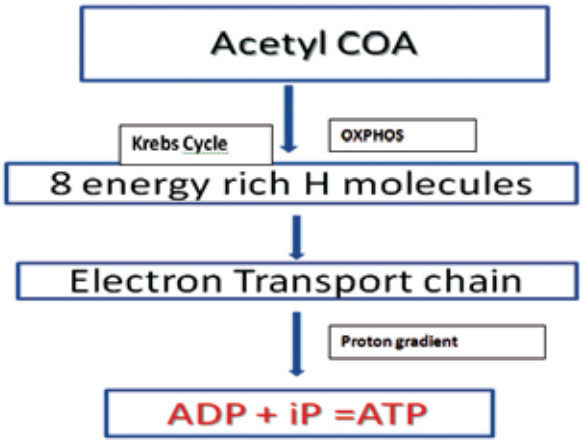
Mitochondrial disorder has the dubious distinction of being the most common inherited neuro metabolic disorder in children, with a 1:5000 life time risk! Energy failure at cellular level is the crux of the matter.It also has a myriad of presentations making early diagnosis difficult.

Mitochondria are considered to be an evolutionary parasite within eukaryotic cells, from over a billion years ago. It enjoys a symbiotic relationship with the host cell in that in return for a constant nutrient supply, it ensures an efficient system of energy production for the cell.

Mitochondria have a dynamic morphology& undergo frequent fission & fusion, existing as a diffuse reticular network rather than discrete organelles.

Energy production at Cellular level





Energy Production & mitochondria

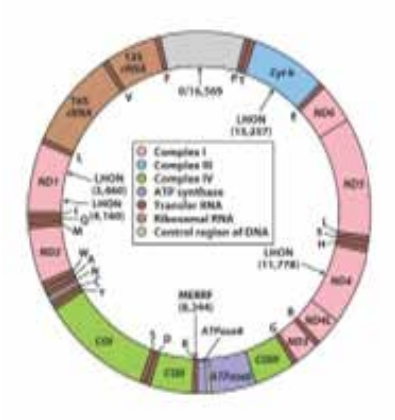
The key event in energy production is the transfer of electrons along the respiratory chain with the proton gradient thus created.

- Respiratory chain is situated at the inner mitochondrial membrane
- It consists of four multi-subunit complexes 1.2.3 & 4
- A series of oxidation reduction reactions take place that culminate in O2 consumption at complex 4 producing of water.
- During this series of electron transfer, extrusion of protons into the inter-membrane space occurs. Proton gradient thus generated is dissipated through ATP synthase(aka Complex 5), wherein ADP &iP condense to form ATP.
- Success & efficiency of this dynamic transfer of electrons rests on the two electron carriers: Co enzyme Q & Cytochrome C

Mitochondrial Genome

This is a small circular double stranded DNA of which up to 2-10 copies are present in each mitochondria. This constitute ~1 % of total cellular DNA and exists 'in peace' with the nuclear genome of the cell.

Mitochondrial DNA (mt-DNA) encodes just 2 ribosomal RNA; 22 t-RNA & 13 polypeptides, while the nuclear DNA (n-DNA)encodes >1000 proteins that are needed for optimal functioning of the mitochondria.



- Complexes 1,3, 4 & 5:- combined control of nuclear & mitochondrial genome
- Complex 2:- Entirely nuclear genomic control
- 75% of pediatric mitochondrial disorders are n-DNA mutations, while 25% are mt-DNA.

Nuclear DNA (n-DNA) mutations

- Obey mendelian inheritance & is usually autosomal recessive.
- Two types:-
  1. Structural mutations :- Code for the respiratory complexes
  2. Non-structural mutations:- Affect replication, repair & metabolism of mitochondria

POLG1:- (Polymerase Gamma)

- Commonest among the n-DNA mutation& is a non-structural one.
- Results in depletion of mitochondria both in CNS & liver.
- Severe neonatal presentation with refractory epilepsy & hepatic failur

Mitochondrial DNA(mt-DNA) mutations:-

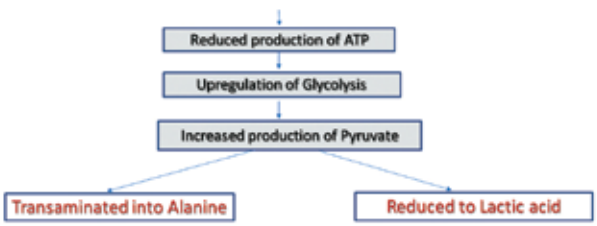
Almost universally maternally inherited & therefore, follow a non-mendelian inheritance. At the time of zygote formation, all the mt-DNA

from the sperm is denatured; hence not incorporated into the zygote. To date only one paternally inherited mt-DNA mutation has been identified.

- Homoplasmy is the state where,within a cell, the entire mitochondrial genome is identical.
- Heteroplasmyis when native mt-DNA co exists with mutant mt-DNA
- Threshold refers to the minimum amount of mutant mt-DNA needed for manifest symptoms & signs. This significantly varies between individuals, tissue types & the specific mutations

In cases of point mutations of mt-DNA, it is a 100% risk in all offsprings

What happens when mitochondria 'misbehave'?



How do mitochondrial disorders present?

Typically, there is no typical presentation!

- Unexplained multi organ failure is the commonest scenario.
- ~ 45% present with neuro-muscular manifestations. In this context, MELAS:- (Mitochondrial EncepalopathyLactic Acidosis &Stroke)deserves a special mention. As the name suggests, presentation is as neonatal stroke. CT scan reveals an infarct that does not conform to a vascular territory& MR angiogram will be normal. EEG is typical & consists of asymmetric, multifocal high signal arising from occipital & parietal lobes.
- Hepatic failure coupled with encephalopathy is another red flag combination

Organ System	What?
CNS	Encephalopathy, myopathy, seizures, Cranial neuropathy…
Heart	Cardiomyopathy & Conduction defects
GIT	Bulbar dysfunction: UMN/Myopathic :- feeding compromised
Lungs	Central respiratory dysfunction Predisposed to infections (posture & aspirations)
Muscle	Myopathy is the commonest presentation CPK,EMG & NCV tend to be normal
Skin	Scaly pruritic Erythema; Reticular pigmentation Eczema, Vitiligo…

Investigations in Mitochondrial disorders:-

Globally, diagnosis has now moved from biochemical to genomic.In practice nevertheless,-following are the investigations that point towards a mitochondrial etiology.

- Lactic Acidosis
- Elevated Alanine in TMS
- CSF Lactate> serum Lactate
- Imaging:-

  CT:- Basal ganglial calcification

  MRI:-Symmetrical cortical & subcortical grey matter changes; basal ganglial involvement

  MRS:- Lactate & N-acetyl Aspartate peaks
- EEG:- Any pattern & type is possible. Typical only in MELAS
- Tissue Biopsy:- Muscle, Liver or skin are preferred. The classical microscopic finding is a sub-sarcolemmal proliferation of mitochondria. Direct measurement of respiratory chain enzyme activity is possible too.Skin fibroblasts can be stored indefinitely& is a renewable source of DNA.Preservation of the biopsy specimen in ideal condition is very vital.

Management strategies…

1. **Acute:-**
   - Stabilise& ensure oxygenation
   - Treat Seizures :Leveterecetam& Carbamazepine preferred choice.

Sodium Valproate is contraindicated because it induces carnitine deficiency; reduces intra mitochondrial fatty acid oxidation &inhibits OXPHOS

- Treat the Lactic acidosis with fluid resuscitation +/- Bicarbonate
- Treat any infection triggers
- IV infusion of Arginine:- Being a source of NO, arginine acts as a cerebral vasodilator and helps reperfusion in MELAS. Available as IV & Oral preparation; latter alone is locally obtainable.

2. Auxillary Treatment:-

'Mitochondrial Cocktail':- Coenzyme Q; Riboflavin ,Thiamine, Carnitine, Vitamin E

- Remove toxic metabolites
- Promote ATP production, bypassing the metabolic defect viathe electron transporter chain mediators

Mitochondrial Cocktail

Drug	Dose
Coenzyme Q (Ecozyme..Maxico)	10-30 mg/kg/day
Riboflavin	50-100 mg/day
Carnitine	100mg/kg/day
Vitamin E	1-2 IU/kg/day
Thiamine (Benalgis)	100mg daily
Vitamic C	5mg/kg/day
Folinic Acid	1-1.5mg/kg/day

3. Long term strategies:-

- Anticipate asymptomatic involvement
  1. ACEi & beta blockers slow down progression of cardiomyopathy
  2. BERA will pick up SNHL & early hearing aids.
  3. Ophthalmology surveillance
- Exercise therapy:- In Mitochondrial myopathy, functioning of mitochondria is definitely improved with exercise.

Points to ponder…

- Cells with high energy requirement particularly vulnerable
- Any age, any organ, in isolation or in combination: Myopathy commonest!
- Deterioration following an inter-current illness is a clue!
- Lactic acidemiais an important but not a very specific or sensitive clue. A value that is <2 has a 97% negative predictive value for a mt-DNA disorder
- Lactate: Pyruvate ratio differentiates between an electron transport chain (ETC) defect and a primary disorder of pyruvate metabolism, when lactate is high. Normal L:P ratio <20.
- CSF lactate> serum lactate is a reliable a clue of mitochondrial encephalopathy,but not an infallible one, as meningitis, sub arachnoid hemorrhage & prolonged seizures do the same.

Clues to a mitochondrial Aetiology:-

1. Valproate induced CNS or hepatic dysfunction.
2. Normal CPK & EMG in a 'definite myopathy'.
3. Unexplained MODS

Meticulous sampling & immediate analysis vital

1. Struggling baby & tight tourniquet can cause a high Lactate!
2. Collect in a vial of 8% perchlorate. keep on ice &analysestat..for Pyruvate!!

- Most important prognostic factor in mitochondrial disorder is myocardial involvement

■

2

Section -2
Case Reports

An unusual case of Para esophageal Bronchogenic cyst

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PVS memorial hospital Kaloor Kochi, Kerala.

Back ground:

Bronchogenic cysts are rare congenital malformation that results from abnormal budding of the tracheal diverticulum of the foregut. It can be intra-pulmonary or mediastinal. Esophageal bronchogenic cysts are uncommon in occurrence.

Case Report

A term female baby (B.Wt - 2.53kg) was born to a primi gravid mother by emergency LSCS because of failed induction. Baby cried immediately after birth. Mother had regular antenatal check-up and the 3rd trimester ultrasonography showed a large cyst in the posterior mediastinum.

Baby had respiratory distress soon after birth, hence admitted in NICU. She was initially managed with HHFNC Oxygen x 2 days, after which distress settled and baby maintained saturation in room air. She was also given IV fluids, IV antibiotics and other supportive measures. On examination there were no other congenital anomalies or dysmorphism. Nasogastric feeds were started by 2nd day which was gradually increased to paladai feeds by day 7. However on day 7 baby had worsening of distress, stridor and feeding difficulty. Barium swallow showed holding up of dye at mid esophagus, but there was no communication with the cyst. CECT chest and MRI thorax with screening of thoracic spine showed the

posterior mediastinal cyst on the right side involving the wall of esophagus extending from the C6 to T11. No intra-spinal extension. Hemi vertebrae noted at C7, D1 and D2 level. (Fig 1 & 2).

Baby was taken up for surgery and approached through right thoracotomy. A cyst of 15x6 cm was extending from the middle of the neck to the gastro esophageal junction on the right side of esophagus. There was a septation at the middle of the cyst. Cyst contained a mucoid jelly like fluid. There was no communication between the cyst and esophagus or to the spinal canal. Upper 2/3rd of the cyst had a common wall with esophagus and lower 1/3 was separate from esophagus. Upper 2/3 of the cyst was excised except the common wall from which mucosa was stripped off completely. Lower 1/3rd was excised completely. The surgery was challenging because of the large size and extensive nature of the cyst.

Post operative period was uneventful, baby recovered well and NG feeds were started second post operative day and changed over to direct breast feeds before discharge.

Histopathology reported as cyst wall lined by ciliated epithelium, the underlying tissue showing seromucinous glands, cartilage and smooth muscles suggestive of bronchogenic cyst. (Fig. 3 & 4)

Discussion:

In 1972 Gray and Skandalakis suggested the classification of foregut cyst based on the anatomic location and embryological origin into esophageal, bronchogenic, and

Neuro enteric cysts. Bronchial cysts results due to the abnormal budding of the Tracheo bronchial tree during embryogenesis (between 4th-6thweeks). The location of the cyst depends on the stage of embryogenesis at which budding have occurred. Most common location is superior and middle mediastinum. It can be para-tracheal, sub-carinal, hilar, para-esophageal and pericardial. An esophageal bronchogenic cyst is uncommon in occurrence. No obvious sex predominance was found.

Symptoms vary with age of presentation, size and location of the cyst. They can present with dyspnea, stridor, difficulty in feeding or can be asymptomatic in newborn period. Later it can present with signs of compressions like dysphagia, airway compression, fever or recurrent infection. In our case due to the large size of the cyst baby became symptomatic soon after birth which is a rare presentation. Diagnosis is usually confirmed by imaging modalities like CT or MRI scan. Cysts are lined by ciliated epithelium and have focal areas of hyaline cartilage, smooth muscle, and bronchial glands in the walls which resembles that of normal bronchial tree. This helps to differentiate bronchogenic cyst from other duplication cysts. Thus diagnosis is confirmed by histology. Treatment is by surgical excision of the cyst .

References

1. Georges R, Deslauriers J, Duranceau A, Vaillancourt R, Deschamps C Beauchamp G, Page A, Brisson J: Clinical spectrum of bronchogenic cysts of the mediastinum and lung in the adult. Ann Thorac Surg 1991,52:6-13.
2. Nobuhara KK, Gorski YC, La Quaglia MP, et al. Bronchogenic cyst and esophageal duplications: Common origins and treatment. J PediatrSurg 1997;32:1408-13.

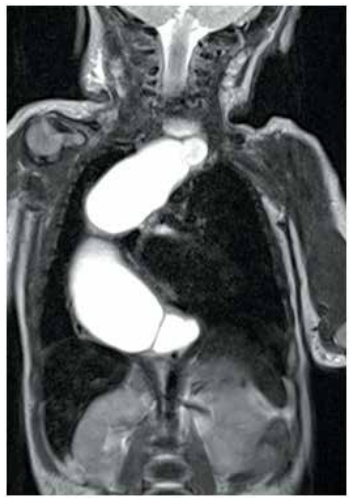

Fig 1: MRI Coronal view showing bronchogenic cyst.

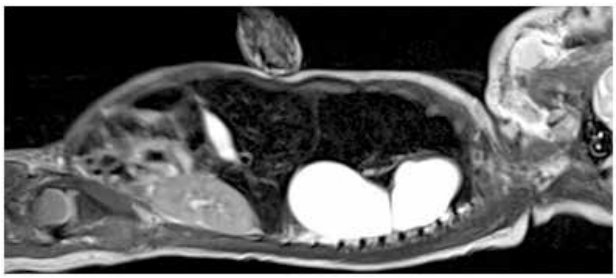

Fig 2: MRI Sagittal view.

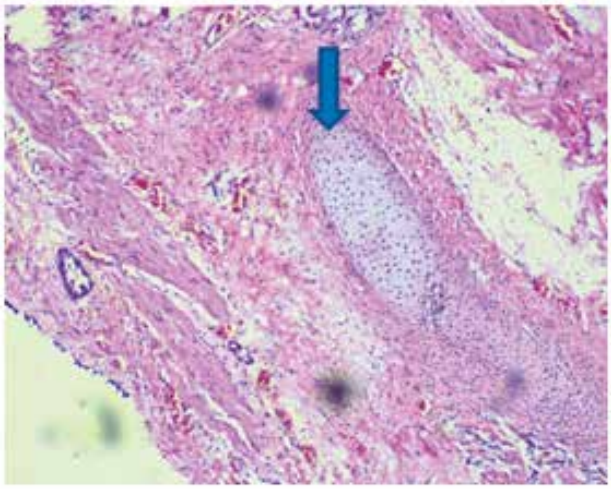

Fig 3. Histopathology showing Cartilage.

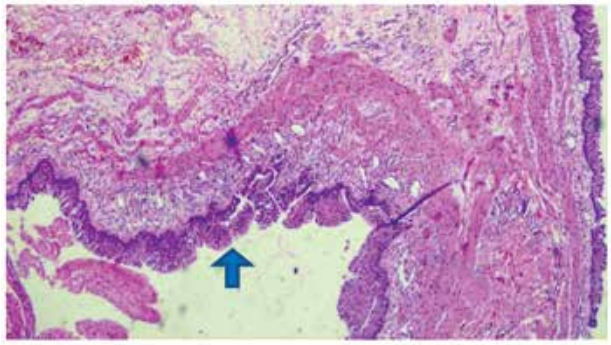

Fig. 4: Histopathology of Respiratory epithelium.

