Exchange transfusion in neonatal hyperbilirubinaemia: a comparison between citrated whole blood and reconstituted blood

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ABSTRACT

Introduction: Exchange transfusion is performed using many different combinations of blood components. No single component is unequivocally the best. The purpose of this study was to determine the efficacy and adverse events of exchange transfusion (ECT) with whole blood and reconstituted blood in neonatal hyperbilirubinaemia.

Methods: The medical charts of all neonates who had undergone ECT over a two-year period were retrospectively reviewed. The demographic features, causes of jaundice, details of the exchange method and ECT-related adverse events of the infants were recorded. A total of 107 ECT procedures were performed in 92 neonates during the study period. The neonates were categorised into those who received whole blood (n is 38) and those who received reconstituted blood (n is 54) for ECT.

Results: There was no significant difference in the demographic characteristics and causes of jaundice between the two groups. ABO blood group incompatibility was the most common cause of hyperbilirubinaemia in both groups. The mean pre-ECT haematocrit of exchange transfused patients with whole blood and reconstituted blood was compatible. Although the mean post-ECT haematocrit in the reconstituted group was higher (39.74 +/- 5.65 versus 38.21 +/- 3.59), this difference was not significant (p is 0.15). The mean post-ECT platelet count was 59,000 +/- 29,400 and 73,000 +/- 21,300 in patients who underwent ECT with reconstituted and whole blood, respectively. A similar number of patients in both groups experienced hypocalcaemia and thrombocytopaenia after ECT. No case of ECT-related mortality was observed.

Conclusion: ECT with either reconstituted or fresh whole blood is an efficient and safe method for reducing hyperbilirubinaemia.

Keywords: exchange transfusion, fresh citrated whole blood, neonatal hyperbilirubinaemia, reconstituted blood

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INTRODUCTION

Neonatal jaundice due to indirect hyperbilirubinaemia is an ongoing problem that warrants hospital admission of newborns. Approximately 5%–10% of all newborns require intervention for pathologic jaundice.[1] Early detection and treatment is important in the prevention of bilirubin-induced encephalopathy. Exchange transfusion (ECT) is a successful form of therapy for severe neonatal jaundice.[1-6] Although the frequency of neonatal ECT has declined markedly in the last two decades,[7] this procedure is still performed in many countries, especially in Asian countries with a high incidence of neonatal hyperbilirubinaemia.

ECT is the replacement of most or all of the recipient's red blood cell (RBC) mass and plasma with appropriately compatible RBCs and plasma from one or more donors. The amount of blood exchanged is generally expressed in relation to the recipient's blood volume. A double volume exchange replaces 90% of the neonate's RBCs. ECT can be performed using many different combinations of blood components, including fresh whole blood and packed RBCs reconstituted with fresh frozen plasma (FFP).[8-10] No single component is unequivocally the best. Since fresh whole blood of the appropriate blood group is not always readily available, reconstituted blood is an alternative blood component for exchange transfusion. This study was conducted to compare the efficacy and disadvantages of these two different blood components for neonatal ECT.

METHODS

All neonates who underwent ECT for neonatal

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Table I. Demographic characteristics of the infants in the two groups.

Characteristic	Group A (n = 38)	Group B (n = 54)
Gestational age (wks)	38.35 ± 1.49*	37.42 ± 2.11*
Weight (kg)	3.02 ± 0.519*	2.87 ± 0.653*
Age of admission (days)	6.03 ± 4.62*	5.51 ± 3.43*
Male	25 (65.8)	32 (59.3)
Caesarean section	12 (31.6)	22 (40.7)
Breastfeeding	35 (92.1)	50 (92.6)

*Data is expressed as mean ± standard deviation or no. (%).
Group A: exchange transfusion with reconstituted blood.
Group B: exchange transfusion with whole blood.

Table II. Biochemical and haematological characteristics of the patients in the two groups.

Characteristic	Mean ± SD		p-value
	Group A	Group B	
Pre-ECT bilirubin (mg/dl)	26.8 ± 5.7	29.1 ± 6.4	0.56
Post-ECT bilirubin (mg/dl)	10.6 ± 3.4	11.7 ± 3.9	0.23
Post-ECT platelet count (µl)	59,000 ± 29,400	73,000 ± 21,300	0.27
Pre-ECT haematocrit	41.2 ± 6.9	41.1 ± 6.2	0.91
Post-ECT haematocrit	39.7 ± 5.6	38.2 ± 3.5	0.17

Group A: ECT with reconstituted blood; Group B: ECT with whole blood; ECT: exchange transfusion

hyperbilirubinaemia in the neonatalogy department of Children's Hospital, Tabriz, Iran, between January 2007 and December 2008 were included in this study. The hospital's committee of ethics in medical research approved this study. The medical records of the patients were reviewed retrospectively, and the following data was collected via detailed questionnaires: the patient's demographic characteristics, causes of hyperbilirubinaemia, the duration of ECT, frequency of exchange, feeding behaviour and adverse events associated with ECT. Based on the type of blood component used for ECT, the patients were categorised into two groups. Group A consisted of 38 patients who underwent ECT with reconstituted blood and Group B comprised 54 patients who received citrated whole blood for ECT. Patients who underwent partial exchange for anaemia or polycythaemia were not enrolled in the study.

