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Gujarat State Chapter

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Greetings for Editors desk

Dr Ravi Parikh

Dear Readers,

It is privilege for me to present third edition of 2023 year neoblaze issue. I have got the bunch of topics and authors which will excite all the readers. I thank all the team of neoblaze for making this happen. I have constant support from Dr Dipen Patel, Dr Prashant Kariya and all my associate editors who meticulously review the articles.

This edition chapter starts with newer modes of ventilation. With survival of extreme premature babies and newer ventilation available this chapter elicits great understanding of reason and way to use newer ventilation techniques. The incidence of NEC in preterm neonates has more or less remain constant over the years and hence a very important care bundles has been described in NEC Chapter which will help to reduce incidence of NEC in your unit if followed meticulously. Cooling therapy in our country is still under debate. The chapter on cooling nicely bring out the indication and usefulness of the therapy in HIE babies. This is followed by very important topic of improving neurodevelopment outcomes in preterm babies. This chapter has been written in two parts and is very nice to read and implement. First part is in this edition and second part will be in next edition. This is followed by very important case discussion of a worsening baby in NICU and its management.

I am sure you will be able to appreciate the hard work of all the authors in giving new information to all the readers. I hope you will be able to enjoy each chapter.

With Warm Regards,

Dr Ravi Parikh

Consultant Neonatologist

Setu Newborn Care Centre

Ahmedabad.

President's Message

Dr Dipen Patel

Dear Friends,

नमस्ते।

I feel proud to be part of the release of 3rd Issue of NeoBlaze for the year 2023, the official quarterly E-Bulletin of NNF, Gujarat State Chapter.

I congratulate the Editor : Dr. Ravi Parikh; Associate Editors : Dr. Ronak Patel, Dr. Manan Parikh, Dr. Reshma Pujara, Dr. Jatin Unadkatfor tirelessly working for this E-bulletin. I thank Dr. Prashant Kariya for providing technical help. I thank all the Authors Dr. Snehal Patel, Dr. Neha Tiwari, Dr. Vishal Gohil, Dr. Binoy Shah, Dr. Kamal Parikh, Dr. Prakash Vaghela, Dr. Chirag Gabani, and Dr. Rajpal Jat for submitting clinically important articles.

NeoBlaze has enormous potential in enhancing the knowledge of the readers with regard to the neonatal science. I am glad that, it is growing in this direction.

I also thank the members of NNF Gujarat State Chapter for continuous support and guidance.

धन्यवाद ।

Prof. (Dr.) Dipen V. Patel

President,

NNF Gujarat State Chapter

Hon. Secretory's Message

Dr Prashant Kariya

Dear esteemed members of NNF Gujarat,

It is with immense pleasure and honor that I address you as the Honorable Secretary General for the third edition of Neoblaze. As we gear up for our much-awaited annual conference, Gujneocon, I am excited about the promise it holds for delivering the best in academics and entertainment.

Our commitment to excellence is reflected in the anticipation surrounding Gujneocon. This conference is not just an event; it's a convergence of minds dedicated to advancing knowledge and practices in neonatology. We are determined to provide a platform that not only enriches your academic pursuits but also ensures a memorable and enjoyable experience for all attendees.

I extend my heartfelt gratitude to all the members of NNF Gujarat for their active participation in celebrating Breastfeeding Week in a grand way. Your dedication to promoting such crucial initiatives underscores the spirit of unity within our community. It is through collective efforts like these that we can create a lasting impact on healthcare practices and public awareness.

As we look forward to Gujneocon, I am reminded of the profound role that education plays in our lives. Education is not merely the transfer of knowledge; it is a journey that shapes our perspectives, hones our skills, and empowers us to contribute meaningfully to society. Nelson Mandela once said, "Education is the most powerful weapon which you can use to change the world." This sentiment encapsulates the transformative potential inherent in the pursuit of knowledge.

In the field of neonatology, continuous learning is not just a professional obligation; it is a moral imperative. Our commitment to providing the best in academics at Gujneocon is a testament to this belief. It is through ongoing education and collaboration that we can push the boundaries of what is possible in neonatal care and ensure the well-being of our tiniest patients.

In conclusion, I eagerly anticipate the opportunity to meet and engage with each one of you at Gujneocon. Let us come together, not just as healthcare professionals but as a community dedicated to advancing the frontiers of neonatal care. Together, we can make a difference that resonates far beyond the confines of our conference.

With warm regards,

Dr. Prashant Kariya

Honorary Secretary, NNF Gujarat

National Neonatology Forum - Gujarat State Chapter

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Volume 3 - Issue - 3, JULY - SEP. 2023

Newer non invasive and Invasive ventilation Strategies

Dr. Snehal Patel
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Introduction: Why do we need newer ventilatory strategies?

With the development of neonatal medicine and intensive care units, the concepts and methods of managing respiratory problems in neonates have been changing continuously. Respiratory distress syndrome (RDS) is a major cause of respiratory failure in preterm infants due to immature lung development and surfactant deficiency. Important aspects such as exogenous surfactant therapy, use of noninvasive ventilation and different ventilation modes to avoid intubation, ventilation-induced lung injury and comorbidities have led to an increased interest in RDS management. (1).

The conventional modes of ventilation have certain limitations. Although they are popularly used and are well understood, often they fail to match the patient-based requirements. Over the years, small modifications in ventilators have been incorporated to improve patient outcome. The ventilators of newer generation respond to patient's demands by additional feedback systems. (2).

The aim of newer ventilation strategies is to limit VILI (ventilator induced lung injury) and hence the consequences like Bronchopulmonay dysplasia and chronic respiratory morbidities . In this article, we will discuss the newer invasive and non-invasive modes of ventilation and their mechanism of action. These modalities use more sophisticated techniques to improve patient-ventilator interaction and transfer control of ventilation from operator to patient. (5)

Physics of Mechanical ventilation :

The ability of ventilator to initiate, maintain and terminate an assisted/artificial breath derives its basis from "Equation of motion." The equation of motion postulates that the pressure necessary to deliver a breath has two components: 1. the pressure to overcome elastic recoil of the lungs and chest wall and 2. the pressure to cause flow through the airways. (2)

$$P = P\text{resistive} + P\text{elastance}$$

P resistive is given by Volume (V) * Airway resistance (R)

P elastance is given by Volume (V) * Lung elastance (E)

In critical care settings, all the parameters of equation of motion change with time. A ventilator setting appropriate for one point of time would not be optimal with patient deterioration or improvement. (7) Conventional modes of ventilation only deliver the set parameters and take no feedback from patient variables. Thus, all the classical volume/pressure control modes are "**Open**

Loop" (the feedback loop is absent). The newer modes target to make alterations with the changing lung and take feedback from patient parameters, thus completing the feedback loop and are "**Closed loop**" type. (8,9) The control, cycle or the limit variables undergo self-adjustment and these variables are no longer limited to single parameter determinant but if the threshold of one component is reached they shift to the other alternate set parameter and thus the loop is completed.

