

## Exchange transfusion in neonates: An experience from a tertiary care center in North India

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Received - 20 July 2019

Initial Review - 12 August 2019

Accepted - 03 September 2019

### ABSTRACT

**Background:** Blood exchange transfusion (ET) involves replacement of affected neonate's blood with compatible donor blood. Although the use of ET has decreased over years, it still remains a popular emergency rescue procedure for newborns with severe jaundice. **Objective:** The study was done to describe the indications and complications associated with ET in a 20 bedded neonatal unit of a tertiary care center in North India. **Materials and Methods:** This was a retrospective observational cohort study of neonates who underwent ET from July 2014 to May 2019. Demographic profile, indications and etiology, details of ET procedure, and related adverse events were noted from medical records and chart review. **Results:** Of 2310 admitted neonates, 77 (3.3%) underwent 103 ETs during the study period with an average rate of 23.3 ETs per year. Hyperbilirubinemia was the most common indication for ET in 53 (68.8%) neonates. Rhesus (Rh) hemolytic disease was the single most frequent etiology for hyperbilirubinemia seen in 43 (55.8%) neonates. A total of 77 adverse events related to ET were seen in 53 (68.8%) neonates whereas 17 (22%) had more than one adverse event. The most common complication was thrombocytopenia in 40 (51.9%) neonates. Overall, mortality was 7 (9.1%); none were attributable to ET. **Conclusion:** The study identifies Rh hemolytic disease of newborn as the most common etiology leading to ET in newborns. Although ET is a relatively safe procedure, the high incidence of adverse events suggests vigilant monitoring and in-depth expertise for performing and managing complications of the procedure.

**Key words:** Exchange transfusion, Newborns, Indications, Adverse events

Blood exchange transfusion (ET) in newborns is an age-old intervention which involves the replacement of affected neonate's blood with compatible donor blood. ET was primarily used in rhesus hemolytic disease of newborn (RHDN) to decrease the mortality associated with it and prevent sequelae of kernicterus due to hyperbilirubinemia in newborns [1]. Subsequently, its use has been extended to hyperbilirubinemia due to other hemolytic and non-hemolytic causes, severe sepsis, severe fluid and electrolyte disturbances, inborn errors of metabolism, disseminated intravascular coagulation, severe anemia and polycythemia [2]. With improved prenatal care of rhesus (Rh) negative isoimmunized pregnancies (anti-Rh D immunoglobulin and intrauterine transfusions) as well as postnatal intensive phototherapy, there is marked decrease in the requirement of ET in last few decades. Revised American Academy of Pediatrics (AAP) guidelines for hyperbilirubinemia and use of postnatal immunoglobulin in RHD have also contributed to the decline [3-5].

As a result, ET has become a rarely performed procedure in nearly every developed country with a rate of 3/100,000 live births in the United States [6]. Consequently, skills required for this life-saving procedure has declined leading to concerns for the

adverse events associated with it. The associated complications are thrombocytopenia, electrolyte and acid-base disturbances, cardiovascular instability, hypothermia, arrhythmias, apnea, seizures, and sepsis. Despite declining indications, ET still remains an emergency rescue procedure for severe hyperbilirubinemia in many resource-limited developing countries [2]. Late referrals, delayed diagnosis of severe hyperbilirubinemia and substandard phototherapy devices are some of the main reasons. This study was conducted with the aim to describe indications and complications of ET at a tertiary care center in North India.

### MATERIALS AND METHODS

This was a retrospective observational cohort study conducted in a 20-bedded level III neonatology unit of a tertiary care teaching institute. All neonates who underwent blood ET from July 2014 to May 2019 were screened for inclusion. Those who had undergone double or single-volume ET were included in the study. Newborns, who underwent partial ET for severe anemia or polycythemia and those with incomplete records, were excluded from the study. For hyperbilirubinemia due to RHDN, indications for ET were cord hematocrit (Hct) <30% or

cord total serum bilirubin (TSB) >5 mg/dl; rate of rise of TSB >1 mg/dl/h despite intensive PT; any TSB >12 mg/dl in the first 24 h and TSB >20 mg/dl in the neonatal period; and the presence of hydrops at birth or history of previous sibling requiring exchange due to Rh isoimmunization and index patient born with pallor, hepatosplenomegaly, and positive direct Coombs test.