Congenital Afibrinogenemia
A Newborn Infant with Umbilical Cord Bleeding

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Abstract

Congenital afibrinogenemia is an extremely rare inherited coagulation disorder caused by a defect in fibrinogen synthesis. In the neonatal period, they may present with gastrointestinal hemorrhage, cord bleeding, hematomas or ecchymoses after traumatic vaginal delivery or rarely hemarthroses. In addition to marked prolongation of PT and PTT, a prolonged thrombin time and unmeasurable fibrinogen level is diagnostic. We describe a case of congenital afibrinogenemia in a three day old newborn infant who presented with umbilical cord bleeding.

Key Words:

Congenital Afibrinogenemia, newborn, cord bleeding.

Introduction

The hemostatic mechanism in a newborn infant differs from older children and adults[1]. Disorders of fibrinogen synthesis are subdivided into two types; Type I, or quantitative abnormalities (afibrinogenemia and hypofibrinogenemia), and type II, or qualitative abnormalities (dysfibrinogenemia and hypodysfibrinogenemia)[2]. Congenital afibrinogenemia is an autosomal recessive disorder in which there is absence of fibrinogen and was first described in 1920 by two German physicians, Fritz Rabe and Eugene Salomon[3]. It is a rare bleeding disorder that affects both male and female of all races with an estimated prevalence of 1 in 10,00,000[2]. Most of the patients are descendents of consanguineous mar-

riage. Afibrinogenemia is associated with mild to severe bleeding and maybe confused with hemophilia.

Case Report

A three day old female infant born by normal vaginal delivery to a healthy 23 year old primi gravid mother, with a birth weight of 2510gms was referred to our hospital for evaluation of umbilical cord bleeding. Baby was breastfed soon after birth. She passed urine and meconium within 24 hours. She developed bleeding from umbilicus about 60hrs of life which increased in spite of pressure bandage, suturing and repeated dose of FFP and Inj. Vitamin K. She was the product of a 2nd degree consanguineous marriage. Mother had pregnancy induced hypertension one week before delivery and was on medications. There was no family history of bleeding disorder.

On admission, baby was afebrile, tachypneic and was in shock with weak pulses and a BP of 42/20mm Hg. Her weight was 2.51kg (10th Percentile) and length was 52cm (75-90 Percentile). There was no dysmorphic features. Physical examination revealed a pale skin, bleeding from umbilical cord and a huge hematoma over right parietal region. There was no organomegaly and rest of the physical examination was unremarkable.

Laboratory investigation showed hemoglobin of 11.1g%, leucocyte count - 12,000/mm3 and platelet count 3,00,000/mm^3. A peripheral blood smear was normal. Bleeding time was 2 minutes (by ivy method), clotting time was longer than 20min, Prothrombin time (PT) was >50 seconds, Partial thromboplastin time (PTT) was >150 seconds, thrombin time (TT) >60 secs and plasma fibrinogen was unmeasurable(<100mg/dl).

Electrolytes, RFT, LFT, TFT, CRP and CSF study were within the normal limits. Urine and blood culture were also negative and FDP was <500ng/ml. Cranial ultrasound was normal. Fresh plasma, packed cell and fibrinogen with cryoprecipitate were transfused and bleeding stopped. Her PT and PTT were persistently prolonged and she required multiple transfusions with fresh frozen plasma and packed cells. These findings were consistent with congenital afibrinogenemia.

Baby's general condition improved over the next few days, she tolerated feeds and was active. She was discharged on the 17th day of hospitalization and the parents were counseled regarding potential risk of future bleeding risks, long term treatment and probability of recurrence in future pregnancy.

Discussion

Fibrinogen (Coagulation Factor I), is a glycoprotein synthesized by the liver, which is essential for blood coagulation. When injury occurs, fibrinogen is converted to fibrin protein which attaches to each other to form a stable network to make up the blood clot. Hence, deficiency or functional defects of fibrinogen results in hemorrhage or thrombosis[2]. The normal value of fibrinogen in blood is 150 - 400mg/dL[4].

Disorders of fibrinogen synthesis can present as afibrinogenemia or hypofibrinogenemia (quantitative defects) or dysfibrinogenemia (qualitative defects). Afibrinogenemia is an autosomal recessive disease[2]. It is an extremely rare inherited bleeding disorder which affects both males and females of all races and most of the patients are product of consanguineous marriage. These patients may present with bleed of varied severity.

The diagnostic work up of a newborn infant with bleeding includes a careful history regarding bleeding disorders in family, relevant perinatal history, maternal medications or illness especially infection and any illness or anomalies in the newborn. The crucial step in diagnosing and managing the bleeding infant is to determine whether the infant is sick or well looking. In DIC or liver disease, infant will appear very sick and bleeding may be diffuse from several sites. Whereas in vitamin K

deficiency or isolated clotting factor deficiency, infants will appear generally healthy.[5,6]

In afibrinogenemia, 85% of the cases present as bleeding from cord. Bleeding may also occur in the skin, oral cavity, gastro intestinal tract, genitor-urinary tract or even as intracranial bleed.[5,6] Our patient was relatively well looking with cord as primary bleeding site and also born out of consanguineous marriage, indicating a congenital coagulation defect.

Laboratory evaluation revealed normal platelet count with prolonged PT, PTT and thrombin time. Septic screening was negative. Fibrinogen level was initially undetectable and was persistently low even after repeated transfusions, confirming the diagnosis of congenital fibrinogen deficiency.

Treatment of afibrinogenemia includes replacement therapy with fibrinogen concentrate and transfusion with cryoprecipitate or fresh frozen plasma[5]. Half life of fibrinogen is approximately 3 to 5 days. The frequency and dose of fibrinogen concentrate should be adjusted to maintain a level of fibrinogen above 50mg/dl. [5,6]

In conclusion, congenital afibrinogenemia, a rare genetic disorder should be remembered when a newborn infant present with cord bleeding.

References

1) Andrew M, Paes B, Milner R, Johnston M, Mitchell L, Tollefsen DM, Powers P.Development of the human coagulation system in the full-term infant. Blood 1987;70:165-72.

2) Acharya SS, Coughlin A, Dimichele DM; North American Rare Bleeding Disorder Study Group. Rare Bleeding Disorder Registry:deficiencies of factors II, V, VII, X, XIII, fibrinogen and dysfibrinogenemias.J Thromb Haemost 2004;2(2):248-256

3) Grech H, Majumdar G, Lawrie AS, Savidge GF. Pregnancy in congenital afibrinogenaemia: report of a successful case and review of the literature. Br J Haematol 1991;78(4):571-572

4) Hilgartner MW, Corrigan JJ. Coagulation disorders. In: Miller DR, Baehner RL, (eds). Blood Disease of Infancy and Childhood. 7th ed. St Louis: Mosby,1995:924-86.

5) Andrew M, Brooker AL. Hemostatic Disorders in Newborns. In: Taeusch WH, Ballard RA, (eds). Avery's Diseases of the Newborn. 7th ed. Philadelphia:WB Saunders Company, 1998:1045-1079.

6) Turner TL. Coagulation Disorders. In: Rennie JM,Roberton NRC, (eds).Textbook of Neonatology 3rd ed. Edinburgh: Churchill Livingstone,1999:795-806

Congenital Cystic Hygroma of Neck.

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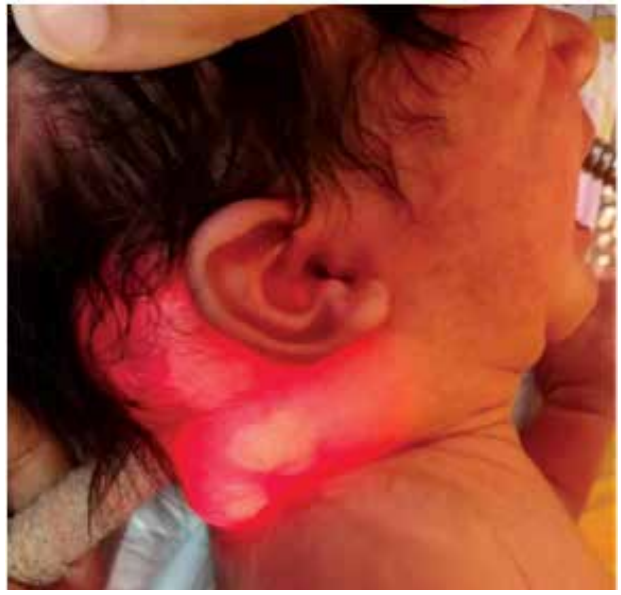
Essential Features:

- Cystic hygromas are congenital malformation of lymphatic system and also known as cystic lymphangioma usually presents as a soft, painless, compressible mass or lump over the lateral aspect of neck, and face region and axilla.
- There are 2 types of cystic hygromas:
  a) Macrocystic (large cysts) and b) Microcystic (small cysts).
- They are brilliantly transilluminant.
- It can also be associated with Trisomy 13,18 or 21, Turner or Noonan Syndrome
- Asymptomatic patient may be treated conservatively with watchful watiting.
- The preferred treatment of cystic hygroma is complete surgical excision; however some recent approaches include sclerotherapy which also gives very good results.
- There is a 15% chance of recurrence after surgical removal of cystic hygroma.



Therapeutic Hypothermia in Asphyxiated Neonates: Experience from "Neobless", Moulana Hospital

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Introduction

Therapeutic hypothermia (TH) is considered as a newer established modality for the treatment neonates with hypoxic-ischemic encephalopathy (HIE). This treatment protocol was implemented in our department since 2016.The aim of this study is to report our experience with total body cooling and neurodevelopmental follow up results.

Patients and Methods

This was a prospective study of newborns admitted with HIE for 2 years (from January 2016 to December 2017). TOBY trial UK guideline for total body cooling was followed .Cooling device was phase changing material (PCM- 'Mira cradle'). The results were analyzed based on maternal and neonatal characteristics, complications during hospital stay and neurodevelopmental outcome (Trivandrum development scale) asper the protocol.

Results

According to inclusion criteria only 30 babies underwent therapeutic hypothermia.Arrival beyond six hours of life was the main factor for exclusion. Overall survival was found to be 84% and overall mortality was recorded as 16%.Out of 84% survivors 80% babies had normal neuro-developmental outcome on follow ups

as per protocol. Out of 25 survived babies 5 (20%) were found to be neuro-developmentally abnormal on discharge. Out of these 5 babies 2 were having severe developmental delay, 2 had moderate developmental delay and one lost follow up.

Conclusion

Our experience with the controlledTH supports its beneficial effect in newborns with HIE. This treatment modality must be considered as a standard treatment in addition to the intensive care support in all eligible cases of perinatal asphyxia.

Key words

Therapeutic hypothermia, Hypoxic ischemic encephalopathy

Introduction

HIE in full term neonate occursamong 1–3 per 1000 live births.[1] It is responsible for almost 23% of total annual neonatal deaths and main cause ofneurologic disability (25%) as per mostrecent studies.[2,3,4] These poor outcomes are mainly because of lack of effective neuroprotective strategy following perinatal asphyxia. Recent meta-analysis justifies efficacy of therapeutic hypothermia (TH) in term infants with moderate to severe HIE.[5,6] No serious or life threatening adverse outcomes were reported to date as per randomized controlled trials.[7] Since theclinical benefits of TH are well established, it is considered as the standard of care in many developed countries. Present study aims to assess the feasibility of using therapeutic hypothermia protocol in our unit and to assess the outcome.

Population and Methods

Population:

30 neonates were recruited for therapeutic hypothermia as per the inclusion criteria fromJanuary 2016 to December 2017.Neobless is a regional referral centre and accredited by IAP/NNF for fellowship training for doctors and nurses with more than 100 admissions per month.

Type of Study and Data Collection:

This was a prospectivestudy including both our inborn and out born babies. Data were collected from patient files, analyzed on the basis of

1. maternal details (age of mother,mode of delivery, acute prenatal and perinatal events)
2. Baby details (Apgar score, and the need of neonatal resuscitation, birth weight, gestational age and gender of the baby)
3. Severity of HIE was assessed prior to cooling (Sarnat and Sarnat grading),
4. Complicationsnoticed during TH
5. Neurodevelopmental follow up details as per the protocol.

Implementation of Hypothermia Protocol:

All babies were selected and treated according to our protocol guidelines.[8] Briefly, neonates born at ≥36 weeks of gestation with at least one of the following:

Criteria A:

Atleast one of the following, 1.APGAR <5 at 10 mins/continued need of resuscitation at 10 minutes,2.acidosis with PH< 7 within 60 mins of life (Umbilical/ABG/CBG) or 3. base deficit 16 within 60 mins of life.

If the neonate meets criteria A, then assess for neurologic abnormality with

Criteria B:

Seizure or moderate to severe encephalopathy consists of altered state of consciousness, abnormal tone or abnormal primitive reflexes.

Neonates meeting criteria A and B are the candidates for cooling.

The exclusion criteria:

Inability to initiate cooling within 6 hours, lethal chromosomal anomaly, severe congenital anomaly, emergency surgical conditions, Intra+uterine infection, severe systemic infec-

tion, major bleeding diathesis, major intracranial hemorrhage.

The whole body cooling was given in this study by using PCM cooling device(MIRA CRADLE). It was started before 6 hour of life. The objective of whole body hypothermiawas to reach a rectal temperature between 33 and 34degree C for 72 hr from the beginning of the cooling. On admission,the newborn kept under the infant warmer off unless the newborn had a temperature less than 33 degree C.Rectal temperature was checked every 15 min until obtaininga temperature of 34 degree C. Hypothermia was continued for 72 hours while the rectal temperature was checked hourlyand the skin probe was held in place continuously. After 72 h of hypothermia, the newborn was gradually warmedfrom 0.2 to 0.4 degree C per hour (6 to 12 h). The newborn wasunder continuous monitoring of cardiopulmonary parameters, urine output, glucose monitoring every 6 to 8 hourly, andBP monitoring every 2 hours.

Statistical Analysis:

The results were expressed as numberand percentage or by the average. Statistical analysis was carried out by SPSS 22.

Results:

Table:1 Maternal Characteristics

Maternal characteristics	Protocol group (n = 30)
Maternal age (average)	22.2
Primigravida	18 (60%)
Antenatal complications, n (%)	
Gestational diabetes	8 (27%)
Gestational hypertension	11(37%)
Perinatal complications	
Abnormal fetal heart rate	12 (40%)
Meconium stained amniotic fluid	10 (33%)
Prolapsed cord	1 (3%)
Retention of the after-coming head	2 (7%)
Shoulder dystocia	2 (7%)

Table: 2 Neonatal Characteristics

Neonatal characteristics	Protocol group (n = 30)
Female gender, n (%)	*11(37%)*
Birth weight (g)	
<2500 gm	*5(17%)*
>2500 gm	*25 (83%)*
Apgar score ≤ 5 at 5 min, n (%)	*18 (60%)*
Apgar score ≤ 5 at 10 min, n (%)	*12 (40%)*
Intubation in the delivery room	
Intubation only	*9 (30%)*
Intubation and chest compression	*6(20%)*

Table:3 Complications during therapeutic hypothermia

Parameters	Protocol group (n = 30)%
Sinus bradycardia	*18 (87%)*
Arrhythmia needing treatment	*0*
Thrombocytopenia (<10,0000/mm3)	*10 (33%)*
Abnormal LFTs	*8 (27%)*
Abnormal Coagulation parameters	*11 (37%)*
Hyperkalemia	*12(40%)*
Abnormal RFTs	*4 (13%)*
High CK-MB	*7 (23%)*
Elevated CRP	*10 (33%)*

Table: 4 - Evaluation of the outcome:

	Protocol group *n 30*(%)
Average duration of hospital stay in days	*8.4day*
Average hour of starting cooling	*3.8hours*
Average time to attain target rectal temperature	*1 hour*
No. and % of Deaths	*5 (16%)*
Babies with normal neurological exam on discharge out of survived babies (25)	*20 (80%)*
Babies with abnormal neurological examination on discharge out of survived babies (25)	*5 (20%)*
%of grade 3 HIE in the neurologically abnormal babies on discharge	*100%*
% of abnormal MRI among neurologically abnormal babies on discharge	*100%*
% Outborn babies among neurologically abnormal babies	*100%*

Out of the total 30 babies, 5 babies died while receiving TH. The main causes were multi-organ dysfunction syndrome, pulmonary hypertension and tension pneumothorax, disseminated intravascular coagulation, myocardial dysfunction and cardiac arrest. Various hematological and biochemical complications noticed in babies receiving therapeutic hypothermia. All these 5 babies were outborn with grade III HIE.

All survived babies (25) were called for neuro developmental follow up as per protocol on 1,3,6,9,12,15,18 months, out of 25 babies 1 lost follow up. Out of 25 babies 5 babies were found to be neurologically abnormal (including baby who lost follow up) on discharge. Out of 4 neurologically abnormal babies on discharge 2 were found to be having severe developmental delay and 2 were reported to be having moderate developmental delay on follow up too. MRI was done in all these 5 babies which showed severe hypoxic ischemic changes. All these 5 babies were outborn with grade 3 HIE according to Sarnat classification. All the rest 20 babies who were neurologically normal on discharge, showed normal development on follow up too.

