NEONATAL JAUNDICE: A REVIEW

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Abstract

Jaundice occurs in most newborn infants. Most jaundice is benign, but because of the potential toxicity of bilirubin, newborn infants must be monitored to identify those who might develop severe hyperbilirubinemia and, in rare cases, acute bilirubin encephalopathy or kernicterus. The focus of this article is to reduce the incidence of severe hyperbilirubinemia and bilirubin encephalopathy while minimizing the risks of unintended harm such as maternal anxiety, decreased breastfeeding, and unnecessary costs or treatment. Although kernicterus should almost always be preventable, cases continue to occur. This article provides a framework for the prevention and management of hyperbilirubinemia in newborn infants of 35 or more weeks of gestation.

Keywords: Jaundice; Extrinsic causes; intrinsic causes; treatment

1. Introduction

A common condition in newborns, jaundice refers to the yellow color of the skin and whites of the eyes caused by excess bilirubin in the blood. Bilirubin is produced by the normal breakdown of red blood cells. Normally, bilirubin passes through the liver and is excreted as bile through the intestines. Jaundice occurs when bilirubin builds up faster than a newborn's liver can break it down and pass it from the body. Reasons for this include:

- Newborns make more bilirubin than adults do since they have more turn over of red blood cells.
- A newborn baby's still-developing liver may not yet be able to remove adequate bilirubin from the blood. Too large an amount of bilirubin is reabsorbed from the intestines before the baby gets rid of it in the stool.

In neonates, jaundice tends to develop because of two factors - the breakdown of fetal hemoglobin as it is replaced with adult hemoglobin and the relatively immature hepatic metabolic pathways which are unable to conjugate and so excrete bilirubin as quickly as an adult. This causes an accumulation of bilirubin in the blood (hyperbilirubinemia), leading to the symptoms of jaundice.

2. Causes

High levels of bilirubin — usually above 25 mg — can cause deafness, cerebral palsy, or other forms of brain damage in some babies. In less common cases, jaundice may indicate the presence of another condition, such as an infection or a thyroid problem. The American Academy of Pediatrics (AAP) recommends that all infants should be examined for jaundice within a few days of birth.

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If the neonatal jaundice does not clear up with simple phototherapy, other causes such as biliary atresia, PFIC, bile duct paucity, Alagille's syndrome, alpha 1 and other pediatric liver diseases should be considered. The evaluations for these include...
blood work and a variety of diagnostic tests. Prolonged neonatal jaundice is serious and should be followed up promptly. Severe neonatal jaundice may indicate the presence of other conditions contributing to the elevated bilirubin levels, of which there are a large variety of possibilities. These should be detected or excluded as part of the differential diagnosis to prevent the development of complications. They can be grouped into the following categories:

2.1 Intrinsic causes of hemolysis

- Membrane conditions
  - Spherocytosis
  - Hereditary elliptocytosis
- Systemic conditions
  - Splenomegaly
  - Sepsis
  - Arteriovenous malformation
- Enzyme conditions
  - Glucose-6-phosphate dehydrogenase deficiency (also called G6PD deficiency)
  - Pyruvate kinase deficiency
- Globin synthesis defect
  - Sickle Cell Disease
  - Alpha-thalassemia

2.2 Extrinsic causes of hemolysis

- All immunity (The neonatal or cord blood gives a positive direct Coombs test and the maternal blood gives a positive indirect Coombs test)
  - Hemolytic disease of the newborn (ABO)
  - Rh disease
  - Hemolytic disease of the newborn (anti-Kell)
  - Hemolytic disease of the newborn (anti-Rhc)
  - Other blood type mismatches causing hemolytic disease of the newborn
  - Breast milk feeding.

2.3 Non-hemolytic causes

- Cephalohematoma
- Polycythemia
- Sepsis
- Hypothyroidism
- Gilbert's syndrome
- Crigler-Najjar syndrome

2.4 Hepatic causes

- Infections
  - Sepsis
  - Hepatitis B
  - TORCH infections
- Metabolic
  - Galactosemia
  - Alpha-1-antitrypsin deficiency
  - Cystic fibrosis
- Drugs
- Total parenteral nutrition
- Idiopathic

2.5 Post-hepatic

- Biliary atresia
- Bile duct obstruction
- Non-organic causes

3. Types of jaundice: 21-24

The most common types of jaundice are:

3.1 Physiological (normal) jaundice: Occurring in most newborns, this mild jaundice is due to the immaturity of the baby's liver, which leads to a slow processing of bilirubin. It generally appears at 2 to 4 days of age and disappears by 1 to 2 weeks of age.