For other neonates with hyperbilirubinemia, the AAP 2004 recommendations for the infants  $\geq 35$  weeks of gestation [7] and weight-based cut-offs for <35 weeks were used [8]. All neonates with hyperbilirubinemia were given intensive phototherapy unit as per unit protocol. Compatible blood that was cross-matched with both newborn and mother was used. ET was done using freshly collected (<7 days) packed red blood cells (PRBC) and plasma that was reconstituted in the blood bank and irradiated before the procedure.

Data were retrieved from medical records of the patient and included maternal details, newborn's demographics, indications for performing the first ET, procedure details, complications attributable to ET (occurring within 72 h after the procedure), and outcome at discharge. Institute ethical committee approved the project. Data were analyzed using SPSS version 20 (IBM Inc., Armonk, NY, USA). Categorical data were expressed as percentages and numerical data as median (interquartile range IQR).

## RESULTS

A total of 2310 neonates were admitted during the study period. A total of 77 (3.3%) neonates underwent 103 ETs during the study period, an average rate of 23.3 ETs per year. The baseline characteristics of study population are shown in Table 1.

Table 2 describes detail of the exchange procedure in study population.

**Table 1: Baseline characteristics of the study population (n=77)**

Variables	n (%)
Gestational age at birth (weeks)	36 (34 <sup>+2</sup> -37 <sup>+2</sup> )*
Birth weight (grams)	2514 (2155-2800)*
Male gender	49 (63.6)
Place of delivery	
Inborn	54 (70.1)
Outborn	23 (29.9)
Mode of delivery	
Cesarean section	58 (75.3)
Vaginal	19 (24.7)
Intrauterine transfusions	38 (49.3)
Duration of hospital stay (days)	13 (9-20)*
Mortality	7 (9.1)
Re-admission	30 (39)
Reasons for readmission	
Top up transfusion	19 (24.7)
Phototherapy	4 (5.2)
Other	7 (9.1)

\* Median (interquartile range)

Hyperbilirubinemia was the most common indication for ET in 53 (68.8%) neonates. RHDN was seen in 43 (55.8%) and was the most common etiology for hyperbilirubinemia. A total of 42 (54.5) neonates underwent ET within first 12 h of life with median age at first ET 11 h (IQR8-168). A total of 20 (25.9%) neonates required more than one ET. A total of 77 adverse events related to ET were seen in 53 (68.8%) neonates as described in Table 3.

The most common adverse event noted was thrombocytopenia followed by dyselectrolytemia and sepsis. Bilirubin-induced neurological dysfunction (BIND) was seen in 8 (10.4%) newborns; of these 7 were outborn babies who had BIND at admission. Overall, 7 (9.1%) neonates died in study and was not related to ET procedure.

**Table 2: Parameters related to exchange transfusion in the study population (n=77)**

Variables	n (%)
Indications	
Hyperbilirubinemia	53 (68.8)
Hyperbilirubinemia+severe anemia	9 (11.7)
Severe sepsis	7 (9.1)
Severe anemia	6 (7.8)
Hyperbilirubinemia+severe sepsis	2 (2.6)
Number	1 (1-2)*
Neonates requiring more than one ET	20 (25.9)
Type of ET	
Double volume	70 (90.9)
Single volume	6 (7.8)
Both	1 (1.3)
Route	
Central (umbilical)	60 (77.9)
Peripheral	14 (18.1)
Both	3 (3.8)
Age at first ET (hours)	11 (8-168)*
Duration (hours)	60 (57-90)*
Peak TSB (n=53)	15.1 (12.3-22.2)*
Etiology of hyperbilirubinemia	n=64 (83.1)
Rhesus hemolytic disease	43 (55.8)
ABO incompatibility	5 (6.5)
Miscellaneous	16 (20.7)

