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Turkish Neonatal Society guideline to the approach, follow-up, and treatment of neonatal jaundice

Türk Neonatoloji Derneği yenidoğan sarılıklarında yaklaşım, izlem ve tedavi rehberi

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Abstract

Jaundice is one of the most common problems in the newborn. It is generally accepted as a physiologic condition; most cases are benign and transient. However, in a small portion of jaundiced newborn infants, serum bilirubin concentrations increase to a level at which irreversible brain damage can occur. The timely diagnosis and management of severe hyperbilirubinemia is essential to prevent acute bilirubin encephalopathy and kernicterus. Kernicterus still occurs although it is almost always preventable. The focus of this guideline is to reduce the incidence of severe hyperbilirubinemia and bilirubin encephalopathy. Therefore, a system-based approach using the recommendations of this guideline should be implemented in all birthing facilities and continued in ambulatory care of the newborn infants.

Keywords: Bilirubin encephalopathy, exchange transfusion, hyperbilirubinemia, kernicterus, newborn, phototherapy

Öz

Sarılık yenidoğan bebeklerde sık görüllen bulgulardan biridir. Normal fizyolojik bir durum olarak kabul edilir; genellikle selim, geçici bir durumdur. Ancak yenidoğanların küçük bir bölümünde geri dönüşümsüz ciddi beyin hasarı için tehdit oluşturabilen düzeylere erişebilir. Zamanında tanı konup tedavi edildiğinde akut bilirubin ensefalopatisi ve kernikterus önlenebilir. Kernikterus her zaman önlenebilir bir durum olmasına rağmen halen görülmektedir. Bu kılavuzun amacı ciddi hiperbilirubinemi sıklığını ve bilirubin ensefalopatisini azaltmaktır. Bundan dolayı bu kılavuzun önerilerinin tüm doğum yapılan kurumlarda ve taburcu etme sonrası izlemde kullanılmasını sağlamak önemlidir.

Anahtar sözcükler: Bilirubin ensefalopatisi, fototerapi, hiperbilirubinemi, kan değişimi, kernikterus yenidoğan

Introduction

Jaundice is yellowish staining of the skin and sclera as a result of increased bilirubin in the body (hyperbilirubinemia). Jaundice is observed only if the serum total bilirubin (TSB) level exceeds 5 mg/dL (1). Although it is generally a benign, transient condition, it may cause severe neurologic sequela by leading to bilirubin encephalopathy if the bilirubin level reaches threatening levels in terms of irreversible, severe brain injury in a small portion of newborns (2).

Kernicterus

Kernicterus is a term that describes the pathologic findings caused by bilirubin toxicity in the brain. The term acute bilirubin encephalopathy is used for the acute symptoms of bilirubin toxicity observed in the first week after birth and kernicterus is used for chronic and permanent clinical sequelae of bilirubin toxicity (3). In recent years, changes related to bilirubin encephalopathy have been defined as bilirubin-induced neurologic dysfunction (BIND). BIND shows a wide spectrum ranging from mild and specific neurologic disorders (isolated auditory neuropathy, movement disorders, dystonia, cognitive disorders, mild mental retardation) to acute bilirubin encephalopathy and post-icteric sequelae (neuromotor/auditory) (4).

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Objective and targets of this guideline

The diagnosis and treatment of jaundice in babies who have no other health problems continue to be a problem (5). The hyperbilirubinemia management recommendations published by the American Academy of Pediatrics (AAP) are used widely (3). However, healthcare systems as well as local traditions, which carry the potential to increase or decrease hyperbilirubinemia in different geographic regions, may have different characteristics (6). Therefore, new guidelines compatible with current conditions have been prepared in many countries.

Currently, responsibility in the management of hyperbilirubinemia is shared by pediatricians other than neonatologists and family physicians because hospitalization times have become shorter. This guideline is for pediatricians and family physicians working in all healthcare institutions, as well as neonatologists working in hospitals.

Approach to babies with jaundice and prevention of jaundice

Primary prevention

A strong correlation between the risk of hyperbilirubinemia and exclusive breastfeeding has been reported (7). Therefore, adequate and successful breastfeeding should be provided. Breastfeeding should be initiated as soon as possible (in the first hour after birth). An increase in the frequency of breastfeeding decreases the possibility of significant hyperbilirubinemia. Mothers are recommended to nurse their babies at least 8-12 times a day in the first days (3).