3.2 Jaundice of prematurity: Occurs frequently in premature babies since they are even less ready to excrete bilirubin effectively. Jaundice in premature babies needs to be treated at a lower bilirubin level than in full term babies in order to avoid complications.
3.3 Breastfeeding jaundice: Jaundice can occur when a breastfeeding baby is not getting enough breast milk because of difficulty with breastfeeding or because the mother's milk isn't in yet. This is not caused by a problem with the breast milk itself, but by the baby not getting enough to drink.

3.4 Breast milk jaundice: In 1% to 2% of breastfed babies, jaundice may be caused by substances produced in their mother's breast milk that can cause the bilirubin level to rise. These can prevent the excretion of bilirubin through the intestines. It starts after the first 3 to 5 days and slowly improves over 3 to 12 weeks.

3.5 Blood group incompatibility (Rh or ABO problems): If a baby has a different blood type than the mother, the mother might produce antibodies that destroy the infant's red blood cells. This creates a sudden buildup of bilirubin in the baby's blood. Incompatibility jaundice can begin as early as the first day of life. Rh problems once caused the most severe form of jaundice, but now can be prevented with an injection of Rh immune globulin to the mother within 72 hours after delivery, which prevents her from forming antibodies that might endanger any subsequent babies.

4. Symptoms: 16-19

The signs and symptoms will depend largely on the cause. Extremely high levels of bilirubin in infants may cause kernicterus, a form of brain damage. Signs of severe hyperbilirubinemia include listlessness, high-pitched crying, apnea (periods of not breathing), arching of the back, and seizures. If severe hyperbilirubinemia is not treated, it can cause mental retardation, hearing loss, behavior disorders, cerebral palsy, or death.

In the physiological group the jaundice is only noted on the second or third day. The baby feeds well, behaves normally and there is no enlarged liver or spleen on examination. The urine may be dark but the stools are normal colour. The bilirubin levels are not significantly raised, below 275 μmol/l. The jaundice resolves over two to three weeks.

Breastmilk jaundice becomes apparent after a few days; the TSB rarely exceeds 275 μmol/l but it is a cause of prolonged jaundice; the baby remains completely well and continues to thrive. It is not a reason to stop breastfeeding.

5. Diagnosis 15, 20, 24

5.1 Exams and Tests 5, 9, 11

All newborns should be examined for jaundice at least every 8 to 12 hours for the first day of life. Any infant who appears jaundiced in the first 24 hours should have bilirubin levels measured immediately. This can be done with a skin or blood test.

Babies should be assigned a risk for later developing jaundice before they leave the hospital. Babies are classified as low risk, low intermediate risk, high intermediate risk, or high risk. Many hospitals do this by routinely checking total bilirubin levels on all babies at about 24 hours of age.

Further testing varies on the infant's specific situation and test results. For example, the possible cause of the jaundice should be sought for babies who require treatment or whose total bilirubin levels are rising more rapidly than expected.

- Testing - A full range of routine and specialty diagnostic testing is available, including MRI and PET scans, evoked potentials (ABR, SEP, VEP); EMG, EEG, video EEG, sleep studies, metabolic and genetic testing, auditory, and neuropsychological testing
- Complete blood count
- Coomb's test
• Measurement of levels of specific types of bilirubin
• Reticulocyte count

The level of albumin in the baby's blood may also be checked. Low albumin levels may increase.

5.2 Non-invasive measurement of jaundice

This method is more accurate and less subjective in estimating jaundice.

5.2.1 Ingram icterometer: In this method a piece of transparent plastic known as Ingram icterometer is used. Ingram icterometer is painted in five transverse strips of graded yellow lines. The instrument is pressed against the nose and the yellow colour of the blanched skin is matched with the graded yellow lines and bilirubin level is assigned.

