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ORIGINAL RESEARCH

Study of neonates with hyperbilirubinemia requiring exchange transfusion

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ABSTRACT
Kernicterus or bilirubin encephalopathy is caused by unconjugated hyperbilirubinemia that develops either as a result of haemolytic process or inability of liver to conjugate bilirubin. It is preventable through the use of phototherapy, intravenous immunoglobulins (IVIg), or exchange transfusion (ET). The exact bilirubin threshold for intervention remains debated, leading to a study focusing on the outcomes of exchange transfusion for high bilirubin levels in term neonates in a NICU setting. Prospective study over 3 years period, carried out in NICU at government teaching institute to determine the outcome and side effects of exchange transfusion and study the neonatal and maternal risk factors resulting in hyperbilirubinemia requiring exchange transfusion. Blood grouping and Rh typing were done for both mothers and newborns. In all newborns, pre-exchange complete blood count, peripheral blood film, coombs test, reticulocyte count, serum bilirubin and post-exchange serum bilirubin, haemoglobin was done. Maternal and neonatal factors, indications, and outcomes were analysed. It was observed that neonates requiring exchange transfusion were mostly term associated more commonly with Rh incompatibility. Exchange transfusion was required among few of the admitted newborns with unconjugated hyperbilirubinemia. The common adverse effect was sepsis. Overall outcome after exchange transfusion was favourable.

Key words: Hyperbilirubinemia, Exchange transfusion, Kernicterus, Rh incompatibility

INTRODUCTION

Neonatal hyperbilirubinemia is one of the most common conditions requiring medical attention in newborn babies. Approximately 60% of term and 80% of preterm babies develop jaundice in the first week of life, and about 10% of breastfed babies are still jaundiced at 1 month of age.[1]While severe hyperbilirubinemia (total serum bilirubin [TSB] level of >20 mg/dL [342.1 µmol/L]) occurs in <2% of term infants, it can lead to permanent neurodevelopmental delay and kernicterus (i.e., chronic bilirubin encephalopathy).[2,3] Furthermore, though preventable, kernicterus occurs in 20% of infants with TSB >30 mg/Dl.[4,5] Bilirubin inhibits mitochondrial enzymes, interferes with DNA and protein synthesis, and alters cerebral glucose metabolism. Unconjugated bilirubin initiates a mitochondrial pathway of apoptosis in developing brain neurons and it inhibits the function of N methyl-aspartate-receptor ion channels.[6] The region most commonly affected are the basal ganglia, particularly the sub thalamic nucleus and the globus pallidus, the hippocampus, the geniculate bodies, various brainstem nuclei, including the inferior colliculus, oculomotor, vestibular, cochlear, and inferior olivary nuclei, and the cerebellum especially the dentate nucleus and the vermis.[7] Kernicterus or bilirubin encephalopathy is caused by unconjugated hyperbilirubinemia that develops either as a result of hemolytic process or inability of the liver to conjugate bilirubin.[8, 9] Kernicterus is preventable through the use of phototherapy, treatment with intravenous immunoglobulins (IVIg), or the use of exchange transfusion (ET) to lower serum bilirubin levels.[10]Despite proven benefit, exchange transfusion might give rise to cardiovascular, biochemical, orhematological complications and mortality rates vary from 0.5 to 3.3%. Thus, current recommendation for exchange transfusion is based on seeking a balance between risk and benefit.[11, 12] Moreover, the introduction of anti-Rh (D)-specific immunoglobulin, intrauterine transfusions, prenatal monitoring, high-intensity phototherapies, and the use

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of nonspecific human immunoglobulin have made considerable contributions to reducing the indications for ET.[13-15]

In haemolytic disease, immediate exchange is needed when 1. Cord bilirubin level >4.5mg/dl and cord hemoglobin level <11g/dl. 2. Bilirubin level is rising >1mg/dl despite phototherapy. 3. Hemoglobin level is between 11g/dl and 13g/dl, and bilirubin level is rising >0.5mg/dl despite phototherapy. 4. Bilirubin level is 20mg/dl or appears to reach 20 mg/dl at the rate it is rising. 5. There is progression of anemia in face of adequate control of bilirubin by other methods.

The bilirubin level at which intervention is necessary and its outcome is still a contentious issue. Hence in the present study we aimed to study outcome of exchange transfusion for hyperbilirubinemia among term neonates in NICU of a tertiary care centre.

AIMS & OBJEVTIVES

1. To determine the outcome and side effects of exchange transfusion in term neonates
2. To study the neonatal and maternal risk factors resulting in hyperbilirubinemia requiring exchange transfusion.

MATERIAL & METHODS

In the present study, 160 patients were enrolled prospectively over 3 years of study period from October 2020 to October 2023. Detailed patient information was taken at the time of admission in NICU. Study was done in Department of Pediatrics, SRTR Government Medical College, Ambajogai, dist. Beed, Maharashtra, India, after getting informed consent from parents. Study was approved by institutional Ethics Committee. Inclusion criteria was all neonates who had bilirubin levels enough for exchange transfusion according to AAP nomogram. Neonates undergoing exchange transfusion due to causes other than hyperbilirubinemia were not included in study.

