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Mini Review

Neonanatal Jaundice: A Mini-Review

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Abstract

Neonatal jaundice is a condition that occurs within the first week of life as a result of excessive accumulation of a bile pigment called bilirubin in the body. It occurs as a usual process in 65-70% of the new-born. However, it may occur due to lack of breastmilk feeding, extreme dehydration or due to some genetic disorders, metabolism disorders, gland malfunction or liver diseases. Sometimes neonatal jaundice can cause complications and even lead to death, if not treated at time. It is important to determine whether the infant's jaundice is physiological or pathological and then treated accordingly. So, the study aims to review the pathophysiology, diagnosis and treatment of neonatal jaundice addressing complexities that have arisen with new technologies. It also discusses the medical and nursing management guidelines regarding the prevention and care of the neonates and their families with jaundice.

Keywords: Neonatal Jaundice; Bilirubin; Phytotherapy; Exchange Transfusion; Immunoglobulins

Introduction

The term Jaundice is derived from the French word '*Juan'* meaning yellow which clinically manifests as yellowish discoloration of the skin, sclera, and mucosa caused by excessive accumulation of bilirubin in the tissue and plasma [1,2].

Neonatal Jaundice is considered as physiological jaundice if it occurs after 48 hours of life or in 2-4 days old new-born; and pathological jaundice if it occurs within 48 hours of life [3]. Mostly it occurs as a physiological process but it also results from red blood cell break down, liver disease, infection, hypothyroidism, or metabolic disorders (pathological process). Jaundice appears visibly if bilirubin level is > 34 µmol/L (2 mg/dL) [1]. In most of the neonates, the jaundice occurs as result of excessive level of unconjugated bilirubin in blood whereas in some infants it occurs due to higher unconjugated bilirubin in blood, which is always pathological. In spite of the advances in treatment and management of neonatal jaundice, it remains an important reason for morbidity and mortality in neonates.

Breastfeeding is very essential for preventing jaundice in neonates as it meets the dietary, emotional, as well as the psychological demands of the neonates [4]. Moreover, it is readily digestible and highly nutritious containing 90% water, 4% lipid, 1% lactose, 1% lactoferrin, 1% polyunsaturated fatty acids (PUFA), vitamins, and minerals (iron, zinc, calcium, sodium, chloride, magnesium, and selenium) [5]. It is a rich source of Bifidus factor, lymphocytes, macrophages, IgA, IgM, and certain immune system constituents. It also releases oxytocin, thereby improving the bond between mother and child [6]. Therefore, breast milk should be feed exclusively for six months in infants.

Pathophysiology

The pathophysiology of jaundice is explained on the basis of metabolism of bilirubin, which occurs in three stages: prehepatic, hepatic, and post-hepatic [7,8].

Prehepatic

Erythrocytes are removed from the circulation after completion of their lifespan and degraded by the macrophages of the reticuloendothelial system present in spleen and liver. The hemoglobin is broken into globin and heme. The globin may be reutilized for hemoglobin formation. In the reticuloendothelial cells of spleen, liver and bone marrow, heme released from the RBC undergoes a series of reactions to form the final product bilirubin. Heme is cleaved by heme oxygenase to form biliverdin (a green pigment) which is reduced by biliverdin reductase to bilirubin (yellow pigment) [9,10].

Hepatic

The bilirubin released from the reticuloendothelial system is lipophilic in nature and therefore it is transported in the plasma in a bound form to albumin. As the albumin-bilirubin complex enters the liver, bilirubin dissociates and is taken up by the hepatocytes by a carrier mediated active transport chain and bound to proteins in the cytosol to decrease the outflow of bilirubin back into the plasma.

In the liver, bilirubin is conjugated with two molecules of glucuronate supplied by UDP glucuronate by bilirubin glucanosyltransferase (of smooth endoplasmic reticulum) to form water soluble bilirubin diglucuronide [9,10] which is conjugated bilirubin.

Posthepatic

Conjugated bilirubin is now entering through the bile into the bile ducts and stored in the gallbladder, and then reaches intestine.

The intestinal mucosa unable to absorb the conjugated bilirubin due to its hydrophilicity and large molecular size. Specific bacterial enzymes namely β-glucuronidases of intestine, hydrolyses bilirubin glucuronides to liberate bilirubin and metabolize bilirubin to urobilinogen (colourless compound), a small part of which may be reabsorbed into the circulation. Urobilinogen can be converted to urobilin in the kidney, which imparts characteristic yellow colour to urine and excreted out. A part of urobilinogen is converted by bacteria to stercobilin which gives characteristic brown colour to the feces [9,10].

Causes of neonatal jaundice

Factors that cause neonatal jaundice include a change in normal blood volume and haemoglobin concentration, a reduction in the average lifespan of red blood cells, and interruption in maturation of liver enzymes. The intestinal bacteria are lower in number in infants than in adults, as a result there is higher level of bilirubin in the body [3].