Newer Ventilatory modes:

Volume guarantee ventilation : Wide fluctuations in tidal volume in ventilated infants are among the mechanisms of respiratory instability, which can lead to frequent fluctuations in SpO2. Volume guarantee ventilation (VG) is a pressure-controlled ventilation mode. Breathing in VG is pressure-limited with a decelerating flow. VG uses a feedback loop for automatic adjustment of PIP to deliver a set tidal volume based on variations in lung compliance, airway resistance, and spontaneous respiratory effort of the patient. (1)

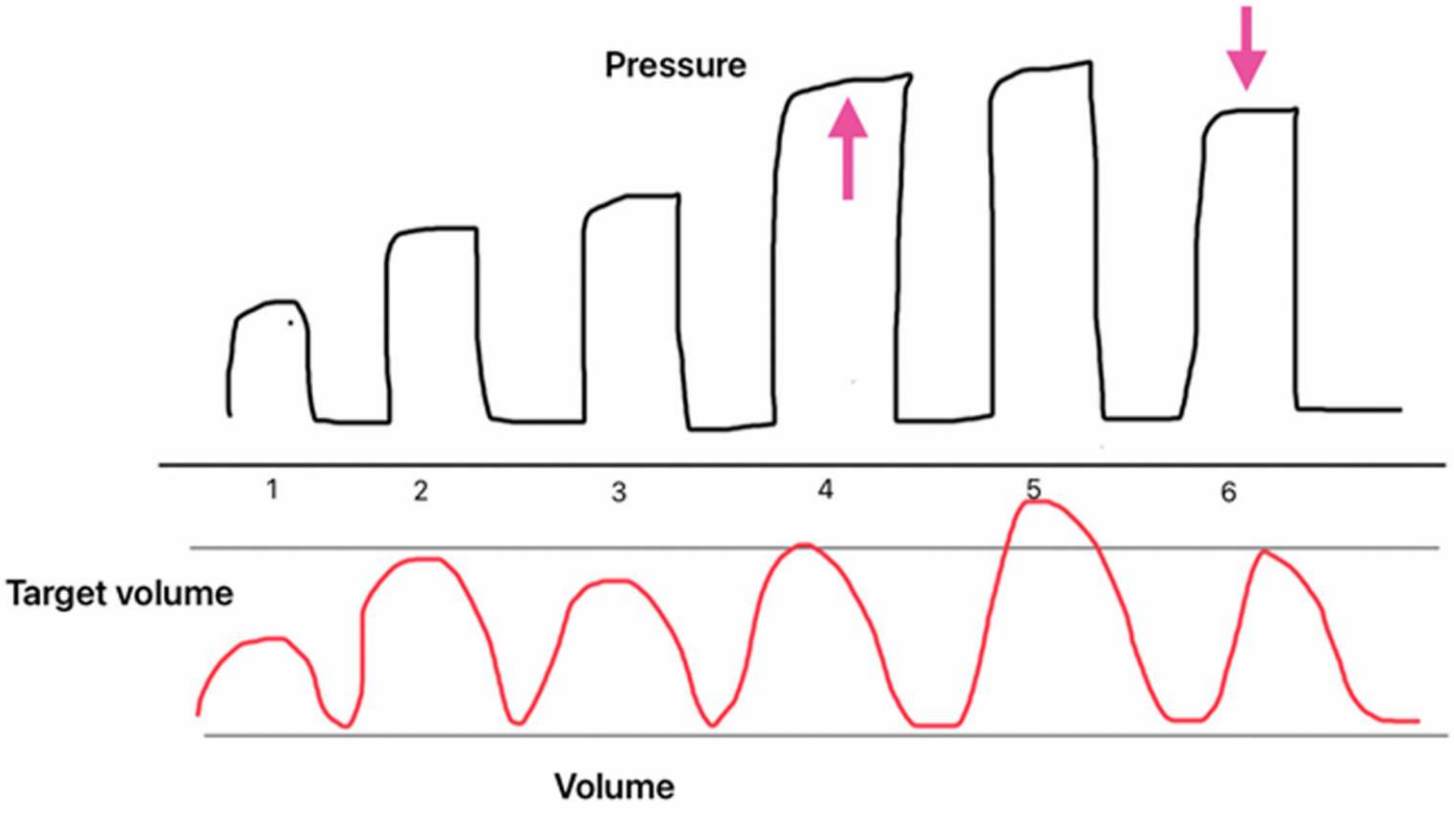


Figure 1: Scalars of volume guarantee ventilation

The VG mode can be used in combination with assist- control (A/C), synchronized intermittent mandatory ventilation (SIMV) or pressure-support ventilation (PSV). The effects of VG vary when combined with different modes in preterm infants. The VG periods of A/C and SIMV were associated with a lower PIP and fewer incidences of excessively large tidal volumes in preterm infants with RDS. The incidence of hypocapnia was lower in A/C VG than in A/C alone. Despite similar morbidity, mortality, and incidence of pulmonary

TABLE 1 : summary of different mode in combination with Volume guarantee ventilation

Mode	A/C+ VG	SIMV+ VG	PSV+VG
Trigger	Ventilator-time Patient-flow/pressure	Ventilator-time Patient-flow/pressure	patient-flow/pressure
Control	Volume	Volume	Volume
Breath	All breaths Mechanically supported	Only intermittent mandatory breaths are supported	If a breath delivers tidal volume below desired, it is transitioned to mechanically supported
Use	Patient with normal respiratory drive, but respiratory muscles are not very strong	Patient with normal respiratory drive, but respiratory muscles are not very strong.... It is an attempt to reduce ventilator assisted breath or to wean from respiratory support	Spontaneously breathing patient requires a substantial level of support and has a vigorous ventilatory drive

inflammation between PSV +VG and SIMV +VG, PSV+VG provided more breaths with tidal volume closer to the set value without over-ventilation and hypocarbia in ventilated preterm infants with Respiratory distress syndrome.

Proportion assist Ventilation :

PAV is a promising newer mode with the advantage of improving ventilator patient synchrony. It is a form of synchronized partial ventilator assistance with a unique feature that ventilator assists in proportion to patients' breathing effort. (3) In other words, it amplifies patient's ventilatory effort giving patient freedom to adopt his own breathing pattern. PAV unloads respiratory muscles and unaltered respiratory pattern allows synchrony between ventilator and patient's neural ventilator drive. Parameters like I:E ratio and inspiratory time are completely patient driven and further add to successful patient synchronization.

Limitation : If the patient worsens or improves, the proportion of assistance may need to be reset according to newer clinical situation. This has, however, has been addressed in newer modification of "PAV+" mode, which is capable of sensing patient lung mechanical properties and adjusting accordingly. (3) A technical important aspect of PAV is that there should be minimal air leak in the system; this would cause the ventilator to over assist or cause auto cycling.

