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Dear Esteemed Members,

Greetings from NNF Delhi!

It gives me a feeling of immense pleasure about the success of our Monthly Bulletin **NeoClips** (Neonatal Clinical Practice). This idea has emerged as a unique proposition from the minds of experienced neonatologists teaming up with young budding counterparts.

In this section we are covering a few important topics like HHHFNC and OSCE on neonatal jaundice. My sincere congratulations to the team which gave physical shape to the idea, chaired by Dr T. J. Antony, co-chaired by Dr Avneet Kaur with very dedicated hard- working Editor in chief Dr Naveen Gupta for their untiring efforts. My special thanks to Dr Swati Upadhyay for working hard on the OSCE section and Dr Sidharth Nayyar for the journal review.

With Best Regard

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 happiness to see the success of NNF Delhi monthly E- Bulletin which was launched in February 2022 with the name of '***NeoClips' (Neonatal Clinical Practice***). Every month it's getting better & better. And credit goes to the Chief editor Dr Naveen Gupta & their exceptional team. OSCE is being covered as system wise which would be very helpful for Neonatal fellow/Residents/Postgraduates. This month we have an interesting case, image & excellent review by Dr Ashish Jain.

We are requesting all the esteemed members to contribute to these E-bulletins. We shall be giving the due credits to all the contributors.

This month NNF Delhi is organizing Advance NRP Workshop (25th June 2022) at CNBC Hospital (Course Coordinator: Dr. Mamta Jajoo) and NEOMAP Workshop (26th June 2022) under the aegis of NNFI along with UNICEF

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

Chief Editor, Neo Clips

Dear Friends,

Greetings from the NeoClips team. We hope you enjoyed reading previous issues of NeoClips.

In this issue, we have come up with some interesting articles.

A premature baby with functional intestinal obstruction is covered as a case report.

Nasal CPAP is considered the gold standard for the treatment of respiratory distress of prematurity. However, nasal trauma is observed with CPAP prongs and masks in these tiny preemies. HHHFNC has come up in recent years to overcome these issues. The current status and recommendations about the use of HHHFNC have been covered in the review article.

Journal scan covers an interesting paper on the effect of treatment of clinical vs electrographic seizures.

The image section covers the exciting case of a newborn with facial dysmorphism and stippled epiphysis.

Picture of the month includes a case of the neonatal hairy pinna.

Neonatal jaundice is covered in the OSCE section of this month.

We hope that you will enjoy reading this issue. Please share your feedback with us. It will help us improve the journal.

Dr Naveen Parkash Gupta

A Case of Functional Intestinal Obstruction of Prematurity (FIOP)

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Index case is a preterm (31 weeks), appropriate for gestational age, male baby with birth weight of 1380 grams, second of diamniotic, dichorionic twin concieved through IVF conception, born to 43 years old G2L1A1 mother through emergency LSCS in view of preterm labour with fetal distress with preterm premature rupture of membranes at 31 weeks. The mother received antenatal steroids.

Baby cried immediately after birth, had respiratory distress in delivery room. Delivery room continuous positive airway pressure (CPAP) was started and baby was shifted to NICU on CPAP support. Baby was continued on CPAP in view of respiratory distress. Inj Piperacillin with Tazobactam were started after sending sepsis work up in view of history of preterm premature rupture of membranes (PPROM). Baby was shifted to heated humidified high flow nasal cannula (HHHFNC) at 18 hrs of life. Caffeine was started at 48 hours of life in view of repeated apneas. Initial sepsis workup was normal. Baby was weaned to room air at 48 hrs of life.

The baby developed abdominal distension and bilious vomiting at 24 hours of life. X-ray abdomen was suggestive of dilated bowel loops and there was no gas in rectum (Fig1). Repeat Xray abdomen at 48 hours of life showed dilated bowel loops and rectal gas shadow was seen (Figure 2).

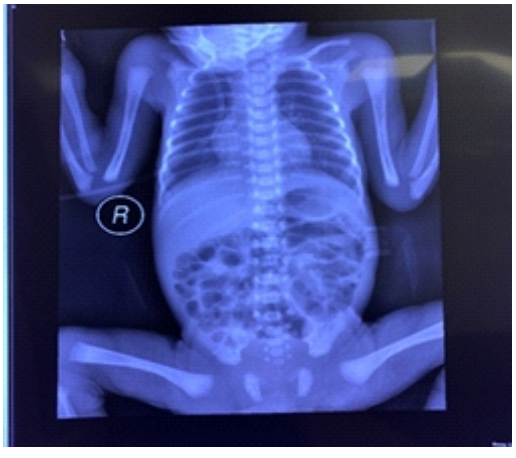

Fig 1. X ray at 24 hours of life

Abdominal distension persisted. The baby continued to have bilious aspirates and bowel loops were visible on clinical examination with no tenderness on palpation.

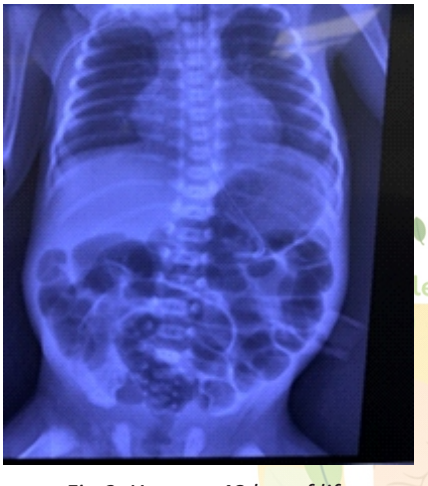

Fig 2. X ray at 48 hrs of life

Possibility of sepsis/ meconium plug/ hypomotility disorder of prematurity/ hirschsprung disease or

colonic aganglionosis was kept. Baby was kept nil per orally and parenteral nutrition was started. Repeat sepsis screen and electrolytes were within normal range. Baby passed speck of meconium post rectal wash. Gastrograffin enema was done which didn't show signs of Hirschspurng or aganglionosis (Figure 3).

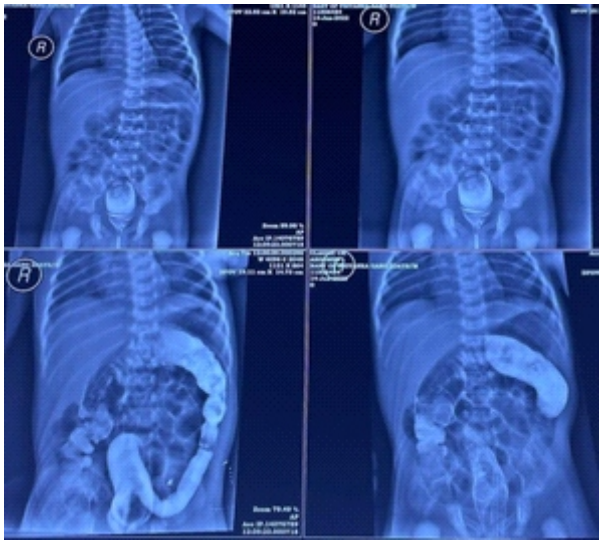

Fig 3. Gastrograffin study at 4th day of life

Pediatric surgery consult was taken and baby was started on repeated rectal washes. Post rectal washes, distension and bilious aspirates reduced. Provisional diagnosis of Hypomotilility disorder of prematurity was kept. Rectal washes were continued for 4 days. Sepsis work up with blood culture and electrolytes were repeated three times and they were normal. Abdominal distension gradually reduced with passage of meconium following rectal stimulation. Baby was started on feeds on 7th day of life, and was increased gradually.

Thereafter baby's course in NICU remained uneventful and he stayed 2 weeks more for weight gain. Caffeine was stopped at 34 weeks PMA. At the time of discharge baby was on full oral and breast feeds. He was gaining weight and was passing stools without stimulation. Baby was discharged with weight of 1.530 kg.

At 1 month follow up baby remained stable, passing stool regularly with weight of 1.980kg

Discussion

Functional intestinal obstruction of pretmaturity (FIOP), previously known as hypomotility disorder of prematurity is characterised by a partial or complete failure of meconium evacuation due to hypomotility of the immature bowel.

Peristaltic function in the immature bowel of preterm infants is disorganised. The peristaltic pressure at 25 weeks of gestational age is estimated to be about half in the term neonates[1,2]. The impaired GI motility and associated increased viscosity of meconium results in meconium impaction at the terminal ileum and sometimes colon leading to obstruction. This presents as feature of intestinal obstruction.

