Neo Clips

NATIONAL NEONATOLOGY FORUM DELHI

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DR LALAN BHARTI
President, NNF Delhi

DR KUMAR ANKUR
Secretary, NNF Delhi

DR NAVEEN PARKASH GUPTA
Chief Editor, Neo Clips

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DR LALAN BHARTI

M.D, FIAP, FNNF
Fellow ADVAC (South Africa)
President NNF Delhi 2022
HOD Paediatrics, JPC Hospital
Govt. of Delhi
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Dear Esteemed Members ,

Greetings from NNF Delhi !

It gives me a feeling of immense pride & pleasure to bring to you the first Monthly Bulletin **NeoClips** (Neonatal Clinical Practice) of NNF Delhi. This idea has emerged as a unique proposition from the minds of experienced neonatologists teaming up with young budding counterparts. The idea to engage, empower and enrich members with each other's experience and knowledge. My sincere thanks and heartiest congratulations to the team which gave physical shape to the idea, chaired by Dr. T. J. Antony, cochaired by Dr.Avneet Kaur with a very dedicated hard working Editor in Chief Dr Naveen Parkash Gupta for their untiring efforts.

I am also thankful to all the contributors for the successful release of this first edition. They have worked with enthusiasm in collecting information from various credible sources. We are very hopeful that this monthly **NeoClips** would assist our members in providing better neonatal care. We would request all the members to give their feedback to help us improve the subsequent issues and also to use this space to share their clinical experiences.

I would like to take this opportunity to extend my sincere thanks to all the esteemed members for reposing their faith in me to lead NNF Delhi as President.

To reduce neonatal mortality to single digit, we need to focus on strengthening the basic care for all newborn and scaling up of low cost & high impact models of care like NRP, KMC, early initiation and promotion of exclusive breast feeding. In this direction, NNF Delhi has started multipronged strategies this year by having various programs like multiple basic and advanced NRP, mentoring and handholding of SNCU, Lactation Workshop, Perinatology Workshop, CPAP/NIV Workshop, Preterm Package Course, Vascular Access Workshop, Basic Nursing Care Workshop, KMC Workshop & QI Workshop etc.

We are also trying to collaborate with Govt of Delhi, WHO and other professional bodies to roll out a govt run program in Delhi for the cause of newborn and take NNF to greater heights.

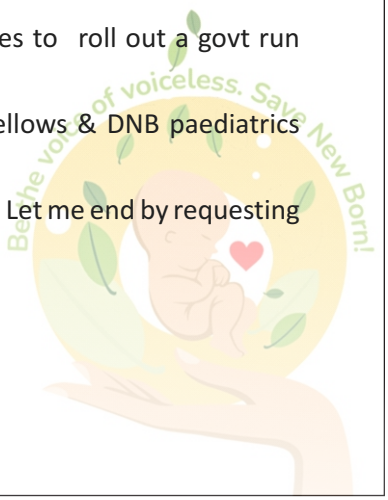
We are also planning to start a much needed **fresher/crash course** for our NNF/IAP Fellows & DNB paediatrics residents which would help them to prepare for their exit exam.

None of these programs can succeed without active participation of you, the NNF member. Let me end by requesting you to join in various programs and make them a success.

With Best Regard

L Bharti

Dr. Lalan Bharti
President, NNF Delhi



From Secretary's Pen

DR KUMAR ANKUR

Secretary, NNF Delhi

Dear friends,

Warm greetings from National Neonatology Forum, Delhi!

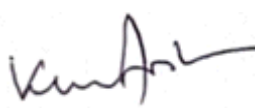
It gives me immense pleasure in announcing that NNF Delhi is releasing monthly E-bulletin from February 2022 with the name '***NeoCliPS' (Neonatal Clinical Practice)***. This bulletin will be an amalgamation of various evidence based clinically relevant topics. It will include Case of the month which would be the case discussed in the monthly meeting that particular month. We will also include an evidence based review article in our guest lecture column. To make it more interesting we are going to add a Journal Scan of the month and Image of the month. Objective Structured Clinical Examination (OSCE) will be the flavour of the day. We plan to include ten OSCE scenarios in each bulletin. This would help the NNF/ IAP fellows and DNB students to sharpen their skills and prepare for their exit exam while helping the others refresh their knowledge.

We are extremely fortunate to have stalwarts who are spearheading this committee (Dr. T J Antony, Dr. Avneet Kaur). However, my special thanks to Dr. Naveen Parkash Gupta who is the chief editor and taking a lot of pain to make it more useful. I am sure it's going to be hit from day one.

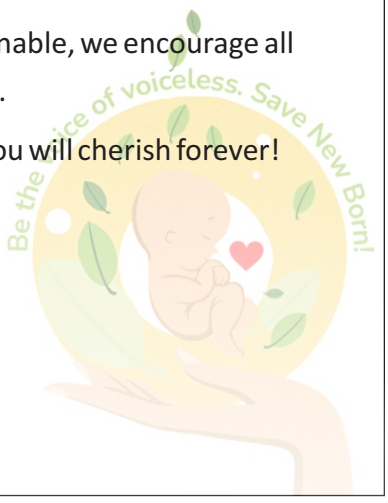
We request all the esteemed members to contribute to this E bulletin. All contributors will be given due credit.

We all know that such projects need significant financial resources. To make it sustainable, we encourage all of you to advertise your Hospitals/Clinics/Labs in our NeoClips at a very nominal rate.

We eagerly look forward to your feedback and hope to give you an experience that you will cherish forever!



Dr. Kumar Ankur
Secretary, NNF Delhi



Editor's Desk

DR NAVEEN PARKASH GUPTA

Cheif Editor, Neo Clips

Dear Friends,

Greetings from National Neonatology Forum, Delhi.

We are excited to announce the release of NeoClips (Neonatal Clinical Practice), a monthly newsletter of NNF Delhi branch. We hope to get eminent Neonatologists and Paediatricians to share their knowledge and experience through this newsletter. We therefore request all the esteemed members of the Delhi NNF to contribute to this journal and make it a success.

We have divided newsletter into different sections.

The Case report section would highlight an interesting case or an unusual presentation of a condition in the neonatal period. In the review section we hope to review a topic of common interest and summarise the current evidence and best practice.

The Picture of the month section would have a picture of a common / interesting condition, while the Image section would have interesting Xrays/ CT / MRI or ultrasound images of interest to neonatologists.

Journal scan will highlight recent research paper of interest or some pathbreaking research paper which has led to change in neonatal practice.

Our Fellows and trainees are a very important part of the Forum, and so for them, we have a section on OSCE (Objective structured Clinical Examination) to help them prepare for their exams.

I, on behalf of the editorial committee, would like to thank the office bearers of Delhi NNF for giving us this opportunity to start this bulletin. Special thanks to Dr Lalan K Bharti (President NNF) and Dr Kumar Ankur (Secretary NNF) in showing faith in us.

I would also like to thank the editorial committee members who have put their heart and soul into this first issue. Thank you Dr Antony, Dr Avneet, Dr Swati and Dr Siddharth for helping me bring out this first issue. I look forward to your cooperation for all the subsequent issues.

