
بسم الله الرحمن الرحيم

Challenges of prolonged jaundice in neonates

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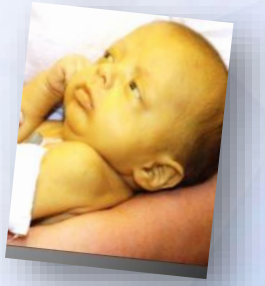

نوزادی نارس ۳۸ روزه با وزن تولد ۸۰۰ گرم و
سن حاملگی ۲۸ هفته با زردی به شما مراجعه می کند

Definition of prolonged jaundice

Prolonged neonatal jaundice is defined as:

- *visible jaundice persisting beyond day 14 in term neonates*
- *visible jaundice persisting beyond day 21 in preterm infants*

15 to 40% of well, breastfed infants at 2 weeks,
and 9% at 4 weeks of age have jaundice

Importance of prolonged jaundice

- One of the criteria of pathologic jaundice
- Underlying disease(R/O cholestasis)
- The level of bilirubin (bilirubin encephalopathy)
- Parental worrisome

Investigations

Etiology of prolonged jaundice:

- *Unconjugated (Indirect hyperbilirubinemia)*
- *Mixed/Conjugated(Direct hyperbilirubinemia or Cholestasis)*

Prolonged unconjugated hyperbilirubinemia

- ***Breast milk jaundice***
- ***Hemolysis***

– *Coombs positive*

- Rh, ABO incompatibility, Anti-Kell, anti-Duffy…

– *Coombs negative*

- Red cell membrane defects e.g. sphero/elliptocytosis, Red cell enzyme defects e.g. G6PD, pyruvate kinase deficiency, Hemoglobinopathy, infection

- ***Increased enterohepatic circulation***

- Pyloric stenosis, Intestinal obstruction

- ***Decreased conjugation***

-Crigler–Najjar syndrome

- Gilbert's disease

- Hypothyroidism

-Prematurity

Hypothyroidism

- *UGT activity in congenital hypothyroidism is deficient and may remain suboptimal for weeks or months.*
- *Because about 10% of congenitally hypothyroid neonates may develop prolonged, exaggerated jaundice, testing for thyroid function should be performed in these cases.*

Pyloric Stenosis

- *May be associated with unconjugated hyperbilirubinemia at the time vomiting begins.*
- *Hepatic UGT activity is markedly depressed in the jaundiced neonates.*
- *The mechanism of diminished UGT activity may be caused by the presence of the variant (TA)7 UGT1A1 gene promoter, which is associated in adults with Gilbert syndrome*

Breast Milk Jaundice

- *The majority of infants with prolonged jaundice will turn out to have breast milk jaundice a diagnosis of exclusion.*
- *Peak levels as high as **20 to 30** mg/dl*
- *Presence of the variant (TA)7 UGT1A1 gene promoter may be associated with prolonged breast milk jaundice*
- *Breast milk jaundice is apparently related to a **change in the composition or physical structure of the milk***

Breast Milk Jaundice

- ***Pregnane- 3-α,20-β-diol****(a* ***progesterone*** *metabolite) found in the breast milk fed to affected neonates, was historically thought to be the cause of this disorder because this substance was shown to be* ***a competitive inhibitor of UGT in vitro.*** *Although milk and urine of mothers of these neonates contain this pregnanediol isomer, the inhibitory effect of this hormone has been questioned*

- ***Nonesterified long-chain fatty acids.*** *This suggests that certain of these fatty acids act as* ***inhibitors of hepatic UGT,*** *causing retention of unconjugated bilirubin*

- *(In rat) suggest that milk from mothers of neonates with this syndrome contains* ***β-glucuronidase, an enzyme that could deconjugate bilirubin and consequently enhance enteric reabsorption of bilirubin****, thereby increasing the hepatic bilirubin load.*

Crigler-Najjar syndrome:

- ***Type I*** *:is a rare AR disease, complete absence of hepatic UGT activity*

Severe unconjugated hyperbilirubinemia develops during the ***first 3 days*** *of life and progresses in an unremitting fashion, with TB concentrations reaching 25 to 35 mg/dL during the first month of life. Kernicterus often occurs in the neonatal period.*

- ***Type II*** *is more common than type I and typically benign. Although unconjugated hyperbilirubinemia occurs in the first days of life, TB levels generally do not exceed 20 mg/dL. Fasting, illness, and anesthesia may cause temporary increases in bilirubin to above baseline.*

