Original Article

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Comparison of the Transfusion Complications in Term and Preterm Neonates with Jaundice

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ABSTRACT

BACKGROUND AND OBJECTIVE: Blood exchange as a method for treating of abnormal increase of bilirubin in the first week of life, has always been faced with serious potential side effects. Therefore prevention and early detection of these complications is important. Given the higher prevalence of jaundice in preterm neonates, this study was done to compare the complications of transfusion in term and preterm neonates with jaundice..

METHODS: This cross-sectional study was done on 50 neonates with hyperbilirubinemia and treated with blood transfusions using available sampling method. Samples were investigated for several variables such as platelets, calcium, glucose, potassium, sodium, bicarbonate and clinical signs during transfusion, and up to 24 hours after it.

FINDINGS: From total of 50 neonates in this study, 22 neonates were preterm (44%) and 28 neonates were term (56 percent). The most common complication of blood transfusions in all neonatal was thrombocytopenia (48%). The most common complication in term neonates was reported thrombocytopenia (85.67%) and metabolic acidosis (2.57%) in preterm neonates, respectively ($p<0.05$). The complications of hyperglycemia (5 term neonates and 3 preterm neonates), hypoglycemia (only 2 preterm neonates), hyponatremia (only in 4 preterm neonates), and a serious complication of hyperkalemia (only in one neonate) were observed. This difference was not statistically significant.

CONCLUSION: The results showed that thrombocytopenia (in term neonates) and metabolic acidosis (in preterm neonates) are the most frequent complications of blood transfusion.

KEY WORDS: *Blood Transfusions, Hyperbilirubinemia, Neonatal Jaundice*.

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Introduction

One of the most common problems leading to hospitalization in the first week of neonatal abnormal is increment of bilirubin level (greater than 5 mg / dl) which can be seen as jaundice (Jaundice) in clinical practice (1-3). Jaundice can be seen in 60% of term infants and 85% of preterm infants during the first weeks of life (4).

Typically, an increase in bilirubin level starts at 24 hours after birth, continues its upward trend and by the end of the first week will decrease its level, however, in some cases bilirubin levels continue to rise and leads unsafe conditions (5). In previous studies, Asian race, history of treated jaundice in sister or brother, preterm delivery, iso-immune hemolytic disease, antigenic and ABO blood type incompatibility and glucose 6 phosphate dehydrogenase deficiency (G6PD), is considered as risk factors for hyperbilirubinemia (1,3,6).

The results of Boskabadi et al. study showed that the most common predisposing and known factors of jaundice complications are related to blood group and RH incompatibility and G6PD deficiency (7). Atleast 481000 newborns suffer from severe hyperbilirubinemia every year around the world, of these 114,000 infants will die and 63,000 of them experience its debilitating effects. It is noted that at least 75 percent of these babies are living in Africa and Asia (8, 9).

Phototherapy is as first line treatment of hyperbilirubinemia and in case of ineffectiveness treatment the exchange transfusion is used (2, 10). Umbilical vein is considered as a convenient way to achieve an artery in newborns. Catheterization through the umbilical vein is an effective, useful and common solution for blood transfusion in babies with jaundice (11, 12).

There are some significant challenges in this method. In the umbilical vein catheterization procedure, usually catheter placed in the great hepatic vein or inferior vena cava which is associated with the risk of infection and bacteremia (11).

However, the delay in treatment and indirect bilirubin deposition in the central nervous system cause kernicterus (3, 6, and 13). Kernicterus is a preventable complications caused by increased levels of bilirubin in the blood of newborns. Now kernicterus are relatively common complication in United States creating concerns (5). Over the years, the level of total bilirubin is known as one of the main criteria of the blood transfusion in newborns. Thus, the maximum total bilirubin for low-risk neonatal are defined according to gestational age, birth weight and postnatal age.

However, the criteria of Kernicterus in high risk infants (including hypothermia, infection, brain hemorrhage and hemolysis) is defined in lower number (14, 15). Indications for blood transfusion are hemolytic diseases (RH and ABO incompatibility, abnormality of red blood cells), metabolic diseases (liver failure, congenital defects of the liver) and reabsorption of bilirubin (low volume of feces and intestinal obstruction).

Also for non-hemolytic jaundice, in the first 48 hours of life, more than 20 mg/dl of bilirubin, and after the first 48 hours, 25 mg/dl of bilirubin blood transfusion is done (16). Blood transfusion may be associated with potential and dangerous side effects such as hemolysis due to incompatible red blood cells, thrombocytopenia, electrolyte imbalance, infections, necrotizing enter colitis, thrombosis (17). In this regard, Shayan and colleagues presented most frequent complications of blood transfusions in the order of metabolic acidosis and thrombocytopenia (18).