Dear Reader I hope you enjoy this inaugural issue. Please send us your feedback and suggestions on how to improve. We look forward to hearing from you.

Dr Naveen Parkash Gupta

Unusual Case of Neonatal Respiratory Distress

Amit Yadav
NNF Fellow, BLK Max Supspeciality Hospital, Delhi
Ankit Parakh
Pediatric Pulmonologist,
BLK Max Supspeciality Hospital, Delhi
Aparna Prasad
Consultant Neonatology,
BLK Max Supspeciality Hospital, Delhi
Kumar Ankur
Head of Department Neonatology,
BLK Max Supspeciality Hospital, Delhi

Case - This 43 day old baby presented with complaints of noisy breathing, on and off, for 15 days, with difficulty in breathing and low grade fever for 2 days. The chest x ray showed a right opaque hemithorax with trachea shifted to right side (Fig.1).

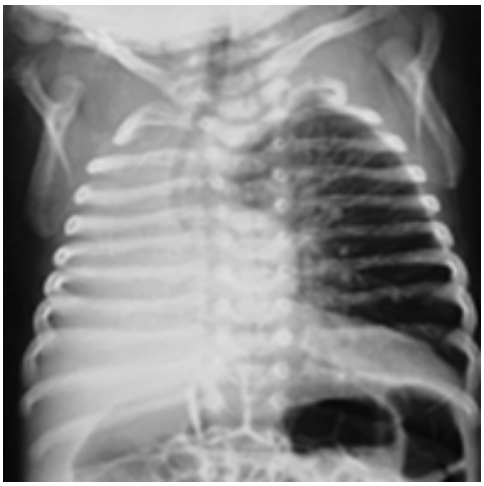


Fig. 1

A CT scan of the chest was done which showed complete collapse of right lung with obliteration of right main bronchus, by tissue with soft tissue density. (Fig. 2)

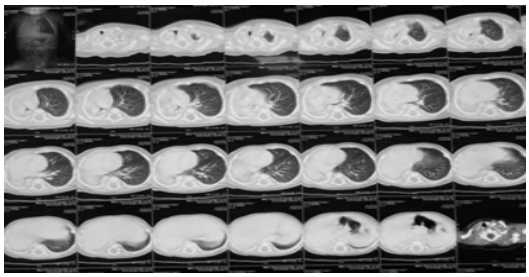


Fig. 2

Rigid bronchoscopy was performed to identify the cause of obstruction, but was not successful. Baby was referred to our hospital. On admission, the child's vitals were stable, but he was breathing with subcostal and suprasternal retractions. Chest examination revealed reduced breath sounds on the right side with bilateral conducted sounds. At this time the differential diagnosis included a viral infection, conditions with mucoviscidosis e.g. Primary ciliary dyskinesia and cystic fibrosis or a congenital lung lesion.

A CT reconstruction of the lung was done using the previous CT scan images and the results were suggestive of an aplastic right lung.

Bronchoscopy, using a 2.8 mm flexible bronchoscope, was performed to evaluate the status of the airway and to look for a cause for the noisy breathing. This showed complete tracheal rings, suggestive of tracheal stenosis, and the bronchoscope could not be negotiated beyond the trachea, on the right side. (Fig.3)

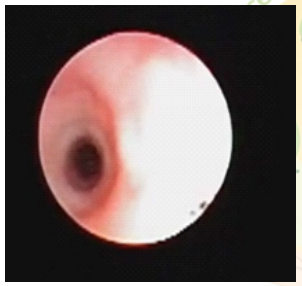


Fig. 3

The diagnosis therefore was Aplasia of right lung with tracheal stenosis. Intravenous antibiotics were therefore stopped, and parents were counselled regarding the condition of the child and a tracheoplasty was offered.

We were unable to do a repeat CT scan of the chest and also were not able to estimate the length of the tracheal stenosis.

Review of literature

Pulmonary hypoplasia includes a spectrum of problems which includes hypoplasia, aplasia, or agenesis of selected or all lung segments. The lesions may be lobar, unilateral, or bilateral. Some degree of the pulmonary hypoplasia spectrum is reported to be found in 7 to 26% of all neonatal autopsies. Primary pulmonary hypoplasia is rare. Cases of primary pulmonary hypoplasia have been described in the literature with varying degrees of severity ranging from bilateral hypoplasia of the lungs to simple hypoplasia of an isolated lobe. Most cases of pulmonary hypoplasia are secondary to conditions that limit fetal lung growth. It may be caused by an embryologic defect of the lung or vascular tissues, or an in-utero vascular accident. Lung aplasia is thought to be caused by abnormal blood flow in the dorsal aortic arch during the 4th week of gestation. Cases of isolated lobar defects with or without tracheobronchial abnormalities (tracheal stenosis), has only been rarely reported. The trachea is composed of 14–21 C-shaped hyaline cartilage rings connected by annular ligaments. Tracheal Stenosis is a fixed narrowing of the tracheal lumen due to intrinsic cartilaginous defects. The epidemiology of tracheal stenosis is unknown, however one study has suggested an incidence of 1 in 64,500 births. Frequently, cartilage rings are constricted and 'complete' at the dorsal end, with an O-shape, rather than the normal C-shape. Diagnosis of unilateral lobar pulmonary hypoplasia requires a high index of clinical suspicion and experience with reading neonatal radiographs. The radiographic findings will vary depending on the extent of lung involvement. In right-sided lobar pulmonary hypoplasia due to an accessory diaphragm, the heart and the trachea are displaced toward the right and the right heart border or superior mediastinum is obscured. A number of associated anomalies have been described in patients with pulmonary hypoplasia, but none has been specifically associated with patients with lobar hypoplasia. Clinically, infants with unilateral lobar pulmonary hypoplasia may have variable presentations depending on the extent of lung involvement and comorbidities. Some infants present with severe respiratory distress in the first few hours of life whereas some may be completely asymptomatic.

Diagnosis is usually made by chest X-ray and CT scan, and invasive procedures like bronchography, bronchoscopy and angiography can be avoided. The typical CT findings are opaque hemithorax with mediastinal shift towards the affected side with absence of lung parenchyma; pulmonary and bronchial tree as seen in our case.

Asymptomatic cases rarely require any treatment especially when no other anomalies are present.

Learning points

- Aplasia of lung is a rare lung malformation.
- Antenatal scans may not pick up the anomaly.
- Congenital cystic adenomatoid malformation may accompany aplasia of lung.
- A newborn with an opaque lung warrants bronchoscopy.
- CT scan confirms the diagnosis.
- Regular follow up, prevention of chest infection, immunization and adequate nutrition are the key factors in management

Caffeine: What do we know in 2022

Naveen Parkash Gupta
Senior Consultant Neonatology,
Madhukar Rainbow Children's Hospital, Delhi
T J Antony
Director and Head of Department Neonatology,
Fortis Memorial Research Institute, Gurgaon

Introduction

Methylxanthines are the drug of choice for apnea of prematurity (AOP). Caffeine is preferred over aminophylline owing to wide therapeutic index and long half-life. The use of caffeine has increased tremendously following the landmark study titled Caffeine for Apnea of Prematurity (CAP). This trial was designed to assess safety of caffeine use in preterm and very low birth weight babies. The clear benefits and safety of caffeine therapy demonstrated in the CAP trial led to its increased use in very low birth weight babies. It is now one of the most commonly used drugs in NICU.