It usually presents typically within first 2 weeks of life with most cases reported at around day 10 of life [3,4,5]. In our case the features were noted within 24 hours of admission.

Neonates <1500gms tend to present commonly in 2nd week of life & those >1500gms are often diagnosed within 1st week of life [4].

VLBW and ELBW preterm infants, however suffer a pathological form of this disorder and experience severe consequences which include clinical bowel obstruction and functional intestinal perforation (FIP) or also termed as spontaneous intestinal perforation (SIP).

Maternal & Obstetric factors which may increase the risk of FIOP are smoking, hypertension, magnesium sulphate use, diabetes, prenatal steroids, placenta abruption, caesarean section, preterm pre-labour rupture of membrane, oligohydramnios, opioid administration [6,7,8,9,10].

On examination there will be abdominal distension associated with visible and/or palpable bowel loops, feed intolerance. As opposed to NEC, features of peritonitis like tenderness or erythema are absent and they are usually haemodynamically stable with unremarkable inflammatory markers.

Diagnosis:

- Plain radiographs typically show features of lower

intestinal obstruction with multiple dilated loops. Pneumatosis, fixed bowel loops, and portal gas which are characteristics of NEC are absent.

- Contrast enema is both diagnostic and therapeutic
- Ultrasound scan shows hypoechoic meconium filled bowel loops with proximal distension.

Treatment:

- Rectal stimulation with glycerine chips is frequently used to encourage meconium passage
- Rectal washouts with warm saline about 10ml/kg

Table 1 showing clinical, radiological and operative features of FIOP[11].

	Clinical signs	Radiological findings	Operative findings
1	Abdominal distension with or without visible or palpable bowel loops	Generalised dilated bowel loops without air-fluid levels	Dilated small bowel containing meconium pellets
2	Failure to pass meconium or passing only smears of meconium usually with rectal stimulation	Microcolon ex-tending to distal terminal ileum on contrast	Small or collapsed colon with palpable thick meconium
3	Feed intolerance with or without bilious nasogastric aspirate	Meconium plugs in the colon or terminal ileum on contrast study	Change in calibre at terminal ileum but bowel lumen is in continuity
4	Haemodynamically stable except in perforation.	Pneumoperitoneum in the advanced stage.	Localised perforation usually at the terminal ileum.
5	Absence of signs of peritonitis like tenderness, oedema, and erythema	Absence of characteristic signs of NEC like pneumatosis, portal gas, and fixed loop	Bowel looks healthy without inflammatory or necrotic changes

is other alternative and could be repeated up to 2-4 times per day.

- Contrast therapy with Gastrograffin enema: its high osmolality allows it to draw fluid into bowel lumen and soften the inspissated meconium. This procedure should ideally take place under fluoroscopic guidance to monitor contrast flow.
- N- acetylcysteine exerts a mucolytic effect by breaking disulphide bonds in mucoproteins hence reducing viscosity. It can be administered via NGT, rectally or through stoma.
- Surgery is indicated for failed conservative management or perforation which can occur rarely

Monitoring:

Active evaluation of response on a daily basis when FIOP is managed conservatively is very important.

- Evaluation of response to treatment: means the passage of a good amount of meconium with reduction of abdominal distension clinically and/or resolution of dilated bowel loops radiologically[12]. Successful treatment is achieved when there is complete meconium evacuation as evidenced by changing stools.

- Identify and management of complications: Fluid and electrolytes abnormalities occurs with Gastrografin and NAC use. Gastrografin enema can cause hypovolaemia as it draws fluid into the gastrointestinal tract lumen[13]. Hypernatremia and hepatic derangement have been reported with NAC[14,15]

Differential diagnosis:

Cystic Fibrosis and Hirschsprung's disease are often suspected as underlying pathologies in pre-term infants presenting with functional intestinal obstruction.

Conclusion:

Functional intestinal obstruction of prematurity contributes significantly to the morbidity and mortality of ELBW and VLBW preterm infants. This case summarises the characteristic clinical and radiological features of FIOP as well as its management options. Surgery is reserved for failed conservative management or perforation

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Heated Humidified High Flow Nasal Cannula (HHHFNC)

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Background

CPAP (Continuous Positive Airway Pressure) is well-established as a mainstay of Non-Invasive Ventilation for many years, but the need for a similar alternative was always perceived. This was because the CPAP therapy is associated with a significant incidence of nasal injury (40% to 80%) in various studies, interfaces used in CPAP are bulky for the tiny babies [where it is most needed], and the application of the interfaces need regular training and astute monitoring for the optimal results. Moreover, the complex circuit requirements like that of a ventilator, CPAP pneumothorax, CPAP Belly and Infection are other important concerns.

Hence, HHHFNC evolved as an easy and user-friendly alternative to CPAP, that proved to be gentler on noses and had very simple usability with efficacy similar to CPAP in a significant proportion of the babies.

What is HHHFNC:

High flow nasal cannulae (HFNC) unlike the CPAP prongs are smaller (Less than 1 cm in length), thinner, tapered cannulae that do not snugly fit the nares allowing expiration. The cannulae occupy only up to 50% of the nostrils without occluding them. The oxygen or blended oxygen and air at flow rates of > 1 L/min is delivered through them. One should understand the difference between the HFNC and the LFNC (low flow nasal cannulae) that are commonly used. Oxygen delivered by 'low flow' nasal cannulae (LFNC) typically refers to the use of flow rates of less than or equal to 1 L/minute. It uses unblended, unheated and non-humidified gas (that is 100% oxygen). LFNC are commonly used in convalescing preterm infants, often with chronic lung disease, and does not provide significant support to the infant's pulmonary function (apart from the provision of oxygen). In contrast, 'high flow' nasal cannulae (HFNC) have been used for administration of oxygen or blended oxygen and air to newborn infants via nasal cannulae at higher flow rates. The use of high flow rates in preterm infants may provide positive end-expiratory pressure (PEEP). In HFNC systems, circuit flow is adjusted according to clinical effect and, although a pressure relief valve is often used, the circuit pressure cannot be routinely measured.

Mechanism of action & advantages of HHHFNC

The HHHFNC may be beneficial to the neonate with respiratory distress syndrome and pulmonary ailment by the virtue of the following mechanisms.

1. It provides a warmed and humidified flow of air and/or air-oxygen mixture (via a blender) to the neonate. This increases the clearance of the secretions and prevents broncho-constriction eventually leading to better comfort and tolerance of respiratory support.
2. The flow of the gas washes out end expiratory gas in oropharynx and nasopharynx thus reducing the dead space and improving minute ventilation. This leads to a reduction in the inspiratory effort and the work of breathing resulting in reduced diaphragmatic load and injury.
3. A nasal inspiratory flow at a higher rate reduces the nasal resistance, increases the dynamic

compliance stabilizes the airways,which results in early weaning leading to a reduction in ventilator induced lung injury.(VILI)

4. The generation of the positive pressure by the higher flows helps in the recruitment of atelectatic lung regions and improves oxygenation.

5. The HHHFNC also has the advantage of reduced gastric distension and better nutritional care, as sucking feeds and Kangaroo care are more easily attempted with HHHF than CPAP.

What are the perceived limitations of HHHFNC?

- Pressure is highly variable and cannot be measured or regulated
- There are no alarms with most HFNC systems
- Distending airway pressure generated by HFNC may lead to lung injury (overexpansion or atelectasis) and contribute to the development of BPD in infants
- Inability to select properly sized prongs could increase the risk for VILI and gastric insufflation

In what situations is HHHFNC used:

HHHFNC is utilized in NICU for infants with mild respiratory dysfunction. The different scenarios, the neonatologists are using HHHFNC currently are as follows. However, the evidence for the use is existent only in few situations (marked as italics)

1. Neonates with bronchopulmonary dysplasia (to assist weaning from FiO2).
2. Slow n-CPAP weaners
3. Neonates with an FiO2 requirement of <0.3
4. Neonates 34-36 weeks corrected gestational age as primary support
5. Neonates not deemed stable enough to be trialled self-ventilating in air
6. *Respiratory support post extubation*
7. Apnea of prematurity
8. Post-op respiratory support.
9. *Babies with nasal trauma from NCPAP*
10. Newer indications like; During intubation (recent), stabilization in delivery room
11. Anesthetic Induction; THRIVE: (Trans Nasal Humidified Rapid insufflation ventilatory Exchange)

In what situations the HHHFNC should be avoided:

1. Blocked nasal passage (choanal atresia)
2. Trauma/ surgery to nasopharynx
3. Smaller babies with respiratory distress as the primary therapy
4. Severe cardiovascular instability

Setting up of HHHFNC (Steps)

Placement of the Machine: Before beginning, we must check the integrity of the equipment and accessories and place the unit on a low shelf below the level of the head of the neonate. We must then install the water chamber and fill it up to the designated mark with distilled water. Thereafter the presterilized heated breathing tube is connected to the designated spot on the unit and locked as per design.