In another study that was done by Eghbalian, in addition to the introduction of thrombocytopenia as a common complication of blood transfusions, hypocalcemia was introduced as a common complication too (19). Because of its importance, the America Academy of Pediatrics in their practice guide considers new epidemiological studies as an important issue for documentation of related side effects to jaundice(20).

Therefore, it is necessary to be identified the complications of blood transfusion in infants, because it can specify the priority in care and treatment and also in prevention of jaundice complications in newborns. The majority of studies did not divided these effects according to two groups' term and preterm infants. However, this study aims to identify complications of blood transfusion in newborns and also try to examine priority of prevalence of blood transfusion complications in term and preterm in two groups. Therefore, this study aimed to determine the

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effects of blood transfusion in term and preterm infants with jaundice.

Methods

In this cross-sectional study, 50 infants with hyperbilirubinemia treated with blood transfusions were selected by convenience sampling method in Kermanshah Imam Reza hospital and divided into preterm and term groups.

Before performing blood transfusions, full explain of effects and benefits of blood transfusions were given by the physician for parents and informed consent for the invasive procedure was obtained. All newborns with jaundice without any problems and with normal laboratory tests except total bilirubin before blood transfusion were enrolled. Newborns with jaundice and other diseases that require blood transfusions and also infants had similar problems (acidosis, sepsis, thrombocytopenia, hypocalcemia) were excluded from the study.

All babies after the admission and laboratory tests (CBC, BUN, Cr, Na K, BS, Bill (T, D), ABG) were placed under heating, umbilical catheter was placed by a specialist or assistant in sterile conditions and blood transfusion was performed under cardiopulmonary monitoring. Blood products including packed red blood cells and fresh frozen plasma (FFP) or fresh whole blood with lifetime of less than 7-5 days were used. Blood volume required for each baby was calculated according to the formula (85- 100 cc/kg). Per 100 ml transfused blood, 1 cc intravenous calcium was administered slowly to prevent from hypocalcemia. Blood transfusion usually was took 90-120 minutes. Vital signs, hypocalcemia, tetany, and irritability were observed by doctors and nurses during this period. One hour after Blood transfusion (Bill (T, D), ABG, Cr, Na, K, BS, CBC, and Bun) were re-examined. Platelet count less than 150000/mm3 as thrombocytopenia, blood sugar more than 180 mg/dl as hyperglycemia as and less than 45 mg/dl as hypoglycemia were considered. In addition, sodium less than or equal 130 mmol/l was considered as hyponatremia and sodium over 150 mmol/l as developed hypernatremia and calcium less than 7 meq/dl in preterm infants and less than 8 in term infants as hypocalcemia and potassium greater than or equal 5/5 meq/l was considered as hyperkalemia. In addition, acidosis was defined as PH less than 7.32 and bicarbonate less than 20 meq /l (19).

Moreover other complications such as necrotizing enterocolitis (NEC) (clinical signs such as abdominal distention, vomiting, and positive guaiac tests associated with intestinal pneumatosis in supine abdominal radiographs or gas in the portal vein), seizure, and cardiac arrest in infants during the blood transfusion or 24 hours after it were considered (19). Blood transfusion-related death in this study was defined as the newborn death 24 hours after blood transfusions except in situations that there was no other obvious cause.

All infants during blood transfusion procedure were monitored by a nurse for general appearance and the symptoms of seizure and cardiac arrest. Statistical analysis was done using SPSS version 19. Transfused blood volume and the number of complications after transfusion were analyzed by Pearson correlation coefficient and to compare complications between term and preterm groups, chi-square test and Fisher exact test was used. $p<0.05$ was considered as significant.

Results

Of 50 studied infants, 22(44%) infants were preterm and others (56%) were term. 64% of these 50 infants suffered from complications after blood transfusions.

The most common complication of blood transfusions in total of neonatal was thrombocytopenia in 24 patients (48%) (Fig1). The most common complication of term neonatal was thrombocytopenia (67.85%) and in preterm infants was metabolic acidosis (2.57%), ($p<0.05$). Another complication was hyperglycemia that in 5 cases of neonates and 3 cases of preterm were observed that statistically was not significant. Hypoglycemia was reported in 2 (9%) preterm infants. Hyponatremia was observed in 4 preterm infants (18.18%) and the incidence of this complication was significant between term and preterm infants ($p<0.05$). Dangerous complications of hyperkalemia was observed only in one term infants (table 1). No case of hypocalcemia, cardiac arrest, NEC, neonatal death and convulsions were observed.