Mechanism of Action: Caffeine is a nonspecific inhibitor of two of the four known adenosine receptors, in particular A1 and A2A, located at multiple sites in the brain. It is rapidly distributed in the brain, with CNS levels approximating plasma levels. Caffeine is respiratory stimulant. It Increases CO2 sensitivity, improves tidal volume and minute ventilation, decreases hypoxic depression of breathing and enhances diaphragmatic function.

Indications: Apnea of prematurity.

Dose: Loading - 20 mg/kg of caffeine citrate IV over 30 minutes or orally.

Maintenance – 5-10 mg/kg/dose of caffeine citrate IV over 10 minutes or orally every 24 hours. Maintenance dose should be started 24 hours after the loading dose.

The ratio of caffeine citrate to caffeine base is 2:1 (e.g. 20 mg of caffeine citrate = 10 mg caffeine base).

Pharmacokinetics: Orally administered caffeine citrate is rapidly and completely absorbed. There is almost no first-pass metabolism. Approximately 86% is excreted unchanged in the urine, with the remainder metabolized via the CYP1A2 enzyme system in liver.

Since the enzymes mature with increasing age, half-life of caffeine reduces as the baby approaches term gestation. Its mean half-life is around 100 hours.

Adverse effects: Side effects are generally mild and may include the following:

CNS – irritability, tremors, jitteriness

CVS – Tachycardia, increased blood pressure, arrythmias

GIT -- Feed intolerance – Increases GI secretions, lowers GES tone

Higher loading dose may lead to decrease cerebral and intestinal flows.

Increased oxygen expenditure and energy consumption – overall slowing of growth

Mean weights of babies on caffeine were lower than their counterparts in CAP trial, during the initial few weeks. The difference was not present at end of 3 weeks.

Evidence from CAP trial: The CAP trial was pragmatic randomized placebo controlled trial done to assess safety of caffeine in very low birth weight babies. They randomized 2006 babies between 500-1250 grams who were at risk of apnea of prematurity. The hypothesis was that infants treated with caffeine would have higher rates of death or adverse long term neurological outcome. A pragmatic approach was chosen. Babies were included if they weighed

between 500gms and 1250 gms at birth, were less than 10 days old and their attending clinicians felt that they were eligible for methylxanthine treatment.

Caffeine was started to treat apnea, prevent apnea and before planned extubation. It was discontinued at median gestational age of 35 weeks. The dose of caffeine citrate used in study was 20 mg/kg/dose as loading dose followed by 5 mg/kg/day as maintenance dose. Maintenance dose was increased to 10 mg/kg/dose if apneas persisted.

Results:

Outcome	Caffeine (%)	Placebo (%)	Unadjusted OR (95% CI)	OR adjusted for center (95% CI)
Pharmacologic therapy for PDA closure	29.3%	38.1%	0.67	0.67 (0.55-0.81)
Surgical PDA closure	4.5	12.6	0.33	0.32 (0.22-0.45)
Bronchopulmonary dysplasia	36.3	46.9	0.65	0.63 (0.52-0.76)
Composite death or disability at 18-21 months	40.2	46.2	0.78	0.77 (0.64-0.93)
Composite death or disability at 5 years	21.1	24.8	0.81 (0.65-1.02)	0.82 (0.65-1.03)
Composite death or disability at 11 years	31.7	37.6	0.77 (0.59-1.01)	0.78 (0.59-1.02)

Short term outcomes – The study showed that use of caffeine led to a decrease in bronchopulmonary dysplasia, severe ROP, and a reduction in the number of babies requiring therapy for patent ductus arteriosus.

Long term outcomes - At 18 months there was an improvement in the rate of survival without neurodevelopmental disability (mainly a reduction in cerebral palsy)

At five years (n=1640) it was seen that neonatal caffeine therapy was with a significantly improved rate of survival without disability in children with very low birth weight.

On Assessment at 11 years there was a reduced risk of motor impairment (adjusted OR 0.66 (95% CI, 0.48 to 0.9))**.** There was no significant effect on combined motor, academic and behaviour impairments.

How does caffeine lead to decrease bronchopulmonary dysplasia and improve neurodevelopmental outcomes:

Caffeine is not a lung drug per se - it minimizes interventions for respiratory control abnormalities in the very preterm infant that result in lung injury that persists into childhood. (Alan jobe AJRCCM 2017*).* Babies in caffeine group were extubated a week earlier in caffeine group than in placebo in CAP trial. Postmenstrual age (PMA) at last use of any positive airway pressure_(mean, 31.4 weeks caffeine; 32.8 weeks placebo) explained 53% (95% CI, 22-100%) of the benefit of caffeine on motor impairment 11 years later.

When to start caffeine therapy

- In post hoc analysis of CAP trial, it was seen that starting caffeine early (< 3 days) resulted in larger reduction in days of respiratory support. (Davis et al)

- 4 systematic reviews have been done on early vs late caffeine.
- Few systematic reviews suggest that early caffeine leads to less bronchopulmonary dysplasia in both cohort studies and randomized controlled trials. In cohort studies, neonates treated early with caffeine also showed decreased risks of patent ductus arteriosus, brain injury, retinopathy of prematurity and postnatal steroid use. However, the mortality rate was increased.
- Majority of data included in these systematic reviews is observational.
- A recent systematic review (Sandra et al, Pediatric research 2020) suggested critical/serious risk of overall bias in all but one of the studies included. They concluded that no conclusions can be drawn at this time about the optimal timing of caffeine therapy.

Does higher dose confer more benefit

Dose used in CAP trial was 20 mg/kg/dose loading dose followed by 5 mg/kg/day. Maintenance dose was increased to 10 mg/kg/day if baby had further apneas.

6 randomized controlled trials have evaluated higher dose of caffeine and 3 metanalyses have been published. Loading dose ranging from 20-80 mg/kg and maintenance doses from 3-20 mg/kg/d have been used in these studies.

No impact on mortality or BPD was seen. Higher dose did have short term benefits in the form of lesser extubation failures, and lesser duration of mechanical ventilation. However, evidence is of low quality and risk of bias in studies are very high. Due to imprecision, it is not possible to determine whether high dose caffeine is more effective and safer than a low dose.

Guidelines – There are many published guidelines for caffeine use in very low birth weight infants.