Select appropriate size nasal cannula:

One should select the appropriate size of the nasal cannula. One may refer to the product details of the machine that is being used. All the companies provide a chart with the recommended sizes for the term and the preterm babies (Figure 1). The size should be such that, prongs must be smaller than 50% of patient's nares (Figure 2).

Application of the Nasal Cannula

Remove the paper protector from the nasal aspect of the wiggle pads (base tape). Ensure the baby's skin is

F&P Optiflow™ junior

Nasal Cannula

	OPT312 PREMATURE	OPT314 NEONATAL	OPT316 INFANT	OPT318 PEDIATRIC
PERFORMANCE SPECS				
Max Flow Rate (L/Min)	8	8	20	25
Cannula Weight	9 g	9 g	13 g	13 g
Approximate Age Range	< 32 weeks	27 weeks - 6 months	37 weeks - 3.5 years	1 year - 6 years
Approximate Weight Range	< 2 kg	1-8 kg	3-15 kg	12-22 kg
Compatible with	Unique Swivel connection RT330	Unique Swivel connection RT330	Unique Swivel connection RT330 & 900PT531	Unique Swivel connection RT330 & 900PT531
Compatible Humidifier	MR850	MR850	MR850, Airvo 2	MR850, Airvo 2

Fig. 1 : Different types of Optiflow nasal cannula

Fig. 2 : The cannula size should be 50% or less of the internal nare diameter

dry and check the integrity of the nasal septum. Insert one prong into each nostril so that the bridge is just touching the septum. Holding the cannula/wiggle pad wings, apply slight tension so as to straighten the bridge of the cannula then fix the nasal aspects of the wiggle pads onto the baby's cheeks. On one side lift the outer edge of the wing and holding the paper tab remove the paper and press the wiggle pad into place. Do the same on the other side. (Fig 2). Once the cannula is applied check that the bridge has naturally moved 2mm away from the septum. Be sure that the baby, particularly baby's ears are not lying on the

cannula's coil tubing. It is recommended to change the cannula and circuit every 7 days

Connection of the Cannula to the tubing:

The swivel connector of the HF Nasal Cannula may be connected (clicked into) to the blue tubing before application. This allows humidified high flow oxygen/air to be given while the cannula is being applied.

HHHFNC Delivery Systems:

There are 2 kinds of delivery systems available for HHHFNC.

A system similar to bubble CPAP where you should have a compressed source of air and oxygen, blender, humidifier, and circuit meant for delivering high flow and appropriate interphase (Figure 3,4,5).

Airvo – 2 – Airvo 2 generates a high flow of warm and humidified gases which can be delivered to neonates through a variety of nasal interphases (Figure 4,5).

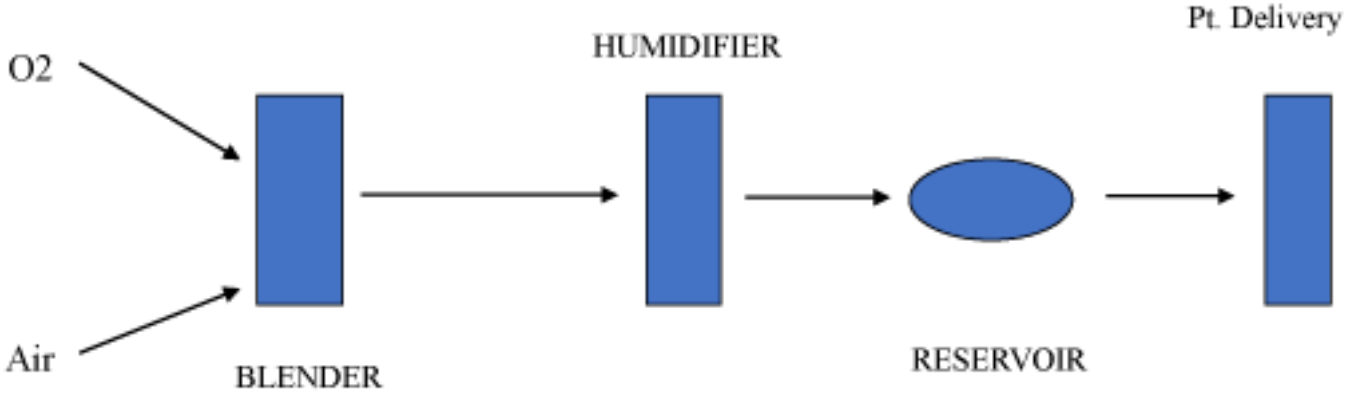

Fig.3 : Basic set up of HHHFNC

Fig. 4 : Setup for HHHFNC

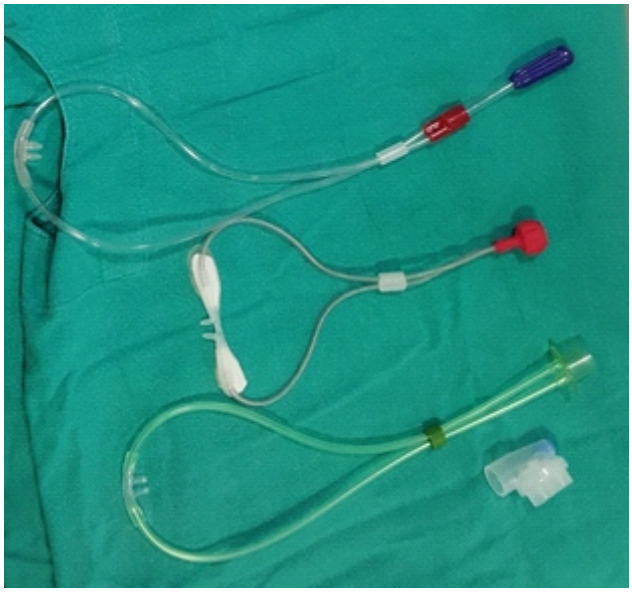

Fig. 5 : Interphases for HHHFNC

Nasal interphase:

Various nasal cannulas are available to deliver HHHFNC. Sizes of cannula varies as per weight of baby.

Recommended Settings (Initiation / Maintenance/ Weaning & discontinuation)

- Prongs: Must be smaller than 50% of patient's nares (tight fit of nasal cannulae may generate pressure of 6-10cm H2O at flow as low as 1,5-2 L/min)
- Flow 4-8 L/min (lower flow 5-6 L/min may be sufficient for smaller babies.)
- Fio2 <40%
- Operating temperature set at 34 - 35º C for flow rate < 5 L/min and 36 - 38º C at > 5 L/min (to prevent condensation- manufacturer's recommendation)
- Use appropriately sized nasal cannula. The following is a guide but the diameters of nares may vary.

Weight	Cannula type	Outer diameter
< 1.4 kg	Premature	0.14 cm
1.4 – 2.6 kg	Neonatal	0.19 cm
>2.6 kg	Infant	0.27 cm

Maintenance of HHHFNC

1. Do not use a chin strap with High flow. Active mouth closure is not required.
2. Watch for “rain-out" as this can cause a lavage to the infant resulting in apnea.
3. The baby may be nursed prone, skin to skin (kangaroo cuddle), supine or side lying.
4. All infants on high flow should have a nasogastric tube in place
5. Infants may be offered breast or bottle feeds whilst on HHHFNC.

Monitoring of a baby on HHHFNC

Continuous monitoring of Temperature, heart rate, respiratory rate and SaO2

Nasal and/or oro-pharyngeal suction may be necessary if baby has a lot of secretions.