Late preterm babies carry a risk in terms of inadequate feeding and hyperbilirubinemia; they should be closely monitored in terms of feeding and jaundice.

Water or sugared water should not be given to newborn babies under any circumstances (8).

Secondary prevention

Specification of blood groups: (3)

- ABO and Rh(D) blood groups and unusual isoimmune antibodies should be tested in all pregnant women.
- If the maternal blood group is not known or the maternal blood group is 0 or Rh (-), direct Coombs test, ABO and Rh(D) blood group should be tested in the cord blood.

Clinical evaluation: All newborns should be followed up in terms of development of jaundice. Skin color should be checked on the first examination after birth and presence

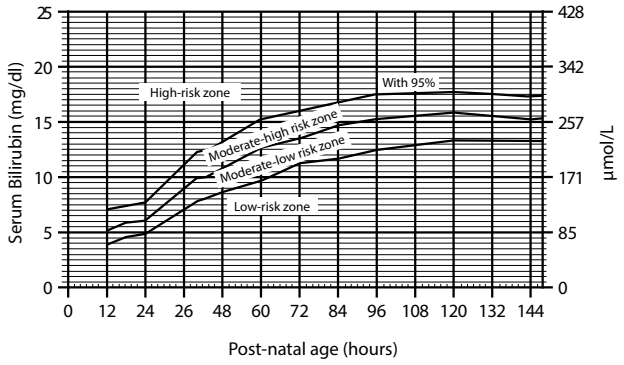

Figure 1. Babies' risk states according to the postnatal age and transcutaneous or STB values. In babies in whom bilirubin levels are measured at ≥2 different times, these values are marked on nomogram and the rate of elevation in the bilirubin level is evaluated. If the bilirubin level is elevating towards the upper percentile curves, hemolysis is considered and the baby is monitored and investigated accordingly (9, 16)

of jaundice should be evaluated every 8-12 hours together with vital signs. Visual evaluations of jaundice should be performed when the baby is naked in a light environment (preferrably natural light). Skin color should be evaluated after the skin is pressed with a finger.

Jaundice developing in the first 24 hours should be considered pathologic unless the opposite is proven. These babies should be investigated in terms of hemolytic disease and other pathologic causes.

Laboratory evaluation

The bilirubin level should be measured in all babies who develop jaundice. Each bilirubin measurement should be interpreted according to the "bilirubin nomogram" prepared by age in hours (Figure 1) (9). Use of these nomograms enables follow up of the course of bilirubin values and the prediction of babies who will subsequently develop hyperbilirubinemia. The following tests should be performed in babies who develop treatment-requiring hyperbilirubinemia, who skip percentiles on repeated bilirubin measurements, and who have no explanatory cause for jaundice in the history and on physical examination (3);

- Maternal blood group and the baby's blood group
- Direct Coombs test
- Complete blood count and peripheral smear
- Reticulocyte count
- Total, direct bilirubin levels
- Glucose 6 phosphate dehydrogenase (G6PD) level
- Reducing substance in urine
- Serum albumin level if the serum total bilirubin level approaches the exchange transfusion threshold level

- Serum electrolytes if pathologic weight loss is present
- Complete urinalysis, urine culture, and sepsis markers if increased direct bilirubin level or late-onset jaundice are present
- In prolonged jaundice, thyroid functions in addition to the above-mentioned tests. Cholestase investigations should be performed, if direct bilirubin is increased.

Bilirubin assessment methods

The gold standard is to measure serum total bilirubin (STB) level with analysers in the laboratory. However, blood samples should be obtained for this; the procedure is painful and adequate blood cannot always be obtained (10).

Non-chemical photometric devices enable bedside measurement of bilirubin level and a small amount of a capillary blood sample is required. When serum total bilirubin levels exceed 14.6 mg/dL, TSB values are measured lower. Under these circumstances, bilirubin should be evaluated with standard laboratory method (11).