Neurally adjusted ventilatory assist Ventilation :

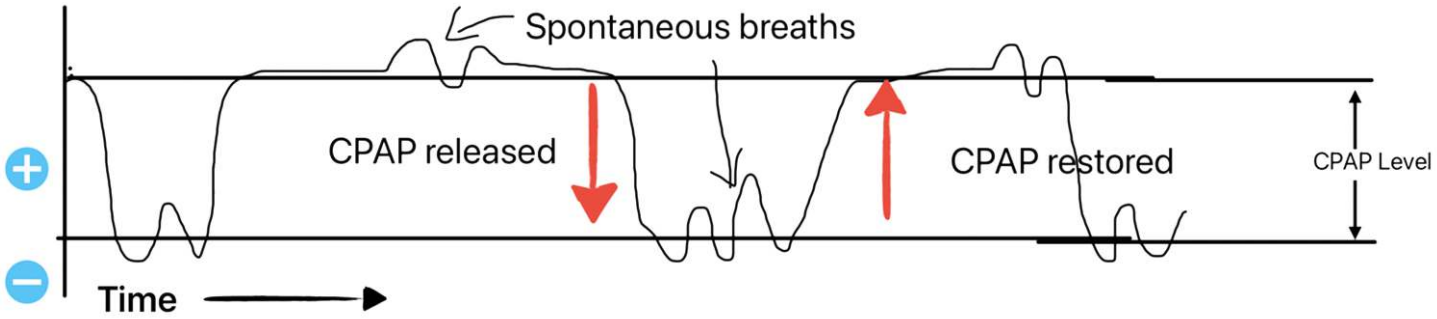
The modality neurally adjusted ventilatory assist (NAVA) works like PAV but uses the electrical activity of the diaphragm (EAdi) as a measure of breathing effort. The EAdi signal is registered by a nasogastric tube (EAdi catheter) mounted with four electrodes placed at the level of the diaphragm. Based on the generated electrical activity of the diaphragm, the ventilator determines the

driving pressure to unload work of breathing. The clinician needs to set the so-called NAVA-level, which determines the driving pressure (cmH2O) is generated per µV of EAdi increase above the tonic activity. Initially a NAVA level is set that generates a similar PIP as the controlled mode used before switching to NAVA. Next the gain is adjusted as per EAdivoltage .EAdi is a relatively stable signal that is less affected by movement or airflow artefacts. Spontaneous breathing effort is essential for successful NAVA ventilation and in its absence a controlled back-up mode should take over.

The clinical application of NAVA has mainly been assessed in cross-over observational studies in both preterm and term newborn infants. Compared with more controlled modes of ventilation, NAVA reduces the PIP, the fraction of inspiratory oxygen, and the work of breathing in infants with respiratory distress syndrome (RDS) or evolving BPD. (4)

Airway pressure release ventilation (APRV) :

APRV is a bi-level mode representing open-lung ventilation strategy. It provides two levels of continuous positive airway pressure (CPAP) with an inverse I:E ratio of 2:1 or more. (4) The rationale of using prolonged high-pressure phase is to prevent alveolar collapse and maintain alveolar recruitment. The release phase (expiratory phase) brings down mean airway pressure and plays a significant role in maintaining normocarbia. The mode has dual functionality; in presence of spontaneous breathing the patient can breathe in any phase of respiratory cycle with supported breaths thus bringing down needs of sedation. In absence of spontaneous



breathing activity, the bi-level pressure acts as time-cycled inverse ratio ventilation. The tidal volume generated mainly depends upon respiratory compliance and difference between the two CPAP levels.

Limitation : APRV should be used with caution in hypovolemic patients as increased intrathoracic pressure further lowers venous return.

Mandatory minute Ventilation :

It is a modality that targets minimum preset minute volume . The patient is allowed to breathe spontaneously, and all breaths are pressure supported. At regular intervals (for example every 10s), the ventilator estimates the minute volume based on the spontaneous rate and VT in that short period. If the estimated minute volume is below the set target, extra mechanical inflations are started

to guarantee the preset minute volume. These mechanical inflations can be pressure or volume targeted. The actual rate of mechanical inflations depends on the spontaneous effort of the patient. If the spontaneous minute volume is above the target, no mechanical inflations are added. Observational studies have evaluated MMV in newborns, demonstrating MMV maintains adequate gas exchange with less mechanical support than SIMV. (4)

Noninvasive ventilation :

NIPPV : Several modes of NIPPV have been described in literature, namely nasal intermittent mandatory ventilation (NIMV), non-invasive pressure support ventilation, and bi-level CPAP .(5) It can be further classified as **synchronized NIPPV (SNIPPV) and non-synchronized (machine-triggered) NIPPV (NS-NIPPV)** (5)

Application of NIPPV combines NCPAP with additional intermittent breaths above the baseline and the modifiable parameters are positive end expiratory pressure (PEEP), peak inspiratory pressure (PIP), respiratory rate and inspiratory time (Ti) The periodic breaths increase tidal volume leading to enhanced removal of CO2, sustained alveolar ventilation during episodes of apnea and increased FRC. This mode of NIV has a greater ability to reduce apneic and bradycardic episodes in preterm infants compared to NCPAP. Most ventilators can be used to provide NS- NIPPV but SNIPPV can only be generated by Infant Flow SiPAP and Infant Flow Advance. Infant star Ventilation was a famous ventilator for SNIPPV before 2009. For synchronization, the most frequently used device is the Graseby capsule (GC), which is placed in the subxiphoid area to track the respiratory effort (5).

Advantages of SNIPPV include improved thoraco-abdominal synchrony, reduced need of intubation and lower incidences of desaturations, bradycardias and central apnea. Decrease in BPD and air leakage was also noted with SNIPPV.

Nasal high frequency oscillatory ventilation : (nHFOV)

Nasal HFOV provides an oscillatory pressure waveform to the airways, without synchrony with the infant's breath, aiding to enhance CO2 elimination and alveolar recruitment . Additionally, it has been reported to significantly decrease desaturations and frequency of apnea and bradycardia episodes . The frequent adverse effects observed with nHFOV are upper airway obstruction due to increased secretions, thick, viscous secretions and abdominal distention. A recent study compared nHFOV to NCPAP in preterm infants (28–34weeks) with moderate to severe respiratory distress post- INSURE. They found a significant decrease for intubation requirement when using nHFOV. Further studies are required to assess and compare various devices and interfaces to deliver nHFOV and to compare nHFOV to the more commonly used NIV techniques. (4).

NIV -NAVA:

NIV-NAVA is similar to invasive NAVA but ventilation mode of delivery is via nasal prongs or single nasal-pharyngeal tube or a

mask. NIV with NAVA is feasible and well tolerated in preterm infants with physiological benefits, such as improved patient-ventilator synchronization and reduced peak inspiratory pressure (PIP), FiO2, frequency, and length of desaturations. NIV with NAVA improved diaphragmatic unloading, possibly leading to a reduction in the WOB. A significant improvement in the WOB-related indices was also observed in infants with severe bronchiolitis after transition from NCPAP to NIV NAVA. The benefits of both NAVA and NIV-NAVA are similar, namely better patient-ventilator interaction and synchrony and improved gas exchange efficiency. The ease of use of NIV-NAVA will undoubtedly promote its growing use in NICU worldwide. (4).