Discussion

In this Prospective study, we present our experience to prove role of TH in the management of neonates with moderate and severe HIE and beneficial effect of total body cooling on survival and long-termneurological outcome for newborns.[9,10,11]

Two principal methods of cooling exist: selective headcooling and the total body cooling. No superiority of eithermodality is supported by the existing evidence.[12,13] However, the selective head cooling is associatedwith a large gradientof intra-cerebral temperature.[13] The distribution of the intra-cerebral temperature is morehomogeneous in the case of total body cooling.[14,15]

In this study, we used total body cooling for hypothermia. The best neuroprotective effect is obtained when treatmentstarted before 6 hours of life. Ideally an amplitude-integrated electroencephalogram (aEEG) assessment for abnormal findings should be done prior to treatment initiation and during cooling was highly supported.[16, 17] (But because of high cost of equipment and non- availability in our centre, we have not used this).

Starting the hypothermia protocol before 6 h of life need a rapid assessment of the severity of HIE. Hourly evaluation is required for these neonates to determine the stage of HIE. This need increased awareness about TH to obstetricians and peadiatricians. It also requires good neonatal transport service facility.

There were no side effects documented in this study. The worsening of neonatal infection is main concern of cooling therapy in low- and middle-incomecountries.18 Babies diagnosed with HIE are mostly started onempirical antibiotic treatment if the etiology of asphyxia isunclear. Though we had 10 cases of elevated CRP on day 1, none of these has progressed to septic shock, or caused death.[19]

Fully established level 2/3 ICU facility with 1:1 nursing care and 24 hour medical person cover is a must before considering to start TH. We should be able to manage the multi system problems of perinatal asphyxia. Considering the incidence of perinatal asphyxia, there should be at least one centre in each district with facility for TH.

Various newer modalities of neuro protection are under trial in management of HIE along with therapeutic hypothermia (some of them are: Erythropoietin Melatonin

IGF-I, Xenon etc) and hope some of these will come in standard guidelines for day to day clinical use.[20]

Conclusion

Therapeutic hypothermia should be given to eligible cases of perinatal asphyxia. Our experience from 30 cases has shown definite

beneficial effect in moderate HIE. No major complications have been encountered due to cooling. We suggest to have a multicentre study from Kerala.

References:

1. E. M. Graham, K. A. Ruis, A. L. Hartman, F. J. Northington, and H. E. Fox, "A systematic review of the role of intrapartum hypoxia-ischemia in the causation of neonatal encephalopathy," American Journal of Obstetrics & Gynecology, vol. 199, no. 6, pp. 587-595, 2008.
2. J. E. Lawn, S. Cousens, and J. Zupan, "4Millionneonatal deaths: when? where? why?"TheLancet, vol. 365, no. 9462, pp. 891-900, 2005.
3. C.M. Robertson andM.Perlman, "Follow-up of the term infant after hypoxic-ischemic encephalopathy," Paediatr Child Health, vol. 11, no. 5, pp. 278–282, May 2006.
4. T. W. Pin, B. Eldridge, and M. P. Galea, "A review of developmental outcomes of term infants with post-asphyxia neonatal encephalopathy," European Journal of Paediatric Neurology, vol. 13, no. 3, pp. 224-234, 2009.
5. M. A. Tagin, C. G.Woolcott,M. J. Vincer, R. K.Whyte, and D. A. Stinson, "Hypothermia for neonatal hypoxic ischemic encephalopathy: an updated systematic review and meta-analysis," Archives of Pediatrics and Adolescent Medicine, vol. 166, no. 6, pp. 558-566, 2012.
6. S. E. Jacobs,M. Berg, R.Hunt et al., "Cooling for newborns with hypoxic ischaemic encephalopathy," The Cochrane Database ofSystematic Reviews, vol. 1, 2013.
7. S. Jacobs, R. Hunt, W. Tarnow-Mordi et al., "Cooling for newborns with hypoxic ischaemic encephalopathy," Cochrane Databaseof Systematic Reviews, 2007.
8. "Therapuetic hypothermia with intracorporeal temperature monitoring for hypoxic perinatal brain injury" NICE guidelines for therapeutic hypothermia, 2010.
9. G. Simbruner, R. A. Mittal, F. Rohlmann et al., "Systemic Hypothermia after Neonatal Encephalopathy: outcomes of neo.neuro.network RCT," Pediatrics, vol. 126, no. 4, pp. e771-e778, 2010.
10. S. Shankaran, A. R. Laptook, R. A. Ehrenkranz et al., "Whole body hypothermia for neonates with hypoxic-ischemic encephalopathy," New England Journal of Medicine, vol. 353, no. 15, pp. 1574–1584, 2005.
11. D. J. Eicher, C. L. Wagner, L. P. Katikaneni et al., "Moderate hypothermia in neonatal encephalopathy: efficacy outcomes," Pediatric Neurology, vol. 32, no. 1, pp. 11-17, 2005.
12. A. D. Edwards, P. Brocklehurst, A. J. Gunn et al., "Neurological outcomes at 18 months of age after moderate hypothermia for perinatal hypoxic ischaemic encephalopathy: synthesis and meta-analysis of trial data," BritishMedical Journal, vol. 340, no. 7743, article c363, 2010.
13. G. Dixon,N. Badawi, J. J. Kurinczuk et al., "Early developmental outcomes after newborn encephalopathy," Pediatrics, vol. 109, no. 1, pp. 26–33, 2002.
14. A. R. Laptook, L. Shalak, and R. J. T. Corbett, "Differences in brain temperature and cerebral blood flowduring selective head versus whole-body cooling," Pediatrics, vol. 108, no. 5, pp. 1103– 1110, 2001.
15. M. Thoresen and A.Whitelaw, "Cardiovascular changes during mild therapeutic hypothermia and rewarming in infants with hypoxic-ischemic encephalopathy," Pediatrics, vol. 116, pp. 92-99, 2000.
16. R. Sahni and U. M. Sanocka, "Hypothermia for hypoxicischemic encephalopathy," Clinics in Perinatology, vol. 35, no. 4, pp. 717-734, 2008.
17. A. J. Gunn, T. R. Gunn, M. I. Gunning, C. E.Williams, and P. D. Gluckman, "Neuroprotection with prolonged head cooling started before postischemic seizures in fetal sheep," Pediatrics, vol. 102, no. 5, pp. 1098-1106, 1998.
18. V. Kumar, J. C. Shearer, A. Kumar, and G. L. Darmstadt, "Neonatal hypothermia in low resource settings: a review," Journal ofPerinatology, vol. 29, no. 6, pp. 401-412, 2009.
19. E. Chakkarapani, J. Davis, and M. Thoresen, "Therapeutic hypothermia delays the C-reactive protein response and suppresses white blood cell and platelet count in infants with neonatal encephalopathy," Archives of Disease in Childhood:Fetal and Neonatal Edition, vol. 99, no. 6, pp. F458–F463, 2014.
20. George SA, Bennet L, Weaver-Mikaere L, Fraser M, Bouwmans J, Mathai S, et al. White matter protection with insulin like-growth factor 1 (IGF-1) and hypothermia is not additive after severe reversible cerebral ischemia in term fetal sheep. Dev Neurosci(2011) 33:280–7.doi:10.1159/000329923

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Staphylococcal scalded skin syndrome in a very low birth weight preterm infant

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INTRODUCTION

Staphylococcal scalded skin syndrome (SSSS) is an exfoliative dermatitis produced by the toxins of some strains of staphylococci, predominantly phage group 2, particularly strains 71 & 55. It has been reported predominantly in children under 5 years of age with few cases only reported in very preterm infants. In these cases the disease can be life threatening . We are reporting such a case.

CASE REPORT

First of twin /late preterm/35 weeks /1.045kg/SGA/girl/ LSCS(Twin pregnancy, IUGR) born to 27 year old G2P1L1 mother. Mother had hypothyroidism and on eltroxin during pregnancy.

Baby cried immediately after birth. No active resuscitation required. Second twin weight was 1.93 kg.

Problems in the baby - IUGR , Suspect sepsis (received IV antibiotics), Anaemia (received packed RBC transfusion - leucodepleted).

On post natal day 23 baby developed watery nasal discharge. Treated with saline nebulisation and nasal drops. On post natal day 25 baby developed peeling of skin, initially in the perioral area. Base of the lesion was erythematous. Subsequently baby developed peeling of skin over forearm, hand, abdomen and buttocks. Nasal swab culture and sensitivity showed heavy growth of staphylococcus, sensitive to Linezolid. Sepsis screen - negative. Blood culture and sensitivity - no growth. Treated with IV Linazolid for 7 days. Baby initially was very sick, required IV fluids and other

supportive measures. Baby improved with IV antibiotics and skin lesions improved with topical applications .

Both the parents or caregivers did not have any evidence of staphylococcal infection nor was there any outbreak in the NICU or any nasal swab cultures positive

DISCUSSION

SSSS is anexfoliative dermatitis produced by the toxins of some strains of Staph aureus.[1,2] caused predominantly by phage group 2 of staphylococci particularly strains 71 and 55 . Staphylococci are found in nasopharynx and less commonly on umbilicus, urinary tract, superficial abrasions, conjunctiva and blood and spread hematogenously. Predominantly affect children less than 5 years of age. It is very rare in extremely low birth weight infants. In these cases the disease might cause significant complications and can be life threatening. SSSS should be suspected in infants with generalised exfoliative lesion and positive Nicholsky sign.[3] SSSS is caused by staphylococcal exfoliative toxins A or B, which split the granular layer of the skin, induce proteolysis, and might exhibit superantigen activities, such as epidermolysis and lymphocyte mitogenicity. This syndrome which is rare in premature infants, is characterized by blistering and superficial desquamation of the skin and is caused by two epidermolytic toxins (ETA and ETB) produced by Staphylococcus aureus.

Out breaks of SSSS have been reported in NICU' s due to handling of the babies by infected or asymptomatic carriers of staphylococci. SSSS caused by MRSA producing exfoliative toxin is life threatening infection of neonates. Diagnosis of SSSS is mainly based on clinical features. Tzanck preparation from a freshly denuded area may reveal many acantholytic cells with out inflammatory cells. Culture specimen should be collected from the nose, throat or pyogenic focus on the skin for isolation of staphylococci. Systemic antibiotics are the main stay of treatment[4]. Major complications of SSSS are serious fluid and electrolyte disturbances[5]

Conclusion

Staphylococcal scalded skin syndrome in very low birth weight preterm babies are very rare. In these cases the disease can be life-threatening. Prompt diagnosis and appropriate antibiotic therapy is essential for survival. Early diagnosis and early treatment with parenterally administered beta-lactamase resistant penicillins are important to prevent life threatening complications of this syndrome.

Classical SSSS appearance - peri-oral and on abdomen

Lesions perioral

References:

1. Makhoul IR, Kassis I, Hashman N,Sujov P. Staphylococcal scalded-skin syndrome in a very low birth weight premature infant. Pediatrics. 2001 Jul;108(1):E16
2. Patel GK. Staphylococcal scalded skin syndrome management AMJ club Dermatology 2003,4: 165-175
3. Haveman LM, Fleer A, Gerards LJ.Staphylococcal scalded skin syndrome in two very low birth weight infants. J Perinat Med. 2003;31(6):515-9
4. Murono.K.Fujita.K microbiologic characteristics of exfoliative toxin producing staphylococcus aureus.
5. Fitzpatricks Dermatology 17th edition (chp-178)

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Perinatal testicular torsion -not an uncommon entity

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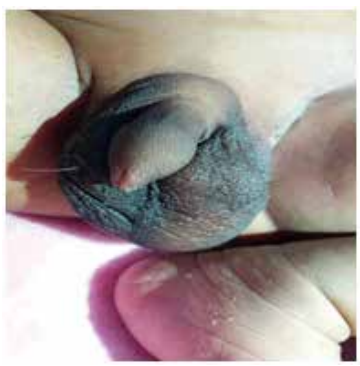
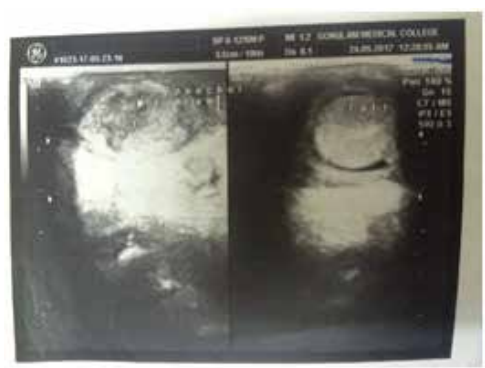
Introduction

Perinatal testicular torsion is a rare condition with incidence of 1 in 7500 live births. 70% are prenatal and 30% post natal. Post natal torsion present as acute scrotum, whereas prenatal torsion may be missed usually as it is a non-tender hard mass. Management of prenatal torsion is controversial. We are reporting 3 such case series presenting within a period of one year.

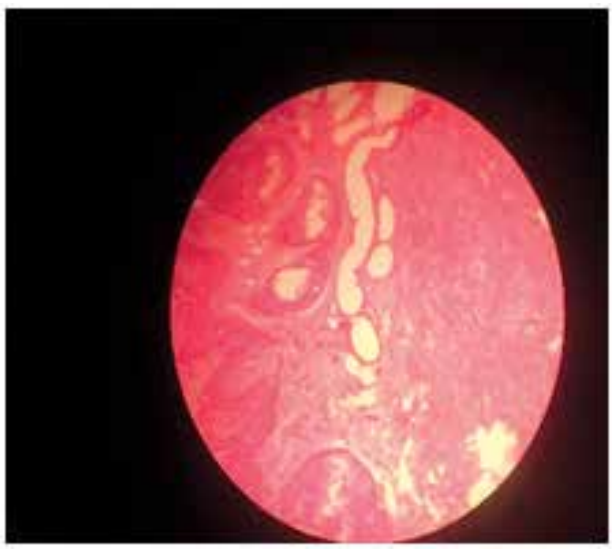
Case report:

Case 1: Term male baby 3.26 kg born to a 33 year old G3P2L2 mother with gestational diabetes by normal vaginal delivery. Asymptomatic baby on routine examination showed right hemi- scrotum darker with normal rughae. Right testis was hard, mobile, non-tender and larger than the left.





USG scrotum with Doppler showed right testis to be mildly enlarged, with peripheral calcification and no vascularity. Central hypo echoic area showing infarction and necrosis. Left testis was normal Scrotum on exploration showed right testis atrophic with torsion. Right testis was removed and left orchidopexy done.



Histopathology showed areas of hemorrhage and ischemic necrosis Only outlines of seminiferous tubules with extravasated RBCs seen. Spermatic cord and epididymis showed viable tissues.

Case 2: Term 3.4kg baby born to a 25 year old primi mother by normal delivery. Right testis was hard, USG doppler showed heterogenous echo pattern with no vascularity. Left testis was normal with left sided hydrocele. Right orchidectomy and left orchidopexy done.

Case 3: Term 2.8 kg baby born to 28year old G2A1 mother by normal delivery. Left testis was hard. USG doppler showed heterogenous echo pattern with no vascularity. Right testis was normal. Left orchidectomy and right orchidopexy done.

Discussion:

Testicular torsion was first described in 1840 by Delasiauve and reported in the newborn by Taylor in 1897. Prenatal torsion produce minimal to no discomfort and few localized findings. Possible etiologies of perinatal torsion include difficult labor, breech presentation, high birth weight, an over reactive cremasteric reflex and multiparity. These factors potentially increase intra uterine pressure as well as pressure in the birth canal during parturition. Such pressures may stimulate a brisk cremasteric response in the setting of loose tunica-scrotal attachment.

Usually extra vaginal-Testis, epididymis, and tunica vaginalis twist on the spermatic cord. The degree of torsion varies from 180° to more than 720°. The severity of torsion depends upon the degree of twist. Prenatal testicular torsion may be unilateral or bilateral, and bilateral torsion can be synchronous(67%) or asynchronous(33%). Antenatal ultrasound is not that sensitive. Careful routine postnatal physical examination can diagnose it.

Salvageability depend on time elapsed since torsion. Torsion in prenatal period far from birth can present as an absent or a nubbin testis. Torsion in the prenatal period several weeks back present as a regular, firm, painless scrotal mass, often in the upper part of the hemiscrotum, smaller than the contralateral normal testis, very much attached to the scrotal wall, without acute inflammatory signs, and which does not transmit light. When Torsion occur in the prenatal period near birth (several days), a firm and painless scrotal mass, bigger or similar in size than the contralateral normal testis, is seen without acute inflammatory signs and which does not transmit light. Torsion inprenatal period very near to birth (few days or several hours) will present with acute inflammatory scrotal signs: a painful, enlarged, bluish or reddish hemiscrotum; an enlarged and sometimes elevated testis - not transmitting light, thickened and painful cord. Doppler USG is 89.9% sensitive, 98.8% specific; USG alone is equivocal. USG will show enlarged, heterogenous testis,

thickened tunica albuginea with rim like hyperechoic reflections (calcifications) at the transitional zone between testis and tunica albuginea in case of prenatal torsion. Hypoechoic central area may also be evident which shows necrosis. Short duration of torsion is characterized by mixed echogenecity. Prolonged intrauterine torsion shows calcification and a hypervascular ring of tunica with a hypodense centre.

