



Efficacy of exchange transfusion in the treatment of neonatal hyperbilirubinemia in Duhok and the factors affecting it

KEYWORDS

ADRs, Pharmacovigilance, Causality.

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ABSTRACT *Introduction* Neonatal jaundice is an in-progress problem needing hospital admission of newborns. Exchange transfusion (ET) has been known as an effective treatment for severe neonatal jaundice. Although the frequency of neonatal exchange transfusion has declined markedly in the last two decades, this procedure is still performed in many countries

Aim is to shed light on the Exchange transfusion to assess the efficacy of this procedure in lowering bilirubin level and factors affecting this efficacy.

Materials and Methods A cross sectional prospective study included neonates who underwent exchange transfusion for treatment of neonatal hyperbilirubinemia in Heevi Pediatric Teaching Hospital in Duhok, north of Iraq from June 2014 to June 2015. Neonates with hyperbilirubinemia underwent urgent double volume exchange transfusion with whole blood compatible with neonate's and mother's blood. All patients had serum bilirubin levels (TSB), blood group and Rh, reticulocyte count, coomb's test, complete blood count, and peripheral blood film. Data collected included age, initial serum bilirubin levels, Hematocrit, cause of hyperbilirubinemia (hemolytic or non-hemolytic) and rate of TSB lowering after the procedure, the rate of TSB change 8 hours after the procedure, the change of hematocrit after the procedure and duration of procedure were all studied. Data were analyzed statistically using SPSS 19, Fisher's exact test and Pearson Chi-square were $P < 0.05$ is significant.

Results The neonates were 132. The mean initial TSB is 24.34 mg/dl (SD 5.13). The mean lowering of TSB after exchange transfusion is 8.8 mg/dl (SD 3.63) with a percentage of 36.15% while the initial PCV is 49.62 (SD 9.6). The procedure needed to be repeated in 44 cases (33.3%). The mean duration of the procedure was 56.48 minutes (SD 12.64). The mean age at which the procedure is done is 4.48 days (SD 2.2). In 44 cases (33.33%), the cause was hemolysis. The serum bilirubin rebounded 8 hours after the procedure in 77 cases (58.3%) and the hematocrit dropped in 81 cases (61.83%). The age of patients, initial serum bilirubin and duration of procedure have no significant effect on the efficacy while non hemolytic causes significantly increase the efficacy of the procedure

Conclusion The mean TSB, mean hematocrit, age at which the procedure is done are comparable to other studies but the efficacy in lowering TSB is less. The procedure lowers bilirubin more effectively in non hemolytic hyperbilirubinemia. Serum bilirubin rebounds and hematocrit falls significantly after the procedure in most cases.

Introduction

Neonatal jaundice is an in-progress problem needing to hospital admission of newborns and approximately 5-10 percent of all newborns require intervention for pathologic jaundice. Exchange transfusion (ET) has been known as an effective treatment for severe neonatal jaundice [1]. The most common indication of exchange transfusion is ABO-Hemolytic Disease of the Newborn (ABO-HDN) [2]. Therefore, many infants with severe neonatal jaundice should undergo exchange transfusion, even before identification of the exact cause of ABO-incompatibility [3,4]. Early detection and treatment of neonatal hyperbilirubinemia is important in prevention of bilirubin-induced encephalopathy. [5]. Exchange transfusion (ET) removes circulating bilirubin, antibodies in plasma and antibody-coated sensitized red blood cells (RBCs), replacing them with RBCs compatible with maternal serum or neonates' serum and providing albumin with new bilirubin site [6]. Whole blood used for exchange transfusion either compatible with neonates' serum or plasma or mother's serum is commonly used [7].

Although the frequency of neonatal exchange transfusion has declined markedly in the last two decades, this procedure is still performed in many countries, especially in Asian countries with a high incidence of neonatal hyperbilirubinemia [8]. ET 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 [9,10].