Blood gases if on supplemental oxygen or on clinical grounds

Weaning

It may not be possible to wean flow rate if FiO2 > 0.3

Attempt to reduce by 1 L/min 24 hourly if FiO2 < 0.25-0.3 in babies >1.5Kg

Attempt to reduce by 0.5L/min 12 hourly if FiO2 < 0.25-0.3 in babies < 1.5 Kg

Attempt to stop if requiring 2.0 L/min or less

Clinical instability, increased work of breathing or significant increase in FiO2 consider pneumothorax

Simplified weaning

- 1 L/min every 24h if FiO2 < 30%
- 1 L/min every 12h if FiO2 = 21%

Table 1. Consented guide to initiation and alteration of nasal high flow therapy in neonates (9) .

Current weight	Initiation of flow	Escalation of flow	Weaning flow	When to discontinue
<1500 grams	4-6 lpm	FIO2 > 35% or RR, WOB	by 0.5 lpm q 12-24 hrly	flow = weight (kg)
1500-3000 grams	5-7 lpm	FIO2 > 35% or RR, WOB	by 0.5 – 1 lpm q 6-12 hrly	2 lpm
More than 3000 grams	6-8 lpm	FIO2 > 35% or RR, WOB	by 0.5 – 1 lpm as indicated	2 lpm
Comments	Max flow 8 lpm	by 1-2 lpm q 15-20 min	Typically slower wean with BPD	

If cycling of HHHFNC and CPAP is being utilized:

- HHHFNC should be administered during the day allowing for increased parental interaction and sucking feed attempts. CPAP should continue at night time.
- CPAP and HHHFNC have different tubing and pressure relief valves (CPAP white/HHHFNC blue), so the entire system needs to be alternated.
- The same humidifier base may be utilized.

Failure of HHHFNC

If the baby is requiring FiO2 > 0.5 or has CO2 retention, acidosis or apnea s/he is likely to need alternative support.

Complications

1. Potential for asynchrony in breathing may result in the infant becoming tired over long periods; therefore, good assessment of work of breathing is required.
2. Potential for nasal erosion (although less than with nasal CPAP) remains.
3. There is some concern about unknown end distending pressure and varied results gained in research studies; therefore, ensure that the prongs do not seal the nares and reduce flow as able.
4. "Rainout" in circuit resulting in lavage and aponea. Use designated circuit (RT330) and check for "rainout" regularly, draining the circuit as required.

Cleaning and maintenance:

It is important to carefully follow manufacturer's instructions to keep the device clean. Single-patient use accessories must be disposed of between patients to prevent cross-contamination. The interfaces can be washed in warm water with mild dishwashing detergent added and rinsed in drinking quality water. Additionally standard aseptic techniques to minimize contamination should be followed when handling the unit and accessories. This includes proper hand-washing, avoiding hand contact with connection ports, safe disposal of the used consumables and suitable storage of the unit after cleaning and disinfection. The accessories and filters must be changed per schedule and regular servicing done to keep the devices safe and extend the life of consumables.

Conclusion:

HFNC is an important part of neonatal respiratory care and has role in preterm > 28 weeks GA in postintubation setting as well as can be applied successfully as primary support, though it is less effective than CPAP which should be readily available as rescue therapy to prevent increased risk of intubation. Further research into its use in extremely preterm infants, approach to assess surfactant necessity and optimal pathway to weaning will improve its usability and benefits.

Key messages

1. HHHFNC should be given at flow rates between 2 and 8 L/min in term and most preterm infants.

2. No more than 50% of the area of the aperture of the nares should be occluded.
3. Gas conditioning with warmth and humidity is important.
4. HHHFNC can be used as means of respiratory support in post-extubation state and in babies having nasal trauma on CPAP

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Neonatal Hairy Pinna (Hypertrichosis pinnae auris)

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A newborn baby girl, gestational age of 38 weeks and birthweight 4200 grams (> 97th percentile), was referred to our centre in view of respiratory distress at birth. Mother had pre-gestational diabetes mellitus. She had infrequent follow-ups with poorly controlled blood sugar levels during pregnancy and a HbA1c of 9.3% at 12 weeks of gestation.

Baby was started on non-invasive ventilation in the neonatal intensive care unit (NICU) and respiratory distress improved in 24 hours. The baby was noted to have extensive hypertrichosis of the pinnae **(Figure 1),** while the rest of the body was relatively lanugo free. She had doll-like facies. There were no other apparent features of dysmorphology. Echocardiography revealed mild biventricular hypertrophy without any signs of hypertrophic obstructive cardiomyopathy (HOCM). Electrocardiography and cranial ultrasonography were normal. The baby had transient asymptomatic hypoglycemia for which intravenous fluids were administered and feeds were continued. Baby was euglycemic and improved in next 48 hours. Rest of the laboratory parameters including hematocrit, calcium and bilirubin were unremarkable. Screening for congenital hypothyroidism was done at 48 hours of life which revealed a normal TSH for age. Genetic analysis was denied by the parents.

Discussion:

Hypertrichosis, defined as an increase in the non-androgen-modulated hair on the body, may be congenital or acquired, localised or generalised. Our case presentation includes a rather unusual but potentially pathognomonic feature, localized hypertrichosis of ear pinnae, with sparing of the rest of body skin. Its recognition may be a useful clue pointing to gestational diabetes mellitus (GDM) in poorly followed pregnancies. Association between neonatal hairy pinna and maternal diabetes has been reported infrequently in the past. The neonates described in these reports had localized hairy pinna without hypertrichosis of the body. The degree of hirsutism has traditionally been linked to the adequacy of diabetic control in the mother. Hypertrichosis pinnae may also be hereditary, and a Y-linked inheritance has been suggested.

An association between diffuse hypertrichosis, maternal diabetes mellitus and congenital hypothyroidism has been reported. Diffuse neonatal lanugo has been reported more frequently especially in Indian population. This is a self-limited entity and the pinnae are relatively spared in them. Androgen mediated hypertrichosis of neonates can also happen secondary to exposure to maternal androgens due to conditions like polycystic ovarian syndrome. In most of these conditions, the excessive hair fall off during infancy without any specific treatment.

Localized hypertrichosis of the ear pinnae may represent a potential marker of infant of diabetic mother and thereby alert physicians to suspect other associated conditions.

Fig 1: Localised hypertrichosis of the left ear pinna

A newborn with depressed nose and stippled epiphysis

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Clinical Presentation

A male infant weighing 1900 grams was born at 38 weeks gestation to a second gravida with Rheumatic Heart Disease, taking warfarin since last 6 years with no change in medication during pregnancy. The baby was small for date and had nasal hypoplasia with depressed nasal bridge (Figure 1). USG cranium revealed ventriculomegaly and Xray revealed stippled epiphyses (Figure 2).

Suspicion: Warfarin Embryopathy (Di Sala Syndrome)

Differential Diagnosis: Epiphyseal stippling can also be seen in

a. Chondrodysplasia punctata
b. Fetal alcohol syndrome
c. Hypothyroidism
d. Acrodysostosis.

Key information regarding Warfarin Embryopathy:

a. Warfarin, a low-molecular weight oral anticoagulant (about 1000 Daltons) easily crosses the placenta and blocks the recirculation of vitamin K, interferes in vitamin K reductase activity which leads to a decrease in vitamin K-dependent mineralisation inhibitors (osteocalcin and Gla matrix protein) in cartilage resulting in ectopic calcium deposits in the epiphysis and epiphysial stippling.
b. The greatest susceptibility to warfarin embryopathy is between 6th and 9th weeks of the gestational period
c. Features include facial dysmorphism (hypoplastic nasal bone and depressed nasal bridge), upper airway obstruction (choanal atresia, laryngomalacia), skeletal changes (short stature, brachydactyly, stippled epiphyses, hypoplastic nails) and CNS abnormalities (ventriculomegaly, intellectual disability, optic atrophy, deafness).

Prognosis: After reviewing 418 pregnancies with maternal ingestion of warfarin, live birth occured in 83.7%, spontaneous abortion in 8.6%, stillbirths in 8.4%. premature deliveries in 4.6% and neonatal death occurred in 2.9% cases.

Prevention: Women on lifelong warfarin therapy should strictly avoid conception or switch over to high-molecular weight anticoagulant (heparin-20 000 Dalton) throughout pregnancy.