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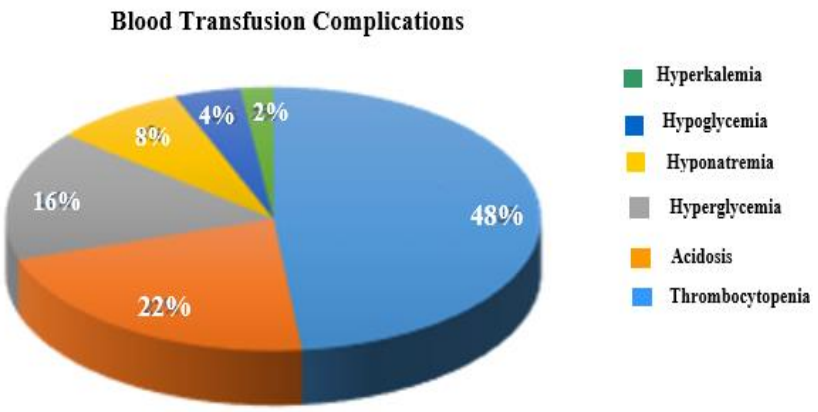

Figure 1. Frequency of blood transfusion complications in infants with jaundice

Table 1. The frequency of blood transfusion complications in term and preterm infants

Complication after blood transfusion	Term N(%)	Preterm N(%)	P- value	Total N(%)
Thrombocytopenia	19(67.85)	5(22.72)	0.002	24(48)
hypoglycemia	5(22.72)	3(13.63)	0.986	8(16)
hypoglycemia	0(0)	2(9.09)	0.189	2(4)
Hyponatremia	0(0)	4(18.18)	0.032	4(8)
Hyperkalemia	1(3.75)	0(0)	0.998	1(2)

Discussion

In this study, complications related to blood transfusions was observed in 64% of cases that this amount have been reported (74%) in research of Patra, and 61.75% in the Eghbalian and colleagues study (21, 22). The results showed that the most common complication of blood transfusion in the neonates is thrombocytopenia (48.3%), which study of Eghbalian and colleagues, Badiee and colleagues, Steiner and colleagues and Sabzehei and colleagues were in line with it (22-25).

Davutoglu and colleagues in addition to introducing thrombocytopenia as a common complication reported that this complication is transient. Introducing thrombocytopenia as a transient sign minimizes concerns about the persistence of this effect and its risks (20). Khera and colleagues in their study introduced the thrombocytopenia as the most important effect of phototherapy in neonatal jaundice (26). This makes it necessary that more extensive studies must be done to compare the effects of blood transfusion and phototherapy treatment. This hypothesis may be introduced that reduction of the platelets number in jaundice can act independent of the type of used treatment, however, there is a need for more investigations in its various aspects. Metabolic acidosis (21.7%) was the second most common complication. Masood and colleagues also showed that metabolic acidosis is a common complication following blood transfusion and it was due to aging of blood products (27). Therefore, it is recommended if the life of blood product was more than 7-5 days, PH must be controlled and in case of low PH, bicarbonate must be added to correct it. Also high-volume transfusion as much as possible be prevented (23, 24). Shayan and his colleagues indicated that hypoglycemia was observed in 29% of cases and this complication in our study was seen in 16% of cases which is probably due to the dextrose in the blood product (18).

While hypoglycemia was not observed in the study of Eghbalian et al. In the present study hypoglycemia was observed in 4% of cases. In addition in study of Masoud and colleagues was observed in 7 cases which can be due to transfusion with high volumes or lack of sufficient blood glucose after blood transfusion (22, 27). It is recommended that after blood transfusions, the baby blood sugar must be checked and corrected. In our study, hyponatremia was observed in 8% of patients. In addition, in the study Shayan and

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colleagues was seen in 11% of cases, whereas this effect was not seen in the study of Eghbalian and colleagues (18,22). Another complication of blood transfusions was hyperkalemia that only one term infants in our study suffered from hyperkalemia. In line with this study, Shayan and colleagues also reported hyperkalemia in only in one infant, while the Eghbalian and colleagues reported hyperkalemia in 6 cases (22, 18). The causes of hyperkalemia in blood transfusion could be the age of blood products, its administration speed and function of the kidneys.