Our neonatology department routinely uses the 2004 American Academy of Pediatrics hyperbilirubinaemia guidelines[3] for the management of admitted newborn infants. All the neonates with severe hyperbilirubinaemia who were studied received phototherapy immediately after admission and the total serum bilirubin was measured 4–6 hours after the initiation of phototherapy. Infants with unresponsive hyperbilirubinaemia underwent urgent ECT with one of the available blood components (fresh whole blood or reconstituted blood). All of the patients underwent isovolemic double volume ECT via the insertion of an umbilical vein catheter under aseptic conditions. Stored RBCs collected on citrate-dextrose-phosphate-adenosine (CDPA) anticoagulant with FFP were used for ECT in Group A and by adjusting the haematocrit of reconstituted blood to 45%. Patients in Group B received fresh whole blood containing CDPA anticoagulant.

During the ECT procedure, calcium gluconate was administered intravenously after every 100 ml of blood was removed. ECT-related adverse events were defined as any complication that was not present before ECT, which occurred within three days after the exchange. Thrombocytopaenia was defined as platelet count < 100,000/µL and hypocalcaemia as total serum calcium < 8 mg/dL or ionised calcium < 1 mmol/L.

All data was analysed using the Statistical Package for the Social Sciences version 13.0 (SPSS Inc, Chicago, IL, USA). The data was summarised using descriptive statistics. The Pearson's χ^2 test and student's *t*-test were used to compare the categorical variables. A p-value < 0.05 was considered to be statistically significant.

RESULTS

A total of 95 patients underwent ECT between January 2007 and December 2008. Three neonates were excluded from the study due to incomplete data recordings in their medical charts. The demographic data was similar between the two groups, with no statistically significant differences (Table I). A total of 107 ECT procedures were performed on 92 patients over the two-year period. 13 patients (four in Group A and nine in Group B) had two ECT procedures, while two patients from Group B underwent three ECT procedures.

The most common cause of jaundice was ABO incompatibility in 48 (52.2%) cases. Rh isoimmunisation, glucose-6-phosphate dehydrogenase deficiency and weight loss of more than 10% of the birth weight was determined as a cause of hyperbilirubinaemia in 9.8%, 3.3% and 10.9% of the patients, respectively. There were no significant differences in the causes of hyperbilirubinaemia between the infants in the two groups. 13 (14.1%) patients experienced thrombocytopaenia (five in Group A, eight in Group B). Although the mean platelet count after ECT in Group A was lower than that in Group B, there was no significant difference in the post-ECT

platelet count between the two groups. The pre- and post-ECT values of various parameters are shown in Table II. None of the thrombocytopaenic neonates required platelet transfusion. Although the mean post-ECT haematocrit in Group A was higher than that in Group B (39.74 ± 5.65 vs. 38.21 ± 3.59, respectively), this difference was not statistically significant ($p = 0.15$). The calcium level was reduced in eight (8.7%) patients (three in Group A and five in Group B). No death was reported among the patients in the two groups.

DISCUSSION

A few systematic studies have been conducted on the causes of hyperbilirubinaemia and the complications of ECT.[1,5,6,9] It has been reported that less than 0.1% of pregnancies with ABO incompatibility require treatment with ECT. However, significant hyperbilirubinaemia and severe haemolytic disease were found in 21.3% and 4.4% of the ABO-incompatible patients studied by Sarici et al, probably due to the ethnic and geographical characteristics of the population under study.[11] In our study, the most common cause of ECT was ABO incompatibility, and this finding is similar to those of other studies.[5,12] ABO incompatibility was common in neonates who required more than one ECT. Yigit et al suggested the use of group O RBCs re-suspended in AB plasma for the ECT in cases of ABO haemolytic disease.[13] Although the re-exchange rate was higher among our patients who underwent ECT with whole blood, this difference was not significant. The difference in the results may be due to the lower number of neonates in our study. Both the stored whole blood and reconstituted blood are deficient in platelets.

Although we used fresh whole blood (less than three days old), the most common ECT-related adverse event in this study was thrombocytopaenia. It is recommended that platelets should not be added to reconstituted blood during an exchange. Platelet transfusion is indicated only for infants with significant thrombocytopaenia (≤ 50000/μl), or for those who are bleeding.[7] Over a ten-and-a-half-year study period in two large perinatal centres in Cleveland, OH, USA, 67 infants who had undergone ECT for hyperbilirubinaemia were identified, and adverse events were found to have occurred in 73% of the exchanges, with hypocalcaemia (29%) and thrombocytopaenia (44%) being the most common.[9]

Neonatal exchange with citrated blood could be associated with a decline in serum calcium due to the presence of citrate. In both groups, calcium gluconate was administered intravenously after every 100 ml of removed blood. In our study, hypocalcaemia was the second most common adverse event of ECT. Only four patients were treated with intravenous calcium. The mean post-ECT haematocrit in neonates with reconstituted blood was higher than in those with whole blood, but the difference was not statistically significant. This may be due to the adequate mixing of whole blood during the ECT procedure and the adjustment of the haematocrit of reconstituted blood to 45%.

In a study of 40 ECTs with heparinised whole blood or citrated composite blood, it was shown that the use of citrated reconstituted blood was associated with significant post-ECT increases in serum osmolality, blood glucose and haemoglobin as well as a decrease in ionised calcium without clinical complications.[14] Sharma et al reported 25 cases of ECT by reconstituted blood and concluded that adjusting the haematocrit of reconstituted blood to 50% ± 5% enhances the ability to maintain normal haemoglobin after ECT.[15]

In conclusion, our study has shown that ECT with either whole or reconstituted blood is an efficient and safe method for reducing hyperbilirubinaemia. Considering the high demand for ECT in our country and the limited availability of fresh whole blood, it is recommended that reconstituted blood be made available as an option for neonatal ECT in emergency situations.

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