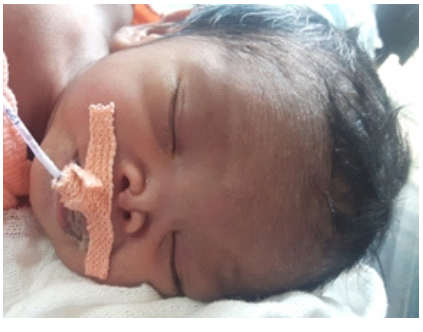

Fig 1 : Facial dysmorphism

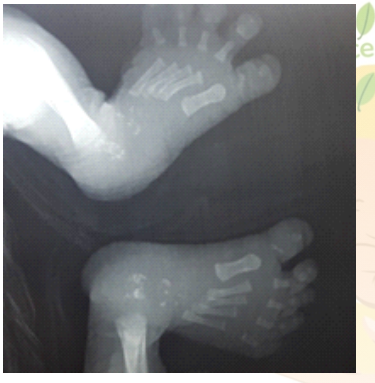

Fig 2 : Xray both feet showing stippled epiphysis

Journal Scan

JAMA Network Open

Original Investigation | Pediatrics

Effect of Treatment of Clinical Seizures vs Electrographic Seizures in Full-Term and Near-Term Neonates A Randomized Clinical Trial

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Research Question- In term or near-term neonates with seizures (P), does treatment of all electrographic and clinical seizures (I) compared to treatment of only clinical seizures (C) improve survival free of disability (O) at 2 years of age (T).

Hypothesis

Population	**Neonates more than 35 weeks' gestational age with neonatal seizures in < 48 hours after birth.**
Intervention	**Treatment of all electrographic and clinical seizures**
Control	**Treatment of clinical seizures alone (aEEG covered)**
Outcome	**Neurodevelopmental assessments at 2 years of age**

METHODS

- **Design:** Randomized controlled trial
- **Allocation:** Randomization was stratified by site and diagnosis using computer-generated block randomization with variable block sizes
- **Blinding:** Neither clinicians nor parents could be blinded to study
- **Follow-up period:** 2 years
- **Setting:** 13 participating centers across 3 countries (Australia, Austria, and Singapore) between March 2012 and February 2016
- **Patients:** 212 infants

Inclusion criteria: Neonates more than 35 weeks' gestational age who were less than 48 hours of age who had a diagnosis of either:

- Neonatal encephalopathy including coma, stupor, or depressed mental state
- HIE with at least two of following: (1) apgar score less than 5 at 5 minutes of birth, (2) cord blood gas or arterial blood gas within 1 hour of birth with pH of less than 7.1 or base excess less than -12, or (3) need for ongoing respiratory support at 10 minutes after birth
- Suspected neonatal seizures from any cause

Exclusion criteria: Diagnosis of nonconvulsive status epilepticus or cerebral dysgenesis subsequently diagnosed on neuroimaging

Seizures were treated according to a standard algorithm with phenobarbital as first-line treatment and phenytoin as second-line treatment.

Primary Outcome: Neurodevelopmental assessments at 2 years of age by blinded assessors using Bayley Scales of Neurodevelopment, 3rd edition

Analysis and Sample Size:

Researchers anticipated 40% background rate of death or neurodisability and approximately 50% of included neonates will have seizures due to HIE. Researchers calculated sample size based on a 12% reduction in death or severe disability anticipated with the electrographic seizure treatment group. With 80% power and two-sided 0.05 significance, a goal of 260 neonates in each group was calculated to determine a significant difference in outcome. The trial was concluded early due to a lack of equipoise at some sites as the trial progressed so that 212 infants were randomized.

Patient follow-up: 172 infants (81%) with follow-up data analyzed for primary outcome

Results

Primary Outcome (Total N = 172) No significant difference in odds of death or disability in neonates with clinical and electrographic seizures treated compared to those with only clinical seizures treated (44% vs. 31%, OR 1.83, 95% CI 0.96-3.49)

Secondary Outcomes Cognitive scores were lower in 80 survivors in electrographic and clincial seizure group as compared to 82 survivors in clinical seizure group (97.4 vs 103.8; MD -6.5; 95%CI -1.2 to -11.8; p=0.02)

Conclusion - In a group of neonates with acute symptomatic seizures, treatment of electrographic and clinical seizures with currently used anticonvulsants did not significantly reduce the risk of death or disability at 2 years compared to treatment of only clinical seizures.

Reviewers Comments The present trial evaluated whether aggressive treatment of electrographic seizures in addition to clinical seizures improved neurodevelopmental outcomes.[1] They found no difference in death or severe disability at 2 years. These results remained consistent even after adjusting for seizure burden and HIE.

The WHO 2011 recommendations on the treatment of neonatal seizures recommend treatment of all clinical and electrographic seizures.[2] These were based on the best available evidence at the time, but there has always been a concern regarding safety of usage of AEDs for a long term in neonates as they are neurotoxic.[3-5] Even with access to cEEG monitoring, neonatal seizures are frequent, difficult to recognise and difficult to treat[6] leading onto inappropriate usage of AEDs. Consensus on the timing of administration of AEDs is also unclear as although there is evidence that treatment of neonatal seizures may be time-critical, but more research is needed to confirm this.[7] Thus a lot of research is needed in this context. The present study by Hunt et al tried to evaluate the safety of AEDs. The study failed to make definitive conclusion on long term neurological outcomes due to early termination, but it does suggest that aggressive treatment of electrographic seizures will not help in achieving any additional long term benefits. The research questions still unanswered are the AED of first choice (phenobarbitone vs levetiracetam), timing of first dose, duration of treatment, timing to stop and effectiveness and safety of newer AEDs.

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Question 1.

24 years old G2A1 mother with "O Negative" blood group has been following up in your associated antenatal clinic. The husband's blood group is "B positive". There is a history of one spontaneous abortion 2 years back. Maternal ICT at 12 weeks of pregnancy was negative. Now she is 24 weeks gestation and ICT has become positive with anti-D titers 1:64.

a. What is the anticipated risk to the baby?

b. What is the next step in management?

c. Would you administer Anti-D to this mother?

d. What would be the indication for cordocentesis in this case?

e. What are the criteria for intrauterine transfusion in such cases? What are the methods for intrauterine transfusion?

f. What investigations would you perform on the baby after birth?

g. This mother comes to you in the next pregnancy again and anti-D titers are 1:1028 at 18 weeks of pregnancy. How would you proceed?

Question 2.

A 38-week male infant weighing 3200 g was born after an uncomplicated pregnancy. The mother is a 35-year-old primipara with A Rh-positive blood group. The baby's course in the hospital was uneventful and the baby was roomed in with his mother. Although the mother needed significant help in establishing effective breastfeeding, the baby was exclusively breastfed at discharge and thereafter. Prior to discharge, jaundice was noted at the age of 48 hours. The total serum bilirubin level was 10.5 mg/dl.

a. What are the major risk factors for the development of severe hyperbilirubinemia in infants more than 35 weeks of gestation?

b. What are the risk factors for neurotoxicity in babies with hyperbilirubinemia?

c. Which chart would you use pre-discharge to designate the risk of subsequent severe hyperbilirubinemia?

d. What is the risk of developing subsequent severe hyperbilirubinemia in this baby? What would be your follow up recommendation based on that?

e. The baby was discharged at the age of 48 hours and comes to you 2 days later with marked jaundice and icterus up to soles. The results of his physical examination are otherwise normal, but his weight is now 2800 g. Mother reports nipple crack and breast engorgement. His total serum bilirubin level is 19.5 mg/dl and his conjugated (direct) bilirubin level 0.6 mg/dl. There is no pallor or splenomegaly. The complete blood count and peripheral-blood smear are normal. The infant has type A Rh-positive blood. What would be your next line of management?

f. What score would you use to assess the neurological status of this baby? What are its components? How do you interpret the score?

g. What is the possible reason for hyperbilirubinemia in this baby?

Question 3.

You have started intensive phototherapy for the above-mentioned baby in room with mother. You repeat a serum bilirubin after 6 hours, but it has not dropped and is same. You visit the room and find that the baby is lying on bed and phototherapy unit is

placed high above and is fixed at maximum possible distance.

a. What corrective action would you take in this baby?

b. What is the mechanism of action of phototherapy?

c. What factors affect the dose and efficacy of phototherapy?

d. What are the criteria for defining intensive phototherapy?

e. What is the irradiance footprint of phototherapy?

f. What are the advantages of LED phototherapy over conventional phototherapy?

g. How frequently would you monitor serum bilirubin values in a baby receiving phototherapy?

h. What are the criteria for stopping phototherapy and checking rebound serum bilirubin values?