Ventilation mode	Ventilator in market
HFOV and nHFOV	Sensor medics , SLE6000 , dragger VN600, fasaana HFO
PAV	Puritan Bennett 840 ventilator
Mandatory minute ventilation	Bragger Babylog VN 500/600
NAVA	Servo I ventilator
APRV	Vela ventilators , diamond series Evita XL, Evita XL Neo
PRVC	Servo 300 , mauqe servo i

KEY POINTS :

1. **Understand patient first as per pathophysiology, select ventilator with appropriate mode and be with patient, chase your settings as per patient's response and get best synchronization possible.**
2. **Teach scalars to your nursing staff. They should be able to pick up problems before ventilator alarms.**
3. **Check PCO2 levels regularly. Cerebral vascular fluctuations can impair neurological outcome .**
4. **Shift to non-invasive mode as soon as possible.**

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Neonatal necrotizing enterocolitis : Prevention

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INTRODUCTION:

Necrotizing enterocolitis (NEC) is one of the most common gastrointestinal emergencies in the newborn infant. It is a disorder characterized by ischemic necrosis of the intestinal mucosa, which is associated with severe inflammation, invasion of enteric gas-forming organisms, and dissection of gas into the intestinal wall and portal venous system. [1]Despite advances in NICU care, the estimated mortality rate associated with NEC ranges between 20% and 30%, with the highest rate among infants requiring surgery. Although early recognition and aggressive treatment of this disorder has improved clinical outcomes, NEC accounts for substantial long-term morbidity in survivors of neonatal intensive care.Hence, preventive efforts have focused on identifying interventions that will reduce the risk and severity of this disorder.

EFFECTIVE INTERVENTIONS

Efforts to minimize the frequency or severity of NEC are directed at reducing exposure to risk factors and finding interventions that will prevent the disorder [2-6]. Since NEC occurs almost exclusively in preterm infants, prevention of preterm birth would have an impact on NEC incidence. Unfortunately, this goal has not yet been met.

1.Antenatal corticosteroids(ACS)— ACS could reduce mucosal uptake of macromolecules, decrease colonization with aerobic bacteria, reduce bacterial translocation, and increase activity of enzymes such as lactase, maltase, sucrase, and Na/K-ATPase, which have been correlated with a reduction in NEC. As a result, ACS should be given to all women at risk for preterm delivery within seven days.

2. Human milk feeding- The unique properties of human milk promote an improved host defence and gastrointestinal function. Several well controlled clinical trials have demonstrated that human milk feeding can reduce the incidence of NEC. The protective effect of human milk appears to be dose dependent. Mechanismsinclude:

Lowers gastric pH.

Enhances intestinal motility.

Positively impacts the gut microbiota through antimicrobial effects and prebiotic and probiotic components, thereby lowering the risk of microbial dysbiosis, an important factor in the pathogenesis of NEC.

Human donor milk is considered a safe alternative when the mother's own milk is not available. In a meta-analysis of nine trials (1675 neonates), rates of NEC were lower in infants receiving donor breast milk compared with formula feeding (4 versus 7 percent; relative risk [RR] 0.53, 95% CI 0.35-0.81). [7]

3. Standardized feeding protocol —This provides a consistent approach to initiation of

minimal enteral feedings, timing, and rate of advancement of feeding, timing of fortification, addition of additives like vitamins and iron, and criteria when to withhold and restart feeds.

Observational studies have shown that they are associated with lower rates of NEC. In a meta-analysis of 15 observational studies (18,160 preterm neonates) comparing rates of NEC before and after implementation of standardized feeding protocols, rates were considerably lower after implementation (risk ratio 0.22, 95% CI 0.13-0.36).[8] The protocols used in these studies varied substantially withregard to timing of initiation and timing and speed of advancement. This suggests that standardization rather than any specific feature of the protocol is the key aspect of this intervention.

Feeding protocols need to consider:

- **Timing of initial trophic feedsand rate of advancement of feeding** – Trophic feeding provides infants very small amounts of milk to help prime the intestinal tract. It might improve the activity of digestive enzymes, enhance the release of digestive hormones, and increase intestinal blood flow and digestive motility in premature infants. The optimal timing of initiation of trophic feeding and volume of feeds for reducing NEC remains uncertain. There have been concerns that initiation of enteral feeds within the first week of life for very preterm (<32 weeks, VPT) and VLBW infants would increase the risk of NEC. However, available data support that trophic feeding does not increase the incidence of NEC compared to enteral fasting.

Timing of progressive enteral feeds – A meta-analysis of VLBW infants demonstrated that delaying the introduction of progressive enteral feeds (after four days of age) was not associated with a reduced risk of NEC, and that the delay was associated with a longer time to establish full enteral feeds.[9]

Rate of advancement of enteral feeds – A systematic review of 14 trials of VLBW infants reported that faster rates of advancing feeds (30 to 40 mL/kg/day) compared with lower rates (15 to 24 mL/kg/day) did not increase the risk for NEC or mortality.[10]

- **Colostrum** – Oral colostrum care (OCC) consists of administering drops of maternal colostrum into an infant's mouth within the first day of life. Most of these early volumes are absorbed directly in the mouth with some traveling to the gastrointestinal tract. One meta-analysis reported that OCC may reduce the incidence of NEC, late onset sepsis, IVH and the time to full feeding in infants ≤ 32 weeks' gestation [11]. Further research efforts are needed to determine whether there is any benefit of human colostrum in preventing NEC.

- Asepsis precautions while feed preparation and administration to prevent contamination is important to prevention GI colonisation and sepsis.

4. Antibiotic stewardship — Observational evidence suggests that infants who receive prolonged antibiotic therapy are at increased risk for NEC. In a meta-analysis of 13 studies (7,901 infants), empirical antibiotic therapy for five or more days was associated with

increased risk of NEC (adjusted RR 1.51, 95% CI 1.22-1.87). [12-14]Antibiotic stewardship aimed at reducing unnecessary antibiotic therapy and limiting the duration of empiric antibiotic therapy in infants with sterile cultures may reduce the risk of NEC. Also,current evidence does not support the use of prophylactic antibiotics to reduce the incidence of NEC for high-risk premature infants.

5. Avoid gastric acid suppression — Gastric acidity may play a role in preventing the cascade of infectious and inflammatory events leading to NEC. H2 blockers such as cimetidine, ranitidine, and famotidine suppress gastric acidity. Observational data from large case series have reported that H2 blockers are associated with an increased risk of NEC.

There are little data on proton pump inhibitors (PPIs) on the incidence of NEC. However, PPIs also should be avoided, since they also reduce gastric acid production and would be expected to have a similar impact on the microbial community in the gut.

6. Transfusion-associated NEC (TANEC) — The practice of holding feeds during and after transfusion is supported by observational studies that have reported an association with onset of NEC within 48 hours following a blood transfusion among infants receiving feeds during and after transfusion. In a meta-analysis of 7 observational studies (7492 neonates), the incidence of NEC was substantially lower in neonates who had feeds held after transfusion compared with those who did not (0.7 versus 2.4 percent; RR 0.47, 95% CI 0.28-0.8). [15-17]

While these observational data cannot establish a causal relationship, the consistent temporal relationship has raised concern for causality. However, it is also plausible that the association between transfusion and NEC is mostly due to the adverse effects of severe anaemia rather than the transfusion itself. It has been proposed that severe anaemia (e.g., haematocrit<25 percent), causes intestinal injury to the gut through hypoxic or immunologic mechanisms, and a subsequent blood transfusion may trigger the development of NEC due to additional changes in viscosity, inflammation, and perfusion to the gut.