Transcutaneous bilirubin (TcB) measurement: Total serum bilirubin is measured on the surface of the skin, thereby reducing the number of blood samples. Its widespread use decreases the frequency of severe hyperbilirubinemia and hospital readmissions for phototherapy (PT) (12). However, TcB measurement is not reliable in babies receiving PT and in babies with dark skin color (13).

In the presence of high bilirubin levels; when TcB exceeds the 75th percentile on the bilirubin nomogram, serum bilirubin level should be measured as measurements show STB to be low (14).

The following babies should not be evaluated through TcB:

- Babies with a TcB value of >12 mg/dL
- Babies with jaundice in the first 24 hours
- Babies for whom a treatment decision has been made
- Babies receiving phototherapy treatment

Direct bilirubin measurement: Direct bilirubin should be measured in association with total bilirubin in order to evaluate cholestasis in all babies with jaundice who require treatment and in ill babies who have prolonged jaundice.

If the direct bilirubin level is above 1 mg/dL, when the total bilirubin level is below 5 mg/dL or if the direct bilirubin level is higher than 20% of the total bilirubin level, when STB is above 5 mg/dL a diagnosis of direct (conjugated) hyperbilirubinemia is made (3). Other than this, a direct bilirubin level above 2 mg/dL is always pathologic (15).

Special evaluations directed to the reason of jaundice

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is associated with acute hemolysis and may result in severe hyperbilirubinemia and bilirubin encephalopathy. In the presence of hemolysis, enzyme levels may be found to be high; they should be remeasured three months later and the baby should be kept away from agents that cause hemolysis (5). In most of these newborns, marked hemolysis findings including anemia and reticulocytosis are absent. It has been reported that there is also a defect in bilirubin conjugation in babies with G6PD deficiency who develop severe hyperbilirubinemia (UGT promotor gene mutation) (16).

In babies with severe jaundice, reducing agents in urine should be tested as a screening test for galactosemia. It should be kept in mind that indirect hyperbilirubinemia may predominate in the first days of life.

Risk evaluation before discharge

Each newborn should be evaluated in terms of development of severe hyperbilirubinemia before discharge; this is especially important in terms of newborns who are discharged before the 72nd hour. STB or TcB measurement should be performed in all babies before discharge from hospital (3). Blood sample obtained for STB during screening of metabolic diseases prevents repeated blood sampling. It has been recommended that risk factors [low gestational age (<38 weeks), being breastfed, excessive weight loss especially in babies who have a weak suck, observation of jaundice in the first 24 hours, isoimmune hemolytic disease (G6PD deficiency), history of sibling who previously received PT, cephal hematoma or diffuse echymosis] should be specified in addition to bilirubin measurements and these should be used in association (17).

Families should be given information and written guidelines related to jaundice. If the bilirubin level measured before discharge is in the high-risk zone (>95th percentile), the newborn should not be discharged.

Follow-up after discharge

The times of follow-up visits depend on the age of the baby at the time of discharge and the presence of risk factors. Babies, who are discharged before the expected peak of STB reached, should be followed up in the elevation period and the bilirubin level should be measured, if necessary.

Generally, babies who are discharged early should be seen earlier (3).

- Babies who are discharged before 24 hours should be seen in the 72nd hour of their life,
- Babies who are discharged between 24 and 48 hours

should be seen in the 96th hour of their life,
- Babies who are discharged between 48 and 72 hours should be seen in the 120th hour of their life.

If a baby has risk factors for hyperbilirubinemia but it will not be possible to follow up the baby, discharge should be postponed until the time period during which the risk of hyperbilirubinemia is at the top, passes.

At each follow-up visit, the newborn's body weight, weight loss percentage, frequency and color of urine and stool, presence of jaundice, as well as nutritional status should be evaluated.

In babies with jaundice requiring treatment, the auditory brainstem response (ABR) test which is performed to evaluate hearing should be repeated when the baby becomes 3-4-month old.

Prolonged jaundice

Prolonged jaundice is defined as jaundice lasting more than 2 weeks in term babies and more than 3 weeks in preterm babies (15). In prolonged jaundice, increased direct bilirubin level is always pathologic and causes of cholestatis should be investigated.