Question 4.

A 5-day old male newborn is admitted to with severe jaundice. He is a first-born child, via cesarean delivery at a gestational age of 39+6 weeks, with APGAR scores of 9 at 1 and 5 min after birth. The blood types of both the baby and the mother are B positive. Maternal ICT was negative. Total serum bilirubin (TSB) is reported as 24.5 mg/dl. There is no cephalhematoma, bruise or sub galeal bleed. There is no encephalopathy. Baby is otherwise well to examine. There is no significant weight loss. The glucose-6-phosphate dehydrogenase deficiency screen and direct Coombs test are negative. Blood examination shows hemoglobin level is 12.2 g/dL with a reticulocyte of 10%. There is family history of recurrent blood transfusion and gallstones in father and paternal uncle. You have started intensive phototherapy for this baby while preparing for exchange transfusion.

a. What would be your differential diagnosis in this baby?

b. What are the diagnostic criteria for Hereditary Spherocytosis (HS)?

c. What is the spectrum of clinical features of HS in neonatal period?

d. What investigation would you advise to confirm the diagnosis of HS?

e. What is the most common genetic defect involved in HS?

f. What are the short- and long-term complications associated with HS?

g. What are the treatment modalities for HS? What is the definitive treatment and when should it be offered?

Question 5.

You are following up a 3-day old baby in your OPD. The baby was born at 38 weeks with birth weight of 2.9 kg. Mother is O positive and baby A positive. There was no jaundice in first 24 hours. Baby is exclusively breast fed and was discharged at 40 hours of life with transcutaneous bilirubin (TCB) of 6.5 mg/dl. TCB in your OPD at follow up at 72 hours is 15.5 mg/dl. Baby is otherwise well to examine without any significant weight loss.

a. What would be your next step?

b. What is the principle behind TCB?

c. In which conditions would you avoid using TCB?

d. What are the indications for doing serum bilirubin while monitoring a baby with TCB?

e. Up to what age can you do TCB in neonates?

f. What are the common devices available?

g. What is the latest upgrade in TCB machine and how is it different from previous version in terms of intended use?

h. Name one more method for non-invasive measurement of bilirubin in neonates.

Question 6.

A 28-day old boy baby presents to you in OPD with history of high coloured urine. On enquiring, mother clearly gives history of *pigmented* stools. Baby is exclusively breastfed and thriving well. You note

icterus and request for total and direct bilirubin. Total serum bilirubin is 15 mg/dl and direct bilirubin is 13 mg/dl. You plan to evaluate the baby for neonatal cholestasis.

a. What investigations would you plan for this baby?

b. USG abdomen reveals normal gall bladder morphology and contractility and no evidence of choledochal cyst. LFT shows moderately elevated ALT and *normal GGT.* What would be your differential diagnoses?

c. What would be your next step in managing this baby? What is the current consensus on role of HIDA scan in evaluation of neonatal cholestasis?

d. You plan liver biopsy for this baby. Liver histology shows cholestasis, giant cell hepatitis, hepatocellular necrosis, portal fibrosis. Biopsy specimen is subjected to immunohistochemistry which shows absent canalicular staining with BSEP antibodies. Electron microscopy showed amorphous bile. What is the most probable diagnosis?

e. What are the medical and surgical treatment options available for this condition?

f. What is the expected course of disease and what are the anticipated long-term complications?

Question 7.

You have been called to attend delivery of a term baby with suspected Rh isoimmunization. Mother is A negative with positive ICT (anti-D titers 1: 64) since 24 weeks of pregnancy. The baby is born and has pallor and splenomegaly. Cord Bilirubin is 8 mg/dl and Hb is 7.5 g/dl. Retic count is 8%. Baby's DCT is +++. You had immediately shifted the baby to NICU and started intensive phototherapy while preparing for exchange transfusion.

a. What are the indications of exchange transfusion for hyperbilirubinemia in neonates?

b. What percentage of circulating RBCs are removed by double volume exchange transfusion? How much drop in bilirubin levels is expected by DVET?

c. Baby's blood group is B positive. What type of blood would you use for exchange transfusion in this baby?

d. Baby's weight is 3 kg. How would you calculate the amount of blood needed for double volume exchange transfusion?

e. What are the complications associated with exchange transfusion?

f. You have requested the blood bank for desired blood product and type, but it is not available anywhere at present. What would you do?

g. What are the indications of IV Immunoglobulin in neonatal jaundice?

Question 8.

A 19-day old term born 3.2 kg birth weight baby boy has been brought to you with complain of yellowish discoloration of body. The baby was born by caesarean section. You note that baby is icteric till soles. The baby had already received phototherapy twice after birth for serum bilirubin of 18 and 22 mg/dl on days 4 and 9 of life. The baby is thriving well. There is no pallor, no hepatosplenomegaly. There is no cephalhematoma, bruising or any evidence of concealed bleed. Baby has been on breast feeds as well as formula feeds. Baby's vitals are stable. There is no setting of blood group incompatibility. Baby's DCT is negative, and CBC is WNL. You request for a total serum bilirubin, and it is 22 mg/dl again with direct bilirubin only 0.5 mg/dl.

a. What additional investigations would you carry out?

b. What are the probable causes of marked prolonged unconjugated hyperbilirubinemia in neonates?

c. G-6-PD levels for this baby are very low. What advice would you give to the family?

d. How is the neonatal presentation of G-6-P-D deficiency different from classical presentation later?

e. What are the congenital non haemolytic unconjugated hyperbilirubinemia clinical

syndromes? Which of these has most severe presentation and what is the definitive treatment for same?

Question 9.

A term 38-week gestation, boy baby with birth weight 2920 g was born to a 28-year-old primigravida mother by caesarean section for fetal distress. It was a booked pregnancy with regular antenatal visits and normal antenatal ultrasounds. Breast feeding was initiated at 3 hours of life and continued thereafter. Baby passed urine and stools on the first day of life. Baby was noted to have icterus till soles on day 3 of life. The baby was admitted in NICU, and phototherapy was started. Investigations showed TSB of 26.2 mg/dL with direct fraction of 1.2 mg/dL at 72 hours of life. Baby had pallor and splenomegaly of 2 cm below LCM. There was no encephalopathy, no cephalhematoma or bruise. The blood group of the baby and both the parents was A Rh (+). Direct coombs test of the baby was positive (++++). Haemoglobin was 12 g/dL. Glucose 6 phosphate dehydrogenase enzyme levels were normal. Peripheral smear showed evidence of haemolysis with reticulocyte count of 8.5%. Maternal ICT was positive.

a. What would be your most probable diagnosis?

b. What investigations would you plan in this baby to confirm the diagnosis?

c. What are the current recommendations for routine antibody screening during pregnancy?

d. You did exchange transfusion in this baby along with intensive phototherapy. Now the baby is ready for discharge after 1 week of hospital stay. How would you plan the long term follow up this baby?

Question 10.

A 28-day old well thriving neonate has come to you for routine follow up visit. Mother does not have any medical concerns. However, as a routine practice, you ask the colour of stool and mother says it is “white”. She takes out the diaper and you find pale unpigmented stool. You plan to evaluate the baby. Lab tests reveal conjugated hyperbilirubinemia and a raised GGT. Next you plan an USG abdomen.

a. What USG findings would suggest Biliary atresia?

b. What are the clinical forms of Biliary atresia?

c. What are the characteristic histologic features in biliary atresia?

d. What is the initial surgical management? Before what age should it be preferably done to achieve best outcomes?

e. How would you medically support this baby?

f. What are the ways to reduce the risk of ascending cholangitis after surgery? What are its clinical implications?

g. When will you refer this baby for liver transplantation?

h. What screening method may be utilised in office practice for early detection of Biliary atresia?