The level of bilirubin concentration at which ET should be indicated remains the subject of disagreement, since the incidence of bilirubin encephalopathy also depends on other variables such as gestational age, the presence or absence of hemolysis and the newborn's clinical status. Current recommendations for performing ET are based on seeking a balance between the risks of encephalopathy and the adverse events related to the procedure [11].

We did this study to shed light on the Exchange transfusion in Heevi Pediatric Teaching Hospital to assess the efficacy of this procedure in lowering bilirubin level and factors affecting this efficacy and also the frequency of the need to repeat the procedure.

Materials and Methods

This cross sectional prospective study included 132 neonates who underwent exchange transfusion for treatment of neonatal hyperbilirubinemia in Heevi Pediatric Teaching Hospital in Duhok, north of Iraq from June 2014 to June 2015.

Those neonates (first 28 days after birth) who had indirect hyperbilirubinemia and underwent exchange transfusion

(according to guideline tables printed in Nelson Text book of pediatrics) were included in the study.

Neonate with hyperbilirubinaemia underwent urgent exchange transfusion with whole blood compatible with neonate's and mother's blood. All of the patients underwent double volume exchange transfusion through a catheter inserted in the umbilical vein under aseptic conditions. Fresh anticoagulated whole blood was used. During procedure, calcium gluconate was administered intravenously after removal of every 100 ml of blood.

All patients had serum bilirubin levels (TSB), blood group and Rh, reticulocyte count, coomb's test, complete blood count, and peripheral blood film. Data collected included age, Initial serum bilirubin levels, Hematocrit (PCV), cause of hyperbilirubinemia (hemolytic or non-hemolytic) and rate of TSB lowering after the procedure, the rate of TSB change 8 hours after the procedure, the change of hematocrit after the procedure and duration of procedure were all studied.

Data was analyzed statistically using SPSS 19, Fisher's exact test and Pearson Chi-square were $P < 0.05$ is significant.

Ethical approval was taken from Research Ethics Committee of the Directorate of Health in Duhok.

Results

The mean initial TSB is 24.34 mg/dl(SD5.13). The mean lowering of TSB after exchange transfusion is 8.8 mg/dl(SD3.63) with a percentage of 36.15% while the initial PCV is 49.62%(SD 9.6). The mean duration of the procedure was 56.48 minutes(SD12.64). The mean age at which the procedure is done is 4.48 days(SD 2.2).

The exchange transfusion was repeated in 44 cases(33.3%).

The age distribution of patients shows a higher percentage of TSB lowering with advancing age but no significant difference was detected as shown in Table- 1-

Table-1-Relation between TSB lowering and the age of neonate

Age days	<10%	10-20.99%	21-30.99%	31-40.99%	41-50.99%	51 and more	Total
1-2	0	2	7	6	6	3	24
3-4	0	6	8	17	8	6	45
5-6	2	7	6	13	17	2	47
7 and more	0	3	1	6	3	3	16
Total	2	18	22	42	34	14	132

P=0.376

The relation between initial TSB and the rate of TSB lowering as in Table -2- shows the highest lowering rate with exchange transfusion is in the neonates with TSB level of 20-29.9 mg/dl but there was no significant relationship.

Table-2-The relation of TSB lowering to the initial TSB level

Initial TSB mg/dl	<10%	10-20.99%	21-30.99%	31-40.99%	41-50.99%	51 and more	Total
9-19.9	0	4	1	6	7	3	21
20-29.9	2	11	14	31	25	9	92
30 and more	0	3	7	5	2	2	19
Total	2	18	22	42	34	14	132

P=0.354

The duration of procedure as shown in Table-3- seems to affect the rate of TSB lowering so that the duration of 50- 64 minutes is associated with more lowering but this effect is not significant.