Jaundice lasts longer in babies who are breastfed compared with those fed with formula (18). The majority of cases of prolonged jaundice are breastmilk jaundice. However, other causes should be excluded to make a diagnosis of breastmilk jaundice. In babies with prolonged jaundice, thyroid function tests (TSH, sT4), urinalysis, and urine culture should be performed in addition to the above-mentioned tests, which should be performed in babies with jaundice after taking the history and performing a physical examination. If the direct bilirubin level is not elevated, measurement of liver enzymes is not needed.

Treatment

In treatment, the objective is to prevent the elevation of bilirubin levels to levels that will be harmful to the brain and to rapidly decrease increased bilirubin levels. PT is frequently used for treatment; in some cases, exchange transfusion or intravenous immunoglobulin (IVIG) is used. Treatment indications vary by the baby's gestational age, postnatal age, bilirubin level, and the presence of hemolysis. It is appropriate to use AAP guideline graphs (3), which consider both gestational week and risk factors, in babies with a gestational age above 35 weeks and to use the tables prepared according to birth weight, in babies aged under 35 weeks (19).

Babies in whom jaundice is observed in the first 24 hours and whose bilirubin levels rapidy increase should be evaluated in terms of hemolysis.

Indicators of hemolysis are as follows (15, 20):
1. Jaundice in the first 24 hours
2. Direct Coomb's test (+) and accompanying laboratory findings
   a. Findings of hemolysis on peripheral smear
   b. Increased reticulocyte count
   c. Reduction in hemoglobin and hematocrit levels
3. G6PD deficiency in association with increasing serum total bilirubin level
4. >0.2–0.5 mg/dL increase per hour in the bilirubin level
5. Increasing or persistantly high STB levels despite phototherapy

Phototherapy

The objective of phototherapy is to decrease the need for exchange transfusion by decreasing the bilirubin level and to prevent the development of bilirubin encephalopathy. It is not used in place of exchange transfusion. While making the treatment decision, direct bilirubin is not substracted from total bilirubin; treatment is initiated according to the TSB level, the rate of increase in serum bilirubin level, the baby's birth weight, gestational age and postnatal age, and the presence of risk factors. For treatment threshold levels for the initiation of phototherapy, Figure 2 is used in babies aged over 35 weeks and Table 1 is used in babies aged under 35 weeks (3, 19).

Efficiency of phototherapy: Wavelength and intensity/strength of light, the body surface area exposed to light, and the rate of reduction in the bilirubin level determine the efficiency (21). The most efficent light is blue-green light and its wavelength is between 460 and 490 nm. LED

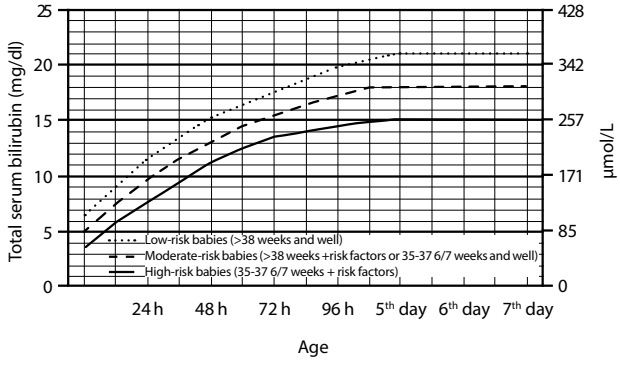

Figure 2. Phototherapy threshold levels according to the postnatal age in babies with a gestational age of ≥35 weeks (3). Risk factors: Isoimmune hemolytic disease, G6PD deficiency, asphyxia, marked lethargy, inability to maintain heat, acidosis, sepsis, albumin <3 g/dL (if measured). Unless all risk factors are excluded, the baby is considered at low risk and the lower curve is used. When making the treatment decision, direct bilirubin is not substracted from total bilirubin; the total bilirubin level is used

Table 1. Phototherapy and exchange transfusion threshold levels in babies with a gestational age below 35 weeks

Birth weight (g)	24-48 hours	49-72 hours	After the 72nd hour
<1000	4 (10)[a]	5 (11)	6 (12)
1000–1499	5 (12)	7 (14)	8 (16)
1500–1999	7 (15)	9 (16)	10 (17)
≥2000	8 (17)	12 (18)	14 (19)

[a]The first figure shows phototherapy threshold level and the figure in brackets shows exhange transfusion threshold level (mg/dL). If risk factors are present, 2 units below these values are accepted. Risk factors: Isoimmune hemolytic disease, G6PD deficiency, asphyxia, marked lethargy, inability to maintain heat, acidosis, sepsis, albumin <3 g/dL (if measured) (18)

lamps that have longer half life and lower infrared emission are also efficient.