5.2.2 Transcutaneous bilirubinometer: This is hand held, portable and rechargeable but expensive and sophisticated. When pressure is applied to the photoprobe, a xenon tube generates a strobe light; and this light passes through the subcutaneous tissue. The reflected light returns through the second fiber optic bundle to the spectrophotometric module. The intensity of the yellow color in this light, after correcting for the hemoglobin, is measured and instantly displayed in arbitrary units.

6. Treatment

A major concern with jaundice is the risk of very high concentrations of bilirubin reaching the brain and causing damage. But studies show that most babies who suffer such brain damage have underlying illnesses or conditions, such as complete inability of the liver to process bilirubin.

Doctors usually use phototherapy, or light treatment, to bring down bilirubin levels. The infant is placed under special fluorescent lamps that convert the excess bilirubin into a water-soluble form that can be excreted in bile and urine. The infant receives treatment usually in an incubator, for approximately two to three days.

An old traditional herbal remedy for neonatal jaundice with a newly identified risk. Yin-chen (Artemisia scoparia) is a very popular intravenous herbal preparation used for the treatment of neonatal jaundice in China. Bilirubin-protein titration studies with the horse radish peroxidase method have shown that the herb is highly effective in displacing bilirubin from its protein binding. Free bilirubin is liberated in this process and this could increase the risk of brain damage in jaundiced infants. With the present state of knowledge, the use of traditional herbal therapies should be strongly discouraged in neonates.

6.1 Phototherapy

Infants with neonatal jaundice are treated with colored light called phototherapy. Physicians randomly assigned 66 infants 35 weeks of gestation to receive phototherapy. After 15±5 the levels of bilirubin, a yellowish bile pigment that in excessive amounts causes jaundice, were decreased down to 0.27±0.25 mg/dl/h in the blue light. This shows that blue light therapy helps reduce high bilirubin levels that cause neonatal jaundice. Exposing infants to...
high levels of colored light breaks down the bilirubin. Scientists studied 616 capillary blood samples from jaundiced newborn infants. These samples were randomly divided into three groups. One group contained 133 samples and would receive phototherapy with blue light. Another group contained 202 samples would receive room light, or white light. The final group contained 215 samples, and was left in a dark room. The total bilirubin levels were checked at 0, 2, 4, 6, 24, and 48 hours. There was a significant decrease in bilirubin in the first group exposed to phototherapy after two hours, but no change occurred in the white light and dark room group. After 6 hours, there was a significant change in bilirubin level in the white light group but not the dark room group. It took 48 hours to record a change in the dark room group’s bilirubin level. Phototherapy is the most effective way of breaking down a neonate’s bilirubin.

Phototherapy works through a process of isomerization that changes the bilirubin into water-soluble isomers that can be passed without getting stuck in the liver.

In phototherapy, blue light is typically used because it is more effective at breaking down bilirubin (Amato, Inaebnit, 1991). Two matched groups of newborn infants with jaundice were exposed to intensive green or blue light phototherapy. The efficiency of the treatment was measured by the rate of decline of serum bilirubin, which in excessive amounts causes jaundice, concentration after 6, 12 and 24 hours of light exposure. A more rapid response was obtained using the blue lamps than the green lamps. However, a shorter phototherapy recovery period was noticed in babies exposed to the green lamps. Green light is not commonly used because exposure time must be longer to see dramatic results.

Light therapy may increase the risk of nevi, or skin moles.

Increased feedings help move bilirubin through the neonate’s metabolic system.

The light can be applied with overhead lamps, which means that the baby's eyes need to be covered, or with a device called a Biliblanket, which sits under the baby's clothing close to its skin.

6.2 Exchange transfusion: 15, 17, 19

Indications

Less frequently, when neonatal jaundice is more severe, and fluorescent light therapy is unable to break down all circulating bilirubin, exchange transfusion is often used. High levels of bilirubin in the blood can lead to brain damage and other serious problems. In these cases, exchange transfusion is a life-saving procedure designed to counteract the effects of serious jaundice, infection, or toxicity. The procedure involves the staged removal of the infant's blood and replacement fresh donor blood or plasma.

