International Standard Serial Number (ISSN): 2249-6807

International Journal of Institutional Pharmacy and Life Sciences 9(6): November-December 2019

INTERNATIONAL JOURNAL OF INSTITUTIONAL PHARMACY AND LIFE SCIENCES

Pharmaceutical Sciences **Review Article……!!!**

Received: 12-10-2019; Revised: 21-11-2019; Accepted: 24-11-2019

NEONATAL JAUNDICE

Dolly S. Patil*, Lokesh G. Barade, Harshal L. Tare

TSPM'S Trimurti Institute of Pharmacy, Jalgaon, Maharashtra, India.

Keywords:

Jaundice, Extrinsic causes Intrinsic causes, Exchange transfusion, Bilirubin meter

For Correspondence:

Dolly S. Patil

TSPM'S Trimurti Institute of Pharmacy, Jalgaon, Maharashtra, India

E-mail:

dollypatil2612@gmail.com

ABSTRACT

Jaundice occurs in most new born babies. Most jaundice is benign, but because of the potential toxicity of bilirubin in newborn babies must be monitored to identifying those who might develop severe hyper bilirubinemia and, in rarer cases acute bilirubin encephalopathy. Rarely, if bilirubin levels are sufficiently high, bilirubin can cross the blood brain barrier and cause a damaging condition called kernicterus. Neonates on exclusive breastfeeding have a different pattern of physiological jaundice as compared to artificially feed babies. This article is focus on reduce the incidence of server hyper bilirubinemia and bilirubin kernicterus while minimizing the risks of unintended harm such as maternal anxiety, decrease breastfeeding and Unnecessary costs or treatment.

INTRODUCTION:

A common conditions in infants, jaundice or icterus is the condition characterized by yellow coloration of the skin and white of the eyes, mucous membrane and deeper tissues due to increased bilirubin level in blood.[1] The high prevalence of neonatal hyper bilirubinemia reflects developmental red blood cells, hepatic and gastrointestinal immaturities that results in imbalance favoring bilirubin production over hepatic-enteric bilirubin clearance.[2,3] Neonatal jaundice occurs in more than 60% of late preterm and term newborn, peaking at 3-5days of life and usually resolving by 2week of age.[4] This common clinical finding is the result of an imbalance between production and elimination of bilirubin, a breakdown product of hemoglobin. Bilirubin formation in newborns is 2 to3 times greater than in adults owing to the shorter life span in adults owing to the shorter life span of fetal hemoglobin compared to adult hemoglobin. Severe neonatal hyper bilirubinemia, defined as total serum bilirubin (TSB)[4] concentrations> 221µmol/L (12.9 mg/ DL), ha been estimated to occur in up to 10% newborns.[2,3] Neonatal jaundice is the discoloration of skin and sclera color to yellowish in a newborn by bilirubin.[5] Therefore it can create concern in the physician anxiety in parents. According to neonatal – perinatal Database(NNPD) in the incidence of neonatal hyper bilirubinemia in-house live-births is 3.3% while in extramural admission morbidity due to hyper bilirubinemia accounted for 22.1%.[6]

The mechanism of neonatal jaundice is the imbalance between bilirubin production and conjugation, which results in increase in bilirubin levels.[7] The imbalance is mainly because of the immature liver of the neonate and the rapid breakdown of the red blood cells, which may be multifactorial.[8,7,9,10] The main causes of increased bilirubin mostly are: race, genetic polymorphism, inherited and acquired defects e.g. spherocytosis, Gilbert 's syndrome, Najjar 1 and 2 Molecular genetic studies have shown the correlations between the neonates hyper bilirubinemia and different genetic variation which can change in enzyme activity.[11,12]

CAUSES:

In neonates, jaundice tends to develop because of two main factors first the breakdown of fetal hemoglobin as it is replaced with adult hemoglobin and the second one is the relatively immature hepatic metabolic pathways which are unable to conjugate so excrete bilirubin as quickly as an adult. This causes an accumulation of bilirubin in the blood, leading to the symptoms of jaundice. They can be grouped into the following categories:

Intrinsic causes of hemolysis:

1. Membrane conditions
    - Spherocytosis

- Hereditary elliptocytosis

2. Systemic conditions
    - Splenomegaly
    - Sepsis
    - Arteriovenous malformation
3. Enzyme conditions
    - Glucose-6-phosphate dehydrogenase deficiency
    - Pyruvate kinase deficiency
4. Globin synthesis defect
    - Sickle cell disease
    - Alpha-Thalassemia

Extrinsic causes of hemolysis:

1. All immunity
    - Hemolytic disease of the newborn (ABO)
    - Rh disease
    - Hemolytic disease of the newborn
    - Other blood type is matches causing hemolytic disease of the newborn
    - Breast-milk feeding

Non-hemolytic causes:

- Cephalonematoma
- Polycythemia
- Sepsis
- Hypothyroidism

Hepatic causes

1. Infections
    - Sepsis
    - Hepatitis B
    - TORCH infections
2. Metabolic
    - Galactosemia
    - Alpha-l-antityrypin deficiency
    - Cystic fibrosis
3. Drugs