Devices with a strength of at least 8-10 μW/cm^2/nm are used for phototherapy (22). For intensive phototherapy, devices with a strength of at least 30 μW/cm^2/nm is recommended; devices with strength above 65 μW/cm^2/nm may have adverse effects (21). The body surface exposed to PT is increased instead of using devices with strengths above these values. Intensive PT is given from both above and below by using two separate PT devices or tunnel PT devices.

In preterm babies, devices stronger than 15-40 μW/cm^2/nm are avoided (23). There is evidence indicating that higher values increase mortality, especially in babies weighing less than 1000 g (23).

For phototherapy to be considered efficient, a reduction of 0.5 mg/dL per hour should be obtained in the bilirubin level measured 4-6 hours after treatment is initiated. A linear reduction is not observed in serum bilirubin levels. The higher the baseline level is, the faster is the reduction. In cases of severe hyperbilirubinemia, use of intensive PT decreases the severity of bilirubin neurotoxicity and the need for exchange transfusion (24).

In babies with hemolysis or direct Coombs positivity with a gestational age of <37 weeks or in babies who received PT in the first 3 days, STB is measured after PT is discontinued (check for "rebound"). However, the baby does not need to stay in the hospital for this.

Use of phototherapy: Intensive phototherapy is used for patients with a bilirubin levels 3 mg/dL below the exhange transfusion threshold level. Unidirectional phototherapy is used in patients with lower bilirubin levels. If the baby is receiving PT in an incubator, PT lights are adjusted such that they are vertical to the incubator surface to minimize reflection and loss of efficiency (3). If the serum total bilirubin level is at the exhange transfusion threshold level, coating the bed in which the baby lies with aluminium foil or white material increases the efficiency of PT (25). During phototherapy, no cream or oil etc. should be applied on the baby's body. In addition, the efficieny increases as the device is moved closer to the baby (3). However, halogen and tungsten lamps should not be too close to the baby because they may lead to burns (25). A space of 35-40 cm is left between the baby and these devices (26).

PT is applied continuously if the bilirubin levels are close to the exchange transfusion threshold level. After the bilirubin level is reduced, the baby is given to the mother for nursing by interrupting PT for half an hour in order to provide mother-baby bonding (3).

PT is stopped when the serum total bilirubin level reduces below 13-14 mg/dL or when it reduces 2-3 mg/dL below the phototherapy initiation threshold level in term babies who have no risk factors (3).

Phototherapy complications: Insensible fluid loss is increased and the stool consistency softens in babies who receive phototherapy. Eruptions occur on the skin and disappear after treatment is discontinued. Adequate hydration, nutrition, and temperature control are important. Neutral ambient temperature should be provided and the baby's body weight and wet diapers should be followed up daily in terms of hydration. In addition, the mother-baby bond may be affected.

The eyes should be covered to prevent retinal injury. Purulent conjunctivitis has been reported in relation to long-term use of eyepatches (27).

Hypocalcemia may be observed in relation to an increase in calcium exretion in urine in preterm babies (28). It is very rarely manifested clinically and spontaneously recovers in 24 hours after PT is discontinued (29).

Phototherapy may disrupt the day-night circadian rhythm and may lead to frequent crying and jitteriness (30).

Bronze baby syndrome is observed in babies with a high direct bilirubin level (31). It is harmless and returns to normal after PT is stopped.

Use of PT is contraindicated in babies who have congenital porphyria or who use photosensitizing drugs (3). Long-term use of PT increases oxidative stress, lipid peroxidation, and riboflavin deficiency (32, 33).