Masoud and colleagues, Steiner and colleagues and Badiee and colleagues have reported the hypocalcemia after blood transfusion which can be due to citrated blood and binding of citrate with ionized calcium in newborn (23,24,27). While in this study and the study of Shayan and his colleagues hypocalcemia was not observed in infants which could be due to intravenous administration of calcium during blood transfusions (1 cc per 100 cc of blood products) (18).

In the present study similar to study of Sanpavat, the incidence of complications in preterm infants compared to term was higher, but Shayan and colleagues reported that the complications of blood transfusion in term neonates are more that preterm neonates which could probably due to more deletion of preterm cases from the study because of similar side effects before the transfusion (18,28). Eghbalian et al reported the incidence of cardio-respiratory arrest and seizure 5% and 4.2%, respectively, whereas cardiopulmonary arrest and seizure was not observed in this study which is different compared to mentioned report (22). In study of Patra and colleagues, Eghbalian and colleagues and Shayan and colleagues did not observed no cases of necrotizing enterocolitis after blood transfusions which is consistent with the results of this study (18,21,22). Since the Jaundice in early detection can be rapidly treated with simple actions and prevent from its dangerous complications, quick phototherapy and timely detection of jaundice can reduce the requirement to blood transfusion in future years. In addition, regarding to more and perfect education of doctors and nurses and midwives and greater accuracy in care and diagnosis of nursing and educating mothers, we can reduce the need for blood transfusions.

Overall, the mortality rate decreased following blood transfusion and in healthy infants decreased to less than 1 percent. But given the high prevalence of complications of blood transfusion in newborns, the need to use public education by the media and the establishment of free training classes for pregnant mothers. This action provide sooner refer of infants with jaundice to health centers. In addition to better diagnosis and treatment of these infants, there is a need to constant and careful monitoring during blood transfusion, administration of platelets in thrombocytopenia, revision of blood products PH (If it is not fresh) by sodium bicarbonate, and the need for frequent monitoring of vital signs and necessary tests during blood transfusions.

The study showed that thrombocytopenia and metabolic acidosis was the most frequent complications of blood transfusion in newborns and the ratio of all blood transfusion complications in preterm infants is higher than term infants. Due to the complications of blood transfusion, platelet count and doing Gasometery after transfusion is necessary to realize the complications caused by blood transfusions and to fix it. In this regard, it is recommended that blood transfusions are performed by trained and skilled personnel and infants during the blood transfusion locate under close surveillance of vital signs and laboratory tests.

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References

1.Kaabneh MA, Salama GS, Shakkoury AG, Al-Abdallah IM, Alshamari A, Halaseh RA. Phenobarbital and phototherapy combination enhances decline of total serum bilirubin and may decrease the need for blood exchange transfusion in newborns with isoimmune hemolytic disease. Clin Med Insight Pediatr. 2015;9:67-72.

2.Orimadegun AE, Akingbola TS. Routine administration of intravenous calcium during exchange blood transfusion for treatment of severe neonatal hyperbilirubinaemia: a systematic review of quantitative evidence protocol. 2015;13(1):134-45.

3.Sgro M, Kandasamy S, Shah V, Ofner M, Campbell D. Severe neonatal hyperbilirubinemia decreased after the 2007 canadian guidelines. J Pediatr. 2016 ;171:43-7.

4.Esfandiarpour B, Ebrahimi H, Karkan MF, Farahmand N, Karambin MM. Neonatal exchange transfusion for hyperbilirubinemia in Guilan (the north province of Iran): a 3-year experience. Turk J Pediat. 2012;54(6):626-31.

5.Bhutani V, Vilms R, Hamerman-Johnson L. Neonatal exchange transfusion for hyperbilirubinemia in Guilan (the north province of Iran): a 3-year experience. The Turkish J Pediat. 2012;54;30(6):626-31.

6.Alizadeh Taheri P, Sadeghi M, Sajjadian N. Severe neonatal hyperbilirubinemia leading to exchange transfusion. Medical journal of the Islamic Republic of Iran. 2014;28(1):1-2014.

7.Boskabadi H, Ashrafzadeh F, Azarkish F, Khakshour A. Complications of neonatal jaundice and the predisposing factors in newborns. J Babol Univ Med Sci. 2015;17(9):7-13.

8.Bhutani VK, Zipursky A, Blencowe H, Khanna R, Sgro M, Ebbesen F, et al. Neonatal hyperbilirubinemia and Rhesus disease of the newborn: incidence and impairment estimates for 2010 at regional and global levels. Pediat Res. 2013;74(1):86-100.