	AAP Guidelines 2016	European Guidelines 2019	NICE Guidelines 2020	Expert (Barbara Schmidt – PI of CAP trial)
Initiation	Optimal time to start unknown (1B) No recommendation if dependent on mechanical ventilation. >28 weeks: for apnea (2A)	Used to facilitate extubation (1A) Early (prophylactic) considered for those at high risk of requiring mechanical ventilation (2A)	Use "routinely" in any baby ≤ 30 weeks as early as possible (2A)	GA > 30 weeks – Wait until apnea develops GA < 30 weeks and ventilated – Start caffeine as you wean on ventilator settings GA < 30 weeks and some or no respiratory support – Start caffeine early
Dose	20 mg/kg loading dose 5–10 mg/kg maintenance (1A)	20 mg/kg loading dose 5–10 mg/kg maintenance (1A) Maintenance dose up to 20 mg/ kg/day "may be more effective but needs further testing in randomized trials"	20 mg/kg loading dose 5 mg/kg/day maintenance up to 20 mg/kg/day if apnea persists (2B) Consider higher dose than 20 mg/ kg/day if therapeutic efficacy not achieved	20 mg/kg loading dose 5–10 mg/kg maintenance (1A)
Discontinuation	33–34 weeks PMA, or 5–7 days off positive pressure	Not addressed	33–35 weeks PMA if baby stable	33-35 weeks PMA if baby is stable (off respiratory support for at least 5-7 days)
Drug levels	Not needed	Not needed	Yes, with higher doses	Not needed

Practice points

- Caffeine citrate as prescribed in the CAP trial is safe and effective for infants with apnea of prematurity, those requiring assisted ventilation to treat apnea and those about to be extubated.
- In AOP, caffeine is associated with decreased risk for BPD, PDA treatment, and neurological impairment.
- Caffeine therapy may be discontinued at around 33–35 weeks postmenstrual age in most infants if they are stable and off respiratory support for at least 5-7 days.
- The most immature infants and those with bronchopulmonary dysplasia may require longer treatment.
- Optimal timing of starting caffeine therapy is not clear.
- High dose or early use without further trials shouldn't be tried in clinical practice outside of research settings.

Suggested Readings:

1. Kreutzer K, Bassler D. Caffeine for apnea of prematurity: a neonatal success story. Neonatology. 2014;105(4):332-6. doi: 10.1159/000360647.
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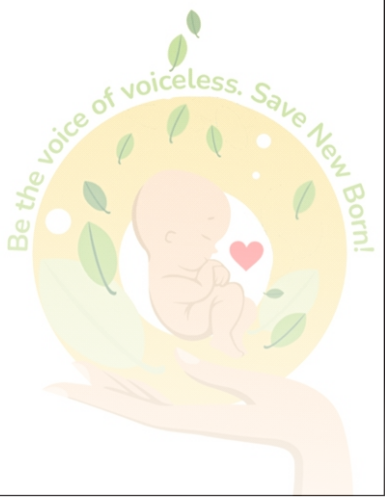


A newborn with restricted movements of left arm

Swetha.K, Devendra Singh Somvanshi
NNF Fellow, Madhukar Rainbow Children's Hospital, Delhi
Naveen Parkash Gupta
Senior Consultant Neonatology, Madhukar Rainbow Children's Hospital, Delhi

Clinical presentation – 3 days old term appropriate for gestation age baby presented with restricted movements of left upper limb

Examination findings – Upper limb adducted, internally rotated and forearm extended (figure). Moro reflex was asymmetric (video)

Suspicion – Lt side Erb's paresis

Condition –

Neonatal brachial plexus palsy (NBPP) is an uncommon condition, with an incidence that ranges from 0.04 to 0.3 percent of live births. Potential mechanisms include stretching/traction, compression, infiltration, and oxygen deprivation. Shoulder dystocia and macrosomic babies (birth weight > 4 kg) are risk factors. Good physical examination makes the diagnosis. It is advisable to do chest radiograph to rule out fracture clavicle.

Treatment – Involves early physical and occupational therapy with goal to prevent contractures. It includes passive range of motion exercises at all relevant joints beginning in latter half of first week after birth, supportive splints if needed to prevent finger flexion or elbow contractures, and muscle strengthening.

Surgery is needed only in severe cases or functional recovery doesn't happen in 3 to 9 months.

Prognosis – Spontaneous recovery occurs in many cases of NBPP by 1-3 months though in some children functional impairment persists till 18 months. Highest recover rate is seen in C5 and C6 palsy (95%) followed by C5 to C7 palsy (64%) followed by C5 to T1 palsy (21%). Early clinical recovery (within 2-4 weeks), elbow flexion and near normal strength by 3 months are favorable prognostic indicators.

Image Section

Anil Batra
Senior Consultant Neonatology,
Madhukar Rainbow Children's Hospital, Delhi
Charu Jha, Pinaki Dutta
NNF Fellow,
Madhukar Rainbow Children's Hospital, Delhi

Clinical Presentation – Repeated airleaks bilaterally requiring multiple chest tubes followed by milky fluid draining from chest tube on 15th day of life in a preterm 33 weeks, 950 grams baby.

Suspicion – Esophageal perforation

Supporting findings – On reviewing Chest xray there was a xray in which nasogastric tube was going towards right side (figure 1a)

Investigations – Upper gastrointestinal contrast study showing contrast leaking from esophagus

Management– Conservative treatment. Feeding jejunostomy was done in child and continuous feeds were given.

Key message –

1. Most of esophageal perforations are iatrogenic involving cervical esophagus.
2. Iatrogenic perforations in distal esophagus are uncommon.
3. A high index of suspicion is warranted in infants with a sudden deterioration of respiratory status, especially following procedures involving the pharyngeal region.

Management of esophageal perforation is conservative. Aim is to give rest to the esophagus and establishing an alternate route of feeding.