When high-strength PT devices are used, especially in preterm babies below 1500 g, the incidence of patent ductus arteriosus (PDA) may increase (34).

Potential long-term adverse effects of phototherapy: There is evidence indicating that phototherpy increases the risk of asthma, allergic rhinitis, and conjunctivitis by influencing the immune system and Th2/Th1 balance (34).

Although it has been reported that phototherapy increases the number of melanocytic nevi and leads to formation of atypical nevus, it has not been shown to lead to an increase in melanoma or other skin cancers (34). Studies related to adverse effects including malignant melanoma, DNA injury, and skin changes are insufficient (21).

Use of prophylactic PT is not recommended because of these adverse effects.

Exchange transfusion

Exchange transfusion is performed when serum bilirubin levels reach treatment thresholds (Figure 3, Table 1) specified according to the baby's postnatal age and the potential risk factors in terms of bilirubin toxicity, despite intensive PT and IVIG treatment, if necessary, or when the STB is above exchange transfusion threshold levels and persists above this level despite 6-hours of intensive PT or when the baby has findings of acute bilirubin encephalopathy (3, 19). In babies with a postnatal age above one week, G6PD deficiency should be considered primarily if an acute increase in STB above 0.2 mg/dL per hour is observed; intensive PT should be initiated and preparations for exchange transfusion should be initiated.

Free unconjugated bilirubin (not bound to albumin) can cross the blood-brain barrier because of its lipophilic property. There is a risk for the development of kernicterus at lower bilirubin levels, when the albumin levels are low, as the level of free bilirubin will increase.

If the serum albumin level is below 3 g/dL, the baby is considered to carry risk in terms of hyperbilirubinemia and the treatment threshold level is specified accordingly. The bilirubin/albumin ratio is not used alone to make a decision of exchange transfusion, but it is used in associaton with STB levels to support the treatment decision for exchange transfusion (Table 2) (3). Albumin infusion is not recommended (20).

Exchange transfusion should be performed by individuals experienced in this field. The procedure is performed in open beds to prevent heat loss. Keeping the baby nil per oral is not required and the stomach is emptied via a nasogastric tube before the procedure, if necessary. Resuscitation materials are prepared. The baby is monitored

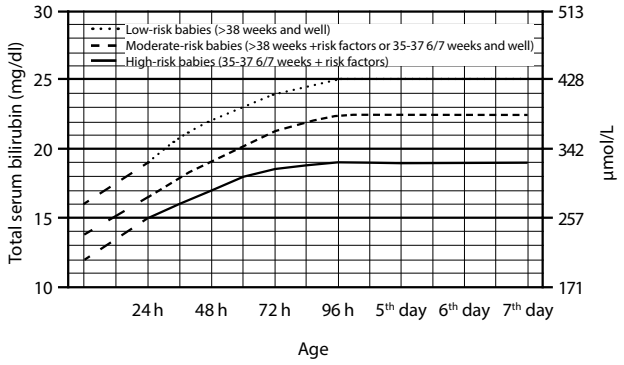

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Table 2. Bilirubin/albumin ratio at which exchange transfusion should be planned according to the baby's risk category

Risk category	B/A ratio at which exchange transfusion should be planned STB mg/dL/Alb, g/dL
Gestational week >38 weeks	8
Gestational week 35 0/7–36 6/7 weeks and well	
Gestational week >38 weeks and baby at risk	7.2
Gestational week 35 0/7–36 6/7 weeks and baby at risk	6.8

B/A: bilirubin/albumin; STB: serum total bilirubin

throughout the procedure and intensive PT is continued before, during and after exhange transfusion. The STB level is measured within 2 hours of the procedure. Informed consent must be obtained from families.

Characteristics of the blood to be selected

Generally, erythrocytes and plasma are mixed by blood banks such that the hematocrit level is reduced to 50-60%. If ABO incompatibility is present, O erythrocytes and AB plasma are used (35). If ABO incompatibility is absent, normal saline or albumin can be used instead of plasma. If there is no blood group incompatibility, exchange transfusion should be performed with blood of the same blood group as the child's blood group. In patients with

subgroup incompatibility, blood that is negative in terms of the antigen causing incompatibility is used. If whole blood is to be used for exchange transfusion, it should be fresh whole blood (<24 hours). Cross-match of the donor blood is performed with the maternal blood if exchange transfusion is to be performed urgently in the delivery room and in cases of intrauterine transfusion. In all other cases, cross-match of the donor blood is performed with the baby's blood (3). Compatible blood for exchange is decided according to the baby's and mother's blood groups.