Evidence of hemolytic disease is absent (although it may occur coincidentally), stool color is normal, and neonates are otherwise healthy

Gilbert syndrome

- *Benign disorder that affects about **6%** of the population and produces a chronic unconjugated hyperbilirubinemia. Both defective **hepatic uptake of bilirubin and decreased hepatic UGT1A1 activity have been demonstrated***

- *When mutations in both the gene for **G6PD** and the promoter for UGT occur, the degree of neonatal hyperbilirubinemia has been severe*

History

- History of blood group incompatibility
- Family history of prolong jaundice, hematologic and liver disease
- Method of feeding and weight gain (birth weight & current weight)
- Lethargy
- Urine color
- Color of stool
- Bleeding/bruising /hematoma

Examination

- Jaundice
- Pallor
- Hydration status
- Dysmorphic features
- Cataracts
- Hepatosplenomegaly
- Hypotonia and encephalopathy
- Petechia/ ecchymosis
- Look in the nappy – color of stool and urine

Investigations

- Total and conjugated bilirubin(don't rely to previous results)
- CBC, retic
- U/A,U/C
- Check result of routine metabolic (heel prick) screening (including screening for congenital hypothyroidism, galactosemia and G6PD deficiency)

نوزادی نارس ۳۸ روزه با وزن تولد ۸۰۰ گرم و سن حاملگی ۲۸ هفته با زردی به شما مراجعه می کند کدام عبارت صحیح نیست؟

الف) با توجه به سن حاملگی نوزاد زردی طبیعی است و نیاز به بررسی ندارد

ب) باید بیلی روبین مستقیم نوزاد اندازه گیری شود

ج) باید نتایج آزمایشات غربالگری بررسی شود

د) باید هموگلوبین نوزاد اندازه گیری شود

Treatment

نوزاد ۱۵ روزه ای با سن حاملگی ۳۹ هفته بدلیل زردی پوست به درمانگاه مراجعه کرده است. در معاینه نوزاد کاملاً سالم است. وزن زمان تولد ۳۰۰۰ گرم و هم اکنون ۳۵۰۰ گرم می باشد. نتایج آزمایشات انجام شده به شرح زیر است:

Bilirubin: Total= 9 Direct= 0.7 , Hb= 14 reticulocyte= 0.5%

G6PD=Normal TSH=3 U/A, U/C=NL

مناسب ترین درمان برای این نوزاد کدام است؟

الف) دادن اطمینان خاطر به مادر و چک بیلی روبین چند روز بعد

ب) قطع شیر مادر به مدت ۴۸ الی۷۲ ساعت و چک بیلی روبین ۷۲ ساعت بعد

ج) شروع فنوباربیتال خوراکی و چک بیلی روبین ۴۸ ساعت بعد

د) شروع فتوتراپی درمنزل و چک بیلی روبین ۲۴ ساعت بعد

Treatment of prolonged jaundice

- No treatment (reassurance to family, wait and watch)
- Phototherapy (based on the level of bilirubin)
- Treatment of hemolysis (folic acid and f/u)
- Brief interruption of breast milk nursing
- Phenobarbital
- Others(Hypothyroidy , HPS,….)

Brief interruption of breast milk nursing

- *Interruption of nursing and substitution with formula feeding for 1 to 3 days usually causes a prompt decline of the TB concentration to about half or less of the original level.*
- *May be useful to confirm the diagnosis*
- *Failure to respond in this manner indicates that the neonate's jaundice may be unrelated to breast milk, and other causes should be sought*

- *An alternative way is to confirm that the TB is primarily unconjugated, that thyroid function tests are normal, and that there is no evidence of urinary infection. In the situation in which the infant is thriving and the TB does not reach dangerous levels, it may be prudent to observe the infant.*
- ***So, It is not recommended unless bilirubin concentrations reach levels that might be of danger to the infant, or there is severe parental anxiety***

Effective nursing practices that prevent early "starvation" in breastfed newborns

may reduce not only

the incidence of breastfeeding jaundice,

but also the severity of breast milk jaundice

Phenobarbital and prolonged jaundice

- Increase hepatic uptake, conjugation, and excretion of bilirubin
- Long term toxicity
- Excessive sedation in neonates
- Much less effective in premature infants
- Has been reserved for specific high risk population
- Can differentiate between type I and type II of Crigler Najjar syndrome, the response to phenobarbital in patients with type II

Other treatments

- Levothyroxine for Hypothyroid neonates
- Surgery for treatment of HPS & GI obstructions
- Herbal medicine
- Maternal diet


Thanks for your attention