Radio nucleotide scan: Technetium - 99m pertechnetate is the agent of choice, dose of at least 5 mCi. Typically, immediate radionuclide angiograms are obtained, with subsequent static images as well. In the healthy patient, images show symmetric flow to the testes, and delayed images show uniformly symmetric activity. The appearance of testicular torsion on scintigraphy depends upon the chronicity. In acute torsion (usually <7 h): blood flow may range from normal to absent on the involved side, and a nubbin sign may be visible. The nubbin sign is a focal medial projection from the iliac artery representing the reactive increased flow in the spermatic cord vessels terminating at the site of torsion. Static images show photopenic area in the involved testis. In the subacute and late phases of torsion (missed torsion), often increased flow to the affected hemiscrotum via the pudendal artery with a photopenic testis and a rim of surrounding increased activity on static images - described as rim, doughnut, or bull's eye sign.

Management: For long standing intrauterine torsion, there is no urgency; these neonates should be operated on electively when the child is in optimal clinical status to confirm the suspected diagnosis, to remove the affected testis, and to explore the contralateral normal one. If torsion occurs in the prenatal period very near to birth or in the postnatal period within the first month of life immediate exploration should be carried out. Early surgical exploration may detect asynchronous torsion and allow its correction. Whether contralateral orchidopexy is justified is controversial.

Postnatal torsion will be presenting with considerable tenderness and swelling of a previously normal testicle. Testicular salvage rate in acute torsion: 85-97% - when operated within 6 hrs ,55-85 % @6-12 hrs, 20-80 % @12-24 hrs and <10% if > 24 hrs.

Conclusion:

Prenatal testicular torsion is not so rare, but usually missed as it is asymptomatic and later present as cryptorchid. Careful postnatal physical examination and documentation is essential , especially in avoiding future medico legal complications. Also note that in torsion in the immediate prenatal period, the testis may be salvaged if promptly operated.

References:

1. John M Gatti, Janine Pettiford. The Acute Scrotum; Ashcraft's Pediatricsurgery 6th edn page 702-704. Text book editors: George W Holcomb III, J Patrick Murphy, Daniel J Ostlie.
2. Tomm Lissauer. Physical Examination of newborn; Fanaroff & Martin's NEONATAL-PERINATAL MEDICINE 10th edn page 396. Text book editors:Richard J martin, Avroy A Fanaroof, Michele C walsh.
3. Muhammad Riaz-Ul-haq et al , Neonatal Testicular Torsion; a Review article. Iran J Pediatr. 2012 Sep; 22(3): 281-289.
4. P R H Callewaert and Philip Van Kerrebroeck.New insights into perinartal testicular torsion. Eur J pediatrics 2010; 169(6):705-712.

Tracheo-Oesophageal Fistula - 12 year experience in a tertiary centre

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Introduction

Oesophageal atresia (OA) with or without Tracheo- oesophageal fistula (TEF) is a congenital defect which requires immediate surgical management once diagnosed. The outcome depends on many factors, mainly the associated congenital anomalies and the type of TEF. Despite the improvement in survival, the morbidity associated with surgical repair remains high. Waterston and Montreal have suggested different classifications that will determine the prognosis of the patient. Waterston's classification is based on the birth weight, associated anomalies & preoperative pneumonia. But Montreal system is based on ventilator dependence and associated major anomalies only.

AIMS & OBJECTIVES

- To study the clinical profile, risk factors affecting mortality, and short term outcome after surgery of cases of TEF managed in our tertiary care center for a period of 12 years.
- To compare the survival rate as per the Waterston and Montreal systems of prognostic classification.

Methods:

Retrospective observational study of case records of newborns admitted with diagnosis of Tracheo- oesophageal fistula/Oesophageal Atresia (TEF/OA) for a period of 12 years from January 2004 to December 2015.

Results:

Out of the total 41 babies, majority were male - 27 (65.85%) & term babies - 25 (60.99%). Overall survival rate was 29 out of 41 (70.7%). Mortality was higher in those associated with pre-operative pneumonia, congenital anomalies and prolonged ventilation. 70.74% had anastomotic stricture requiring dilatation, 7.31% had anastomotic leak. The maximum number of patients (87.80%) were in type C of the Gross classification scale. The survival rate was least in type C of Waterston's classification scale (61.53%) and group 2 of Montreal's classification scale (30%).

MATERIALS & METHODS

A retrospective analysis of departmental database of newborns admitted and treated with diagnosis of Tracheo-oesophageal fistula/ Oesophageal Atresia (TEF/OA) for a period of 12 years from January 2004 to December 2015 was done. Patient's clinical profile, associated anomalies, surgical procedure, postoperative complications, and short term outcomes at 6 months after delivery were studied. They were classified based on the Gross classification, Waterston and Montreal system of classification and survival rate was calculated.

RESULTS:

A total of 41 patients were enrolled in the study of which 27(65.85%) were males and 14 (34.14%) were females. Out of this, majority 25(60.99%) were term babies. 29 (70.73%) were low birth weight with mean wt of 2212 g and 32 (78.04%) were outborns. Antenatal USG had shown polyhydramnios in 18 (43.9%). After delivery, 34 (82.92 %) babies presented with respiratory distress, 29 (70.73%) had excessive secretions and 13 (31.7%) had cyanosis. Preoperative aspiration pneumonia was present in 17(41.46 %).

Associated anomalies were present in 19 (46.34%) neonates, of which 9 (22) had cardiac anomalies, most common being PDA with Ostium secundum ASD (4 cases), followed by congenital cyanotic heart disease in 3 babies. Other anomalies were genitourinary and gastrointestinal 7 each, skeletal anomalies 3, and Down's syndrome with multiple anomalies 1. Three or more of VACTERL association were present in 5 babies (12.19%).

We could do ligation of the fistula & primary anastomosis in 35 (85.36%) babies of which 24 (68.6%) babies survived. Gastrostomy with esophagostomy and ligation of fistula was done in 5 babies and all of them survived and these patients had undergone gastric pull up procedure later. One patient could not be operated and that baby died. In 29 (70.73%) babies, surgery was done with in 48hrs. Prolonged ventilation was required in 12.2%. Post operatively 29 (70.74%) babies had anastomotic stricture and required dilatation of stricture. 3 (7.31%) babies had anastomotic leak of which one baby expired. None of our patients had recurrence of fistula.

Overall mortality was 29.2% (12) in this cohort. Male babies had higher mortality rate (9 died, 22%, P value-0.427). Being tertiary referral centre, majority of the babies were outborns (78.04%), but mortality was less in this group (21.87%). Mortality was higher in the group of patients associated with congenital anomalies (36.84%, P-0.359) and in patients with preoperative pneumonia (41.47%, P-0.058). Those associated with cardiac anomalies had higher mortality rate compared to others (44.45%). Those patients requiring prolonged ventilation had higher mortality (40%).

Prognostic classification:

Survival and mortality based on various classification of TEF.

Gross classification	Number	Survival – Number & %	Died Number & %	P-Value
A	1 (2.4)	1 (100)	0	0.701
B	1 (2.4)	0	1 (100)	
C	36 (87.8)	26 (72.22)	10 (27.78)	
D	2 (4.9)	2 (100)	0	
E	1 (2.4)	0	1 (100)	

The maximum number of patients (87.80%) were in type C of Gross classification. Overall survival rate in our study was 70.7%. The survival rate according to Waterston's classification was type A (77.78%) type B (73.68%) and type C (61.53%). Survival of Group1 of Montreal system was 83.87% and that of Group 2 was 30% (P-value <.05)

Montreal classification				
	Total No &%	Survival & %	Mortality &%	P-Value
Group 1	31 (75.6)	26(83.87%)	5 (16.13)	<.05 *
Group 2	10 (24.4)	3 (30%)	7 (70)	

Waterston classification				
	Total No &%	Survival & %	Mortality &%	P-Value
Type A	9 (21.95%)	7 (77.78%)	2 (22.22%)	0.137
Type B	19 (46.34)	14 (73.68%)	5(26.31)	
Type C	13 (31.7%)	8 (61.53%)	5 (38.46)	

Comparison with other studies:

Variables	PVS Hospital Kochi	Tandon et al KGMU,Lucknow)[1]	Peter Manning et al (Mott Hospital Michigan) [2]
Duration & Number	12y & 41	2yrs & 127	50yr & 428
GA & B.wt	Term, LBW	Term & Normal wt	term, LBW
Asso Congenital anomalies	46.34%	41%	34%
VACTERL asso.	12.19%	5%	17.5%
Anastomotic leak	7.31%	9%	8.5%
Esophageal stricture	70.73%	40%	19%
Overall survival rate	70.7%	80%	82%
Waterston classification	Type A(77.78%) Type B(73.68%) Type C(61.53%)	Type A(100%), Type B(82%), Type C(22%)	Type A(100%), Type B(83%) Type C (63%)

DISCUSSION:

There was a male preponderance (1.9:1) in this study. This was also shown in other larger studies worldwide. Although there was no significant relationship seen between time of surgical intervention and place of birth, it is seen in developing countries that the most important factor influencing the outcome is the prompt diagnosis and quick referral to the tertiary center, especially in India.[3]

Mortality was higher in those associated with congenital anomalies. 3 or more of VACTERL association were present 12.19%. Those with preoperative pneumonia had higher mortality. In babies treated for TEF and EA, the single most important factor improving survival in those babies is the prevention of pneumonia[4]. Post-operative anastomotic leak was less in our study, whereas anastomotic stricture, which required dilatation was higher (70.74%) compared to the study by Scott et al in which it was reported as 16 % and 35% respectively[5]. The maximum no of cases were in the type C of Gross classification in our cohort. The survival rate was least for type C (61.53%) of Waterston's classification & Group 2 of Montreal system (30%).

CONCLUSION

1. Mortality was higher in babies associated with preoperative pneumonia, congenital malformation and prolonged ventilation.
2. 70.74% of the operated patients developed anastomotic stricture which causes significant morbidity in these patients.
3. Most common was type C of Gross classification
4. Overall survival rate in our hospital was 70.7 %
5. Survival rate was least in Type C (61.53%) of Waterston's classification & Group 2 (30%) of Montreal classification.
6. Montreal system of classification is more reliable than Waterston's classification for prognostication. However because Montreal classification is according to ventilator dependency (after surgery), pre-operative prognostication is difficult as per this classification.

REFERENCES

1. R. K. Tandon, Satendra Sharma, Shandip K. Sinha, Kumar Abdul Rashid,Ravi Dube, S. N. Kureel, Ashish Wakhlu, J. D. Rawat. Esophageal atresia: Factors influencing survival - Experience at an Indian tertiary centre. J. Indian Assoc Pediatr Surg / Jan - Mar 2008 / Vol 13 / Issue 1
2. P B Manning, R A Morgan, A G Coran, J R Wesley, T Z Polley, Jr, D M Behrendt, M M Kirsh, and H E Sloan. Fifty years' experience with esophageal atresia and tracheoesophageal fistula. Beginning with Cameron Haight's first operation in 1935. Ann Surg. 1986 Oct; 204(4): 446-453.
3. R. K. Verma, S. S. Nath, G. K. Sinha.Retrospective study of esophageal atresia with tracheoesophageal fistula -three year experience .Indian.J.Anaesth; 2003;47(2):111-115
4. Louhimo I and Lindahl H. Oesophageal atresia: Primary results of 500 consecutively treated patients. J. of Paediatric Surgery 2006; 18 (3): 217-29.
5. Scott A. Engum, MD; Jay L. Grosfeld, MD; Karen W. West, MD; Frederick J. Rescorla, MD; L. R. Tres Scherer III, MD. Analysis of Morbidity and Mortality in 227 Cases of Esophageal Atresia and/or Tracheoesophageal Fistula Over Two Decades. Arch Surg. 1995; 130(5):502- 508 ■

3

Section -3

Algorithm & Formulary

Algorithm for management of urinary tract dilatation following postnatal ultrasound

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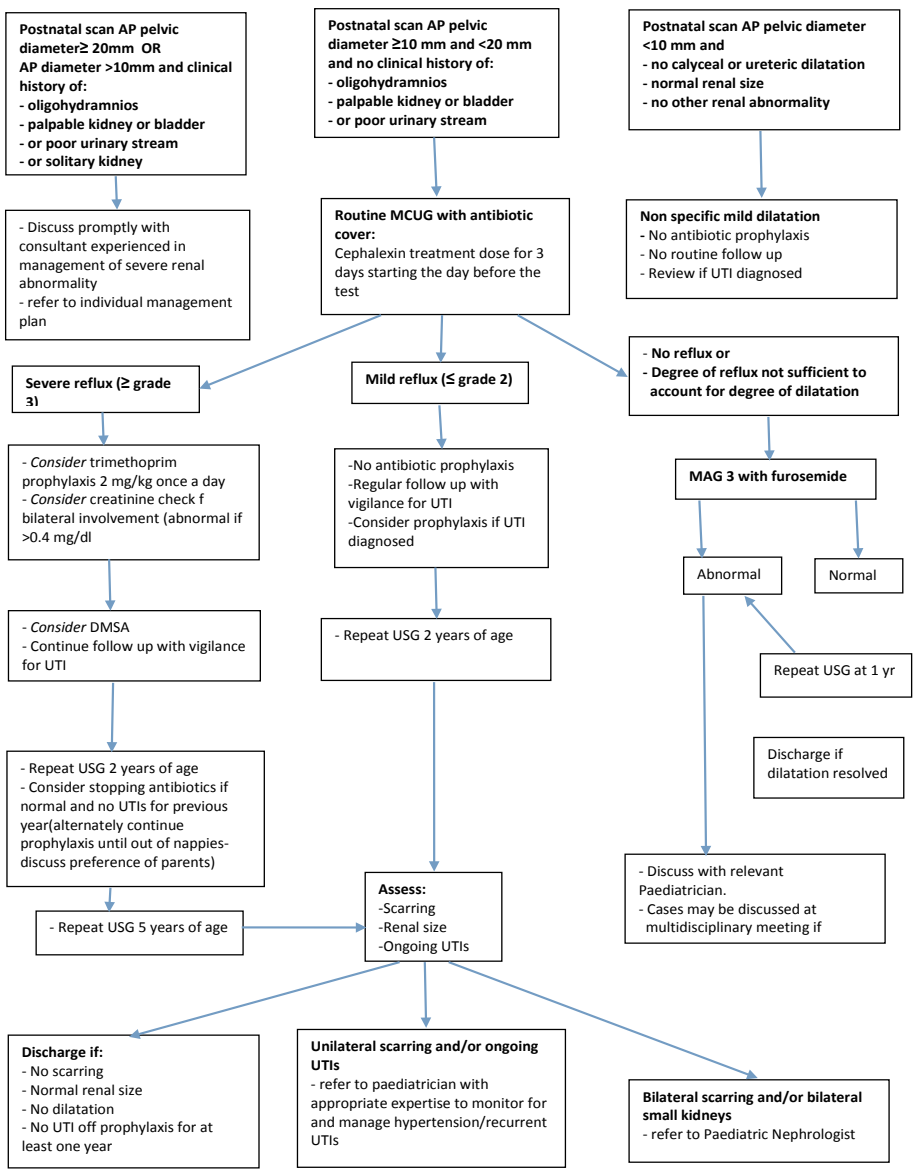

References:
1. Mallik M,Watson AR. Antenatally detected urinary tract abnormalities:more detection but less action.Pediatr Nephrol 2009;23(6):897-904
2. NICE guidelines UTI in children August 2007

Algorithm for management of NAIT

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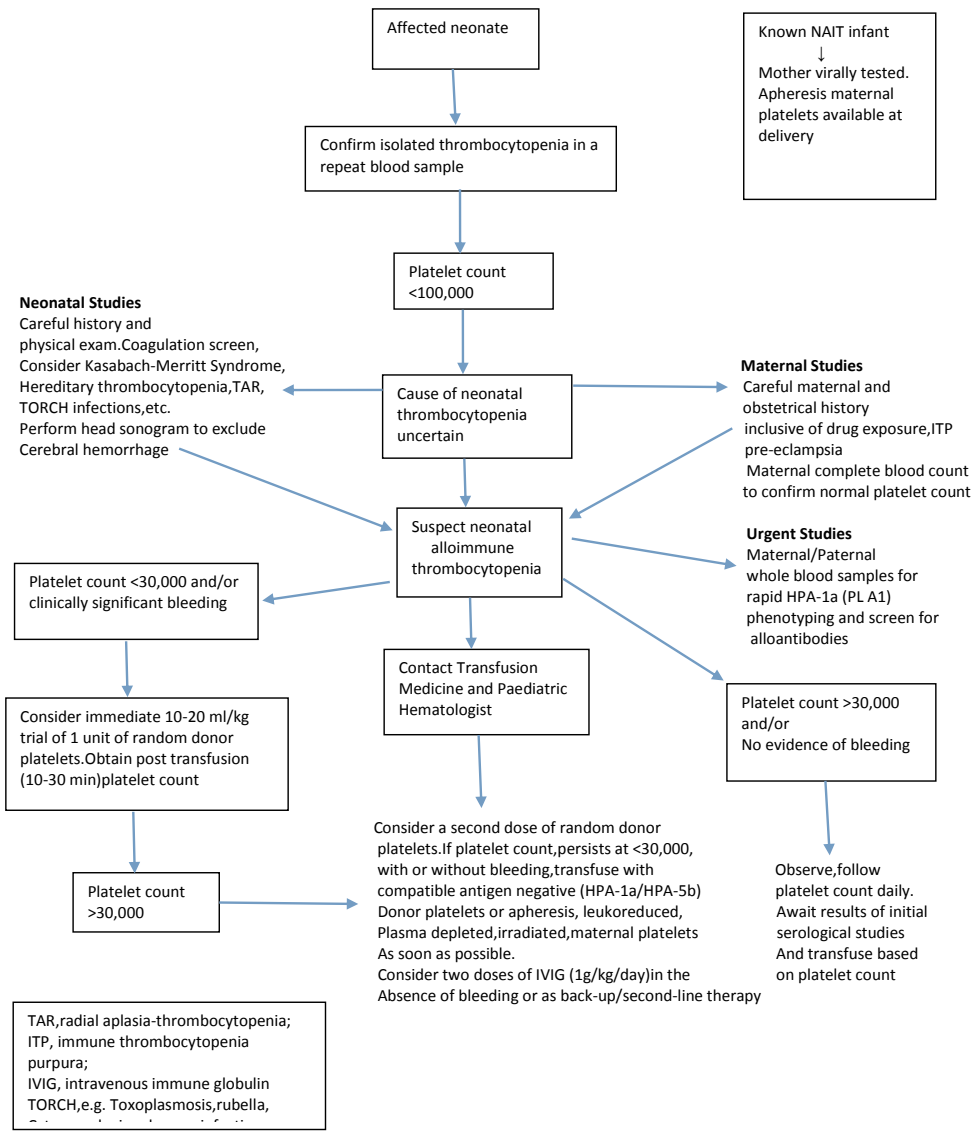

Algorithm for the management of unexpected alloimmune neonatal thrombocytopenia (NAIT).(Adapted from Blanchette VS, Johnson J, Rand M.The management of alloimmune neonatal thrombocytopenia.Bailliere's Clin Haematol 2000;13:365-390, with permission from Elsevier.)