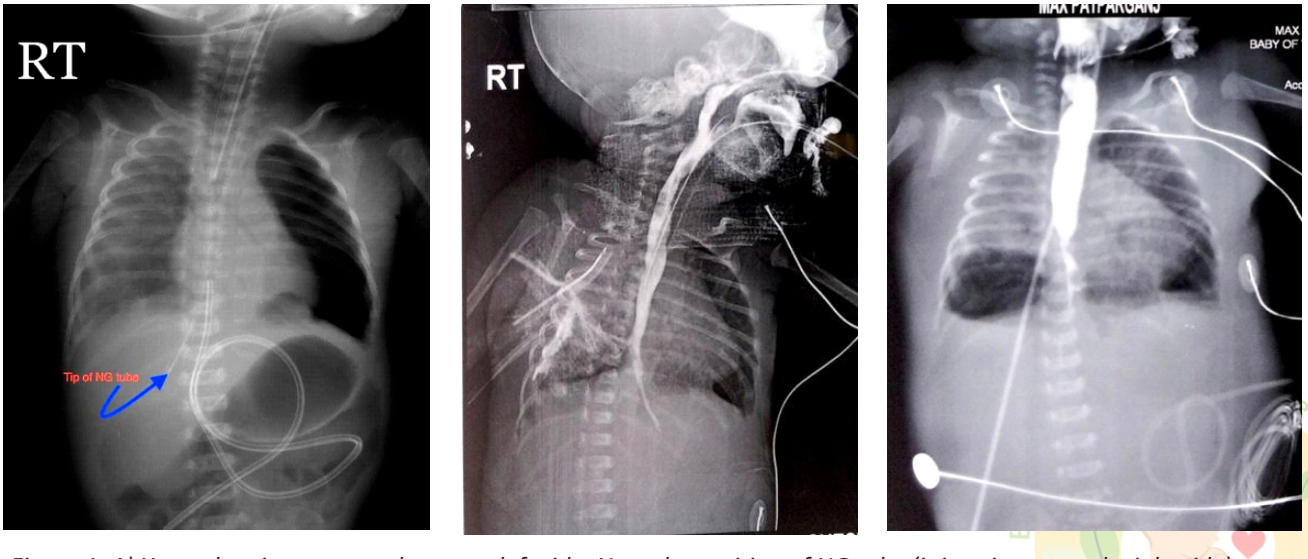


Figure 1: A) X-ray showing pneumothorax on left side. Note the position of NG tube (it is going towards right side).
B) Upper GI contrast study Showing contrast leaking from lower esophagus.
C) The perforation had been healed but a slight narrowing is obvious at the site of perforation.

Journal Scan

Reviewers

Sidharth Nayyar

Senior Consultant Neonatology, Cloud Nine Hospital, Faridabad

Avneet Kaur

Senior Consultant and Head of Department Neonatology, Apollo Cradle, Motinagar, Delhi

Research

JAMA | Original Investigation

Effect of Minimally Invasive Surfactant Therapy vs Sham Treatment on Death or Bronchopulmonary Dysplasia in Preterm Infants With Respiratory Distress Syndrome

The OPTIMIST-A Randomized Clinical Trial

Peter A. Dargaville, MD; C. Omar F. Kamlin, DMedSci; Francesca Orsini, MSc; Xiaofang Wang, PhD; Antonio G. De Paoli, MD; H. Gozde Kanmaz Kutman, MD; Merih Cetinkaya, PhD; Lilijana Kornhauser-Cerar, PhD; Matthew Derrick, MBBS; Hilal Özkan, MD; Christian V. Hulzebos, PhD; Georg M. Schmölzer, PhD; Ajit Aiyappan, MD; Brigitte Lemyre, MD; Sheree Kuo, MD; Victor S. Rajadurai, MD; Joyce O'Shea, MD; Manoj Biniwale, MD; Rangasamy Ramanathan, MD; Alla Kushnir, MD; David Bader, MD; Mark R. Thomas, MD; Mallinath Chakraborty, PhD; Mariam J. Buksh, MD; Risha Bhatia, PhD; Carol L. Sullivan, MD; Eric S. Shinwell, MD; Amanda Dyson, MMed; David P. Barker, DM; Amir Kugelman, MD; Tim J. Donovan, MPH; Markus K. Tauscher, MD; Vadivelam Murthy, MD; Sanoj K. M. Ali, MD; Pete Yossuck, MD; Howard W. Clark, DPhil; Roger F. Soll, MD; John B. Carlin, PhD; Peter G. Davis, MD; for the OPTIMIST-A Trial Investigators

OPTIMIST (cOllaborative Paired Trials Investigating Minimally Invasive Surfactant Therapy) trial

What is known already

1. In preterm babies < 30 weeks, CPAP is better than elective ventilation and surfactant administration in terms of decrease in composite outcome of death and bronchopulmonary dysplasia at 36 weeks postmenstrual age. (RR 0.91(95% CI 0.84-0.99)). (1)
2. Surfactant was administered at a higher FIO2 threshold (0.4-0.6) in CPAP group in these trials

What is still unknown

Whether the benefits of initial CPAP would have been greater if lower threshold of surfactant administration was used in CPAP group.

Research Question - For preterm infants with respiratory distress syndrome supported with continuous positive airway pressure (CPAP), does selective administration of surfactant via a thin catheter at a low oxygenation threshold improve survival without bronchopulmonary dysplasia compared with continuation of CPAP?

Hypothesis

Population	25-28 weeks neonates with respiratory distress supported with CPAP
Intervention	Surfactant administration via thin catheter at low FIO2 threshold
Control	Sham treatment
Outcome	Composite of death and BPD at 36 weeks PMA

Methods

Study design - International, multicenter randomized clinical trial of a blinded intervention conducted at 33 tertiary-level neonatal intensive care units.

Randomization and blinding - Infants were randomized 1:1 to the MIST group or the sham treatment (control) group via a computer-generated code linked to a corresponding opaque sealed envelope. Stratification done by study center and gestational age. Clinicians and parents were blinded to the study intervention with screening of the infant's bedspace from external view.

Participants – 25-28 weeks preterm with RDS on CPAP needing FIO2 more than 0.3 were eligible neonates.

Intervention - Infants were randomized to the MIST group (n = 241) and received exogenous surfactant (200mg/kg of poractant alfa) via a thin catheter. Surfactant was given in 3 aliquots with interval of 10 seconds between each aliquots.

Control - Control group (n = 244) received a sham (control) treatment consisting only of transient repositioning.

CPAP was continued thereafter in both groups unless specified intubation criteria were met. Babies were intubated when FIO2 needs were 0.45 or above.

Primary Outcome – Composite of death and BPD at 36 weeks postmenstrual age (PMA)

Sample Size Calculation - The study aimed to recruit 606 infants, providing90%power to detect an absolute risk reduction of 13% (RR reduction of 33%) in primary outcome, which for the control group was projected to be 38% based on observational data.

Results - Infants were enrolled between December 16, 2011, and March 26, 2020. Recruitment ceased on March 26, 2020 due to the COVID-19 pandemic. 488 infants were randomized by that time and 485 were included in analysis.

There was no difference in primary outcome (risk difference [RD], −6.3%[95%CI, −14.2%to 1.6%]; relative risk [RR], 0.87 [95%CI, 0.74 to 1.03]; *P* = .10)

The study does show a benefit in terms of reduction of BPD in survivors by 17% (RR, 0.83 [95%CI, 0.70 to 0.98]) but we should infer this finding cautiously as the results might have been altered by various limitations in the study itself.

Conclusion of study - Among preterm infants with respiratory distress syndrome supported with CPAP, minimally invasive surfactant therapy compared with sham (control) treatment did not significantly reduce the incidence of the composite outcome of death or bronchopulmonary dysplasia at 36 weeks postmenstrual age.

Limitations of study –

1. After slow recruitment, enrollment ceased at the onset of the COVID-19 pandemic at 81% of the planned recruitment target, meaning that the study was underpowered for detection of a treatment effect of the magnitude originally hypothesized.
2. Although the intervention was successfully blinded to the treating clinicians, members of treatment teams were likely to have participated in the care of enrolled infants at some time during hospitalization, raising the possibility of performance bias.