Table-3-The relation between TSB lowering and duration of the procedure

Duration min.	<10%	10-20.99%	21-30.99%	31-40.99%	41-50.99%	51 and more	Total
35-49	1	3	5	11	13	5	38
50-64	0	14	14	26	14	6	74
65-79	0	1	3	1	2	2	9
80 and more	1	0	0	4	5	1	11
Total	2	18	22	42	34	14	132

P=0.133

The cause of hyperbilirubinemia significantly relates to the rate of TSB lowering so that non hemolytic hyperbilirubinemia is more effectively lowered than in cases of hemolysis as shown in Table-4-

Table-4-The relation between TSB lowering and the cause of hyperbilirubinemia

cause	<10% n. %	10-20.99% n. %	21-30.99% n. %	31-40.99% n. %	41-50.99% n. %	51and more	Total
Hemolytic	0	5	8	20	4	7	44
Non hemolytic	2	13	14	22	30	7	88
Total	2	18	22	42	34	14	132

P=0.015

The TSB measurement 8 hours after the procedure showed increased TSB in 77 cases(58.3%) due to the rebound while in 47cases (35.6%) TSB decreased and in 8 cases (6.1%) TSB didn't change. The relation of TSB 8 hours after the procedure to different variables shows significant increase TSB with the age where it is significant at age 1-4 days and the duration of the procedure where it is significant when duration is 35-49 minutes and 65-79 minutes while no significant relation to initial TSB and cause of hemolysis as shown in Table-5-

Table-5-The change of TSB after ET by 8 hours and its relation to variables

Variable	Increased TSB (%)	Decreased TSB (%)	No-change TSB (%)	P
AGE days				
1-2	18 (57%)	5 (20.8%)	1 (4.2%)	0.022
3-4	26 (57.8%)	15 (31.9%)	4 (8.9%)	
5-6	26 (55.3%)	18 (38.3%)	3 (6.4%)	
7 and more	7 (43.8%)	9 (56.2%)	0 (0%)	
Initial TSB mg/dl				
9-19.9	12 (57.1%)	8 (38.1%)	1 (4.8%)	0.088
20-29.9	56 (60.9%)	32 (34.8%)	4 (4.3%)	
30 and more	9 (47.7%)	7 (36.8%)	3 (15.8%)	
Duration min.				
35-49	24 (63.2%)	10 (26.3%)	4 (10.5%)	0.048
50-64	41 (55.4%)	30 (40.5%)	3 (4.1%)	
65-79	6 (66.7%)	3 (33.3%)	0 (0%)	
80 and more	6 (54.5%)	4 (36.4%)	1 (9.1%)	
Type				
Hemolytic	26 (59.1%)	15 (34.1%)	3 (6.8%)	0.121
Non hemolytic	51 (58%)	32 (36.4%)	5 (5.7%)	

Hematocrit (PCV) measurement done 8 hours after the procedure shows that in 38 cases(28.78%) PCV increased while in 81 cases (61.83%) it decreased and in 13 cases(9.39%) there was no change. The relation of these changes to variables shows that PCV significantly increase when the procedure is done at the age of 1-2 days while significantly decreases when done at age of 5 days and more. Also the duration of the procedure exerts its effect on PCV after 8 hours while neither initial TSB nor the cause of hemolysis have any significant effect as shown in Table-6-

Table-6- Change of PCV after ET by 8 hours and its relation to variables

Variable	Increased PCV (%)	Decreased PCV (%)	No change PCV (%)	P
AGE days				
1-2	12 (50%)	10 (41.7%)	2 (8.3%)	0.027
3-4	12 (26.7%)	29 (64.4%)	4 (8.9%)	
5-6	10 (21.3%)	31 (66%)	6 (12.8%)	
7 and more	4 (25%)	11 (68.8%)	1 (6.2%)	
Initial TSB mg/dl				
9-19.9	10 (47.1%)	11 (52.4%)	0 (0%)	0.061
20-29.9	21 (22.8%)	61 (66.3%)	10 (10.9%)	
30 and more	7 (36.8%)	9 (47.4%)	3 (15.8%)	
Duration min.				
35-49	12(31.6%)	25(63.2%)	2(5.3%)	0.044
50-64	23(31.1)	42(56.85)	9(12.2%)	
65-79	3(33.3%)	4(44.4%)	2(22.2%)	
80 and more	0(0%)	11(100%)	0(0%)	
Type				
Hemolytic	13(29.5%)	25(56.8%)	6(13.6%)	0.065
Non hemolytic	25(28.4%)	56(63.6%)	7(8%)	