NEONATAL DRUG FORMULARY

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ABBREVATIONS

- SWFI: Sterile Water For Injection
- PO : Per Oral
- IV : Intravenous
- IM : Intamuscular
- Sub Q: Subcutaneous
- PR: Per Rectal

L = Liver	K= Kidney	B.M* = Breast Milk	P=Pregnancy^
Indicates need for caution or need for dose adjustment in hepatic impairment	Indicates need for caution or need for dose adjustment in renal impairment	Refer to explanation of breast feeding categories.	Refer to explanation of pregnancy categories

*Explanation of breast feeding categories:

1. Compatible
2. Use with caution
3. Unknown with concerns

X Contraindicated ? Safety not established.

Explanation of Pregnancy categories.

A : Adequate studies in pregnant women have not demonstrated a risk to the fetus in the first trimester of pregnancy, and there is no evidence of risk in later trimesters.

B: Animal studies have not demonstrated a risk to the fetus, but there are no adequate studies in pregnant women; or animal studies have shown an adverse effect, but adequate studies in pregnant women have not demonstrated a risk to the fetus during the first trimester of pregnancy, and there is no evidence of risk in later trimesters

C: Animal studies have shown an adverse effect on the fetus, but there are no adequate studies in human s; or there are no animal reproduction studies and no adequate studies in human.

D: There is evidence of human fetal risk, but the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risk.

X: Studies in animals or humans demonstrate fetal abnormalities or adverse reaction; reports indicate evidence of fetal risk. The risk of use in pregnant women clearly outweighs any possible benefit.

1. ACYCLOVIR (Antiviral)

Indication: Herpes Simplex infections (HSV), Varicella Zoster infection with CNS and pulmonary involvement, herpes simplex encephalitis.

1. ACYCLOVIR (Antiviral)

Indication:

Herpes Simplex infections (HSV), Varicella Zoster infection with CNS and pulmonary involvement, herpes simplex encephalitis.

Neonatal (Birth to 5 months)

L	K	B.M	P
No	Yes	I	B

DOSAGE ADMINISTRATION :

Condition		Dosage and Frequency	Reconstitution and Administration	Storage, Stability
HSV infection	Premature Infants Neonates	10mg/kg/dose q12hrs x 14-21days 10 mg/kg/hrs q 8 hrs Disseminated disease X 21 days	Compatible with $NS/D_{5\,W}$ Powder reconstitute with SWFI Administer over 1 hour	Reconstituted solution stable at room temperature for 12 hours Do not refrigerate
Varicella	IV PO	10-20mg/kg q8hrs at least 7-10 days 10mg/kg 4 times daily for 7-10 days after exposure		

Adverse Effects, Contraindications & Incompatibility

Adverse effects, Contraindication,Incompatibility	Neutropenia, Crystalluria, Hepatic impairment, risk of transient renal dysfunction, Fat emulsion, Aztreoam, caffeine citrate

2. AMIKACIN (Aminoglycoside)

Indication:

Infections with gram negative organisms and mycobacterial organisms.

L	K	B.M	P
No	Yes	-	D

Dosing chart :

PMA (weeks)	Postnatal(days)	Dose (mg/kg)	Interval(hrs)	Administration	Dilution & Storage
≤29	0-7	18	48	NS/D5W over 30minutes Dilute with compatible solution of 2.5-5mg/ml	
	8-28	15	36		
	≥-29	15	24		
30-34	0-7	18	36		
	≥8	15	24		
≥35	All	15	24		

3. AMOXICILLIN

Indications:

Infections involving upper respiratory tract and urinary tract due to susceptible organisms.

Dose:

20-30mg/kg/day; in divided doses q 12-8 hrs.

UTI Prophylaxis: 10-20mg/kg once daily

L	K	BM	P
No	Yes	1	B

Condition	Dose : Oral	Frequency and Administration
General Dosing	20mg-30mg/kg/day	Divided dose in every 12 hour
Otitis media, Group A or B Streptococcus	30-40mg/kg/day	Divided dose in every 8 hours
UTI, Prophylaxis (Hydronephrosis, Vesicoureteral refluxes)	10-15mg/kg/day	Once daily

Route: PO

Adverse reaction, Precautions:

With prolonged therapy monitor renal, hepatic, and hematologic function periodically.

4. AMPHOTERICIN B

Indications;

Disseminated fungal infections caused by susceptible fungi such as; Blastomycesdematitidis, Histoplasmacapsulatum, Ceyptococcusneoformans, Candida sp., Sporithrixschenkii, Coccidioidesimmitis, Aspergillus sp.

L	K	B.M	P
No	Yes	?	B

Route: IV

Dose	Dosage and Administration	Storage, Stable
Test dose	0.1/kg infused over 30 min or 0.25mg/kg IV on first day over 6 hrs.	Available as powder reconstitute with compatible fluid
Subsequent dose	Increase gradually to 0.5-1 mg/kg/day IV as single infusion over 4-6 hrs.	Stable for 24hr at room Stable for 7 days at refrigerator Do not flush with saline solution

Adverse effects, Contraindications, Precautions:

Fever, Vomiting, Hypokalemia, mild renal tubular acidosis and hypomagnesemia Monitor K, Mg, BUN, Creatinine, Bilirubin, alkaline phosphatase.

5 AMPHOTERICIN B LIPID COMPLEX, LIPOSOME

Drug	Dose Interval	Dilution / Infusion	Special consideration
Lipid complex	5mg/kg Q24H	IV over 2hour	Do not freeze, protect from light Diluted mix stable for 48hrs Do not flush with saline Compatible with DSW Incompatible with NS
Liposomal Indication: Fungal infections resistance to conventional amphotericin B or patients with hepatic or renal dysfunction.	5-7mg/kg Q24H	IV over 2 hours	Reconstituted suspension stable for 24hr Do not freeze, protect from light Compatible with D_5 Incompatible with NS

Adverse effects, Precautions;

Anaemia, thromobocytopenia, hypokalemia, vomiting

Less nephrotoxic than conventional Amphotoxicin B

6. AMPICILLIN

Indications:

Initial empirical treatment with aminoglycosides fo bacterial sepsis and meningitis.

Drug of choice for Listeria monocytogenes and Enterococci.

L	K	B.M	P
No	Yes	I	B

Dose:

Days	Weight	Dose	Frequency
< 7 days	< 2 kg	50-100 mg/kg/day	Divided in q 12 hrs
	> 2 kg	75-150 mg/kg/day	Divided in q 8 hrs
> 7 days	< 1.2 kg	50-100 mg/kg/day	Divided in q 8 hrs
	1.2-2 kg	75-150 mg/ kg/day	Devided in q 12 hrs
	> 2 kg	100-200 mg/ kg/day	Divided in q 6 hrs

Route; IV, IM

PMA(weeks)	Post natal (days)	Interval(hours)	Dilution & Administration
≤29	0-28	12	Reconstitute SWFI, reconstitute solution must be used in 1 hr due to loss of potency.
	>28	8	
30-36	0-14	12	
	>14	8	IV push over 3-5 minutes
37-44	0-7	12	
	>7	8	Compatible with D5W, NS
≥45	All	6	

Adverse effects, contraindication, compatibility;

-Hypersensitivity reaction, diarrhea, interstitial nephritis.

7. AZITHROMYCIN (MACROLIDE)

Indications;

Pertussis, Chlamydia trachomatis, conjunctivitis.

L	K	B.M	P
Y	Y	2	B

Route: IV, PO

Disease	Dose	Duration	50/m compt	Stability & Duration
Pertussis	10mg/kg/dose	ODx5 days	NS, D5W	Lyophilized powder Reconstitute with SWFI
Chlamydia trachomatis Conjuctivitis Pneumonitis	20mg/kg/dose	ODx3days	RL+NS	Dilute prior to administration Infuse over 60 minutes Keep at 24hrs at room temp. 7days at refrigerator

Adverse effects, contraindication, incompatibility

Diarrhoea, vomiting occur in 5-12% of patients

Use with caution in impaired hepatic function and prolonged QT

Do not give as a bolus or IM

L	K	B.M	P
No	Yes	1	B

General Dosing:

30mg/kg/dose twice daily. Slow IV push over 5-10ml.

Route; IV/IM

PMA(wks)	postnatal(days)	Interval(nos)	Dilution/stability
≤29	0-28	12	
	>28	8	Reconstitute with SWFI
30-36	0-14	12	
	>14	8	Stable at room temperature for 48 hours.
37-44	0-7	12	
	>7	8	
≥45	All	6	Administer slow IV push over 5-10 minutes Solution Compatibile with D5W, D10W,NS

Adverse effects, incompatibility, contraindications;

Eosinophilia, elevation of serum transaminase, Monitor for Thrombophlebitis.

Adequate amounts of glucose must.

9. CEFEPIME

L	K	B.M	P
No	Yes	1	B

Indication:

Susceptible gram negative bacteria, including Pseudomonas aeruginosa, Lower respiratory tract infections, cellulitis, and urinary tract infections.

Route: IV, IM

Condition	Dose	Interval	Dilution, Storage, Administration
Term, Preterm ≤14days	30mg/kg/dose	Q12H	Powder reconstitute with SWFI to 100mg/ml concentrate then reconstitute with (D_5W, $D_{10}W$, D_5LR, NS).
Term, preterm>14 days	50mg/kg/dose	Q12H	Stable for 24 hour at room temperature
Meningitis and severe infection	Doses above	Q8H	
Max. Dose	6gm/24hr		IV infusion over 30 – 90 minutes

Adverse effects, contraindication

Rash, diarrhea, elevated hepatic transminase and BUN and creatinine, eosinophelia and positive coomb's test

10. CEFOTAXIM (CEPHALOSPORIN, 3rd GENERATION)

Indication:

Neonatal meningitis

L	K	B.M	P
No	Yes	1	B

General Dosing;

Sepsis: 50 mg/kg / dose IV or IM

Meningitis and Disseminated gonococcal infection: 100mg/kg/day÷q12hrs

Age		Total Daily Dose	Divided	Stability, dilution, storage
0-7 days	< 2000 g	100 mg/kg	q 12 hrs	Powder reconstitute with compatible solution
	> 2000 g	100-150 mg/kg	q 8-12 hrs	Stored at room temperature for 24hours
> 7 days	< 2000 g	150 mg/ kg	q 8 hrs	Infuse IV over 30 minutes
	> 2000 g	150 – 2000 mg/ kg	q 6-8 hrs	

Adverse effects, Precautions and contraindications

Phlebitis, rash, transient neutropenia, eosinophilia,

11 CEFTAZIDIME

Indications:

Susceptible gram negative bacteria, particularly Pseudomonas aeruginosa. Meningitis and neonatal sepsis at risk og aminoglycoside toxicity.

General Dose:

Sepsis: 30 mg/kg/dose IV

Meningitis: 50 mg/kg/dose IV

Route: IV,IM

Dosing interval

Post Natal Age (PNA) and Weight		Dose (mg/kg/day)	Devided in (hrs)	Storage, Dilution, Administration
< 7 days	< 2000 g	100 mg/kg/day	q 12 hrs	IV solution: powder reconstitute with SWFI, stable for 12 hours
	> 2000 g	100-150 mg/kg/day	q 8-12 hrs	Compatible with D_5W, $D_{10}W$, NS
> 7 days	< 1200 g	100mg/kg/day	q12hrs	Administer IV over 30 minutes
	> 1200 g	150/kg/day	q8hrs	

Adverse effects, interaction

May cause phlebitis, diarrhea, rash, neutropenia, thrombocytopenia, false positive coomb's test. Ceftazidime synergetic with aminoglycoside

12. CEFTRIAXONE (Broad spectrum cephalosporin)

L	K	BM	P
Y	Y	1	B

12 CEFTRIAXONE (Broad spectrum cephalosporin)

Indication:

Sepsis and meningitis caused by suscetibile gram negative organisms (E.Coli, pseudomonas, Klebsiella) Gonococcal infections.

Route: IV, IM

Dose:

Disease	Condition (PNA and Age) and Dose		Interval	Dilution with administration
Sepsis and Meningitis	< 7 days	50mg/kg	q24hrs	Reconstitute with compatible solution. Stored at room temp-2days., refrigerated 10 days. IV or IM Infusion IV over 30 minutes Avoid calcium containing solution for 48hours
	> 7 days < 2 kg	50mg/kg	q24hrs	
	> 7 days > 2 kg	50-75mg/kg	q24hrs	
Uncomplicated gonococcal ophthalmia or Prophylaxis	25-50mg/kg * 1 dose.(Max.dose 125mg)		q24hrs	
Disseminated Gonococcal Infection	25-50mg/kg/dose once daily IV or IM for 7 days		q24hrs	

Adverse effects, contraindication, incompatibility

Not recommended for use in neonates with hyperbilirubinemia.

Concurrent administration of calcium containing solution contraindicated. Increase in BUN, serum creatinine, increase in AST & ALT.

13. CEFUROXIME

Indication:

Infections caused by susceptible gram positive and gram negative organisms; not active against Enterococci or Pseudomonas.

L	K	BM	P
No	Y	1	B

Dose: PO 10-20mg/kg divided q 12 hrs.

Condition	Dosage	Administration
<7 Days	50 mg/kg divided q 12 hrs	IV or IM
7-21 Days	75 mg/kg divided q 8 hrs	IV
>21 Days	100 mg/kg divided q 6 hrs	IV
In severe infections may double the dose for all of the above age groups and administer IV only.		

Route: IV,IM,PO

Adverse reactions, Contraindications:

Diarrhea, urticaria, neutropenia, rash elevated liver enzymes.

14. CHLORAMPHENICOL

Indication:

Serious infections due to organisms resistant to other less toxic antibiotics. Useful for infections with Bcteroids, H. influenza, N. meningitides, Salmonella, and Ricketstsia

L	K	BM	P
Y	Y	3	C

Route: IV, PO

Condition	Dose	Interval	Preparation
Loading dose	20mg/kg	Start over 30mints	Powder reconstitute with SWFI Give IV over 15-30 minutes.
(After 12 hours)	≤7 days	25mg/kg/24-Q24H	
Maintenance dose	>7days ≤2kg	25mg/kg/24÷Q24H	
	>2kg	50mg/kg/24÷Q12H	

Adverse reactions, Precautions:

Stomatitis, rash, Serios and fatal blood dyscrasias may occur; Reversible bone marrow suppression, irreversible aplastic anemia, hemolysis in G6PD deficiency and gray baby syndrome.

15. CLINDAMYCIN

Indications:

Infections caused by anaerobic bacteria and susceptible gram positive organisms, second line drug for Bacteriodesragilis infections in infants.