Reviewers Comments

Study enrolment period was very long (2011 – 2020). During this period, neonatal practices of surfactant administration have changed and MIST has has been increasingly used for surfactant delivery. Furthermore, a Cochrane review of surfactant delivery via a thin catheter or endotracheal tube has provided strong evidence in favour of the thin catheter delivery method (for death or bronchopulmonary dysplasia: RR, 0.59 [95% CI, 0.48-0.73]). (2)

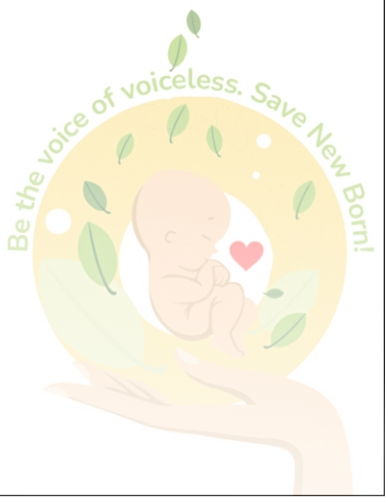
Different guidelines suggest different thresholds of FIO2 for surfactant administration. European consensus guidelines 2019 suggest rescue surfactant at FiO2 > 0.30 on CPAP pressure of at least 6 cm H2O (3). Canadian guidelines 2021 recommend giving

surfactant therapy at FIO2 threshold of 0.5. (4) Both guidelines mention less invasive surfactant administration (LISA) or MIST as preferred approach of surfactant delivery in spontaneously breathing babies on CPAP. (3,4)

Future research – To see effect of different FIO2 thresholds (0.3 vs 0.5) for surfactant replacement therapy through MIST on composite outcome of death and bronchopulmonary dysplasia in preterm babies with respiratory distress on CPAP.

References

1. Schmölzer GM, Kumar M, Pichler G, Aziz K, O'Reilly M, Cheung PY. Non-invasive versus invasive respiratory support in preterm infants at birth: systematic review and meta-analysis. *BMJ*. 2013; 347:f5980. doi:10.1136/bmj.f5980
2. Abdel-Latif ME, Davis PG, Wheeler KI, De Paoli AG, Dargaville PA. Surfactant therapy via thin catheter in preterm infants with or at risk of respiratory distress syndrome. Cochrane Database Syst Rev. 2021;5:CD011672.
3. Sweet DG, et al. European Consensus Guidelines on the Management of Respiratory Distress Syndrome - 2019 Update. Neonatology. 2019.
4. Ng EH, Shah V. Guidelines for surfactant replacement therapy in neonates. Paediatrics & Child Health. 2021 Feb;26(1):35-41.



QUESTIONS

Swati Upadhyay
Senior Consultant Neonatology, Max Superspeciality Hospital, Patparganj, Delhi
Sidharth Nayyar
Senior Consultant Neonatology, Cloud Nine Hospital, Faridabad
Naveen Parkash Gupta
Senior Consultant Neonatology, Madhukar Rainbow Children's Hospital, Delhi

Question. 1

A term newborn is noted to have progressive respiratory distress after birth.

a. What is the diagnosis on chest X-ray (fig. 1)?

b. What investigation will you do to confirm the diagnosis?

c. What is the definitive management for this condition?

d. During anaesthesia induction, the infant is noted to be blue. What could be the possible reason?

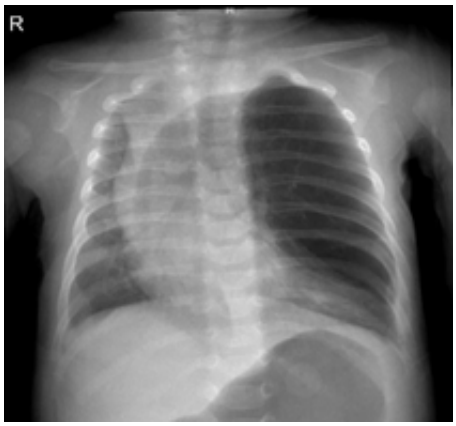


Fig. 1

Question 2

a. Identify the graphs below (Fig. 2 and 3) and mention its use in ventilated babies.

b. Identify phases of respiration have at A, B shown in Fig. 2?

c. Name 2 possible events that occurred between arrows 1 and 2 (Fig.3) in a ventilated baby.

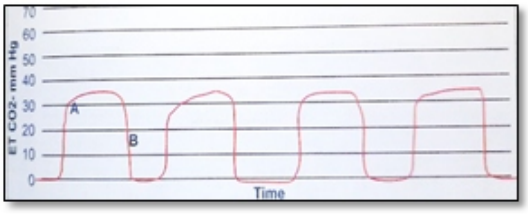


Fig. 2

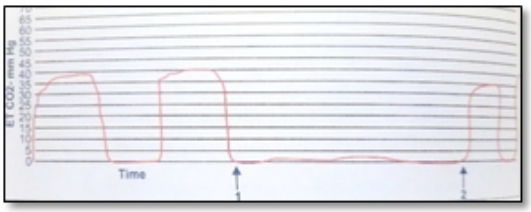


Fig. 3

Question 3

ABG of Baby A and Baby B is mentioned below :

Baby A	**Baby B**
pH 7.40	pH 7.30
pCO2 35 mmHg	pCO2 74 mmHg
pO2 75 mmHg	pO2 50 mmHg
SaO2 92%	SaO2 80%
Hb 6 g%	Hb 13 g%

a. How do you calculate arterial oxygen content?

b. Which of the above 2 babies is more hypoxic and why?

c. What is the normal value of arterial oxygen content?

Question 4

A term baby boy is born limp and gets intubated in labour room. Baby is ventilated and put on SIMV mode

of ventilation with PIP 17, PEEP 6, Fio2 40% and rate 40/min. His initial chest X-ray is shown in Fig. 4.

a. What is the diagnosis?

b. Comment on the position of Endotracheal Tube.

c. Write the formula for calculating LHR? What value of LHR indicates a good prognosis?

d. What should be the timing of surgery in such case?

e. What is the concept of ALARA when doing neonatal X Rays?

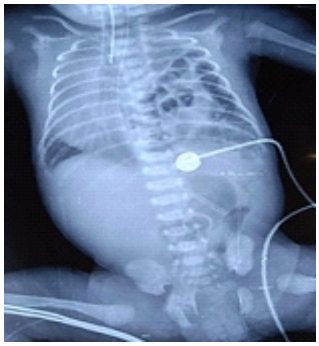


Fig. 4

Question 5

A 2 days old term baby boy is being ventilated for MAS with PPHN on SIMV mode with PIP 28, PEEP 6, Fio2 of 1, f 60/min, Ti 0.35 sec, MAP 14 cmH2O. ABG is as given below.

pH	7.21
pCO2	54 mmHg
pO2	44 mmHg
HCO3	13 mmol/l

a. Interpret this ABG.

b. Calculate the Oxygenation Index (OI)

c. What is the indication of initiating iNO and ECMO based on OI?