Diagnosis

Physical examination

Proper medical history should be taken from the new-born parents like earlier occurrence of jaundice or other conditions that may cause changes in RBC like sickle cell; spherocytosis, or ABO and Rh incompatibility, certain enzyme deficiency like Glutamate 6 phosphate dehydrogenase and pyruvate kinase; genetic disorders like Crigler-Najjar and Gilbert syndromes or diseases related to liver or gallbladder. Appropriate record should be there on sufficient breast milk feeding [3].

Clinical Examination

Dermal staining in new-born

Dermal staining of bilirubin can be used to detect the intensity of jaundice [11]. Dermal staining in new-born advances towards cephalo-caudal direction [12]. The new-born should be always observed in good daylight. The physician should light the skin by applying digital pressure and the underlying colour of skin and subcutaneous tissue should be recorded. New-born should also check the colour of skin beyond the thighs, if it yellowish in colour then bilirubin levels should be assayed for confirmation of jaundice. Clinical assessment is incorrect if a new-born is under the treatment of phototherapy [13].

Measurement of Bilirubin levels

Bilirubin level can be checked by using Transcutaneous bilirubinometer, Bilimeter or biochemical method [14-18].

Bilirubinometer

Transcutaneous bilirubinometer is a non-invasive method for estimation of bilirubin in skin. This method is based on the principle of multi wavelength spectral reflectance for staining bilirubin in the skin [19]. The accuracy of result obtained by this method can be affected by level of skin pigmentation and its width [20].

Bilimeter

The method depends on the principle of Spectrophotometry and it helps to detect the amount of total bilirubin present in the serum. Total bilirubin present in the serum may be in conjugated form or in unconjugated form. Because of the predominant unconjugated form of bilirubin in neonatal jaundice, this method has been considered as a useful technique in neonates.

Biochemical

The gold standard for estimation of bilirubin in serum is the estimation of total bilirubin and conjugated bilirubin which based on the principle of *Van den Bergh* reaction [21,22].

Management

We should follow proper protocols for the treatment of neonatal jaundice such as adequate breast milk consumption, phototherapy, exchange transfusion, Intravenous infusion of immunoglobulins etc. Advice should be given to mother and family member on exclusive breastfeeding to baby continuously for at least 6 months [23].

Infants with jaundice within 24 hours of birth should undergo continuous monitoring and intensity of transcutaneous bilirubin or total serum bilirubin levels should be estimated [24]. It should be noted that babies thar are on breastfeeding and/or born before completion of 38 weeks of gestation have a higher change of developing neonatal jaundice and need firmer supervision and monitoring.

Treatment methods

Phototherapy

Phototherapy is extremely effective and remains as the first line of treatment for managing significantly higher levels of bilirubin [25-29]. After several years of its use as a treatment method for hyperbilirubinemia, nowadays, phototherapy is considered as safe, efficient and without any serious adverse effects in newborns [25], thereby, making it the "cornerstone" for treatment of hyperbilirubinemias [30].

Phototherapy is another option for treatment, when the total serum bilirubin level is between 15 mg/dl to 20 mg/dl in infants of 25 to ≥ 72 hours old. It should be kept in mind that Phototherapy can be practiced only if the blood total bilirubin level is more than five times the birth weight of the [31]. In some cases, phototherapy is started in infants weighing 1.0 kg to 2.0 kg with a bilirubin level of 5 mg/dl to 10 mg/dl [32].

Phototherapy comprises the use of light of a particular spectrum through lamp, pad, blanket, or cover etc. [25,33] which changes the bilirubin present in the skin from unconjugated form to conjugated form, so that it can easily bypass the liver and advances directly to excrete through bile or urine [33,34]. The intensity of hyperbilirubinemia depends on the kind of device used, treatment duration, intensity of light used as well as on place of treatment [25,28,33]. Phototherapy can be safely stopped for up to 30 minutes at a time to enable breast milk feeding and also for other requirements [35]. Bilirubin level falls down within 2 hours of start of treatment and after it the therapy can be interrupted for some time for feeding and bonding [25]. Dehydration may occur due to unaware water loss which may be a concern for exclusively breastfed babies and should be observed accordingly [35,36].

Nursing attentions should be given on proper eye protection for the infant and lessening diaper covers and checking the patches to increase skin surface area treated. To minimize skin damage, plastic covers or optical filters are used to cover the lights in order to screen the ultraviolet rays [25]. Nurses should also monitor the infant's level of dehydration, temperature intensity, and also check for availability of infant's feeding, proper care as well as medical necessities in treatment [33]. Despite various advantages, phototherapy has certain drawbacks like photosensitivity and blistering, blebs, purpura, and bronze baby syndrome etc. [33].