Guidelines for an exchange transfusion include:

- Hemolytic disease of the newborn (Rh disease)
- Life-threatening infection

Fig.2- Picture depicting transfusion in Neonates
• Severe disturbances in body chemistry
• Toxic effects of drugs
• Polycythemia

Procedure

The infant is laid on his or her back, usually under a radiant warmer. The umbilical vein is catheterized with a fluid-filled catheter. The catheter is connected to an exchange transfusion set, incorporating lines to and from a waste container and a pack of donor blood. These are connected by means of a four-way stopcock, to which is also attached the syringe used to remove and replenish the infant's blood. The exchange transfusion now goes ahead in cycles, each of a few minutes duration. Slowly the infant's blood is withdrawn, and the fresh, pre-warmed blood or plasma is injected. After the exchange transfusion, an umbilical catheter may be left in place in case the procedure needs to be repeated within a few hours.

6.3 Home Treatment

• Parents are often asked to watch their newborns for signs of jaundice, which produces a yellow tint to the skin and eyes. Many mothers and their newborns leave the hospital within 48 hours of the baby's birth, often before signs of jaundice develop. It is recommended that your infant have a follow-up exam with your health professional within the first 5 days after birth.

• If your baby has jaundice but does not need phototherapy, your baby's doctor will ask you to watch for and report any signs of increasing jaundice or changes in behavior. To check for signs of increasing jaundice:
  - Undress your baby and look at his or her skin closely twice a day. For dark-skinned babies, look at the white part of the eyes to check for jaundice. Remember that your baby will get cold quickly when undressed. Cover your baby after about 1 minute.
  - Check your baby at the same time of day, in the same room, under the same lighting conditions each time. If you think that your baby's skin is getting more yellow, call your health professional.
  - The best home treatment for jaundice is frequent feedings, whether breast-feeding or bottle-feeding. Feeding your baby frequently (about 8 to 12 times a day) will provide him or her with the fluids needed to get rid of the extra bilirubin.

• Babies with jaundice who are otherwise healthy may be treated at home with a type of phototherapy that uses a fiber-optic wrap, usually a blanket or a band. These wraps usually reduce blood bilirubin levels more slowly than standard phototherapy, so generally they are used only for mild jaundice. Sometimes standard therapy and fiber-optic wrap therapy are used together.

• If your baby is being treated at home for jaundice, it is important that you understand how to use all of the equipment. Ask your baby's doctor for help if you have questions or concerns. You may need to take your baby to a lab each day to get his or her bilirubin checked. A home health nurse may visit to make sure all is going well.

• If your baby has been treated with phototherapy, the yellow tint to the baby's skin and eyes may not disappear immediately. But if the yellow tint intensifies, report it to your health professional.
Sometimes parents try to treat their jaundiced babies on their own without the proper equipment. Placing a baby under lights at home, near a windowsill in the sunlight, or outside in the sun will not lower the amount of bilirubin in his or her blood. Your baby's skin may get burned by the lights or the sun. In addition, your baby may get too cold. Special lights and controlled surroundings are always needed to treat jaundice safely.

Some mothers who breast-feed their babies are concerned that they will need to stop breast-feeding if their babies develop jaundice. The American Academy of Pediatrics encourages women to continue breast-feeding newborns with jaundice who are otherwise healthy and to focus on increasing the frequency of feedings (about 8 to 12 times every 24 hours). If your baby needs help getting enough milk, you can use a lactation aid or ask your doctor or a lactation consultant to help your baby latch on better.

If your baby is hospitalized, you may need to pump your breasts to maintain your milk production. You can then take the milk to the hospital for your baby's feedings.

Conclusion

This review is a compilation of information of neonatal jaundice with respect to its types, etiology, symptoms, diagnosis, treatment and preventive measures. Jaundice is the most common condition that requires medical attention in newborns. The yellow coloration of the skin and sclera in newborns with jaundice is the result of accumulation of unconjugated bilirubin. In most infants, unconjugated hyperbilirubinemia reflects a normal transitional phenomenon. However, in some infants, serum bilirubin levels may excessively rise, which can be cause for concern because unconjugated bilirubin is neurotoxic and can cause death in newborns and lifelong neurologic sequelae in infants who survive (kernicterus). For these reasons, the presence of neonatal jaundice frequently results in diagnostic evaluation. Emphasis is given on diagnostic techniques to detect the presence of jaundice in neonate’s body. Neonatal Jaundice if diagnosed on time can be cured and the overall increase in death rate of neonates due to this condition can be reduced.

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