Question 6

A late preterm baby 2.5 kg had respiratory distress soon after birth. Baby was intubated in delivery room. He had frothy secretions few hours after birth (Fig.5) . Chest radiograph is as shown in Fig. 6.

a. Identify the condition.

b. How do you differentiate a case of esophageal atresia with tracheoesophageal fistula (EA with TEF) from pure esophageal atresia on chest xray

c. Mention 2 antenatal ultrasound findings that can raise suspicion of esophageal atresia

d. Name few postoperative complications in such case

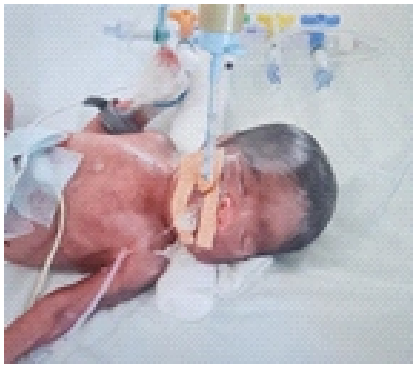


Fig. 5

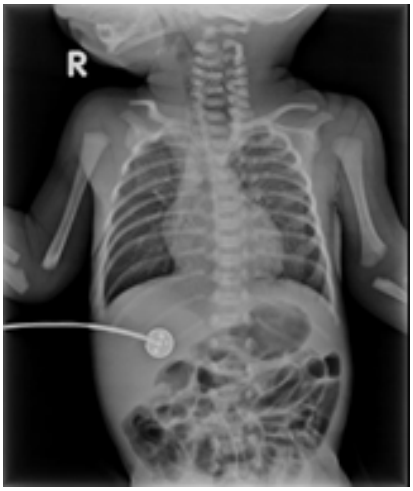


Fig. 6

Question 7

a. Identify the equipment shown in Fig.7.

b. What are the indications for using this?

c. What are its limitations?

d. What size is recommended to be used as per NRP guidelines 2020?

e. Above what weight is it recommended to be used according to recent NRP guidelines 2020?

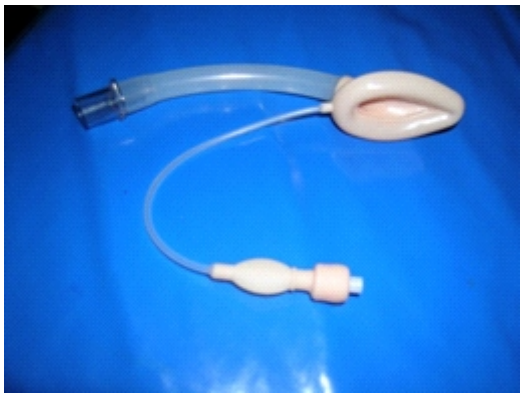


Fig. 7

Question 8

Below are the waveforms (Fig. 8) coming on ventilator screen of a term baby who has suddenly started desaturating.

a. Which kind of waveform is this (Scalar or loop)

b. Identify parameters on y axis in A,B,C waveforms

c. What is the abnormality depicted in B,C waveforms

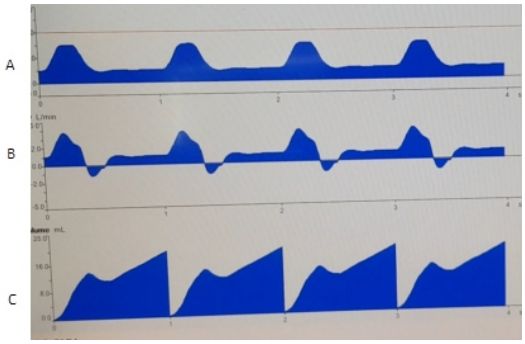


Fig. 8

Question 9

Below are the waveforms (Fig. 9) coming on ventilator screen of a term baby who has suddenly started desturating.

a. Which kind of waveform is this (Scalar or loop)

b. Identify A, B waveforms

c. What is the abnormality depicted in A,B waveforms

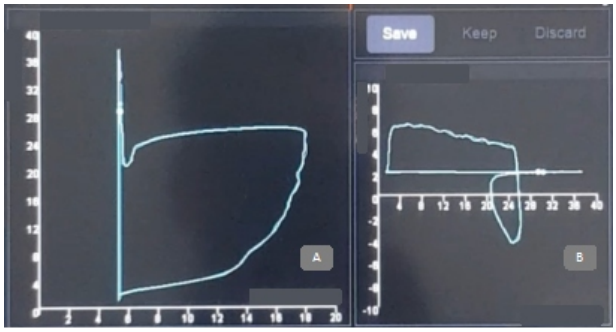


Fig. 9

Question 10

a. Identify the abnormality in this waveform. (Fig. 10)

b. What complications can occur due to this abnormality?

c. Identify the problem in given waveform (Fig. 11)

d. Time constant is product of ....

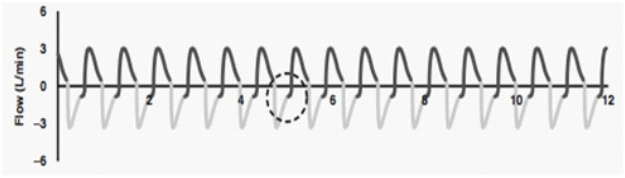


Fig. 10

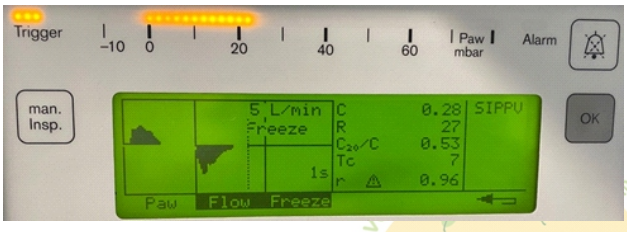


Fig. 11

Answer 1

a. Congenital Lobar Emphysema

b. HRCT thorax

c. Lobectomy

d. These babies may not tolerate PPV at time of anesthesia as it may lead to air trapping in the emphysematous lobe resulting in compression of normal lung leading to respiratory failure and cardiac arrest. In these emergency situations, surgeons should be prepared to do quick thoracotomy and deliver the emphysematous lung, leading to release in compression of the normal lung.

Answer 2.

a. It is a capnograph. It is used for continuous monitoring of paCO2.

b. A=Expiration; B=Inspiration

c. Tube dislodgement (1) and subsequent reintubation into trachea (2) ***OR***

Cardiopulmonary arrest (1) followed by resumption of spontaneous circulation (2) ***OR***

Equipment failure and apnea (1) followed by resumption of respiration (2).

Answer 3.

a. Oxgyen content (CaO2) = 1.37 * Hb% * spo2 + 0.003 * paO2

Oxygen is carried in blood through hemoglobin or it is present in dissolved form. 1 gm of HbF binds to 1.37 ml of oxygen if HbF is 100% saturated with oxygen.

So 1.37*Hb*Spo2 is the oxygen bound to Hb. 0.003*PaO2 is the dissolved fraction.

b. Baby A is more hypoxic as oxygen content of baby A is 7.62 ml O2/dl and oxygen content of baby B is 14.1 ml O2/dl

c. 16-22 ml O2/dl

Answer 4.

a. Congenital diaphragmatic hernia

b. Tip of endotracheal tube is between T3 and T4.

c. Lung to head ratio (LHR) = Lung area/ Head circumference measured on fetal ultrasound where,

Lung area = Longest Diameter of contralateral lung * Perpendicular diameter of contralateral lung.