Answer 1.

a. Rh isoimmunization. Hemolytic disease of fetus and newborn.

b. MCA doppler for MCA-PSV (Middle cerebral artery-Peak systolic velocity) at 1-2 weeks intervals to detect fetal anemia

c. No.

d. MCA-PSV more than 1.5 times MOM (multiple of median).

e. Fetal hemoglobin lower than 2 SD below the mean for gestational age or Hematocrit < 30% with gestation less than 35 weeks. Methods of IUT are intravascular and intraperitoneal.

f. ABO Rh, CBC, DCT, Reticulocyte count, Peripheral smear for hemolysis, S. Bilirubin

g. Plasmapheresis and IVIG may be considered in mother. Start weekly MCA dopplers and if MCA PSV is more than 1.5 MoM, check fetal hemoglobin by cordocentesis. Indications for IUT as mentioned above.

Answer 2.

a. Predischarge TSB or TcB level in the high-risk zone of hour specific normogram, Jaundice observed in the first 24 hours, Blood group incompatibility with positive direct antiglobulin test, other known hemolytic disease (eg, G6PD deficiency), Gestational age 35–36 wk, Previous sibling received phototherapy, cephalhaematoma or significant bruising, feeding problems particularly if nursing is not going well and weight loss is excessive, East Asian race.

b. Isoimmune hemolytic disease, G6PD deficiency, Asphyxia, Sepsis, Acidosis, Albumin less than 3.0 mg/dL, significant lethargy, and temperature instability.

c. Bhutani's hour specific nomogram

d. The baby's serum bilirubin is in the low intermediate risk zone . Therefore the baby is at low to intermediate risk. We should advise for follow up in 2 days.

e. Start intensive phototherapy and correct hydration and feeding as baby has 12.5% weight loss.

f. BIND score or BIND -M score.

BIND score components: Mental status, muscle tone, cry

BIND -M: Mental status, muscle tone, cry, altered gaze

BIND -M incorporates abnormality of the upward gaze, which is another classic sign of bilirubin encephalopathy

In addition to BIND score, there is altered subgaze score which is as follows
Normal gaze - 0
Sunsetting/paralysis of upward gaze - 3

Interpretation:

BIND Score Interpretation

0: No indication of acute bilirubin encephalopathy (ABE)

1-3: Subtle signs of mild acute bilirubin encephalopathy (ABE)

4-6: Moderate acute bilirubin encephalopathy (ABE), urgent bilirubin reduction intervention is likely to reverse the acute damage

7-9: Advanced acute bilirubin encephalopathy (ABE), urgent bilirubin intervention is needed to prevent further brain damage and reduce the severity of sequelae.

Bilirubin-induced neurologic dysfunction (BIND) assessment (score) for term and late preterm infants

Clinical signs	Score
Mental status	
Normal	0
Sleepy but arousable, decreased feeding	1
Lethargic, poor suck, irritable, and/or jittery	2
Semicomatose to comatose, unable to feed, seizures	3
Muscle tone	
Normal	0
Persistent mild to moderate hypotonia	1
Mild to moderate hypertonia alternating with hypotonia	2
Persistent retrocollis and opisthotonos	3
Cry pattern	
Normal	0
High pitched when aroused	1
Shrill, difficult to console	2
Inconsolable crying or weak/absent cry	3
Total BIND score	

BIND-M Score Interpretation

The maximum total score for BIND-M is 12. A score of 1-4 was predicted to be indicative of mild ABE, which is generally considered to be reversible if treated promptly and aggressively.

An intermediate score (5-6) was predicted to be indicative of moderate ABE, which might be reversible with urgent and prompt bilirubin reduction.

Higher scores (7 and above) would likely indicate severe/very severe ABE, probably representing irreversible brain damage in most infants.

g. Breastfeeding jaundice. Increased enterohepatic circulation due to decreased feeding.

Answer 3.

a. Decrease the vertical distance between baby and phototherapy unit. We can increase exposure by double surface phototherapy. Also, phototherapy units can be covered with white cloth for enhancing the efficacy.

b. Structural isomerization, photoisomerization, photooxidation

c. Spectrum of light emitted, spectral irradiance, spectral power, cause of jaundice, TSB level at the start of jaundice

d. "Intensive phototherapy" implies irradiance in the blue-green spectrum (wavelengths of approximately 430–490 nm) of at least 30

W/cm2 per nm (measured at the infant's skin directly below the center of the phototherapy unit) and delivered to as much of the infant's surface area as possible.

e. The area illuminated by the PT device with sufficient spectral irradiance. It is measured with the help of radiance meter.

f. Advantages of LED phototherapy: Less heat generation, less hyperthermia, lesser insensible losses, less power consumption, and more shelf life.

g. If TSB is close to exchange range/ or hemolytic jaundice is anticipated- Repeat value within 2-3 hrs

TSB >25- Repeat in 2-3 hrs

TSB 20-25- Repeat in 3-4hrs

TSB <20- Repeat in 4-6hrs

If continues to fall- repeat in 8-12hrs.

h. For stopping:

TSB less than 3mg/dl below phototherapy range. 2 values for haemolytic jaundice. Single value otherwise. In readmission jaundice stop phototherapy once TSB < 14mg/dl.

For Rebound testing: After 24 hours of stopping (particularly in hemolytic or early jaundice). In readmission jaundice, option of clinical review after 24 hours can be given.

Answer 4.

a. Non–immune-mediated hemolytic jaundice:

Inherited RBC defects:

Enzyme defects: Glucose-6-phospate/ Pyruvate kinase deficiency

Membrane defects: Hereditary spherocytosis/ Hereditary elliptocytosis. Hemoglobinpathies: Severe forms of Thalassemias/ Sickle cell disease

b. The diagnosis of hereditary spherocytosis (HS) in a newborn infant is generally made based on a positive family history, spherocytes on blood film and Coombs-negative hemolytic jaundice of variable severity with an elevated mean corpuscular hemoglobin concentration (MCHC) and a low mean corpuscular volume (MCV). If MCHC/MCV ratio > 0.36, it is likely to be HS. Positive osmotic fragility test. Definitive diagnosis is by genetic testing.

c. During the perinatal period, the clinical manifestation of HS ranges from severe fetal anemia with hydrops fetalis to no clinical symptoms. In the neonatal period, jaundice is the most common manifestation.

d. Eosin-5'-maleimide (EMA) binding test, Acidified Glycerol lysis time test, Genetic testing (Next generation DNA sequencing)

e. *ANK1*, located at 8p11.21, encodes erythroid ankyrin, and its mutations are the most common causes of HS1

f. Anemia, hyperbilirubinemia, folate deficiency, cholelithiasis, aplastic crisis

g. Phototherapy/ Exchange transfusion for jaundice as and when indicated, management of anemia using blood transfusion, folate supplementation. Definitive treatment is splenectomy, and it is usually offered after 5 years of age.

Answer 5.

a. We will do total serum bilirubin

b. Multiwavelength reflectance photo spectrometry

c. Babies less than completed 35 weeks of gestation

Jaundice in first 24 hours of life

Babies more than 14 days old

Babies under phototherapy or post phototherapy

Babies where conjugated hyperbilirubinemia is suspected.

d. TCB measurements greater than 13 mg/dl.

TCB > 75th centile on Bhutani's hour specific normogram. TCB is at 70% of TSB level recommended for phototherapy/ TCB measurement within 3 mg/dl of TSB phototherapy cut off. In other words, if "TCB + 3" would change the management, then TSB should be obtained.

e. 14 days

f. JM-105, JM-103, Bilicheck

g. Draeger JM-105 is indicated for use in neonatal patients born at or after 24 weeks gestation who have not undergone exchange transfusion. The device is indicated for use before, during, and after phototherapy treatment.

h. End Tidal Carbon monoxide measurement

Answer 6.

a. Liver function tests, Fasting ultrasound whole abdomen, sepsis screen, metabolic tests, genetic tests, liver biopsy

b. PFIC (Progressive familial intrahepatic cholestasis) I and II

Inborn errors of bile acid metabolism

c. We shall plan liver biopsy.