UNPROVEN OR INEFFECTIVE INTERVENTIONS

Probiotics — Probioticsare one of the most studied preventive measures for NEC. They have been shown in several studies and meta-analyses to be effective in preventing NEC. However, there is lack of consensus on the optimal regimen and insufficient data for extremely preterm infants and the level of evidence was of low quality due to marked heterogeneity and potential bias amongst clinical trials resulting in significant unanswered questions. Therefore, based on the available information and unresolved concerns, routine use of probiotics to prevent NEC is not recommended.

Oral immunoglobulin therapy — The rationale for oral immunoglobulin therapy is that it may reduce NEC by inhibiting release of proinflammatory cytokines. However, based upon the available evidence, immunoglobulin therapy has failed to demonstrate a

meaningful benefit from this therapy.

Nutritional supplements — Nutritional supplements derived from human milk (e.g., lactoferrin and oligosaccharides) have been investigated as potential strategies to prevent NEC. Other supplements like amino acids arginine and glutamine have also been studied as possible interventions to prevent NEC. However, data either are limited or do not support the use of these interventions to prevent NEC.

KEY POINTS: **Effective strategies to reduce the incidence and/or severity of NEC in preterm neonates include:**

- **Antenatal corticosteroids – Pregnant individuals who are at high risk for preterm delivery before 34 weeks gestation should receive antenatal corticosteroids.**
- **Human milk feeding – Human milk compared with intact bovine milk-formula is associated with a lower risk of NEC. Breast milk feeding should be encouraged for this benefit and because of other well-established benefits of breast milk. If mother's milk is unavailable, pasteurized donor human milk should be used.**
- **Standardized feeding protocols – Standardized feeding protocols provide a consistent approach to initiating and advancing feeds, and criteria for when to withhold and restart feeds.**
- **Avoiding medications that may contribute to NEC – This includes:**
  - **Antibiotic stewardship to avoid prolonged courses of antibiotics whenever possible.**
  - **Avoiding acid suppression unless it is clinically indicated**
- **Holding feeds during and after transfusions – For very low birth weight (VLBW) infants (BW <1500 g) who require red blood cell (RBC) transfusion, we suggest holding feeds during and after the transfusion (Grade 2C).**

Probiotics, oral immunoglobulin therapy or other nutritional supplements are currently not recommended for routine use for NEC prevention.

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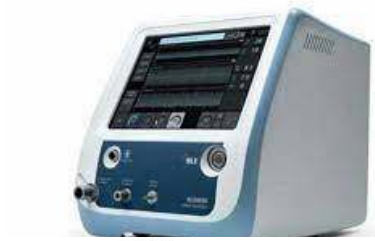




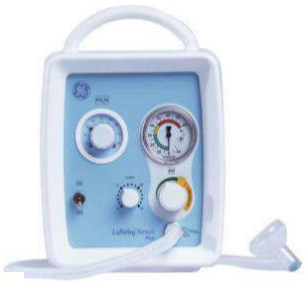








Therapeutic hypothermia (Cooling Therapy) for HIE in LMIC

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HIE is a most common cause of Neonatal Mortality and morbidity not only in India but across the globe. Incidence of HIE 1-2/1000 live birth in High income country (HIC). As compare with HIC, rate of HIE is 20 times higher in Low-& middle income countries (LMIC). Despite of all the efforts to reduce incidence of HIE in form of Neonatal resuscitation program, numbers is still High. In HIC, Therapeutic Hypothermia (TH) is well establishing and standard care of management for HIE. Unfortunately, Advance treatment in form of TH, optimum neonatal care are not happening in LMIC where incidence of HIE high. A few of the centers in India including public sector are offering TH with verities of cooling method for moderate to severe HIE.

There were total 24 RCT were found where 7 from HIC and 17 in LMIC. An individual patient data is not available. All the data regarding TH were extracted in form of inclusion criteria, exclusion criteria, devices and method of hypothermia with target temperature, severity of population, primary and secondary outcomes. Most of the trials had taken Death till discharge, death or severe disability at 18-24 months of age, cerebral palsy as primary outcome. The recent trial (Helix trial) was published in LMIC which had enrolled large number of neonates. It showed no difference/effect on death or disability at 18-24 months. It has been observed that one of the many secondary outcomes (Death before discharge) was significantly increased in hypothermia group. Till the publication of Helix trial, there had been 15 trials from LMIC. Unfortunately, none of the trial reported reduction/increase in neonatal mortality. But metanalysis of these trials suggested that TH could result in a 35% reduction in neonatal mortality(RR 0.64, 95% 0.51-0.81). There was no heterogeneity was observed trials of HIC but Substantial heterogeneity was observed in trials from LMIC. Cord PH, proportion of outborn neonates, Proportion of neonates with severe HIE, admission temperature, illness severity were the reasons for clinical heterogeneity in LMIC trials.

1. Cord PH- Majority of study from HIC had been reported Cord PH to know the intrauterine status. There was reduction in death before discharged in pool data who was reported cord PH <7.0 with moderate to severe HIE. Those who had not reported Cord PH(1 HIC, 8 LMIC), substantial heterogeneity was observed in the event rate. Even the large sample size and high event rate (TOBY, Helix, Catherine) have variable risk ratio.
2. Outborn (extramural birth Neonates)-

Studies with no outborn neonates had been shown significant reduction as compared with those studies who included both. Although, there was significant heterogeneity was found with studies with outborn.

3. Temperature on admission- Passive cooling (<36 Degree) and deeper cooling (<33 degree) has been associated with worse outcome. The studies who had noted temperature more than 36 degree in intervention group showed significant reduction in the risk before discharge. In other way around who had temperature <36 degree showed a significant increased in risk of death before discharged. Increased mortality might be reflected due to direct effect of hypothermia on mortality or suboptimal supportive care during transport. A Hypothermia on admission may be indirect marker of more severe birth asphyxia and lower basal metabolic rate.
4. Severe HIE- there should be linear correlation between the proportion of neonates with severe HIE and the proportion of neonates who died before discharge. Majority of studies had been followed same. The HELIX study had higher number of deaths than expected in the interventional group as compare to other studies. Two other studies had higher number of deaths in control group. These differences may be due to study design or difference in other baseline characteristics of the included population.

The Indian Neonatal Collaborative reported the outcome of 352 neonates with HIE admitted across 17 centers from January 2018 to December 2019. Of these, 59% received TH, Survival to discharge rate among neonates with moderate to severe HIE was 82%. A High degree of variability was observed in the rate of survival at different centers (33-100%). Few trials had survival<75% but sample size <10%. In summarize, TH was not associated with increased survival till discharged.

In summary, TH is the proven treatment for moderate to severe HIE and is likely to decrease death or severe disability and Cerebral palsy at 18-24 months even in LMIC as compared to HICs. Till now in LMIC, significant heterogeneity was found in LMIC as compared to HICs in case of death before discharged. It could be the lack of certainty of encephalopathy being due to an asphyxia insult. Various factors are affecting the outcome in LMICs like Cord PH, variable inclusion criteria, suboptimal treatment, non-uniform treatment for out born neonates, Infection, lack of inadequate advance equipment Servo controlled machine, High secondary outcomes like abnormal coagulation, ventilation, shock ets.