ET- exchange transfusion, TSB-total serum bilirubin

**Table 3: Complications related to exchange transfusion (n=77)**

Variables	n (%)
Thrombocytopenia	40 (51.9)
Dyselectrolytemia	18 (23.7)
Hypocalcemia	16 (20.7)
Hyponatremia	2 (2.5)
Sepsis	8 (10.3)
Hemodynamic disturbances	5 (6.5)
Miscellaneous (apnea, feed intolerance, necrotizing enterocolitis, coagulopathy, hypoglycemia)	6 (7.7)
More than one adverse event	17 (22)

## DISCUSSION

This retrospective study describes the profile of neonates requiring ET and its complications. ET was introduced in 1950's as a gold standard treatment for the management of newborns affected with severe hyperbilirubinemia due to RHDN [1]. The current consensus on performing ET depends on weighing balance between the risks of kernicterus versus adverse effects of procedure [9]. Overall, 3.3% admitted neonates underwent ET in this study which is similar to published literature [10-12] but less than that reported by Salas *et al.* [13] who reported ET in 15.5%. The difference could be due to changing practices across time and different demographic profile of patients requiring ET. RHDN was the most common etiology for ET in our study which is in contrast to other studies reported in literature [10-11,13-24]. Only three studies [25-27] reported it as the most common etiology for ET.

Even though the incidence of RHDN decreased across the globe, the disease is still seen in many developing countries. The possible reasons could be suboptimal antenatal care, poor affordability of anti-Rh D-globulin, lack of awareness among rural population for seeking antenatal care, and referral bias. Many studies reported idiopathic [14-16,19,21-22] cause of hyperbilirubinemia requiring ET which was followed by ABO incompatibility [17,20,23]. ET was done in 9.1% neonates with severe sepsis in the study. Role of ET in severe sepsis was recently studied by a randomized trial which demonstrated a trend toward decrease in mortality and improvement in immunoglobulin and complement C3 levels and acid-base status following ET [28].

This study demonstrated adverse events in 53 (68.8%) newborns. Available literature reports variable incidence of adverse events related to ET ranging from 13% to 93.1% [12-15,19,21-24,27]. The different incidence could be explained by variation in the definitions used, level of sickness, etiologic profile of neonates, and varying expertise for performing the procedure. The most common complication noted was thrombocytopenia (51.9%) which is similar to the published studies [13,15,20,27-29]. Thrombocytopenia following ET occurs due to replacement of whole blood with PRBC, which is deficient in platelets as well as activation of coagulation system leading to consumptive coagulopathy [24].

Hypocalcemia is one of the common biochemical abnormalities after ET and its incidence varies from 11.5% to 48.3% [13-14,20,22,24,27-29]. Hypocalcemia (20.7%) was the second most common adverse event noted in this study. The possible mechanism includes binding of ionic calcium and magnesium by citrate which is used as anticoagulant in donor blood. Most complications were transient and manageable. Although overall mortality was 9.1%, none could be directly attributable to ET. The reported mortality due to ET varies from 0 to 3.3% and our results are comparable to these studies [13-15,19,20-24,27].

The present study adds to limited recent literature available from India, describing indications and complications of ET. Although ET is relatively safe, high incidence of complications mandates strict monitoring of both clinical and laboratory parameters during and after the procedure. Limitations include

retrospective nature of the study and being a single-center study, the data might not be generalizable to other parts of India.

## CONCLUSION

This study identifies rhesus hemolytic disease of the newborn as the most common etiology for exchange transfusion in this part of country. The incidence of adverse events was moderately high which suggests that ET should be performed under settings where expertise for performing and managing complications is available.

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*Funding: None; Conflict of Interest: None Stated.*

**How to cite this article:** Naranje KM, Singh A, Panghal A, Pandita A, Gupta G. Exchange transfusion in neonates: An experience from a tertiary care center in North India. *Indian J Child Health*. 2019; 6(9):503-506.

Doi: 10.32677/IJCH.2019.v06.i09.009