L	K	B.M	P
Yes	Yes	2	B

Dose: General dose 5-7.5 mg. kg / dose

Route: IV, IM, or PO

PNA and Weight		Dose	Divided in	Dilution, stability, administration
< 7 days	< 2000 g	10 mg/kg/day	q12hrs	Pre mixed solution administer over 30 minutes IV,IM, PO IV preparation reconstitute with compatible solution
	> 2000 g	15mg/kg/day	q8hrs	
> 7 days	< 1200 g	10mg/kg/day	q12hrs	
	1200-2000 g	15mg/kg/day	q8hrs	
	> 2000 g	20-30 mg/kg/day	q6-8hrs	
Infants	PO	10-30mg/kg/day	q6-8hrs	
	IV,IM	25-40mg/kg/day	q6-8hrs	

Dosing Interval:

PMA	Post natal days	Interval	Dilution, stability, administration	Major Indication/ Remarks
≤29	0-28 >28	12 8	Pre mixed solution administer over 30 minutes IV,IM, PO IV preparation reconstitute with compatible solution	Gram-positive cocci and bacteroides. Widely distributes to most tissues, esp the lungs. Poor CSF penetration. Psuedomembranous colitis.
30-36	0-14 >14	12 8		
37-44	0-7 >7	12 8		
≥45	All	6		

Adverse effect, Contraindication, Precautions;

May cause Abdominal pain, bloody diarrhea, Fever

Most serious adverse affect is pseudomembrane colitis, Steven - Johnson Syndrome, elevated liver enzyme.

Contraindicated in meningitis, Rapid IV administration may cause hypotension, arrhythmias and cardiac arrest.

16. FLUCONAZOLE

Indications:

Systemic fungal infections including meningitis due to Candida species.

L	K	BM	P
Y	Y	2	L/D

Route: IV,PO

Dose;

Condition/indication	Dosage	Administration
Systemic infection Meningitis	Loading dose 12mg/kg on day 1, then 6 mg/kg/dose q 24 hrs. (Duration of therapy depends on type of infection and may range from 14-28 days.For meningitis duration is 10-12 weeks after CSF culture become negative.)	Infusion over 60 minutes Do not freeze
Oropharyngeal Candidiasis (PO)	Loading dose: 6 mg/kg on day 1 then 3 mg/kg/dose q 24 hrs.	
Prophylaxis	3mg/kg/dose twice weekly IV or PO	

Dosing intervals

PMA	Post natal	Interval
≤29	0-14 >14	72 48
30-36	0-14 >14	48 24
37-44	0-7 >7	48 24
≥45	all	24

Adverse effects, Interaction, contraindications and incompatibility

May cause QT prolongation, elevated liver enzymes, leucopenia, and thrombocytopenia. May increase levels of phenytoin. Contraindicated in patients receiving cisapride

17. GANCICLOVIR

Indication:

Cytomegalo virus, CMV infections

L	K	BM	P
Yes	Yes	3	C

Dose:

6 mg/kg/dose q12 hours IV Treat for a minimum of 6 weeks if possible. Decrease dose by ½ for neutropenia (<500 cells/ mm3).

Administer:

over 60 minutes. Discontinue therapy if neutropenia does not resolve after dose reduction.

18 GENTAMICIN

Indication:

Infections caused by susceptible gram negative organism (Such as E.coli, Pseudomonas, Proteus). Used in combination therapy for newborns sepsis.

L	K	BM	P
No	Yes	2	C/D

Dose:

Post Natal Age (weeks)	Post Natal Age (Days)	Dose (mg/kg)	Interval
<29	0-7	8	48
	8-28	4	36
	>29	4	24
30-34	0-7	4.5	36
	>8	4	24
>35	All	4	24

Route: IV, IM, IT/IVT

Adverse reaction, Contraindication, Precautions;

May cause Ototoxicity (Vertigo or deafness) and Nephrotoxicity at higher dose, may potentiate neuromuscular blockage and aggravate effect of hypermagnesemia.

L	K	B.M	P
No	No	2	C

19. IMIPENEM

Indication:

Effective against gram - negative and gram - positive bacteria, both aerobes and anaerobes, including Pseudomonas aeruginosa and Bacteroide fragilis.

L	K	BM	P
No	Yes	2	C

General dosing: 20-25 mg/kg/dose q12 hrs

Condition	Dose	Frequency
0-4 weeks, < 1200g	20 mg/kg/dose	q 18-24 hrs
PNA <7 Days, 1200-1500g	40 mg/kg/day	Divided q 12 hrs.
PNA > 7 Days, 1500 g	75 mg/kg/day	Divided in q 8 hrs

IV Administer over 30 minutes.

Route: IV

Adverse reactions, Precautions, Contraindications:

Non-CNS infections caused by Enterobacteriaceae and anaerobes resistant to other antibiotics. Seizures common with meningitis and severe renal dysfunction

20. LINEZOLID

Indication:

Pneumonia, bacteremia, MRSA

Route: IV, PO

Indication	Dose	Interval	Administration
Term<14 days	10mg/kg/dose	Q12H	Infuse IV over
Term≥14days	10mg/kg/dose	Q8H	30 min
Preterm	10mg/kg/dose`	Q12H	Protect from Light

Adverse effect, contraindication, incompatible

Gram-positive organisms, incl. MRSA, refractory to vancomycin and other antibiotics. Not used for empiric therapy, don't use with SSRIs

Most common side effects headache, anemia, leukopenia, thrombocytopenia, administer with or without food

21. MEROPENAM (CARBEPENAM)

Indications:

Treatment of multidrug resistant gram negative and gram

L	K	BM	P
No	Yes	2	B

positive aerobic and anaerobic pathogens.

Route: IV

Dose:

Indication	Dose	Interval		Storage Administration
Sepsis	20 mg/kg/dose	<32	0-14; q12h	After reconstitution and dilution infuse IV over 30minute
	20mg/kg/dose		>14; q12h	
		>32	0-7 ; q12h	
			>7 ; q8h	
Meningitis/ Pseudomonas	40mg/kg	Q8h		
Infant ≥3months	30mg/kg	Q8H		

Adverse effects, Precautions, contraindication:

Diarrhea, rash, hypotension, Risk of pseudomembranous colitis

Monitor

Thrombocytopenia and Eosinophilia Renal function, Hepatic function

21. METRONIDAZOLE

Indications:

Anaerobic bacteria and protozoal infections such as, amebiasis, giardia lamblia, trichomonas.

L	K	BM	P
Yes	Yes	3	B

Monitor

Thrombocytopenia and Eosinophilia Renal function, Hepatic function

21. METRONIDAZOLE

Indications:

Anaerobic bacteria and protozoal infections such as, amebiasis, giardia lamblia, trichomonas.

Route: IV, PO

Loading dose: 15mg/5g PO or IV over 60 minutes

Maintenance dose: 7.5mg/kg/dose PO or IV over 60 minutes

PMA (weeks)	Post natal (days)	Amount per dose	Interval
≤29	0-28	7.5 mg/kg	48
	>28		29
30-36	0-14	7.5 mg/kg	29
	>14		12
37-44	0-7	7.5 mg/kg	24
	>7		12
≥45	All	15 mg/kg	8

Adverse effect, Prophylaxis, Contraindications

Neutropenia and rarely seizures, Drug metabolitis may cause brownish discoloration of the urine

22. NYSTATIN

Indications:

Treatment of cutaneous and mucocutaneousCandidal infections.

Route: PO,Topical

Condition	Dose (1 ml=1,00,000 units)	Remarks
Preterm	0.5 mL PO q6 hours	Mucocutaneous candida infections
Term	1 mL PO q6 hours Apply topically with swap to each side of mouth.Use for length of antibiotic therapy and continue for 24 hours after discontinuation of antibiotic therapy, especially in infants <1500 grams .	Prophylaxis against invasive fungal infections in VLBW infants. Do not need if using fluconazole

Adverse reactions, Contraindications:

May cause diarrhea, GI symptoms and contact dermatitis.

23. OSELTAMIVIR

Indication:

Influenza virus (confirmed or suspected)

L	K	BM	P
No	Yes	2	C

Dose:

PMA (weeks)	Dose (mg/kg/dose PO)	Frequency
<38	1 mg/kg/dose	Twice daily for 5 days
38-40	1.5 mg/kg/dose	Twice daily for 5 days
40	3 mg/kg/dose	Twice daily for 5 days
Longer treatment may be necessary for patients who remain severe ill after 5 days of treatment		

Route: PO

Adverse reactions, Prophylaxis and Contra-indications:

Anaphylaxis and serious skin reactions, including toxic epidermal necrolysis, Stevens-Johnson syndrome, and erythema multiforme.

24. PENICILLIN G (IV/IM)

Indications:

Treatment of infections caused by susceptible organisms such as Streptococci, Neisseria), Congenital syphilis and meningitis.

L	K	B.M	P
No	Yes	2	B

Dose:

Indication	Dose/day	Interval	Storage and Administration
Meningitis	75,000 to 1,00,00 IU/ kg/ dose IV or IM	IV over 30 min	Reconstitute the powder – compatible solution Reconstitute solution stable for 3 Days in refrigerator
Bacteremia	25,000 to 50,000 IV/Kg	IV over 15min	
Syphillis	50,000 IV/kg	IV over 15mints	
Gonococcal Infection	75,000 to 1,00,000	IV over 30min	
Group B Streptococcal infection	2,00,000 IU/kg/day in divided doses.	Over 30min	
	4,50,000 IU/kg/day with Meningitis	Over 30min	

25. PIPERACILLIN / TAZOBACTUM

Piperacillin to Tazobactum ratio 8:1

Indications:

Sepsis, intra abdominal infections caused by susceptible beta lactamase prodfucing bacteria.

L	K	BM	P
N	Y	2	B

General Dosing : 50-100mg/kg/dose

Route: IV, Administer IV over 30 minutes

PMA	Postnatal	Interval	Stability
≤29	0-28 >28	12 8	Reconstitute with compatible solution stable for 24hrs at room air
30-36	0-14 >14	12 8	
37-44	0-7 >7	12 8	
≥45	All	8	

Adverse effects, contraindication

Eosinophilia, hyperbilirubinemia, elevation in ALT AST

Steven-Johnson syndrome.

26 TRIMETHOPRIM - SULFAMETHOXAZOLE (Bactrim)

Indication:

UTI Prophylaxis, minor / moderate infections, Pneumocystis jirovecii pneumonia.

Route: PO, IV

Prophylaxis: 2 mg/kg q 12 hrs PO

Treatment: 4 mg/kg q12 hrs PO

Precautions, Adverse effects, Contraindication

Contraindicated in megaloblastic anemia due to folate deficiency. May cause kernicterus in newborns. Blood dyscrasias, crystalluria, glossitis, Steven - Johnson syndrome, hemolysis in patients with G6PD deficiency.

27. VALGANCICLOVIR

Indication:

Symptomatic and congenital CMV

L	K	B.M	P
Yes	Yes	3	C

Dose:

Neonate and infant: 16mg/kg/dose Po, BD similar level to IV Ganciclovir 6 mg/kg/dose BD.

Valganciclovir is prodrug of ganciclovir

The absolute absorption of ganciclovir from Valganciclovir with food was approximate 60%

Adverse effect, Precautions, Contraindication:

Heamatologic adverse effects netropenia, anemia, thrombocytopenia, acute renal failure, abdominal hepatic function etc, use with caution in renal insufficiency, preexisting bone marrow suppression or receiving myelosuppressive drugs or irradiation.

28 VANCOMYCIN

Indication:

Infection due to methicillin-resistant Stphylococcus, beta - lactum resistant streptococcus. Orally for C. difficile colitis.

L	K	BM	P
No	Y	2	C/B

Route: IV

Dose:

Bacteremia 10mg/kg/dose

Meningitis, pneumonia 15mg/kg/dose

GA (weeks) and PNA (days)		Dose	Frequency	Storage, dilution administration
<30	0-7 days	10-15 mg/kg/dose	q 24 hrs	Reconstitute with SWFI and stable for 14 days refrigerator. Dilute prior to administrate Infuse IV over I hour
	> 7 days	10-15 mg/kg/dose	q12 hrs	
30-37	0-7 days	15 mg/kg/dose	q12 hrs	
	> 7 days	15 mg/kg/dose	q 8hrs	
37-44	All ages	10-20 mg/kg/dose	q 12 hrs	

(GA=Gestational Age, PNA= Post Natal Age, SWFI= Sterile Water For Injection)

Adverse effects, Precaution, contraindication

Ototoxicity and nephrotoxicity with concurrent aminoglycoside neutropenia rashand hypotension (red man syndrome),DRESS neutropenia.

Precaution:

Rapid infusion may cause hypotension and erythema multiform like reaction with intense pruritis.

MISCELLANEOUS DRUGS

29. DIGOXIN

Indication:

Congestive Heart Failure (not useful in decompensated PDA in premature infants), paroxysmal supraventricular tachycardia, and atrial fibrillation

L	K	BM	P
No	Yes	?	C

Dose

Age	Digitilizing (Loading) Dose		Total Daily Maintenance Dose	
	PO	IM or IV	PO	IM or IV
Preterm	20-30 mcg/kg	15-25 mcg/kg	5-7.5 mcg/kg	4-6 mcg/kg
Term	25-35 mcg/kg	20-30 mcg/kg	6-10 mcg/kg	5-8 mcg/kg
Digitilize by giving 50 % initially then give remainder divided into 2 doses q 6-12 hrs. Maintenance dose divided q 12-24 hrs.				

Route: IV, IM, PO

Pharmacokinetics:

Route	Onset of action	Peak action
PO	1-2 hrs	2-8 hrs
IM	15-60 min	2-5 hrs
IV	5-30 min	1-4 hrs
Half life m5-45 hrs in full term neonates and up to 170 hrs in premature infants.		

Adverse effects, Contraindications, Precautions:

Toxic cardiac effects and Non toxic cardiac effects

-PR interval prolongation -QT interval shortening

-Snus bradycardia or SA block -ST segment sargging

-Atrial or nodal ectopic beats -Twaveamlitutedamprosn

-Ventricular arrhythmias -Heart rate slowing

30. DOBUTAMINE

Indication:

Inotropic support in low cardiac output states, after cardiac surgery, shock and hypotension.

Dose:

IV Continousinfusion: 2-15 mcg/ kg/ min, adjusted according to response. Maximum dose: 20 mcg/kg/min.

L	K	BM	P
No	No	?	B

Route: IV

Solution preparation calculation

To calculate the amount of drug needed per defined final fluid volume.

Desired find concentration (mg/ml) x defined final fluid volume (ml)=amount of drug to add to final infusion solution.

Calculating infusion rate (ml/hr) = Dose(mcg/kg/min) * Weight (kg)* 60 min/hr

Concentration (mcg/ml)

31. DOPAMINE

Indication:

Hypotension or shock not responding to adequate fluid volume replacement. In low doses increases renal perfusion and urine flow.

L	K	BM	P
No	No	?	C

Dose:

IV Continuous infusion: 2-20 mcg/kg/min.

Typical initial dose: 5-10 mcg/kg/min if given for blood pressure support;

2-3 mcg/kg/min if given to improve renal perfusion.

Low dose:

1-5 mcg/kg/min for increased renal output and renal blood flow.

Intermediate dose:

5-15 mcg/kg/min for increased renal blood flow, heart rate, cardiac contractility, cardiac output, and blood pressure.

High dose:

> 15 mcg/kg/min alpha adrenergic effects predominate, vasoconstriction, increased blood pressure.

Route: IV

Adverse reaction, Precautions:

Dopamine must not be used as a sole therapy in hypovolemic patients. Extravasation may cause tissue necrosis. Do not administer into an umbilical arterial catheter. May cause tachycardia and arrhythmias and increased pulmonary artery pressure.

Calculating infusion rate (ml/hr) =

Dose (mcg/kg/min) * Weight (kg) * 60 min/hr
Concentration (mcg/ml)

32. ENALPARIL/ ENALAPRILAT

Indication:

Mild - severe hypertension afterload reduction in CHF

L	K	BM	P
No	Yes	2	C

Dose:

Enalapril (PO): 0.01mg/kg/day, every 24 hrs; increase dose and interval as required every few days to up to 0.1mg/kg/day divided in 1-3 doses.

Enalaprilat (IV): 5-10 mcg/kg/dose every 8-24 hrs.

Precautions, Adverse effects: Use with caution in renal impairment. Oliguria and increased serum creatinine occur frequently. May cause hypotension, hypoglycemia, hyperkalemia, and bone marrow suppression.

Enalapril converted to enalaprilat by the liver

Enalapriat: IV Begin 10mcg/kg/dose IV over 5 minutes

33. ENOXAPARIN

Indication:

Prophylaxis and treatment of thromboembolic disorders.

L	K	BM	P
Yes	Yes	2	B

Dose: Prophylaxis: 0.75 mg/kg q12hrs

Treatment: 1.5 mg/kg/ q12hrs

Route: Sub Q

Condition	Dose	Interval	Storage, Administration
Term infants	1.7mg/kg per dose	q12hrs	Available as 20mg/0.2mL
Preterm infants	2mg/kg per dose gub Q	q12hrs	40mg/0.4ml
Low risk prophylaxis	0.75mg/kg per dose Sub Q	q12hrs	60mg/0.6mL Preservative free filled syringe

Deep VeinThrombosis:

Infant <2 months 0.75mg /kg/dose q12hrs

≥2 months 0.5mg/kg/dose q12hrs

Max. dose 30mg/dose

Adverse reaction, Precautions, Contraindications:

Bleeding or thrombocytopenia may occur. Use with caution in patients with increased risk of bleeding.

34 EPINEPHRINE

Indication:

Cardiac asystole or profound bradycardia and hypotension, acute cardiovascular collapse, short term use in cardiac failure resistant to other drugs. In order infants may be used subcutaneously for relief of bronchospasm.