Exchange transfusion

Exchange transfusion is designated by cord bilirubin levels greater than 5 mg/dl, bilirubin levels >1 mg/dl every hour, or indirect bilirubin levels > 20 mg/dl [37]. For healthy term babies who were born between the first 25-48 hours of life and had bilirubin levels of 340 µmol/l (19.88 mg/dl); for healthy term babies who were born beyond 48 hours and had bilirubin levels of 430 µmol/l (25.15 mg/dl) [38]. For preterm infants, the following guidelines should be followed: birth weight (BW): >2000 g and bilirubin levels: 260-290 µmol/l (15.20-16.96 mg/dl); birth weight: 1001.00-1500.00 g and bilirubin levels: 170-260 µmol/l (9.94-15.20 mg/dl); and birth weight: < 1000.00 g and bilirubin levels:136 -170 µmol/l [38].

More use of phototherapy has decreased the use of the invasive exchange transfusion (ET) method [25], referring exchange transfusion to only severely emergent cases [25-29]. Lack of adequate phototherapy and facilities, severity of hyperbilirubinemia complicated by genetic factors, and systems deficits make this method a more common treatment in developing countries [30,39]. It removes high-bilirubin aliquots from infant's blood and then scientifically substituting it with "clean" donor blood to get a rapid bilirubin decrease [33,34]. Exchange transfusion is performed with the help of catheters, generally through umbilicus [40]. Administration of blood products involves certain risks like metabolic risks and blood products associated risks, however, these are temporary findings and can be treated well [41,42]. But exchange transfusion method may have some disadvantages that includes apnea [41], necrotizing enterocolitis, renal failure, seizure, and advance to kernicterus [43].

Immunoglobulin and metalloporphyrin's

Infusion of immunoglobulin by intravenous route is considered as the most commonly used principal treatment for higher level of blood bilirubin level in infants with immunological conditions [44], even though it can also be used as an additional therapy to phototherapy as it helps in minimizing the duration of phototherapy [28]. Infants having hemolytic jaundice due immunological disorders have mainly profited from the use of immunoglobulins, thereby reducing the requirement for exchange transfusion therapy [28]. Intravenous infusion of immunoglobulin is generally considered safe with only few occasional complications like hemolysis, sepsis, and renal failure [28].

Metalloporphyrin's works by aiming the enzyme heme oxygenase to limit the formation of bilirubin [28,29] in order to treat hyperbilirubinemia [45]. It can be used as a prevention plan in infants which are more prone to hyperbilirubinemia [29], like infants with very low birth weight and in infants with genetic risk factors such as Gilbert's syndrome, glucose-6-phosphate dehydrogenase, and UGT-1A1 mutations [29] etc. However, the use of metalloporphyrin's in hyperbilirubinemia is still under experiment [45], have not been considered clearly safe in humans [46] and not permitted by the FDA, and are specifically labeled "not recommended" as therapy for to treating hyperbilirubinemia in infants by some strategies [36].

Nursing Guidelines

At first, nurse should follow certain general interventions *i.e.,* minimizing the clothing, providing blanket to maintain the required temperature; checking for dark coloured urine or bilirubin in blood, light coloured stool etc. Under phototherapy treatment, the body weight of baby should be checked; proper knowledge should be provided to the mother about breastfeeding; disease conditions and its treatment, and also the mother should be encouraged to continue the breastfeeding exclusively for at least 6 months. While performing phototherapy, continuous monitoring of new-born and machine (phototherapy light, and temperature) is inevitable, along with it some other factors should also be taken into considerations like proper cover should be there on the eyes and genitalia of new-born; the new-born baby should be checked for the presence of rashes, dehydration, hyperthermia, lethargy, abdominal distension, eye damage, and bronze baby syndrome. Proper medication including fluids administration should be provided to the new-born baby as per the requirements. The nurse should inquire about the health status of both the newborn baby and the mother as a follow up of the treatment and reporting it to the doctor.

Prevention

The best way to prevent neonatal jaundice is adequate and exclusive feeding of breast milk for the first 6 month of life. Formula fed infants usually should have 30-60 milliliters of formula every two to three hours for the first week [47] and if possible, up to 6 months.

Conclusions

Neonatal jaundice is quite common condition in infants occurring during the first week of life which is characterized by hyperbilirubinemia. Various steps have been taken to fight neonatal jaundice like exclusive breastfeeding, phototherapy, exchange transfusion and infusions of Immunoglobulins. At the same time, parents should have proper knowledge on neonatal jaundice to check the occurrence of jaundice and seek medical attention as or when required. Neonatal jaundice is considered as the common cause of neonatal sickness and even death. Therefore, early prevention and timely treatment of neonatal jaundice are very crucial to inhibit neonatal complications as well as neonatal death.

Conflict of Interest

The authors declare no conflict of interest.

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