Study Procedure: Cord blood investigations in the setting of Rh incompatibility were sent. In the probable ABO setting, ABO blood grouping, Rh typing, serum bilirubin, complete blood count, reticulocyte count, and coombs tests were sent from peripheral blood. In suspected case of sepsis, septic workup was done as per unit protocol. Glucose-6-phosphate dehydrogenase deficiency (G6PDH) and minor blood grouping were done whenever suspected. All patients were given phototherapy before and after the procedure. Double volume exchange transfusion was done, Small amount of blood (5 mL/kg) was exchanged in each pass using the pull and push technique. Each pass (starting from the drawing of the baby's blood per umbilical venouscatheter, disposing of that old blood, followed by drawing donor blood and transfusing that blood into the infant) takes approximately 1.5 to 2 minutes for completion.Vital signs including SpO_2 were monitored continuously during the procedure, 4 hourly for 24 hours and 8 hourly thereafter. Complications observed were taken into consideration for immediate intervention.

All infants who were included in study were followed at regular interval up to 12 months of age. BERA was done at 3 months of age, follow up and assessment during later period (6 months and 12 months) was done in terms of attainment of neurodevelopmental milestone.

Data was entered in excel sheet, cleaned and coded. Percentages were computed for categorical variables. Comparison was done by unpaired student t- test with the help of SPSS software.

RESULTS

There were 86 (54%) male and 74 (46%) female neonates, 64 were term and 96 were near term gestation. 89 (56%) neonates having birth weight less than 2.5 Kg. 138 (86%) were born through normal vaginal delivery and 22 (14%) through LSCS. 142 (89%) neonates developed jaundice within 24 hours after birth and remaining 18 (11%) had jaundice within 24 to 72 hours after birth.

Majority of neonates i.e.142 (89%) had Rh incompatibility, 8 (5%) had ABO incompatibility, 2 (1%) had minor blood group incompatibility, 3(2%) hyperbilirubinemia in IDM (no other cause specified), 2 (1%) G6PDH deficiency and 3 (2%) exaggerated physiological jaundice.

Table No. 1: Distribution of study subjects according to adverse events.

Adverse Events	Frequency	Percentage (%)
Hyperglycemia	86	54
Sepsis following exchange transfusion	27	17
Anemia requiring top-up transfusion	34	21
Hypocalcemia	21	13
Thrombocytopenia	10	6
Catheter-related complications	2	1

Table 1 shows that hyperglycemia was the most common adverse event seen in 86 (54%) neonates, followed by sepsis in 27 (17%), anemia in 34 (21%), hypoglycemia in 21 (13%), thrombocytopenia in 10 (6%) and catheter-related complications in 2 (1%).

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Table No. 2: Distribution of study subjects according to outcome.

Outcome	Frequency	Percentage (%)
Bilirubin encephalopathy	10	6
Rebound hyperbilirubinemia requiring phototherapy	18	11
Death	3	2
Hearing impairment	2	1

Bilirubin encephalopathy was observed in 10 (6%) neonates, rebound hyperbilirubinemia requiring phototherapy in 18 (11%) and hearing impairment in 2 (1%). 3 (2%) neonates died even after exchange transfusion as depicted in table 2.

DISCUSSION

Among the neonates, 142 (89%) were with Rh incompatibility, 8 (5%) were with ABO incompatibility which were more comparedto study byDey SK et al where more than three-fourth of babies (33/41, 80.5%) requiring exchange transfusion had Rh incompatibility, and four babies (9.8%) had ABO incompatibility.[9] Arpit K et al in their study found that study most common cause of hyperbilirubinemia requiring exchange transfusion was ABO incompatibility i.e. 42.86%, (n=15). Rh incompatibility constituted 22.85% of cases (n=8). In remaining 34.29% cases (n=12) no specific cause could be found.[1]

Adverse events like hyperglycemia seen in 54%, sepsis in 17%, anemia in 21%, hypocalcemia in 13%, thrombocytopenia in 6% while catheter related complications seen in 1% study cases. Dey SK et al stated that the most common complication related to the exchange transfusion was hyperglycemia (51.2%).[9] Next to hyperglycemia, sepsis following exchange transfusion was the second most common complication found in 19.5% of newborns. Anemia requiring top-up transfusion and hypocalcemia were found in 17.1 and 14.6%, respectively. There were no catheter-related complications. Among the study subjects bilirubin encephalopathy was seen in 10 patients, rebound hyperbilirubinemia requiring phototherapy was seen in 18 patients, hearing impairment was seen in 2 patients while death occurred of 3 patients after ET. Arpit K et al in their study observed that no mortality occurred in our study. [1] None of the enrolled neonate had to undergo repeat exchange transfusion. It is comparable to study conducted by Sanpavat S, where morbidity was noted in 15.3% of cases.[16]Badiee Z also found complication in 14 neonates (20.9%) in hisstudy.[17] Patra K et al showed higher incidence (74%) of associated abnormalities, commonest being thrombocytopenia (44%) followed by hypocalcemia (29%).[18]

CONCLUSION

Rapidly increasing bilirubin levels in neonates is very harmful for neonates and may be life threatening if not treated promptly. Age of onset of jaundice was below 24 hours in most of cases. Rh incompatibility and ABO incompatibility were the most common indications of exchange transfusion. Hyperglycemia, sepsis and anemia were the common adverse event occurred during ET. Exchange transfusion is one of the most effective and safe method of treating hyperbilirubinemia.

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