LHR > 1.4 indicates good prognosis.

d. In congenital diaphragmatic hernia, initial stabilization is important . There is no emergency for surgery since bowel is lying in thorax from 16 weeks of gestation. It is important to manage coexisting pulmonary hypertension in such babies. Once baby is stable hemodynamically, surgery can be performed.

e. ALARA is " As low as is reasonably achievable" which means making every reasonable effort to maintain exposures to ionizing radiation as far below the dose limits as practical.

Answer 5.

a. Mixed respiratory and metabolic acidosis with hypoxemia.

b. Oxygenation index (OI) is calculated as MAP*FIO2*100/PaO2

In this case it is 31.8

c. Indication of starting inhaled Nitric oxide (iNO) if OI > 20 and ECMO if OI > 40

Answer 6.

a. Esophageal atresia with tracheoesophageal fistula

b. In EA with TEF there is gas in stomach on xray because of presence of fistula between trachea

and lower end of esophagus. However, in esophageal atresia without fistula, there is no gas in stomach (Fig.12)

a. Polyhydramnios and nonvisualized stomach on serial ultrasounds in second or third trimester should raise suspicion of esophageal atresia. Type C variety (EA with TEF) is difficult to pick antenatally since fistula allows fluid to flow into stomach.

b. Post operative complications include anastomotic leak (16 percent), esophageal stricture (35 percent), and recurrent fistulae (3 percent)

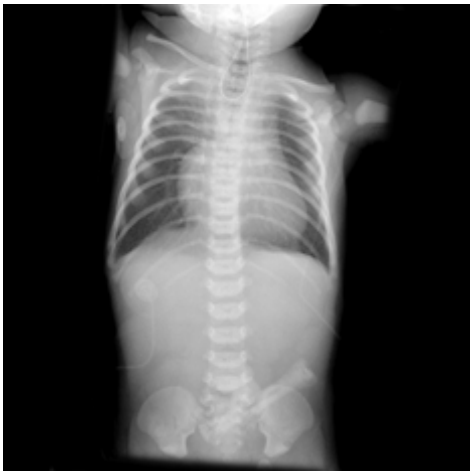


Fig. 12

Answer 7.

a. Laryngeal Mask Airway.

b. As a short-term alternative airway when attempts at face mask ventilation and intubation are unsuccessful.

c. Difficult to administer high pressures as air may leak through seal between pharynx and the mask; Difficult to administer medications; Can not be used in very small babies.

d. Size 1

e. Above 2 kg

Answer 8.

a. These are scalar waveforms as on x axis there is time and y axis there is one variable (either pressure or flow or volume). In loop waveforms, one variable is plotted against other (like pressure volume loop or Flow volume loop)

b. A – Pressure

B – Flow

C – Volume

c. Endotracheal leak is depicted in B,C. In B expiratory flows (waveform below x axis) are smaller than inspiratory flows. In C The expiratory volume is not returning to baseline)

For reference a normal scalar waveform is described below (Fig. 13)

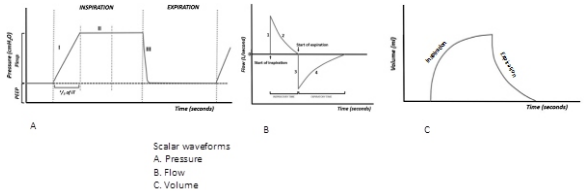


Fig. 13

Answer 9.

a. Loop waveform (one variable is plotted against other variable)

b. A. Pressure Volume loop, B. Flow Volume loop

c. Leak around endotracheal tube. In pressure volume loop expiratory limb of loop is not returning to the point where inspiration is starting on x axis. In case of no peritubal leak, there is no gap between expiratory end point and inspiratory starting point. In flow volume loop again the expiratory limb is not coming back to initial point of beginning of inspiration.

Below figure (Fig. 14) explains the normal pressure volume and flow volume loop waveforms when there is no leak.

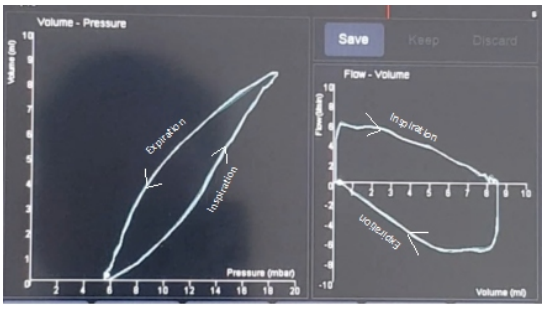


Fig. 14

Answer 10.

a. Air trapping as expiratory flow is less than the inspiratory flow, resulting in more gas entering than leaving the lung leading to generation of Auto PEEP

b. Auto PEEP may lead to pneumothorax

c. Fig. 11 describes long inspiratory time (Ti)

If Ti is adequate, there shouldn't be a gap between inspiratory and expiratory flow waveform as depicted in figure below. (Fig. 15)

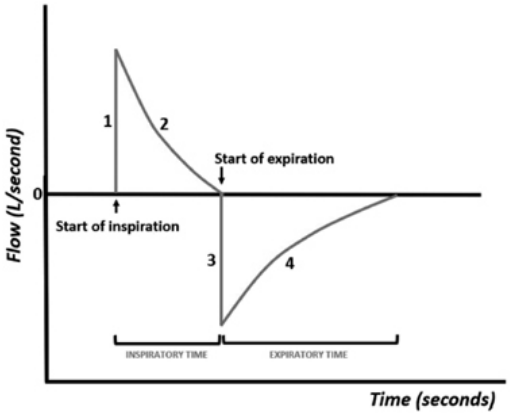


Fig. 15

d. Time constant is product of Compliance and Resistance.

Instructions for Authors

Review Article	**The article should be approximately 2-3 pages long with a word count of 2000-2500 words. Author should summarize key practice points at the end. Please include 5-6 references as suggested reading.**
Case Report	**This would be a summary of the case discussed in that months clinical meeting. Interesting cases even if not presented may also be submitted. It should include the clinical presentation and a brief discussion about the condition. Word count should be 1000-1500. Please include 2-3 references at the end.**
Journal Scan	**Some recent research paper of interest to pediatricians and neonatologists. The structure should include Introduction, Research question, Hypothesis, Methods, Results, Limitations and strengths of study, Reviewers comments. Word count should be approximately 1000 words. Please include 2-3 references if needed at the end.**
Picture of Month	**An interesting case related to neonatal practice. It should have a brief case history and a commentary, all fitting on one page along with the pictures.**
Image section	**Any interesting Xray, Ultrasound, CT or MRI of clinical interest. Brief clinical presentation and about the condition should be summarized on one page along with image.**
OSCE	**About 10-12 questions would be included in this section along with answers.**

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On behalf of committee, I request all members of NNF, Delhi to actively contribute to various sections of the newsletter.

You can contact us at following email addresses:

info@nnfdelhi.org
drgupta.naveen@gmail.com

Please call or Whats App at 9811758133