Discussion

Exchange blood transfusion remains the gold standard for effective treatment of neonatal hyperbilirubinemia. Although exchange transfusion rate was progressively declining over the years, it is still required in up to 7% of neonates admitted to nurseries [12]. In 44(33.3%) cases the cause of hyperbilirubinemia was hemolysis with ABO incompatibility being the most common. This is similar to the results of similar studies where hemolysis due to ABO incompatibility was 30%[13],35%[14] and 21.9%[15]. Other studies showed higher percentage of hemolysis mainly ABO incompatibility like in Iran where it was 49.3%[16] in one study and 38.1% in another one[17]. Exchange transfusion is effective in lowering TSB, removing hemolyzing red blood cells and the antibodies responsible for hemolysis.

Mean initial TSB in our study was 24.34 mg/dl. This is close to other studies in Nepal where it was 24.2mg/dl[18], in Iran and USA where they were 25mg/dl[19,20] and in Thailand where it was 26mg/dl[21]. But it is lower than initial TSB in other studies as in Iran 27.7 mg/dl[22], India 33.5mg/dl[18], Bolivia 31.1mg/dl[23] and Turkey 29.59mg/dl[16]. This variability in initial TSB supports the idea that different factors other than TSB affect the decision to do exchange transfusion.

The mean rate of TSB lowering after exchange transfusion is 36.15% which is lower than results taken from other studies. In Singapore the mean rate was 60.4%[24], in Nepal and Iran 58%[18,20], in India 52.01%[18] and in Brazil 44%[25]. This indicates a lower efficacy of the procedure in our locality and this mandates looking for this in further studies in future.

The initial hematocrit before exchange transfusion in this study is 49.62% indicating that majority of the neonates didn't have anemia. This result is close to the result of an Iranian study where it was 49.5% [20] but higher than a study in Singapore where it was 39.74+/-5.65[24]

The mean age at which the procedure is done is 4.48 days. This is close to results found in an Iranian study where it was 4.97 days [22] but lower than what was present in other studies as in Thailand 6.25 days[21], Singapore 6.03 days[24] and Bangladesh 5.2 days[13]. Although our studies showed increasing efficacy of exchange transfusion with increasing age but this was not significant and also the aforementioned studies showed the same.

The serum bilirubin level at the time of exchange transfusion and the duration of the procedure do not significantly affect the efficacy of the procedure in lowering TSB in the current study in correspondence to different other studies[22,19,21,13,23]

Non hemolytic hyperbilirubinemia is significantly more responsive to exchange transfusion in our study though this comparison has not been made in the other studies we compared with but this is expected because the hemolysed RBCs are a continuous source of bilirubin rendering the procedure less effective.

The TSB measurement 8 hours after the procedure showed increased TSB in most cases and this mandated repeating the procedure in 33.3% of cases. This is due to the rebound of bilirubin while in those cases with TSB remaining the same or decreasing the cause is the efficacy of the procedure in abolishing the source of excess bilirubin. This change of TSB after 8 hours of the procedure is significant-

ly related to age and duration of the procedure.

Hematocrit (PCV) measurement done 8 hours after the procedure shows that in most cases it decreased and this is mostly due to bone marrow suppression following the procedure and technical errors during the procedure.

Conclusion

Exchange procedure is still effective in the management of neonatal hyperbilirubinemia with hemolysis especially ABO incompatibility being the most common cause needing this procedure. The mean TSB, mean hematocrit, age at which the procedure is done are comparable to other studies but the efficacy in lowering TSB is less. The procedure lowers bilirubin more effectively in non hemolytic hyperbilirubinemia. Serum bilirubin rebounds and hematocrit drops after 8 hours in most cases with significant variation with the age and duration. The procedure needs to be repeated in around one third of cases.

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