Hepatobiliary-imino-di-acetic acid (HIDA) scan has limited role in evaluation of NC especially if the baby has clearly documented pale or pigmented stools. The time required (5-7 days) for priming before the scan, especially in patients who are referred late, is a limitation. The sensitivity of scintigraphy for biliary atresia is relatively high (83 %–100 %); however, its specificity is very low (33 %–80 %). A recent meta-analysis of 81 studies has shown a pooled sensitivity and specificity of 98.7 % and 70.4 %, respectively. A non-excreting scan may be seen both in biliary atresia as well as severe hepatocellular dysfunction. However, excretion of the tracer into the bowel despite of biliary atresia is extremely rare and thus an excreting scan may help in ruling out biliary atresia, but without providing any other diagnostic information. Good-quality HIDA scan may not be available everywhere in our country. Since HIDA scan is expensive, time consuming and poorly specific, many centres do not routinely use this test in the evaluation of cholestatic infants because it may delay the diagnostic evaluation without providing definitive diagnostic information. However, others think that it still has a role where the liver biopsy is ambiguous, in the evaluation of preterm infants and in the diagnosis of the uncommon causes like spontaneous perforation of the bile duct.

(Reference: Consensus Statement of the Pediatric Gastroenterology Chapter of Indian Academy of Pediatrics; Italian guidelines for the management and treatment of neonatal cholestasis by Task Force for Hyperbilirubinemia of the Italian Society of Neonatology)

d. Progressive Familial Intrahepatic Cholestasis Type II (PFIC II)

e. *Drugs:* UDCA, rifampicin, cholestyramine

Nutritional rehabilitation: Water soluble vitamins are given at 1–2 times of the age-appropriate RDA. The fat-soluble vitamins are usually supplemented in the following dosage in children: vitamin A—5000–25,000 IU/day PO, vitamin D 400–800 IU/day PO, vitamin E 50–100 IU/day PO and vitamin K 2.5–5 mg/day PO or 2–5 mg intravenous every 3–4 weeks. Adequate sunlight exposure and dietary intake of calcium (800–2000 mg/day PO) is also essential.

Surgical: Biliary diversion procedures, Liver transplantation

f. PFIC patients have a variable prognosis depending on the type of PFIC and severity of genetic defect within each type. Approximately 30% children respond to UDCA therapy and about 70–80% to partial biliary diversion, if offered early in course of disease, before development of cirrhosis. Patients with cirrhosis and end stage liver disease require liver transplant.

Anticipated long term complications: Cirrhosis, Hepatocellular carcinoma, and cholangiocarcinoma

Answer 7.

a. Indications for exchange transfusion: Immediate exchange transfusion is indicated in any infant with acute bilirubin encephalopathy or if TSB is ≥ 5 mg/dl above the threshold for exchange transfusion in AAP chart. It should be considered when TSB reaches the exchange transfusion threshold and is not decreasing despite of intensive phototherapy. In the setting of Rh incompatibility, if the cord bilirubin is more than 5 mg/dl or cord haemoglobin is less than 11 mg/dl, exchange transfusion is recommended.

b. 85% of circulating RBCs are replaced and the bilirubin level decreases by about 50% after double volume exchange transfusion (DVET).

c. B or O Rh negative PRBC suspended in AB positive plasma.

d. 160 ml/kg. For this baby, it will be 480 ml. For dead space loss in circuit, around 20-25 ml extra blood should be taken. 2/3 of the total amount should be PRBC and rest 1/3 plasma (final hematocrit of reconstituted blood should be at least 45).

e. Adverse effects associated with exchange transfusion:

Infection, thrombocytopenia, electrolyte disturbances like hypocalcemia, hyperkalemia, hypo or hyperglycemia, fluid overload, cardiac arrhythmias, coagulopathies, graft-versus-host disease, necrotizing enterocolitis, portal vein thrombosis, and a mortality rate of approximately 0.5% to 2%

f. Continue Intensive phototherapy and give IV Immunoglobulin 0.5-1 g/kg IV over 2 hours.

g. Indications of IVIg: In isoimmune hemolytic disease, administration of intravenous globulin (0.5-1 g/kg over 2 hours) is recommended if the TSB is rising despite intensive phototherapy, or the TSB level is within 2 to 3 mg/dL (34-51 mol/L) of the exchange level. If necessary, this dose can be repeated in 12 hours.

Answer 8.

a. G-6-PD, TSH, sepsis work up.

b. Breast milk jaundice, Hypothyroidism, G6PD deficiency, pyloric stenosis, Crigler Najjar syndrome, Gilbert syndrome, extravasated blood.

c. G6PD deficiency is a genetic disorder. In this condition the person has low levels of an enzyme called glucose 6 phosphate dehydrogenase.(G 6PD). This enzyme stabilises the red cell membrane. It also protects them from substances in the blood that could harm them. In people with G6PD deficiency, either the red blood cells do not make enough G6PD or what they do make doesn't work as it should. Without enough G6PD to protect them, the red blood cells break apart. This can cause anemia and jaundice. Red blood cells that don't have enough G6PD are sensitive to some triggers which can be medicines, foods, and infections. Triggers of hemolysis in kids with G6PD deficiency include illness, such as bacterial and viral infections, some painkillers and fever-lowering drugs, some antibiotics (most often those with "sulf" in their names), some antimalarial drugs (most often those with "quine" in their names), fava beans (also called broad beans), naphthalene (a chemical found in mothballs). Treating G6PD deficiency symptoms is usually as simple as removing the trigger. Often, this means treating the infection or stopping the use of a drug. A child with severe anaemia may need treatment in the hospital to get oxygen and fluids. Sometimes, a child also needs a transfusion of healthy blood cells. The best way to care for your child is to limit exposure to anything that triggers symptoms. We will give written instructions, and a list of medicines and other things that could be a problem for your child with G6PD deficiency.

d. Neonates usually present with severe or prolonged unconjugated hyperbilirubinemia. They may not present with classical hemolytic anemia crisis.

e. Crigler Najjar syndrome-1, Crigler Najjar syndrome-2, Gilbert syndrome. Crigler Najjar-1 is the most severe of these. Liver transplantation is the definitive treatment of Crigler Najjar syndrome type 1.

Answer 9.

a. Minor blood group incompatibility.

b. Blood group typing of parents and baby for Kell, C, c, E, and e. Antibody titres in mother against these antigens.

c. ABO, Rh(D) blood group antigen typing and screening for RBC antibodies at the booking visit.

d. Regular follow up for anaemia till 3 months. BERA at 3 months. Long term neurodevelopment assessment for tone abnormalities/ athetoid CP.

Answer 10.

a. Abdominal ultrasonography findings described in biliary atresia (BA) include the triangular cord sign, abnormal gallbladder morphology (not visualized or length <1.9 cm or lack of smooth/complete echogenic mucosal lining with

an indistinct wall or irregular/lobular contour), no contraction of the gallbladder after oral feeding and non-visualized common bile duct (CBD). A distended gall bladder, however, does not rule out a proximal BA with a distal patent bile duct and mucus filled gallbladder. It is recommended that ultrasound should be done after 4 hours of fasting.

b. Biliary atresia can be grouped into 3 categories:

(i) BA without any anomalies or malformations

(ii) BA in association with laterality malformations (BASM- Biliary atresia splenic malformation)

(iii) BA in association with other congenital malformations:

c. The characteristic histopathology features of BA are bile duct proliferation, bile plugs in ducts, fibrosis, and lymphocytic infiltrates in the portal tracts.

d. The standard treatment of biliary atresia is the Kasai hepatic portoenterostomy with intraoperative cholangiogram to confirm the site of the obstruction before surgery. It should preferably be done before 60 days.

e. *Drugs:* UDCA (Ursodeoxycholic Acid)

Nutritional rehabilitation: Water soluble vitamins are given at 1–2 times of the age-appropriate RDA. The fat-soluble vitamins are usually supplemented in the following dosage in children: vitamin A—5000–25,000 IU/day PO, vitamin D 400–800 IU/day PO, vitamin E 50–100 IU/day PO and vitamin K 2.5–5 mg/day PO or 2–5 mg intravenous every 3–4 weeks. Adequate sunlight exposure and dietary intake of calcium (800–2000 mg/day PO) is also essential.

f. Long loop hepatic portoenterostomy and prophylactic antibiotics after Kasai procedure help in reducing risk of ascending cholangitis. Recurrent cholangitis can progressively worsen liver function.

g. Referral for liver transplantation: Any baby, who has had Kasai's PE and the bilirubin remains >6 mg/dL, three months after surgery, should be referred to a transplant center. Babies with BA who present with decompensated cirrhosis (low albumin, prolonged INR, ascites) are not likely to improve with a Kasai PE and should be referred for liver transplantation.

h. Stool colour card test.

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.**

Contact Us

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

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