Dose:

Severe bradycardia and hypotension:

IV:

0.1-0.3 ml/kg/dose (equivalent to 10-30 mcg /kg/dose) of 1: 10,000solution.

Repeat q 3-5 min as needed.

Continues IV infusion:

Start at 0.1mcg/kg/min, titrate as needed; maximum dose 1 mcg/kg/min.

Route: IV, ET

L	K	B.M	P
No	No	?	C

Adverse reactions, Precautions, Contraindication:

Cardiac arrhythmias may occur, particular premature ventricular contractions and ventricular tachycardia. Renal vascular ischemia, severehypertension with intracranial hemorrhage, and increased myocardial oxygen requirements.

Therapeutic dose may cause hyperkalemia.

Calculating infusion rate (ml/hr) =

Dose (mcg/kg/min) * Weight (kg)* 60 min/hr

Concentration (mcg/ml)

35. HEPARIN

Indication:

Anticoagulation to maintain patency of peripheral and central catheters, treatment of thrombosis.

L	K	BM	P
No	No	1	C

Dose:

Patency of catheters: 0.5-1 Units/ml of IV fluid

Line flushing:

10 Units/ml commonly used, volume of heparine flush is usually similar to volum of catheter.

Systemic heparinization: Initial loading dose: 75 Units/kg given over 10 min (Use 50units/kg if patient is < 35 weeks) followed by continous IV infusion: 28 Units /kg/hr

Route: IV

Adverse reaction, Precautions, Containdication:

Haemorrhage, allergy, thrombocytopenia, elevated liver enzymes.

Calculating Infusion rate (ml/hr) = Dose (Units/kg/hr)* Weight

Concentration (Units/ml)

36. IBUPRUFEN

Indication:

Closure of patent ductusarterious (PDA) for premature infants at age 2 days or greater.

L	K	BM	P
No	Yes	1	C/D

Dose:

Initialdose: 10mg/kg/dose followed by two doses of 5 mg/kg/dose given 24 hours and 48 hours after the initial dose. Administer over 15 minutes. Hold second and third doses if urine output is <0.6 ml/kg/hr; may give when renal function improves.

Adminstor IV by syringe pump over 15 minutes at 24 hour interval

Route: IV

Adverse reactions, Precautions, Contraindication

Contraindicated in premature neonates with at least one of the following.

1. Proven or suspected infection that is untreated.
2. Congenital heart disease in which patency of the ductus arteriosus is necessary for satisfactory pulmonary or systemic blood flow.
3. Active bleeding, especially intracranial hemorrhage or GI bleeding and ulcer diseases.
4. Thrombocytopenia

5. Coagulation defects.
6. Suspected NEC
7. Significant impairment in renal function.

37. INDOMETHACIN

Indication:

Closure of ductus arteriosus, Prevention of intraventricular hemorrhage.

Prevention of intraventriculuar hemorrhage.

L	K	BM	P
No	Yes	1	C/D

Dose:

PDA closure dose (mg/kg): Usually 3 doses per course.

Age at 1st dose	1st(mg/kg)	2nd(mg/kg)	3rd(mg/kg)
<48h	0.2	0.1	0.1
2-7d	0.2	0.2	0.2
>7d	0.2	0.25	0.25

Give doses 12-24 hrs apart.

Longer treatment courses maybe used: 0.2mg/kg/day for up to 5-7 days.

Prevention of IVH for events with a birth weight <1 kg or gestational age

< 28 weeks: 0.1 mg/kg/ q 24 hrs for 3 doses beginning at 6-12 hrs of age.

Infuse IV over 20-30 min

Do not administer if urine output is <0.6mL/kg/hr.

Route: IV

Adverse reaction, Precaution, Contraindication:

May cause transient decrease in urine output. Hyponatremia, hypokalemia and hypoglycemia. Causes platelet dysfunction and decreased GI blood flow. Contraindicated in active bleeding, significant thrombocytopenia, and significant renal impairment.

38. MILRINONE

Indication:

Short term treatment of low cardiac output states (not responding to other treatments); due to sepsis, CHF,

L	K	BM	P
Yes	Yes	2	C

Dose:

Loading dose: 50 mcg/kg IV infused over 30-60 min followed by maintenance infusion.

Maintenance dose: 0.25-0.75 mcg/kg/min. Dose should be titrated based on hemodynamic and clinical response.

Route: IV

Adverse reaction, Precautions, Contraindication:

Monitor for hypotension, electrolyte imbalance, thrombocytopenia, hepatotoxicity and renal impairment.

Calculating infusion rate (ml/hr) =

Dose (mcg/kg/min) * Weight (kg) * 60 min/hr

Concentration (mcg/ml)

39. PROPRANOLOL

Indications:

Tachyarrhythmias, Hypertension, palliation of Tetralogy of Fallot, adjunctive treatment in neonatal thyrotoxicosis.

L	K	BM	P
Yes	Yes	1	C/D

Dose:

Dose	Frequency	Maximum	Administration
Starting oral dose	0.25mg/kg/dose q 6-8 hrs	5mg/kg/day	Protect from light compatible with D_5W and NS
Starting IV dose	0.01mg/kg/ q6hrs over 10 minutes	0.15mg/kg /dose q6hrs.	

Thyrotoxicosis: 2mg/kg/24hr PO Q6-12hr

Route: IV, PO

Adverse effects, precautions and contraindications:

Bradycardia, bronchospasm, hypoglycemia, GI disturbance and hypotension.

40. SILDENAFIL

Indication:

Persistantpulmonary hypertension refractory to inhaled nitric oxide, for those who unable to weaned off of nitric oxide, or in situations where nitric oxide is unavailable

L	K	BM	P
YES	Yes	?	B

Dose: 0.3-1 mg/kg/dose q 6-12 hrs

Route: PO

Adverse effect, Precautions and Contraindication:

Short term worsening oxygenation and systemic hypotension

0.5mg/kg/dose q 6 h - q12h, 0.4mg/kg/dose IVOver 3hr followed bycontinous infusion at 1.6 mg/kg/24 hrs for upto 7 days.

41 ACETAMINOPHEN

L	K	B. M	P
Yes	Yes	1	B/C

Indication: Fever, mild pain

Dose:

PO, PR: 10-15 mg/kg/dose q 6-8 hrs prn.

Neonatal group	Dose (PO)	Dose (PR)
Preterm (28-32 weeks)	10-12 mg/kg/dose q6-8hrs; Max 40 mg/kg/day	20 mg/kg/dose q 12 hrs; Max 40 mg/kg/day.
Preterm (32-36 weeks) and term <10 days	10-15 mg/kg/dose q 6 hrs; Max 60 mg/kg/day	15 mg/kg/dose q 8 hrs; Max 60 mg/kg/day.
Term > 10 days	10-15 mg/kg/dose q 4- 6 hrs; Max. 90 mg/kg/day.	20 mg/kg/dose q 6-8 hrs. Max. 90 mg/kg/day.

Route: PO, PR

Adverse reaction, Contraindication, Precautions:

Hepatotoxicity may occur with serum levels > 200 mcg/ml at 4 hrs or 50 mcg/ml at 12 hrs after overdose. Avoid in G6PD deficiency. Liquid preparation may containing sodium benzoate which can led to gasping syndrome in neonates.

42 FENTANYL

Indication:

Analgesia, short term sedation, adjunct to general anesthesia.

L	K	BM	P
No	Yes	2	C/D

Intermittent :

0.5-4 mcg/kg/dose given by slow IV push, repeat as required q 2-4 hrs.

Continuous IV infusion:

0.5-5 mcg/kg/hr. Tolerance may develop with prolonged use.

Anesthesia: 5- 50 mcg/kg/dose

Route: IV

Adverse reaction, precautions, contraindication:

Physical and psychological dependence

may occur with prolonged use; abrupt discontinuation may result in withdrawal and seizures. Rapid IV infusion may result in skeletal muscle and chest wall rigidity, respiratory distress and impaired ventilation.

50-100 times more potent than morphine on a weight basis.

To prepare infusion

50x desired dose (mcg/kg/hr) x wt (kg) =mcg fentanyl

Desired infusion rate (mL/hr) 50 ml fluid

Calculating infusion rate (ml/hr) =

Dose (mcg/kg/hr) * Weight (kg)

Concentration (mcg/ml)

43. FOSPHENYTOIN

Fosphenytoin dosing is expressed in phenytoin equivalents (Fosphenytoin 1mg PE=phenytoin 1 mg)

Loading dose 15-20mg /kg IM or IV infusion over 10 minutes

Maintenance dose 4-8mg/kg/IM or IV push begin maintenance 24 hours after loading dose

Maximum IV infusion:

3mg/kg/min upto more of 150mg /min

Use with calculation in neonates with hyperbilirubinemia

Adverse effects, precaution, contraindication:

hypokalemia, etc.

44. LEVITIRACETAM

Indication:

Neonatal seizures

Dose : IV, PO : Initial 10 mg/kg once daily , increased gradually by max. 10 mg/kg twice daily every 2 weeks; max. 30 mg/kg twice daily.

Route: IV, PO

Adverse reaction, Precautions: May cause vomiting, somnolence

L	K	BM	P
No	Yes	2	C

45. MIDAZOLAM

Indication:

Sedation and anesthesia and refractory seizures.

Dose:

Moderate (Concious) sedation for mechanical ventilation:

Continous IV infusion : 0.-1 mcg//kg/dose, may repeat q 2-4 hrs as needed.

PO: 0.25 mg/kg/dose.

Anticonvulsant:

Loading dose : 0.15 mg/kg/dose (150 mcg/kg) IV given over at least 5 minutes.

Maintenance infusion; 0.06-0.4 mg/kg/hr (or 1-7 mcg/kg/min)

Route: IV, IM, PO

Adverse reaction, Precautions, Contraindication;

May cause respiratory depression. May cause myoclonus in premature infants. Rapid IV injection may cause hypotension and seizures

L	K	BM	P
Yes	Yes	2	D

46. MORPHINE SULPHATE

Indication:

Analgesia, sedation and treatment of iatrogenic withdrawal.

L	K	BM	P
No	Yes	2	C/D

Dose:

Intermittent: IV, IM, Sub Q: 0.05 mg/kg q 4-8 hrs; max dose: 0.1mg/kg/dose.

Continous IV Infusion: 0.01-0.04 mg/kg/hr.

Route: IV, IM, Sub Q

Adverse reaction, Precaution, Contraindication:

May cause dependence, CNS and respiratory depression, seizures, constipation, bradycardia, peripheral vasodilation and urinary retention.

Neonatal Abstinence Syndrome:

Start when infant has a Finnegan score of > 8 three times or > 10 twice, seizures, or significant weight loss.

Initial PO dose: (based on Finnegan neonatal abstinence scoring)

Scores 8-10 : 0.24 mg/kg/day, divided q 3-4 hrs

Scores 11-13: 0.28 mg/kg/day, divided in q 3-4 hrs.

Scores 14-16: 0.32 mg/kg/day, divided in q 3-4 hrs.

Scores >17 : 0.36 mg/kg/day, divided in q 3-4 hrs.

Calculating infusion rate (ml/hr) =

Dose (mg/kg/min) * Weight (kg)

Concentration (mg/ml)

47. NALOXONE

Indication:

Neonatal respiratory depression secondary to narcotics.

L	K	B.M	P
No	No	?	C

Dose:

Give 0.1 mg/kg/dose IV, IM, ET or Sub Q; doses as low as 0.01 mg/kg may be give, repeat q 2-3 min if needed.

Route: IV, IM, Sub Q, ET

Adverse Drug reaction, Precautions, Contraindication:

May precipitate withdrawal symptoms in neonates with physical dependence to narcotics.

48. PANCURONIUM BROMIDE

Indication:

Skeletal muscle relaxant, paralysis for ventrilator therapy or surgery.

L	K	B.M	P
Yes	Yes	?	C

Dose:

Intermittent : 0.1 mg/kg/dose IV as needed q 30-60 min.

Continous IV infusion : 0.02 -0.04 mg/kg/hr.

Route: IV

Adverse reaction, Precautions, Contraindication:

May cause tachycardia, hypertension, and increased salivation.

Potentaited by acidosis, aminoglycosides, hypermagnesemia and hypokalemia.

Antagonized by; alkalosis, hypercalemia, and caffeine.

49. PHENOBARBITAL

Indication:

Anticonvulsant (first line drug for seizures in neonates), Narcotic withdrawal, may be used for neonatal hyperbilurubinemia and chronic cholestasis.

L	K	BM	P
Yes	Yes	2	D

Dose:

Anticonvulant	Dose and Administration
Loading dose	15- 20mg/kg/IV as single or divided doses. May give additional boluses: 5-10mg/kg/dose; max upto 40 mg/kg total. Administer IV slowly 10-15 minutes
Maintenance dose	3-4mg/kg/day, IV or PO given once daily up to 5 mg/kg/day, once daily.
Hyperbilurebinemia	3-8 mg/kg/day , IV or PO in 2-3 divided doses.

Route: IV, IM, PO

Adverse drug reaction, Precautions, contra-indication:

Abrupt withdrawal may cause status epilepticus, drowsiness , hepatitis, may cause respiratory depression, drowsiness, and hyperactivity.

Drug interactions: Induces liver enzymes.

50. VECURONIUM BROMIDE

Indication:

Skeletal muscle relaxation paralysis for ventilator therapy or surgery.

L	K	B.M	P
Yes	Yes	?	C

Dose:

0.03 - 0.15 mg/kg/dose prn (usually given as 0.1mg/kg/dose q 1-2 hrs).

Route: IV

Adverse reaction, Precaution, Contraindication:

Use with caution in patients with neuromuscular disease. May cause arrhythmias, rash, and bronchospasm. Severe anaphylactic reactions heve been reported.

Interaction:

Neuromuscular blockade potentiate by aminoglycosides, beta blockers, clindamycin, furosamide, magnesium salts, hypoklemia, hypermagnesemia and antagonized by hyperkalemia, caffeine, carbamazepine, phenytoin.

DIURETICS

51. FUROSEMIDE

Indication:

Diuresis in CHF, conditions of fluid overload or pulmonary edema, oliguria not secondary to hypovolemia, and in infants with BPD

Dose:

Intermittent: 1-3 mg/kg/dose IV, IM or PO given q 12-24 hrs.

Continous IV infusion: 0.05 mg/kg/hr, titrate dosage to clinical effect.

Route: IV, IM, PO

Adverse reactions, Precautions, Contraindication;

Electrolyte imbalance, hyponatremia, hypokalemia and hypochromic alkalosis, potentially ototoxic especially in patients with receiving aminoglycosides.

52. HYDROCHLOROTHIAZIDE

Indication:

Diuresis in mild to moderate edema and mild to moderate hypertension. Effectes potentiated when used with furosamide or spironolactone. May improve pulmonary function in patients with BPD.

L	K	BM	P
No	Yes	2	B/D

Dose:

1-2 mg/kg/dose q 12 hrs PO

Route: PO

Adverse drug reaction, Precaution, Contra-indication:

May cause hypokalemia, hyperglycemia, and hyperuricemia. Do not use in patients with significant renal or hepatic impairment.

53. DOMPERIDONE

Indication:

To control nausea, vomiting, and gastro – easophageal reflux.

Dose:

100 - 300 mcg/kg/dose; given to 4-6 times daily prior to feeds.

Route: PO

Adverse drug reaction, Precautions, Contra-indication:

It is contraindicated in moderate or severe hepatic impairment. Dose modification in mild hepatic impairment is not needed. On repeated administration, the dosing frequency of domeperidone should be reduced to once or twice daily depending on the severity of the impairments, and dose need to be reduced.

54. LANSOPRAZOLE

Indication:

Short term treatment of GERD, and erosive esiphagitis.

L	K	BM	P
Yes	No	?	B

Dose:

Route: PO

Adverse reaction, Precautions:May cause GI discomfort, headache, fatigue, Interaction with iron salts, itraconozole, and ampicillin esters.

55 OMEPRAZOLE

Indications:

Gastro esophageal reflux disease, esophagitis, or peptic ulceration.

L	K	BM	P
Yes	No	2	C

Dose:

Neonates; P, IV : 0.5 mg / kg / once daily; may be increases to 2 mg/kg/once daily.

Route: PO, IV

Advrese reaction, Precautions, Contraindication:

Periodic complete blood count and liver function tests with long term therapy.

56. RANITIDINE

Indication:

Prevention and treatment of stress ulcers and GI bleeding aggravated by gastric acid secretion.

L	K	BM	P
Yes	Yes	1	B

Dose:

PO: 2 mg/kg/dose, q 12-8 hrs.

IV: 0.5-1 mg/kg/dose, q 12-8 hrs.

Continous infusion: 0.04 - 0.08 mg/kg/hrs.

Route: IV, PO

Adverse drug reaction, Precautions:May cause nausea, diarrhea, constipation, vomiting and thrombocytopenia.

57. URSODIOXYCHOLIC ACID:

Indication:

For chronic liver diseases associated with cholestasis.

Dose:

10-15 mg/kg/dose; given 1-2 times daily.

Route:

PO; may be given at any time in regard to feeds.