It has been proven that TH is the proven therapy for HIE under optimum neonatal care in case of Moderate to Severe HIE. So, the question would be, should we offer TH in all NICU setups in LMICs? It must be offered in good quality NICU care (Level 3A, 3B, 4). It has been proven that TH would not be effective in suboptimal neonatal care. Doctors, Nursing staff must be experience and competence to treat sick newborn. A Nursing ration must be

1:1 to give optimum neonatal care. All the facilitiesincluding, Ultrasonography, CT, MRI and EEG must be available at bedside. Optimum care includes Ventilation, life support care, Continuous monitoring (Temperature, Blood pressure, Heart rate, Respiration, Oximetry) and 24 x 7 Neonatologists who can manage the neonate both during acute stay and during follow up.

So, what would be inclusion criteria?

It must be offered >36 weeks GA, <6 hrs of the age, admission temperature 36-37.4 C.

1. pH <7 or BE >-16 on cord or arterial blood gas done within 1 hrs of life

   AND

   (i) Apgar score<5 at 10 mins or at least 10 min of positive pressure ventilation

   AND

   (ii) H/o of acute perinatal event(such as but not limited to placental abruption, uterine rupture, cord prolapse)

2. Evidence of moderate or severe encephalopathy.

Prior to initial TH, Parents must be informed cooling details with written consent.

Those who are moribund, have major congenital or genetic abnormalities, neonate with severe IUGR, severe coagulopathy, those with evidence of severe head trauma or intracranial hemorrhage should not offered TH. There is insufficient evidence of the benefit of hypothermia beyond 6h of age.

Most of trials of TH in HIC and some in LMIC used servocontrolled device for either head cooling/whole body cooling. In some trials in LMICs have used non-servo-controlled devices [ice/gel packs or phase change material(PCM)]. A frequent overshoot of temperature beyond target TH were noted in non-servo-controlled devices. It is recommended that servo-controlled devices should be the preferred cooling device for all eligible neonates. However, Non servocontrolled devices included Gel packs/PCM can use in 1:1 nurse: patient ratio with continuous monitoring temperature and take immediate corrective steps to keep the temperature within target range.

There is a strong recommendation that there should be national registry of all neonates with moderate to severe HIE who are being treated with TH. This includes not only acute treatment but also long-term neurodevelopment outcome. These data could be used for monitoring practice, providing feedback to neonatal units offering TH and to frame the policies including safety of device.

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Neurodevelopmental Outcome in Preterm- Measures to improve it

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Consultant Neonatologist,
Ahmedabad

There is increasing survival of sick and very preterm neonates in recent years due to advances in intensive care principles. Our focus should shift from survival to intact survival.

Neurodevelopmental outcome in preterm neonates depend on various factors like gestational age, birth weight, perinatal risk factors, Neonatal complications, sensory input and care during NICUdays. Early identification and intervention play a crucial role in improving their neurodevelopmental outcome.

We can discuss it under following headings:

1. Antenatal intervention to improve neurodevelopmental outcome
2. Delivery room intervention to improve neurodevelopmental outcome
3. NICU practiceswhich can improve neurodevelopmental outcome
4. Red flags in office practice and early intervention

1. Antenatal interventions to improve neurodevelopmental (ND) outcome

a) Administration of antenatal corticosteroids (ACS) to mother for enhancing fetal lung maturity before any anticipated preterm birth is one of the most important strategies to improve neonatal outcomes.

Cochrane systemic review 2017 on ACS says that there is 32 % decrease in Neonatal death, 35 % reduction in RDS and 45 % reduction in IVH and NEC and No significant harm in terms of ND delay or CP.

Indication: We follow the practice of ACS in women at risk of preterm birth from 24to 34 weeks of gestation age (GA). Recently late preterm and early term deliveries are on rise. People have used ACS in them. There has been reduction in RDS and TTNB but increase in transient hypoglycemia and also increase in neurocognitive and neurobehavioral issues at 18 months of age. Till there is further concrete evidence, WHO and GOI suggest to use ACS till 34 weeks of GA only.

Dose : Betamethasone: 12 mg every 24 hrly x 2 doses

Dexamethasone: 6 mg every 12 hrly x 4 doses

b) Antenatal Magnesium Sulfate for Neuroprotection

Effect of magnesium sulfate induced Neuroprotection is multi-pronged like inhibition of calcium influx into the cell, anti-inflammatory effect, vasodilatation and decreased free radical injury. It is indicated for all preterm deliveries < 32 weeks of GA.

Method : 4 gm IV loading over 30 minutes followed by 1 gm per hour maintenance infusion over 12 to 16 hours . Maximum infusion time: 24 hours

Therapy is safe for new born & mother and no increase in resuscitation at birth.

c) Prevention of prematurity, improvement in maternal nutrition and maternal lifestyle changes are our ultimate goal to improve ND outcomes in neonates.

d) In-utero Transfer of Neonate: In centers where there are no facilities to take care of LBW and extremely preterm babies , mother should be transferred to a center where maternal and newborn care can take place under one roof . After delivery transfer of sick preterm babies increases the risk of hypoxia, hypothermia, sepsis and IVH, which further has a detrimental effect on ND outcome.

2. Delivery room intervention to improve ND outcomes:

a) Delayed cord clamping:

NRP recommends delayed cord clamping for at least 60 seconds for all preterm and full term infants not requiring immediate resuscitation at birth. It improves ND outcomes as well as decreases need for inotropes andblood transfusion, also decreases IVH. Cord milking 20 cm of umbilical cord two to three times before clamping has same advantage but not recommended in < 34 wks of GA.

b) Thermoregulation in Delivery Room

- Maintain delivery room temperature around 26 degrees Celsius for all deliveries less than 32 weeks of gestation.
- Use polythene bags or wraps for all deliveries neonates < 32 wks of gestation. Do not dry the neonate before placing inside the plastic bag and head should be covered with cap to prevent evaporative heat loss.
- Use transport incubator to transfer neonate from delivery room to NICU. Otherwise healthy babies should be kept in skin to skin contact with mother immediately after delivery while placenta extraction and episiotomy repair are being conducted.

Cochrane review has shown that early skin to skin contact started soon after birth until the end of first breastfeeding improves breastfeeding success rates and also improves neurological outcomes. We need to sensitize the same to ourselves as well as OBGYN friends for benefit of neonates.

c) Gentle Newborn resuscitation:

- Neonates are resuscitated as per NRP guidelines spontaneously breathing preterm infant < 32 wks with respiratory distress should be supported with CPAP 5 cm of H2O using T Piece device.
- Infant needing positive pressure ventilation are to be provided with PIP and PEEP using T – piece device. Initial setting of the device should be set at 15/5. PIP be increased according to the need.
- Avoid using self-inflating bags for delivering PIP in preterm infants to prevent uncontrolled delivery of tidal

volume.

d) Avoid Hypoxia and Hyperoxia

Pulse oximeter and oxygen blenders capable of delivering set FiO2 must be available for all high risk deliveries. Begin resuscitation with FiO2 21 to 30 % and titrate FiO2 according to SpO2 target.