9.Lawn JE, Blencowe H, Oza S, You D, Lee AC, Waiswa P, et al. Every newborn: progress, priorities, and potential beyond survival. Lancet. 2014;384(9938):189-205.

10.Waterham M, Bhatia R, Donath S, Molesworth C, Tan K, Stewart M. Phototherapy in transport for neonates with unconjugated hyperbilirubinaemia. J Paediat Child Health. 2016;52(1):67-71.

11.Khosravi N, Arab Mohammad Hosseini A. The prevalence bacteremia and determination of the most common organism after exchange transfusion in newborns in akbar abadi hospital (1996-1999). Razi J Med Sci. 2002;9(29):205-8.

12.Ramachandran P, Cohen RS, Kim EH, Glasscock GF. Experience with double-lumen umbilical venous catheters in the low-birth-weight neonate. J perinatol. 1993;14(4):280-4.

13.Olusanya BO, Ogunlesi TA, Kumar P, Boo NY, Iskander IF, de Almeida MF, et al. Management of late-preterm and term infants with hyperbilirubinaemia in resource-constrained settings. BMC pediatrics. 2015.

14.Dennery PA, Seidman DS, Stevenson DK. Neonatal hyperbilirubinemia. New England J Med. 2001;344(8):581-90.

15.Hyperbilirubinemia SO. Practice parameter: management of hyperbilirubinemia in the healthy term newborn. Pediatrics. 1994;94(4):558-65.

16.Front Matter A2 - Gleason, Christine A. In: Devaskar SU. Avery's diseases of the newborn 9th. Philadelpia: W.B. Saunders; 2012. P. 3.

17.Wood AJJ, Dennery PA, Seidman DS, Stevenson DK. Neonatal Hyperbilirubinemia. New England J Med. 2001;344(8):581-90.

18.Shayan K, Omid F, Bayat Mokhtari M, Arjmand Kermani F. The Evaluation of Some Complications of Exchange Transfusion in Neonatal Hyperbilirubinemia in NICU of Bahman22nd Hospital in the Years of 2005-2008. Med Sci J Islamic Azad Univ-Mashhad Branch. 2010;6(2): 109-16.

19.Eghbalian F. Evaluation the complications of exchange transfusion in hospitalized neonates. Sci J Hamadan Univ Med Sci. 2007;14(2):23-7.[In Persian]

20.Davutoglu M, Garipardiç M, Güler E, Karabiber H, Erhan D. The etiology of severe neonatal hyperbilirubinemia and complications of exchange transfusion. Turk J Pediatr. 2010;52(2):163-6.

[DOR: 20.1001.1.15614107.1395.18.9.7.7]
[DOI: 10.22088/jbums.18.9.49]

21.Patra K, Storfer-Isser A, Siner B, Moore J, Hack M. Adverse events associated with neonatal exchange transfusion in the 1990s. J pediat. 2004;144(5):626-31.

22.Ahmadi AH1, Ghazizadeh Z. Evaluation of glucose-6-phosphate dehydrogenase deficiency without hemolysis in icteric newborns. Pak J Biol Sci.2008;11(10):1394-7.

23.Badiee Z. Exchange transfusion in neonatal hyperbilirubinaemia: experience in Isfahan, Iran. Singapore Med J. 2007;48(5):421-3.

24.Steiner LA, Bizzarro MJ, Ehrenkranz RA, Gallagher PG. A decline in the frequency of neonatal exchange transfusions and its effect on exchange-related morbidity and mortality. Pediatrics. 2007;120(1):27-32.

25.Sabzehei MK, Basiri B, Shokouhi M, Torabian S. Complications of exchange transfusion in hospitalized neonates in two neonatal centers in hamadan, a five-year experience. J Comprehen Pediatr. 2015;6(2):2058.

26.Khera S, Gupta R. Incidence of thrombocytopenia following phototherapy in hyperbilirubinemic neonates. Med J Armed Force India. 2011;67(4):329-32.

27.Masood M, Qureshi A, Izhar T. yaqoob M, AI RM: Complications and immediate clinical outcome of exchange transfusion in neonatal hyperbilirubinemia. Pak Paed J. 2005;29(1):3-8.

28.Sanpavat S. Exchange transfusion and its morbidity in ten-year period at king chulalongkorn hospital. J Med Assoc Thai. 2005;88(5):588-92.

[DOR: 20.1001.1.15614107.1395.18.9.7.7]

[DOI: 10.22088/jbums.18.9.49]