L	K	BM	P
Yes	No	1	B

Adverse reaction, Precautions, Contraindication:

Monitor bilurubin levels and LFTs, prior to instituting therapy and periodically throughout the course of therapy.

58. AMINOPHYLLINE

Indication:

Apnea of prematurity, bronchodilation, bronchopulmonary dysplasia, prevention of post - extubation atelectasis.

L	K	BM	P
Yes	No	?	C

Dose:

Apnea:

Loading dose: 4-6 mg/kg PO or infused IV over 30 min.

Maintenance dose: (8-12 hrs after loading dose) 2 mg/kg/dose IV or PO given q 6-8 hrs.

Bronchodilation:

Loading dose: 6mg/kg/ IV or PO, then give maintenance dose: 0.2-0.5 mg/kg/hr.

Route: IV, PO

Adverse drug reaction, Precautions, Contraindication:

May cause tachycardia, jitteriness, vomiting, abdominal distention, hyperglycemia, and seizures.

Aminophylline salt is 80% Theophylline. When changing from IV to PO aminophylline increase dose by 20 %. When changing to PO theophylline no adjustment needed.

59. CAFFEINE CITRATE

Indication:

Neonatal apnea

Dose:

Loading dose: (as caffeine citrate salt): 10-20 mg/kg

L	K	BM	P
Yes	Yes	2	C

Maintenance dose: 5 mg/kg/dose given q 24 hrs.; Begin maintenance 24 hrs after the loading dose.

Route: IV, PO

Adverse drug reaction, Precaution, Contraindication:

Do not interchange caffeine citrate salt formulations with caffeine sodium benzoate. Monitor for cardiac arrhythmias, muscle tremors or twitches, and increased urine output. Consider holding dose if heart rate > 180 beats/min.

60. DEXAMETHASONE

Indication:

Cerebral edema, airway edema prior to extubation, and BPD to facilitate ventilator wearing.

L	K	B.M	P
No	No	3	C

Dose:

Cerebral Edema: PO, IV, IM

Loading dose: 1-2 mg/kg single dose, then maintenance of 1-1.5 mg/kg/day, divided q 4-6 hrs.

Airway Edema or Pre extubation:

IV : Usual 0.25 mg/kg/dose given 4 hrs prior to scheduled extubation and then q 8 hrs for total of 3 doses; range 0.25-1 mg/kg/dose for 1-3 doses; max dose: 1mg/kg/day.

Route: IV, IM, PO

Adverse reaction, Precaution, Contraindication:

Monitor to edema, hypertension, hyperglycemia, hypokalemia, muscle weaknes, and GI bleeding.

61. SALBUTAMOL

Indication:

Bronchodilation, treatment of hyperkalemia

Dose:

Nebulization: 0.1-0.5 mg/kg/dose given q 2-6 hrs.

Inhalation: 100 mcg (1 MDI actuation)/ dose q 2-6 hrs.

L	K	BM	P
No	No	1	C

IV: 4 mcg/kg/dose; repeat if necessary.

Continous infusion: 1-2 mcg/kg/min, adjusted according to response and heart rate up to 5 mcg/kg/min.

Route: Inhalation, IV

Adverse reaction, Precaution, Contraindication:

May cause tachycardia, arrhythmias, tremor and irritable behavior.

62. BERACTANT

Indication:

Surfactant for prevention and treatment of respiratory distress syndrome.

L	K	BM	P
No	No	?	?

Dose:

4 ml/kg intratracheally through ET, divided into aliquots; may give up to 4 doses during the first 48 hrs of life, no more frequently than q 6 hrs apart.

Route: Intratracheal

Adverse reaction, Precautions, Contraindication:

Keep refrigerated and protect from light. Warm at room temperature before administration.

63. CALCIUM GLUCONATE (10%)

Indication:

Symptomatic hypocalcemia, cardiac arrest in the presence of hyperkalemia or hypocalcemia, magnesium toxicity or calcium antagonist toxicity.

L	K	BM	P
No	Yes	2	C

Dose:

Symptomatic Hypocalcemia: 100-200 mg/kg/dose (1-2 ml/kg/dose) slow IV over 5-10 minutes. May repeat dose or follow with continous infusion.

Cardiac arrest: 60-100 mg/kg/dose (0.6-1 ml/kg/dose) IV

Route: IV

Adverse drug reaction, Precautions, Contra indication:

Monitor for hypercalcemia or bradycardia. Use in digitalized patients may precipitate cardiac arrhythmias.

1 ml of 10 % calcium gluconate contains 9.4 mg elemental calcium = 4.5 mEq calcium.

64. CHOLECALCIFEROL (Vitamin D)

Indication:

Nutritional or physiological deficiency.

- Rickets
- Intestinal malabsorption
- Chronic liver disease
- Hypoparathyroidism
- All infants born < 35 weeks who are tolerating full enteral feeds.
- All breastfed babies of vitamin D deficient mothers.

Dose:

400-800 units once daily.

For breastfed babies of vitamin D deficient mothers;

- Mild maternal vitamin D deficiency (25-50 nmol/L): 400 units once daily until 12 months of age.
- Moderate to severe maternal vitamin D deficiency 9(< 25 nmol/L): 100 units once daily for 3 months to be followed by maintenance therapy for 12 months.

Route: PO

Adverse reaction, Precautions, Contraindication:

Anorexia, polyuria, weight lose, sweating, headache, thirst etc.,

65. FERROUS SULPHATE

Indication:

Treatment and prevention of iron deficiency anemia.

L	K	B.M	P
No	No	2	A

Dose:

Dose expressed as elemental iron (fe):

Prophylaxis: 2-4 mg Fe/kg/day. Given in 1-2 divided doses per day.

Therapeutic: 6 mg Fe/kg/day. Give in 1-2 divided doses per day.

Maximum dose: 15 mg/day.

Route: PO

Adverse reaction, Precautions, Contraindication:

May increase red cell hemolysis in vitamin E deficient infants. Nausea, constipation, black stools, lethargy, erosion of gastric mucosa may occur.

66. FOLIC ACID

Indication:

Folic acid deficiency.

Dose:

Premature infants: 50 mcg/24 hrs

L	K	B.M	P
No	No	1	A/C

Route: IV, IM, PO, Sub Q

Adverse drug reaction, Precautions, Contra-indication:

May cause allergic reaction, Large dose may mask the hematologic effects of vitamin B-12 deficiency but will not prevent the progression of neurologic abnormalities.

67 INSULIN

Indication:

Hyperglycemia in very low birth weight infants with persistent glucose intolerance, adjutant therapy for hyperkalemia.

L	K	BM	P
Yes	Yes	1	B

Dose:

Intermittent: 0.1-0.2 Units/kg/ q 6-12 hrs Sub Q or IV.

Continous infusion: 0.01-0.1 Units/kg/hr. Titrate to blood glucose level.

Hyperkalemia: 0.05 Units/kg/ regular insulin + 0.5-1 g/kg/ usimg D10W (Infuse dextrose over 15 min followed by insulin).

Route: IV, Sub Q

Adverse reaction, Precaution, Contraindication:

Neonates are very sensitive to hypoglycemia. Start at lower end of dose and monitor serum glucose closely.

68. INTRAVENOUS IMMUNE GLOBULIN (IVIG)

Indication:

Hypogammaglobulinemia, alloimmune thrombocytopenia.

Dose:

Hypogammaglobulemia: Usual dose 0.5 g/kg as single dose infused over 6 weeks.

Alloimmune thrombocytopenia: 0.4-1 g/kg as single dose infused over 6 hrs.

L	K	BM	P
No	Yes	?	C

Severe hemolysis (Rh or ABO iso): When the total serum bilirubin levels approach or surpass the exchange transfusions limits: 0.-1 g/kg in the first few hours of life; to be infused over 2-4 hrs and the dose can be repeated 2-3 times.

Route: IV

Adverse reaction, Precautions, Containdication:

May cause volume overload, infuse over 2-6 hours, monitor for infusion related side effects.

Start infusion rate at 0.01 ml/kg/min; double rate q 15-30 min. up to a max of 0.08ml/kg/min

69. LEVOTHYROXINE

Indication:

Congenital or acquired hypothyroidism

L	K	B.M	P
No	No	1	A

Dose:

PO: 10-15 mcg/kg/dose daily.

IV, IM: 50-75 % of PO dose.

Route: PO, IV, IM

Adverse reaction, Precaution, Contraindication:

Monitor TSH and T 4 after 2 weeks of therapy. Give oral doses one hour before or 2 hours after feeds, preferably in the morning.

70. MAGNESIUM SULPHATE

Indication:

Hypomagnesemia, Hypocalcemia, torsade de points (polymorphic ventricular tachycardia) and severe persistent pulmonary hypertension of the newborn unresponsive to other vasodilation management, if nitric oxide is not available.

L	K	B.M	P
No	Yes	1	D

Dose:

Hypomagnesemia: 25-100 mg/kg/dose (0.2-0.8 mEq/kg/dose) IV q 8-12 hrs for 2-3 doses.

Maintenance : 0.25-0.5 mEq/kg/day IV.

Hypocalcemia: 100 mg/kg/ IV q 12 hrs for 2-3 doses.

Route: IV, IM

Adverse reaction, Precaution, Contraindication:

May cause heart block, CNS and pulmonary depression, hypotension, intestinal ileus, urinary retention, hypotonia and hypomagnesemia.

71. MCT OIL

Indication:

Caloric supplementation for patients who cannot digest long chain fats.

Dose:

Initial: 0.5 ml every other feeding, then advance to every feeding.

1 ml = 0.93 g = 7.6 caloriers.

Route: PO

Adverse reaction, Precautions, Contraindication:

May cause sedation, ketosis, abdominal pain, and diarrhea. Does not provide essential fatty acid.

72 OCTREOTIDE

Indication:

Treatment of hyperinsulinemic hypoglycemia and as an adjunct treatment for chylothorax.

L	K	BM	P

Dose:

Hyperinsulinemic Hypoglycemia: 1 mcg/kg/dose q 6 hrs Sub Q or IV. Titrate to response: **Max dose:** 10 mcg/kg/dose q 6 hrs.

Chylothorax: Start at 1 mcg/kg/hrSubQ or IV continous infusion.

Titrate upwards as needed up to a max. of 7 mcg/kg/hr. Monitor cycle production.

Route: IV, Sub Q

Adverse reaction, Precautions:

May cause cholelithiasis, biliary sludge, elevated liver enzymes, increased CPK, hypoglycemia, nausea, vomiting, and fat malabsorption.

73. PYRIDOXINE

Indication:

Diagnosis and treatment of pyridoxine dependent seizures and prevention and / or treatment of Vitamin B6 deficiency.

L	K	B.M	P
No	No	1	A/C

Dose:

Initial diagnostic dose in presence of seizures: 50-100 mg IV push or IM.

Maintenance: 50-100 mg per day PO.

Vitamine B 6 : 2-5 Mg / day PO

Route: PO, IV, IM

Adverse reaction, Precautions, Contraindication:

Profound sedation may occur ; be prepared to support with ventilator. Adverse neurological effects may occur with chronic administration.

74. SODIUM BICARBONATE

Indication:

Metabolic acidosis during prolonged resuscitation in the presence of adequate ventilation, treatment of bicarbonate deficit due to renal or GI losses.

L	K	B.M	P
No	Yes	1	C

Dose:

Resucitation: 0.5-1 mEq/kg slow IV push; may repeat in 10 min.

Metabolic acidosis:

Based on the following formula:

HCO3 (mEq) = base deficit (mEq/L) * weight *0.3

Or

HCO3 (mEq) = 0.5 * weight(kg) * (24-serum HCO3)- (mEq/L)

Distal Renal Tubular Acidosis: 2-3 mEq/kg/day.

Proximal Renal Tubular Acidosis: 5-10 mEq/kg/day.

Route: IV, PO

Adverse reaction, Precautions, Contraindication:

May cause cerebral hemorrhage, local tissue necrosis, hypocalcemia, hypernatremia, and hypokalemia.

75. VITAMIN K1 (PHYTOMENADIONE)

Indication:

Prophylaxis and treatment of neonatal hemorrhagis disease, treatment of hypoprothrombinemia secondary to liver disease or malabsorption, vitamine K deficiency.

Dose:

Prophylaxis: 0.5-1 mg IM at birth.

Preterm< 32 weeks gestation:

>1000 g: 0.5 mg IM,

<1000g : 0.25 mg IM.

Term healthy, breastfeed:

1-2 mg at 0,1,2,4 weeks of age.

Severe haemorrhage of neonates:

1-10 mg IV slow IV push.

Route: IV, IM, Sub Q

Adverse reaction, Precautions, Contraindication:

IV administration has been associated with severe reactions resembling anaphylaxis. Monitor response with PT.

MISCELLANIOUS

VITAMINS	DOSE
Hydroxycobalamin	100mg OD
Thiamine	300mg/24hrs
Riboflavin	100mg/24hrs QID
Biotin	10mg daily
Carnitine	50-100mg/kg/24hrs
Folinic Acid	2.5mg-8mg/kg/day
Sodium Benzoate	250mg-500mg/kg/day oral or IV
Arginine	200-600mg/kg/24hrs
Coenzyme Q	5-15mg/kg/24hrs

DRUGS IN RENAL FAILURE

Antimicrobials requiring adjustment in Renal Failure

DRUGS REQUIRING ADJUSTMENT IN RENAL FAILURE

DRUG	Pharmacokinetics			Adjustments in Renal Failure		
	Route Excretion	Normal t1/2 (hr)	Normal Dose Interval	Volume CrCl (mL/min)	Dose	Interval
Acyclovir	Renal	2-4	Q8hr	25-50 10-25 <10	NI NI 50% ↓	Q12hr Q24hr Q24hr
Amikacin	Renal	1.5-3	Q8-12hr	Loading dose 5-7.5 mg/kg; subsequent doses are best determined by serum levels.		
Amoxcillin	Renal	0.7-2	Q8-12hr	10-50 <10	NI NI	Q12hr Q12hr
Amoxcillin /Clavulanate	Renal	1	Q8-12hr	10-30 <10	NI NI	Q12hr Q24hr
Amphotericin B	Renal	Initial 15-48hr Terminal 15 days	Q24hr	Dosage adjustments are unnecessary with preexisting renal impairment.		
Amphotericin B Lipid Complex	Renal (1%)	173	Q24hr	No guidelines established		
Amphotericine B Liposomal	Renal (<10%)	100-153	Q24hr			
Aztreonam	Renal (Hepatic)	1-1.8	Q6-12hr	10-30 <10	50%↓ 75%↓	Nil Nil
Cefepime	Renal	1.1-2.3	Q8-12hr	10-50 <10	NI 50%↓	Q24hr Q24hr
Cefotaxime	Renal	1-3.5	Q6-12hr	<20	50%↓	NI
Ciprolfloxacin	Renal (Hepatic)	1.2-5	Q8-12hr	<30 30-50 <30	200-400mg 250-500mg 250-500mg	Q18-24hr Q12hr Q18hr
Clarithromycin	Renal (Hepatic)	3-7	Q12hr	<30	50%↓	Q12-24hr
Erythromycin	Renal (Hepatic)	1.5-2	Q6-12hr	<10	25-50%↓	NI
Fluconazole	Renal	19-25	Q24hr	<50	50%↓	NI
Gentamicin	Renal	1.5-3	Q8-12hr	>50 <50	NI Usual initial	NI

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					dose	
Imipenem/Cilastatin	Renal	1-1.4	Q6-8hr	41-70 21-40 6-20 <5	50%↓ 63%↓ 73%↓	Q6hr Q8hr Q12hr
Meropenem	Renal	1-1.5	Q8hr	26-50 10-25 <10	NI 50%↓ 50%↓	Q12hr Q12hr Q24hr
Metronidazole	Hepatic (Renal)	6-12	Q6-12 hr	<10	50% ↓	NI
Oseltamivir	Renal	1-10	Q12 – 24 hr	Infuenza treatment10-30 <10	 NI No recommended dosage regimen.	Renal
Penicillin G	Renal	20-50 min	Q4-6 hr	<10	25%↓ 50%-80%	NI NI
Pipercillin/ Tazobactum	Renal	Piperacillin 0.5-1.5 Tazobactum 0.7-1.6	Q6-8 hrs	20-40 <20	30%↓ 30%↓	Q6 hr Q8 hrs
Tetracycline	Renal (hepatic)	8-10	Q6 hrs	50-80 10-50 <10	NI NI NI	Q8-12 hr Q12-24 hr Q24 hr
Valganciclovir	Renal	2.5-3.6	Induction: Q 12 hr IV Maint. Q 24 hr IV/PO	Induction IV 50-69 25-49 10-24 <10	 2.5mg/kg 2.5mg/kg 1.5mg/kg 1.25mg/kg	 Q12hr Q24hr Q24hr 3 times /week
Vancomycin	Renal	2.2-8	Q6-12 hr	>90 70-89 46-69 30-45 15-29 <15	NI NI NI NI NI 10-20 mg/kg	Q6 hr Q8 hr Q12 hr Q18 hr Q24 hr Subsequent doses
Abbreviations: CrCl: Creatinine Clearance, NI: Normal, IV : Intravenous, IM : Intramuscular , GFR: Glomerular Filtration Rate, t1/2: half life						