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Evaluation of the Severity and Duration of Thrombocytopenia following Exchange Transfusion in neonatal hyperbilirubinemia

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Abstract

Background: Infant jaundice is one the most common causes of hospitalization in infant in the first month of birth, which is defined an abnormal increase in blood bilirubin levels. Exchange transfusion is the recommended treatment for neonatal jaundice who do not respond to phototherapy and experience dangerous complication of jaundice and signs of kernicterus. However, this treatment may lead to complications such as thrombocytopenia. This study aimed to investigate the severity and duration of thrombocytopenia following the exchange transfusion in neonatal jaundice.

Material and Methods: This cross section study was performed on 217 infants. Infants with a gestational age of 35 to 42 weeks and bilirubin levels of above 17 mg/dl, who were undergoing treated with exchange transfusion, entered in this study. This study was conducted from 2012 to 2018 in the Ghaem Hospital (Mashhad, Iran). The samples were selected by convenience sampling. The platelet count was measured before exchange transfusion, right after exchange transfusion, 6 hours after exchange transfusion, and platelet count continued until platelet level was normal. At the time of discharge, platelet levels were re-measured.

Results: Among the samples, 104(53.8%) were males and 89 (46.2%) females. Of the infants who were transfused, 15 % had thrombocytopenia. After the exchange transfusion, 80 % of infants had thrombocytopenia. The mean platelet count before the exchange transfusion was 299,180 per mm3 of blood, and it was 105.140 per mm3 of blood after the exchange transfusion. With respect to severity of this complication, 86 % of the thrombocytopenia after exchange transfusion was mild to moderate.

Conclusion: In this study, nearly one-sixth of the infants who needed exchange transfusions had thrombocytopenia that most of them had platelet of more than 100000. Thrombocytopenia is associated with jaundice and can be exacerbated by phototherapy.

Keywords: Exchange Transfusion, Hyperbilirubinemia, Infant, Jaundice, Platelet, Thrombocytopenia

Introduction

Neonatal jaundice is the most common cause of hospitalization in the first month of life (1). Jaundice is caused due to the precipitation of bilirubin pigment in the skin (2, 3). Jaundice is seen in 60 % of term neonates and 85 % of preterm infants during the first week of life. Typically, the increase in blood bilirubin levels begins in the first 24 hours after birth and continues to increase, but a decrease in its level is seen by the end of the first week; however, bilirubin levels continue to increase in some cases. High level of bilirubin creates a dangerous condition in the infant (4, 5). Recent studies have shown that the Asian race, the history of jaundice treated in a sister or brother, preterm birth, Isoimmunization Hemolytic Disease, ABO or RH incompatibility, and g6pd deficiency are hyperbilirubinemia risk factors (6, 7). Boskabadi et al., showed that the most commonly known and predisposing reasons of jaundice were related to the incompatibility of the blood group and RH and the deficiency of g6pd (2). Proper diagnosis and treatment of jaundice have always been one of the challenges of neonatal medicine (5, 8). Kernicterus is the serious brain damage

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caused by unconjugated hyperbilirubinemia, which is associated with high mortality and long-term complications and is estimated to affect about 1.5% of newborns (9). Kernicterus infants who survive usually suffer from mental disorders, seizure , hearing and speech problems , hypotonia, extrapyramidal symptoms , and muscle spasms (10). In phototherapy, a blue fluorescent lamp is used to metabolize bilirubin on the skin surface. One of the jaundice treatments is phototherapy. In phototherapy, infant's skin is exposed to blue fluorescent light. The fluorescent light causes the bilirubin break down with photoisomerization process. In this process, bilirubin is exposed to light becames to lumirubin, which is a water-soluble substance and is easily excreted (11, 12). In the case of failure of phototherapy and occurrence of kernicterus symptoms or high level of bilirubin at the time of referral, exchange transfusion with phototherapy is suggested as the main treatment (2, 9). The maximum total bilirubin that necessitates exchange transfusion depends on the gestational age, chronological age, and birth weight (13, 14). Blood exchange, as a method for treating abnormal increase of bilirubin in the first week of life, has always been faced with serious potential side effects (15) . Exchange transfusion is the replacement of the whole or a large masses of red blood cells and plasma of a the recipient with compatible red blood cells and plasma from a donor (16, 17). Exchange transfusion may have potentially dangerous complications such as hemolysis of incompatible red blood cells, thrombocytopenia, electrolyte disorder, hypocalcemia, hypoglycemia, metabolic acidosis, infection, necrotizing enterocolitis, and thrombosis (13). Thrombocytopenia has been defined as having a platelet count of less than 150,000 per mm3 of blood, irrespective of the gestational age (5). Thrombocytopenia occurs in 1-5% of all infants and in 18-35% of the infants admitted to Neonatal Intensive Care Unit (NICU) (18, 19).Thrombocytopenia is the most common complication of neonatal exchange transfusion (20). Previous studies did not address the severity and duration of thrombocytopenia (20, 21). This study was conducted to determine the severity and duration of thrombocytopenia following an exchange transfusion by monitoring the platelet count before and after the exchange transfusion and platelet count is controlled until it becomes normal.