4. Total parenteral nutrition
5. Idiopathic

Post-hepatic:

- Biliary atresia
- Bile duct obstruction
- Non-organic causes[13-15,16-17]

TYPES OF JAUNDICE:

Several types of jaundice have been reported in neonates including physiological jaundice. Breast feeding/milk jaundice, Hemolytic jaundice including three main subtypes due to Rh factor incompabtility, ABO incompatibility, Glucose-6-phosphatedehydrogenase deficiency.[18]

Physiological Jaundice:

Most cases of hyperbilirubinemia in neonates are in fact physiologic and lead to no serious complications. In rarer cases of physiologic hyperbiliirubinemia, where bilirubin levels reach toxic high levels. Neurodevelopmental abnormalities intellectual deficits, athetosis and loss of hearing. Physiological jaundice usually appears after at least 24 hours of birth and peak after four or five days. In later disappears after about 2 weeks of life. In physiologic jaundice bilirubin is predominantly unconjugated, and bilirubin levels in serum do not become higher than 15mg/DL. More recent guidelines have suggested that even bilirubin levels that reach 17 or 18mg/DL could be considered normal and physiologic in an otherwise healthy full- term neonate.[19.20]

Breast milk/ Breast feeding jaundice:

First described almost 50 years ago, breast milk jaundice benign unconjugated hyperbilirubinemia *associated* with breast feeding, is a common cause of prolonged jaundice in the otherwise healthy feed infant born at term.21-23 Jaundice in breast fed babies usually appears between 24-72 hours of age, peaks by 5-15 days of life and disappear by the third week of life. Higher bilirubin levels have been reported in newborns.[24]

Breast milk jaundice is a benign conditions that resolves without treatments.[25] Clinical experience and quantitative data confirm that when formula is substituted for breast milk hyperbilirubinemia rapid improves.[21-23] Since breast-feeding jaundice was the recognised as a clinical entity, multiple unsuccessful attempts have been made to identify a specific chemical in breast milk that might be responsible causing breast milk jaundice.[21,22,26-28]

Decreased frequency of breastfeeding is associated with exaggeration of physiological jaundice one of thee significant procedures to manage jaundice in a termhealthy babies is the mothers encouragement to breastfeed their babies at least 10-12 times per day.[29] However if bilirubin

levels are higher than 20 mg/DL it is recommended to stop breastfeeding as this could be associated with permanent neurological complication.[6]

HEMOLYTIC JAUNDICE:

Hemolytic jaundice is the type of jaundice that occurs because of excessive destruction of RBC_s resulting in increased blood level of free (unconjugated) bilirubin in this condition, the excretory function of liver is normal, But the quantity of bilirubin increases enormously.[1]

a) Rh factor incompatibility:

Rh hemolytic disease of the newborns (RHDN) results from maternal red-cell alloimmunization.[30] In these cases, the mother's body produces antibodies that attack specific antigens on the RBC_s of the fetus, most likely the Rh antigens. This is most likely to occur when an Rh negative mother has an Rh positive fetus.[31],then maternal immunoglobulin (IgG) antibodies might cross the placenta into the fetal circulation and cause a wide variety of symptoms in the fetus, ranging from mild to severe hemolyticanemia and fetal hydrops.[32,33] Infants who have a risk of developing Rh hemolytic disease of the newborn should be early investigated and treated. Investigations for these infants include packed cell volume,blood group, Rh typing, serum bilirubin, and reticuloytes counts. Immediately following birth these patients should be initiated on phototherapy which should continue until the level of bilirubin decreases significantly.[32]

b) ABO Incompatibility:

ABO hemolytic disease of the newborns (ABO HDN) is the most common maternofetal blood Group incompatibility –ABO. HDN is restricted almost entirely to group A or B bodies born to group O mothers with immune anti-A or anti-B antibodies. Although, HDN has been reported in a baby whose mother was Group A with high titres of anti-B.[34] Babies with O blood group mother should be closely checked and discharged after 72 hours. Routine cord blood screening is not recommended for newborns with O-group mothers.[35]

It has been noted that hemolytic disease of the newborns due to ABO incompatibility frequently occurs during the first pregnancy, and about 50% of infants are affected unlike RH hemolytic disease of the newborns in which the first born-babies are usually spared or free of the disease and subsequent babies are the ones that are affected pregnancies with evidence of fetal sensitization in 3% live birth.[36,37]

ABO incompatibility jaundice usually starts to appear at the age of one day. If it appears earlier. Or it becomes severe etiologies intensive phototherapy is indicated in these cases.[38]

c) GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY:

Glucose -6-phosphate dehyrogenase deficiency is the most common enzyme deficiency involving more than 400 million people worldwide.[39] the management of spherocytosis, G6PD deficiency of an enzyme in RBCS.[33] it is a most vital disease of the path way of hexose monophosphate.[40] it causes significant dysfunction hexose RBCs leading to hemolysis. It should be suspected in any neonate who has a family history with hemolytic dice.[33]