Our aim is to avoid hypoxia and hyperoxia. All this measures improves the ND outcome in PT.

3. Common NICU practice to improve ND outcome

At every opportunity efforts should be made to minimize pain and stress by providing developmentally supportive care (DSC). This includes noise reduction, gentle handling, clustering of procedures, attention to skin and early parenteral participation.

Sick/PT baby's brain is extremely vulnerable. Abnormal inputs from care processes that are not baby friendly can result in developmental and psychological problems. DSC influences the baby's developing brain.

a. Family centered care and KMC:

Allow parents unlimited access to the baby. They must hold the baby, provide comfort, KMC, and gentlymassage the baby. Under supervision can give RT feeding, change diapers and other care process like weighing the baby.

b. NICU environment(light and noise):

NICU light should be dimmed except when skilled procedures are performed. Alarms should be muted once addressed. Their volume be reduced. Avoid loud conversations.

c. Pain management:

Painful procedures must be minimized. Clubbing of blood tests that are not urgent. Lancet pricks are less painful then needle pricks. Talking to baby, tucking the baby, holding hands all have shown to decrease pain. Breast milk and sucrose decrease this pain of procedure. Topical anesthesia, paracetamol and opioid analgesics may be required when more painful procedures are performed

d. Positioning:

Placing the baby “frog legged” for prolonged period in NICU results in external rotation of shoulders and hips and causes tone abnormalities in limbs. Babies must be nursed with head in midline position, hands brought to midline towards the mouth, legs and arms must be flexed and supported at boundaries. They must be contained in nest like position like 'in-utero'. Practice 'tummy time' that is keeping the baby prone for some time when baby is alert.

e. Kangaroo Care:

Kangaroo Mothercare has been the most understood DSC in last decade . Scientific evaluation has demonstrated better sleep, saturation, heart rate, weight gain, exclusive breastfeeding rates, and decrease in infection &early hospital discharge.

Although long durations of KMC are recommended, hospital should provide support for family to stay for long hours, Provide comfortable chairs and privacy to perform KMC. Also need to counsel and educate the family members.

f. Massaging:

Massage reduces behavioral and physiological response to pain and reduces cortisol levels. Better weight gain is demonstrated, bonding with mother improves. Maturation of EEG was shown to be better and developmental score were also better in the study when massage was performed for 15- 20 mins/day.

g. Cue based feeding:

Most NICUs feed babies by the clock every day example 2nd to 3rd hourly. When the baby might need sleeping, nursestarts giving an OG feed. It is recommended to wait for the baby cues that baby is waking up from sleep to decide the right time to feed. Parental involvement is critical to implement cue based feeding.

Even procedures like diaper change and cleaning of baby must be planned based on babies state of wakefulness.

❖ Early intervention and red flags in office practice to be continued in next bulletein...

Pleural effusion associated with peripherally inserted central venous catheter and bed side utility of lung ultrasound

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Abstract:

Acute respiratory distress developed in extremely low birth weight preterm because of bilateral pleuraleffusion, secondary to the migration of a PICC (peripherally inserted central venous catheter) into the pulmonary vasculature. Here we discuss the bed side utility of lung ultrasound for prompt recognition of the problem and rapid treatment are essential and life saving.

Key words:

extremely low birth weight, pleural effusion, peripherally inserted central venous catheter

Introduction:

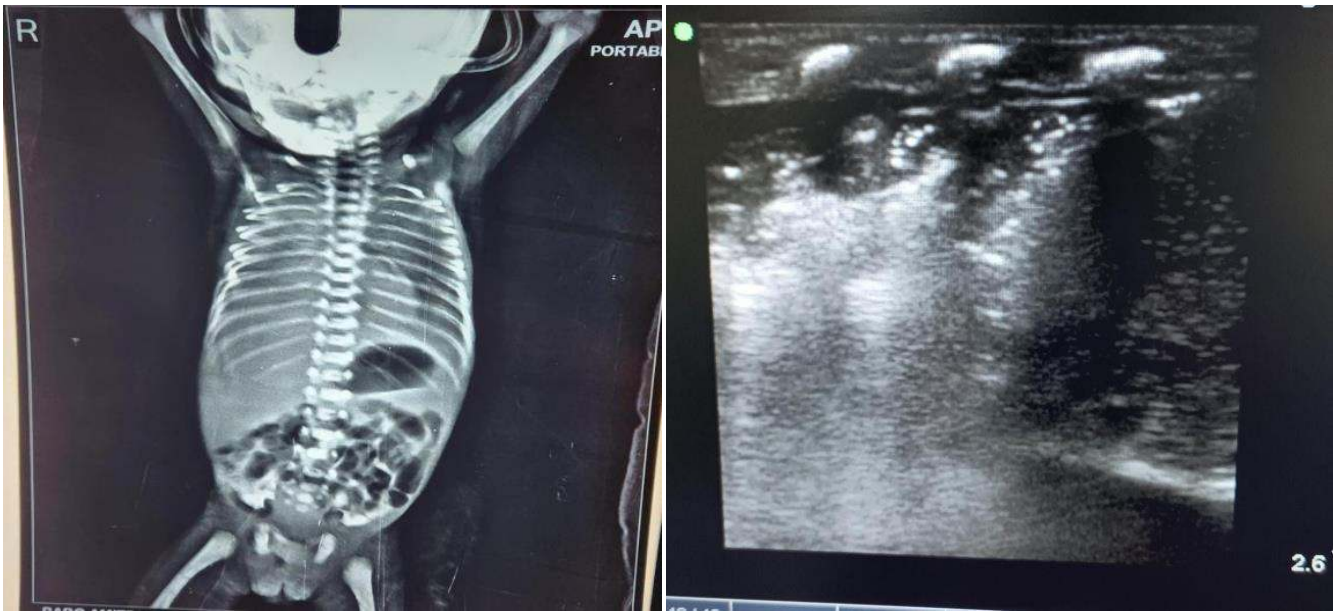
Respiratory distress in extremely low birth weight preterm neonates is very common condition observed in modern medicine practice. The most common cause being prematurity but also associated with sepsis, meconium aspiration, persistent pulmonary hypertension (PPHN), congenital pneumonia and pneumothorax etc. Pleural effusion though rare but is also present as an acute respiratory distress in other wise stable neonates. Utilization of PICC in neonates has been increased in recent times in view of availability of modern NICUs (neonatal intensive care unit) and education of parents towards good outcomes of sick neonates. Most of the neonates diagnosed having pleural effusion are associated with sepsis and with due treatment effusion resolves. Here we will discuss a case of bilateral pleural effusion associated with PICC displacement without sepsis.