Materials and Methods

This cross-sectional study was performed on 217 infants aged 2-14 days with a gestational age of greater than 35 weeks (term and near-term) and a bilirubin level of greater than 17 mg/dl who needed exchange transfusion. The institutional ethical clearance was obtained before initiating the study (IR.MUMS.MEDICAL.REC.1397.466).
Sampling was done at Ghaem hospital from 2012 to 2018 in Mashhad, Iran, by convenience sampling method. During this period, questionnaires were complete and archived by the researcher. The infants whose bilirubin levels met the exchange transfusion criteria, showed clinical signs of kernicterus, or had dangerously high bilirubin levels despite phototherapy were subjected to exchange transfusion. After identifying the infants meeting the inclusion criteria and receiving the physician order for exchange transfusion, blood samples were taken for cross-matching and blood type determination, and the units of blood that were compatible with mother and infant were requisitioned. In infant with RH incompatibilities (the negative RH group), and in ABO incompatibilities (blood group O), usually blood is requested cross match with infant blood group or AB positive blood group, In other cases, the blood used in exchange transfusion, is blood compatible with the maternal blood group.

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The amount of blood requested for each infant was 180cc/kg (270 cc to 720cc) and consisted of two-thirds Pack cells (PC) and one-third fresh frozen plasma (FFP). The sterilized umbilical catheter of proper size was placed by the ward's supervising physician. Given the lack of access to fresh blood and whole blood, in the exchange transfusion, compress red blood cell (PC) and fresh frozen plasma (FFP) are used. After taking the blood through the catheter, the blood exchange was performed by a physician using the sterile technique. The amount of blood needed in each cycle of exchange transfusion is determined based on the infant's weigh. The volume of blood exchanged in each cycle was about 5-8 cc/kg. Of this amount, two-third is compress red blood cell (PC) and one-third is fresh frozen plasma (FFP).The total duration of exchange transfusion was about 45-80 minutes. Blood samples were taken before and after the exchange transfusion using the proper technique and sent to the laboratory for complete blood count (CBC) and platelet count analyses (15). The platelet counts of over 150,000 per mm3 of blood was considered as normal, 100,000-150,000 per mm3 of blood as mild thrombocytopenia, 50000-99999 per mm3 of blood as moderate thrombocytopenia, and platelet counts of less than 50,000 per mm3 of blood was considered as severe thrombocytopenia.

Data collection instruments were a researcher-made questionnaire for collecting neonates' characteristics (age, gender, weight, gestational age, Apgar score) and mothers' blood type, as well as laboratory findings (platelet, bilirubin, hematocrit, direct and indirect Coombs, and reticulocyte). The platelet count was measured before exchange transfusion, right after exchange transfusion, 6 hours after exchange transfusion, and platelet count continued until platelet level goe normal. At the time of discharge, platelet levels were re-measured.

Statistical Analysis

After collecting and coding the data, they were analyzed using SPSS (version 20). In the data analysis stage, first a general description of data was obtained with statistical tables and charts, then the platelet levels before and after the exchange transfusion were compared using T-test. In all tests, $P \leq 0.05$ was considered as the threshold of statistical significance.

Results

In this study, 217 infants were included who were under exchange transfusion in the Ghaem hospital from 2010 to 2018. Among these infants, 17 of them were excluded for having moderate to severe thrombocytopenia before exchange transfusion, 3 of infants were excluded for being aged more than 14 days, and 4 ones were excluded for having a gestational age of less than 35 weeks. Considering sex, 104(53.8%) were males and 89 (46.2%) females. Of the dwith respect to type of delivery, 39.4 % of the infants were born with natural vaginal delivery and 16.1 % were born with cesarean delivery. In 73.1% of them, the cause of jaundice was unknown, in 26.1 % of cases there was an incompatibility of the ABO, and in 0.5% of cases there was an inconsistency of RH. While only 13 cases (6.7%) had thrombocytopenia before the exchange transfusion, 163 (84.4%) cases showed mild to severe thrombocytopenia after the exchange transfusion (Table I and II).