MEASUREMENTOFBILIRUBINLEVELS:

Bilirubin level in a neonatal jaundice can be checked via biochemical method, bilimeter or transcutaneous bilirubinometer.[41-45]

BIOCHEMICAL:

The best method measuring for bilirubin estimation is the total and conjugated bilirubin in assessment based on the vanden bergn reaction[46,47]

BILIMETER:

Bilimeter is used to measure the levels of total bilirubin in the serum is based on spectrophotometry techniques. this is commonly used method in Neonates due to the predominance of unconjugated bilirubin.[41]

TRANSCUTANEOUS BILIRUBINOMETER:

This is a non-invasive method that uses the spectral reflectance of multi wavelengths that are released from the skin bilirubin. This instruments accuracy is usually affected by the pigmentation of the skin and it is thickness.[47] newer devices that use multiwavelength spectral reflectance can eliminate this variability.[48] these devises could help reduce the need to draw blood and improve follow-up for infants a home.

INHIBITION OF BILIRUBIN PRODUCTION

Synthetic metallophyrins in which the centrds iron is replaced by others metals.[49] limit the production of bilirubin by competitively heme oxygenase. In 517v preterm infants who weighed 1500 to 2500. one intramuscular dose (6µmol per kilogram) of tin-mesporphyrin gives with in 24 hours after delivery reduced the requirement for phototherapy by 76 percent and lowered the peak serum bilirubin concentrations by 41 percent.[50] although they are promising metalloporphyrins are not currently approved for use in new. Born infants whether one metalloporphyrin is more safer and effective for newborn infant compared to others is not known none are available for oral administration.

TREATMENT:

PHOTOTHERAPY:

Phototherapy is most common technique used for treatment of hypebilirubinemia in infants four decades[51] efficient phototherapy rapidly reduces the serum bilirubin concentration in the body. The formation of lumirubin, a water-soluble compound, is the rate-limiting step in the elimination of bilirubin by phototherapy.[52] two factors in phototherapy determine the rate of lumirubin formation: the spectrum[52,53] and the total dose of light delivered.[55,56] because bilirubin is a yellow pigmentation, it is likely absorb blue light (with a wavelength of approximately 450mm).[55,56]

The surface area of the infant exposed to phototherapy and the spectrum of light timely phototherapy application in infants who show marked. Potentially hazar dous hyperbillirubinemia is clear and highlighted by the work of mreinil et al, who report that configurational photoisomerization of bilirubin occurs almost instantaneously and is detectable in appericable amounts in the blood of newborns with in 15 min of initiating intensive phototherapy.[59]

a) Conventional Phototherapy:

One can use conventional or fiber-optic phototherapy units provided jaundice is non-hemolytic or its progression is slow.

b) Intensive Phototherapy:

In the circumstances including hemolytic jaundice, rapidly increasing bilirubin, or in effectivenesss of a conventional unit, using of intensive phototherapy is warranted.[60]

c) Exchange Transfusion:

Exchange transfusion remains on important, if infrequently required clinical intervention to reduce the risk for kernicterus.[56,57,61] This technique rapidly eliminates bilirubin from the circulation circulating anti-bodies that target the erythrocytes beneficial in infants who have ongoing hemolysis from any cause.[100] The prevention of Rh (D) hemolytic disease with Rh(D) immunoglobulin and the more effective use of intensive phototherapy have led to a dramatic decline in the number of exchange transfusion .[56,57]

Many complications of exchange transfusion have been reported, including thrombocytopenia, portalvein thrombosis, necrotizing enterocolitis,[63] electrolyte imbalance, graft verus-host disease,[64] and infection. Use of exchange transfusion greatly decreased after introduction of phototherapy[65] and the optimation of phototherapy may further reduce it use.[66]

PHARMACOLOGIC THRAPIES:

Phenobarbitone has been used since the mild-1960_s to increase the conjugation and excretion of bilirubin.[67] However the effect of phenobarbitone is not rapid and take much time to show. When used for 3-5 days in dose of 5mg/kg after birth prophylactincally, it has shown to be effective in babies with hemolytic disease, extravasated blood and in preterm without any significant side effects.[68-74]

Intravenous immunoglobulin:

Early studies[56,57] and a systematic review[75]Suggested administration of intravenous Immunoglobulin (IVIG) to newborn with Rh Hemolytic disease. Significantly reduce the need for exchange transfusion. Two recent randomized controlled trials, however, Showed no benefit from the administration of IVIG to newborns with Rh Hemolytic disease[76,77]and a Cochrane meta-analysis[78] concluded that the efficacy of IVIG was not conclusive in Rh or ABO hemolytic disease of the newborn.

CONCLUSION:

Hyperbilirubinemia is more severe in infants. The yellow coloration of the skin and scores in infants with jaundice is the result of accmulation of unconjugated bilirubin. Government and other public health organization should be arranged seminars, workshops and training for mothers regarding to neonatal jaundice. Parents should be check their ABO blood groups and Rh factor before marriage. Medical scientist should be research on other treatments and technique like phototherapy having no side effects.

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