Case report:

This male neonate was delivered at 30 weeks of gestation to a second gravida mother having nonconsanguineous marriage by means of emergency LSCS (lower segment cesarean section) delivery in view of severe pregnancy induced hypertension and IUGR (intrauterine growth retardation). At birth, baby was IUGR, havingextremely low birth weight of just 600gms with clear amniotic fluid, requiring delivery room resuscitation in form of CPAP (continuous positive airway pressure) and the Apgar score were 1min 5 & 5 min 7. After delivery room stabilization, the neonate was shifted to the neonatal intensive care unit with transport incubator and CPAP support.He was having severe RDS (respiratory distress syndrome) with Silverman Anderson score of 8 and point of care lung ultrasound suggestive of severe RDS. Early surfactant therapy by LISA (less invasive surfactant administration) followed by nasal ventilator support along with other supportive treatments were started. Within next 36 hours baby was hemodynamically stable with FIO2 requirement of only 21% and no other signs of respiratory distress. Considering prolonged TPN (total parenteral nutrition),on day 2, a

20cm PICC was passed through the right saphenous vein and fixed at 18cm at the junction of inferior vana cava and right atrium [1]. On 4th day of life, baby had acute respiratory distress which failed to respond to increased ventilator support.His blood work up turned out to be normal inform of HB 18.9, WBC 5910, PLATELET COUNT 109000, LACTATE 1.1 and CRP within normal limits with sterile blood culture report. Bed side functional 2D Echocardiography was suggestive of normal cardiac function and pulmonary pressure. Bed side lung ultrasound done which suggestive of normal lung fields along with bilateral pleural effusion and displacement of PICC line into pleural cavity (IMAGE A). 2cm withdrawal of the PICC was resulted in prompt relief of respiratory distress within 12 hours and decreased in ventilator support requirement. A subsequent lung ultrasound showed clearing of pleural effusion and six days later PICC was removed without any other complications (IMAGE B). Finally, the baby was discharged with 1.6 kg of weight with intact neurology and normal growth.

IMAGE A



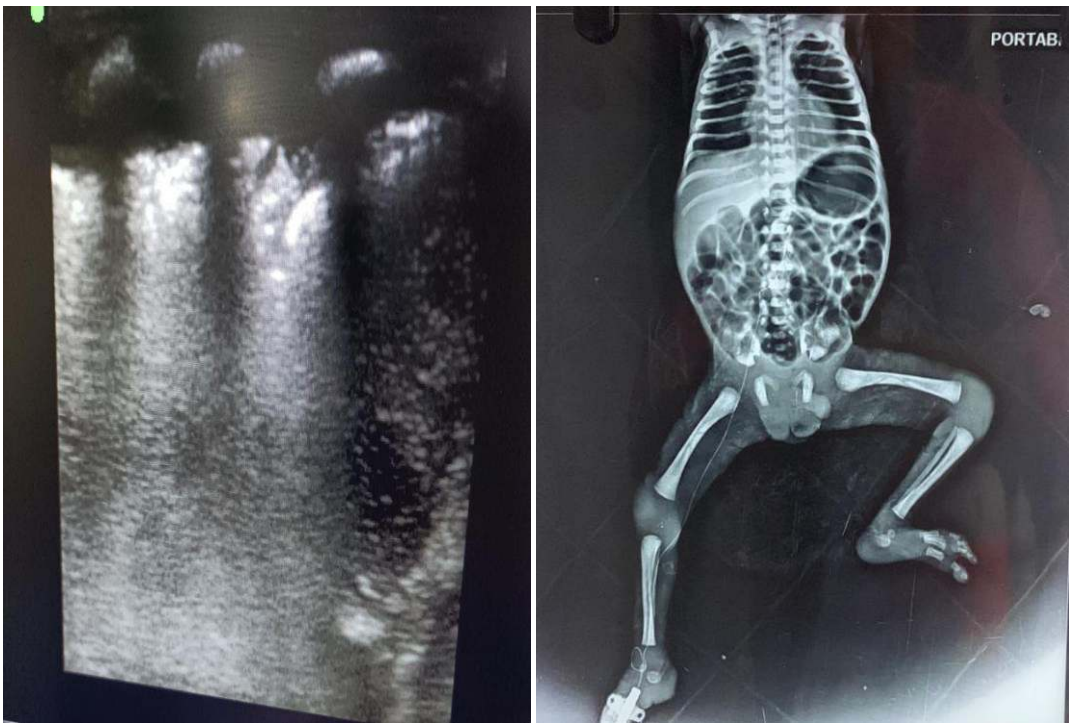


IMAGE B

Discussion

Parenteral nutrition through central lines has been used in the management of small sick newborn infants since 1968. A peripherally inserted central catheter (PICC) made of silicone, polyurethane, or polyethylene provides a prolonged route for administration of parenteral fluids, nutrition, and medications [2]. Preterm neonates admitted to hospital usually require a PICC because of their small and fragile vessels [2, 3]. Femoral, subclavian, and internal jugular and saphenous veins are the most common sites used for PICC catheterization [4]. However there is no significant difference in total PICC related complications between upper and lower extremities PICCs [5]. Although use of a PICC has many advantages for the treatment of neonates, catheter malposition may result in serious complications that could be life-threatening [4]. It is common practice to insert PICC lines for parenteral administration in preterm neonates. Although PICC lines are associated with a number of catheter-related complications, such as infection, catheter block, catheter migration, thromboembolism, and catheter damage, pericardial effusion following PICC insertion is an unusual complication [3, 4]. But in recent times the use of PICC has been drastically increased because of availability of material, skilled doctors, modern NICUs and parents' awareness and willingness to save tiny newborns. A series of complications have been reportedincluding sepsis, thrombosis, vessel perforation, cardiac tamponade and chemical pneumonitis. In this case, bilateral pleural effusions occurred due to PICC go in wrong direction from IVC to pleural cavity [6]. So that TPN & lipid were filled in pleural cavity. The resultant pleural transudate led to acute respiratory distress in the absence of other causes leading to respiratory distress. After withdrawal of the central venous catheter, there was a rapid and complete recovery within 12 hours. It has also been reported that in addition to catheter displacement, other factors, such as the material, length, and size of the catheter, duration of parenteral nutrition, osmolarity, and composition of the infused fluids may severely affect and worsen complications and outcomes related to pleural effusion. Moreover, pleural effusion should be suspected in every newborn who develops respiratory distress with PICC, and all neonatologists should be aware of this clinical emergency and the steps to be taken.

Conclusion:

In this case we understands the necessity for good skin fixation to prevent further onward catheter movement and the importance of reassessment of the catheter position. In case of any unexplained clinical deterioration during parenteral nutrition the possibility of PICC displacement or associated complications should be suspected. Early diagnosis and prompt action is the key to prevent further deterioration.

Recommendation:

The ideal position for central venous catheters is at the junction of the superior or inferior vena cava and the right atrium. To prevent onward catheter movement, we suggest:

(a) Four to five overlapping 2 cm steri-strips be applied starting close to the insertion site to secure the catheter to the skin.

(b) A square of transparent semipermeable dressing be fitted over the insertion site and steri-strips.

(c) The entire length of the catheter is secured to the patient (the catheter is initially loosely coiled and later secured to the skin using narrow strips of transparent semipermeable dressings).

(d) A single piece of tape is crisscrossed under the hub and over the wings of the catheter to stabilize the connection between catheter and hub.

(e) A 2 × 2 cm gauze sponge is placed under the hub and taped, ensuring that the catheter connection of the hub is not kinked.

Transparent dressing or skin closure tapes should not be allowed to encircle the extremity completely, as even with mild venous congestion, such a dressing would act as a tourniquet.

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