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Table I: Mean and standard deviation of platelet count

	Mean (per mm^3 of blood)	Standard Deviation
At admission	316.450	119.19
Before exchange transfusion	299.180	106.87
Right after exchange transfusion	105.140	40.67
6 hours after exchange transfusion	115.770	47.04
Last count	209.310	108.6
Time between last count and exchange transfusion (hours)	52.32	117.27

Table II: Prevalence of thrombocytopenia in different groups

Stage	Group	Frequency	Valid percent
Before exchange transfusion	Normal	180	**93.3%**
	Mild thrombocytopenia	13	**6.7%**
After exchange transfusion	Normal	25	**13.3%**
	Mild thrombocytopenia	82	**43.6%**
	Moderate thrombocytopenia	74	**39.4%**
	Severe thrombocytopenia	7	**3.7%**

Discussion

In this study, nearly one-sixth of the infants who needed exchange transfusions had thrombocytopenia, through most of them had a platelet count of over 100,000. In another study, 36 % of idiopathic hyperbilirubinemia neonates had thrombocytopenia, of which 86% was mild (5).The most common causes of thrombocytopenia in jaundice include ABO and RH incompatibility, polycythemia, infections, infant diabetic mother and Down syndrome (22). The mechanism of thrombocytopenia occurring with jaundice is still unknown, but the presence of blood group antigens and RH on platelet surface may explain some of these observations. In the present study, during the phototherapy, platelet count declined by 5.5 % (17,442 per mm3 of blood). A study by Khera et al. also described thrombocytopenia as the most important adverse effect of phototherapy for treating jaundiced neonates (23). Other studies also reported reduced platelet levels and elevated platelet turnover following phototherapy (22, 24, 25).The mechanism of thrombocytopenia occurring during phototherapy is not yet known. Based on the results of this study, about two-thirds of blood platelets removed from the blood vessels during the exchange transfusion, and unfortunately, due to products used in the exchange transfusion in this center, we did not replace any platelets that may be dangerous. About two-thirds of our neonates showed some degree of thrombocytopenia after the exchange transfusion. However, in other studies, the incidence of thrombocytopenia after the exchange transfusion ranged from 48 to 63 % (15, 20, 26). The relatively high incidence of thrombocytopenia in this study could be due to this fact that other studies used whole blood, but in the hospital of this study, the exchange was performed with packed cells and fresh fluid plasma products.

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In this study, about 84% of the cases of thrombocytopenia following the exchange transfusion were mild to moderate and less than 4 % were severe. Therefore, it seems that by using whole blood, we can overcome this common problem. In addition, it is suggested to re-establish thrombocytopenia and control its complications in infants who have thrombocytopenia or re- exchange transfusion.

In the present study, about 70 % of the removed platelets were replaced within 52 hours after the exchange transfusion. Davutoglu et al., also confirmed the transitory nature of this condition and its common incidence (27). Our results also suggested that thrombocytopenia in neonates after the exchange transfusion was a transient condition. In none of previous studies, the prevalence, severity, and duration of thrombocytopenia were stated, but they were addressed in this study. Due to the high prevalence of thrombocytopenia, proper and rapid diagnosis and patient monitoring is very important. The present study showed that thrombocytopenia was a transient complication after the exchange transfusion in infants. Due to the high prevalence of this complication after exchange transfusion in neonates, the need for early diagnosis and treatment of this complication is evident.

These results also highlighted the necessity of conducting more extensive studies to compare the outcomes of exchange transfusion and phototherapy treatments and to examine the hypothesis that platelet loss in these neonates may be independent of the type of treatment.

Due the complications of exchange transfusion, platelet counting is required after exchange transfusion to correct the complication of the exchange. In this regard, it is suggested that the exchange transfusion should be performed with fresh whole blood by experienced specialist personnel, and the infant treated with exchange transfusion, clinical and laboratory symptoms should be checked thoroughly and if thrombocytopenia is observed, the control of clinical and laboratory symptoms until normalization of the symptoms continues.

Conclusion

In this study, thrombocytopenia was observed in 15% of neonatal jaundice. The exchange transfusion removed about 64 % of the platelets from the blood. The body was usually able to replace 3.5 % of the removed platelets within six hours and replaced about 70 % of them within about 52 hours. Approximately 84 % of thrombocytopenia cases occurred after the exchange transfusion were mild to moderate and less than 4 % of them were severe.

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Conflict of interest

Authors declared no conflict of interst.

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