The blood is irradiated and filtered and warmed in a blood warmer or at room temperature (3, 35). A catheter is placed in the umbilical vein. The exchange transfusion period is 1-2 hours. The amount of blood to be exchanged at one time is 5 mL/kg at most. The rate of exhange transfusion should not exceed 2 mL/kg/minute to prevent fluctuations in blood pressure and thus in intracranial pressure. Double-volume exchange transfusion is performed (3, 35). In this way, 86% of the baby's blood is exchanged. Routine calcium infusion is not recommended during exchange transfusion (20, 36).

Exchange trasnfusion volume (mL)= 2 x total blood volume [(100 mL/kg (preterm baby), 85 mL/kg (term baby)]

$$\text{Erythrocyte volume (mL)} = \frac{\text{Exchange transfusion volume x desired hematocrit}}{\text{Hematocrit of erythrocyte suspension}}$$

Fresh frozen plasma volume= exchange transfusion volume-erythrocyte suspension volume

Drug doses should be repeated or drug levels should be monitored because the procedure will lead to excretion of drugs from the body. Antibiotic treatment is not necessary if infection is not suspected following exchange transfusion (35).

Complications of the procedure include apnea, bradycardia, hypotension, hypertension, hypocalcemia, hypo/hyperglycemia, hyperkalemia, thrombocytopenia, neutropenia, coagulopathy, disseminated intravascular coagulation, metabolic acidosis, vascular spasm, thrombosis, embolism, feeding intolerance, ischemic injury, necrotizing enterocolitis, omphalitis, sepsis and mortality risk (1% in healthy babies, 12% in ill babies) (37).

Intravenous immunoglobulin (IVIG)

IVIG may be used in babies with Coombs (+) Rh or ABO incompatibility and subgroup incompatibility and in babies who have undergone intrauterine transfusion. It is thought to prevent hemolysis by blocking Fc receptors in the reticuloendothelial system. IVIG decreases the need for exchange transfusion by slowing down the rate of bilirubin elevation and by decreasing peak bilirubin levels (3).

Table 3. Exchange transfusion threshold levels in the first 24 hours in babies born with a gestational age below 38 weeks (modified from the reference number 19)

Week	6th hour	12nd hour	18th hour
23–28	5	6	7
29–33	6.5	9.5	12.5
34–37	8.5	11.5	13.5

Standard IVIG (0.5-1 g/kg in 2 hours) is administered in the shortest time possible in babies whose STB increases despite intensive phototherapy and in babies whose STB levels are close to the exchange transfusion threshold level (2-3 mg/dL) or at the exchange transfusion threshold level; it is repeated 12 hours later, if necessary. In babies who have undergone exchange transfusion, IVIG is repeated with the same dose after exchange (3).

Special conditions

Management of Rh hemolytic disease

Before delivery; 0 Rh (-) erythrocyte suspension and AB plasma plus 0 (-) erythrocyte suspension are prepared. Preparation is made such that exchenge transfusion can be performed in the delivery room and IVIG is provided. A team experienced in the field of resuscitation should be present in the delivery room.

As soon as the baby is born; intensive phototherapy is initiated and IVIG is administered. A cord blood sample is sent for hemoglobin (Hb) and STB levels. In babies born with a gestational age above 38 weeks, intensive phototherapy is initiated while preparation for exchange transfusion is being made if the bilirubin level is above 6 mg/dL and the Hb level is <10 g/dL in cord blood. Exchange transfusion is performed if the rate of elevation in STB is above 0.5 mg/dL per hour despite intensive phototherapy and IVIG (38). If the Hb level is below 10 g/dL, but STB is normal, partial blood exchange transfusion is performed for anemia (38).

In babies born with a gestational age below 38 weeks, the decision for exchange transfusion is made according to Table 3.

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