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Original Article

Paediatrics Section

Effect of Low-volume Exchange Transfusion on Neonatal Hyperbilirubinaemia: A Retrospective Cohort Study

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ABSTRACT

Introduction: A double volume exchange transfusion for hyperbilirubinaemia often requires more than one pack of compatible blood to fulfil the calculated volume. This is often unavailable, necessitating exchange transfusion using less than the calculated double-volume. During practice, the authors found that many patients had a positive therapeutic response even when the exchange blood volume was reduced.

Aim: To study the effect of the reduced volume of blood used for exchange transfusion in neonates with hyperbilirubinaemia.

Materials and Methods: A retrospective cohort study was conducted in the Neonatal Intensive Care Unit (NICU), Malankara Orthodox Syrian Church Medical College (tertiary level), Kerala, India, between January 2015 and December 2020. Total 116 patients who underwent exchange transfusion for hyperbilirubinaemia, regardless of gestational age, were included. Pre- and postexchange details, blood chemistry and haemogram were collected from the records and analysed. The patients were grouped into group 1 (80-≤120 mL/kg) and group 2 (>120-≤160 mL/kg) based on the volume of blood used for exchange transfusion. The correlation of exchange blood volume with the percentage drop in bilirubin, rebound rise of bilirubin at six hours, duration of phototherapy, and duration of admission was studied using Pearson's/Spearman's correlation. Data were statistically analysed using Independent samples t-test, Paired sample t-test, and Chi-square test to determine, if there was a significant difference between the groups.

Results: Out of 116 patients, group 1 had 67 (57.78%) patients, and group 2 had 49 (42.24%) patients. The mean±Standard Deviation (SD) gestational age was 37.6±1.57 weeks, and 59 (50.86%) were males. The mean±SD postexchange bilirubin was 13.12±3.85 mg/dL in group 1 and 10.26±2.78 mg/dL in group 2, resulting in a bilirubin reduction of 40.74±12.81% and 53.81±11.67%, respectively. The rebound bilirubin at six hours (13.15±4.32 mg/dL vs 11.23±2.30 mg/dL) made no clinical difference in the management of the patient. The median duration of phototherapy was 48 hours, and the median duration of admission was five days in both groups.

Conclusion: Exchange transfusion with a lower volume of blood, followed by phototherapy, can lead to a clinically acceptable reduction in serum bilirubin. Non availability of the exact 160 mL/kg of blood for exchange is not an adequate reason to delay exchange transfusion.

Keywords: Light-emitting diode phototherapy, Neonatal jaundice, Single volume exchange transfusion, Serum bilirubin

INTRODUCTION

Exchange transfusion is an intervention that was introduced as early as 1940 to reduce the bilirubin in newborns affected with rhesus haemolytic disease and prevent kernicterus in surviving infants [1,2]. The use of this procedure has since then expanded to the treatment of other conditions such as neonatal sepsis, severe anaemia, polycythaemia, and Disseminated Intravascular Coagulation (DIC) [3-5]. Exchange transfusion removes the antibody-coated red blood cells, products of haemolysis mainly unconjugated bilirubin and replaces them with fresh donor blood. The recommended practice is to perform a double volume (160 mL/kg) exchange for treating hyperbilirubinaemia and a single volume (80 mL/kg) exchange for anaemia [6,7].

It has been reported that the optimum amount of bilirubin was removed when the exchange volume was around 160-180 mL/kg [6]. Over the years, blood banks have started separating and dispensing blood components rather than holding whole blood [8]. Consequently, for exchange transfusion, packed red blood cells suspended in plasma are routinely being used. The usual volume of such a pack is around 300-350 mL [9]. This would mean that when the patient is above 2.3 kg, a single pack would not provide the calculated 160 mL/kg [6].

During clinical practice, the authors encountered situations when only one pack of compatible blood (300-350 mL) was available for conducting the exchange transfusion, which translated to around 100-120 mL/kg of blood and, those patients had an acceptable therapeutic response. The Cochrane analysis comparing a single volume (80 mL/kg) exchange to a double volume exchange concludes that there is insufficient data to change the practice of double volume exchange [10]. However, there is no data on how the treatment is affected when the exchange volume is less than the calculated double volume. The present study is an attempt to fill this gap.

The present study was conducted to evaluate the efficacy of exchange transfusion conducted with less than 160 mL/kg of blood among neonates with hyperbilirubinaemia. The objectives of the study were to find the percentage drop of bilirubin based on the volume of blood used and to determine whether these patients required a longer duration of phototherapy, a greater number of days in admission, and their bilirubin level at discharge.

MATERIALS AND METHODS

A retrospective cohort study was conducted in the tertiary level NICU, Malankara Orthodox Syrian Church Medical College (tertiary level), Kerala, India. The study was approved by the Institutional Ethics Committee (MOSC/IEC/550/2021). The data were collected between January 2015 and December 2020 and were analysed from May 2021 to August 2021. Confidentiality was maintained at all steps of the study.

Inclusion criteria: All patients who had undergone exchange transfusion for hyperbilirubinaemia, regardless of gestational age during the study period, were included in the study.

Exclusion criteria: Patients who underwent exchange for other indications like sepsis and anaemia were excluded from the study.

Study Procedure

Details of maternal demographics, newborn demographics, Rh/ABO groups, pre-exchange and postexchange bilirubin levels, haemoglobin levels, sodium, potassium, calcium, platelets, reticulocyte count, duration of phototherapy, complications and outcome at discharge were collected from the medical records. Direct antibody tests were performed, and patients were categorised as negative, weak positive, 1+, 2+, 3+ and 4+ [11]. All neonates were given Light Emitting Diode (LED) phototherapy prior to and postexchange transfusion.

Method of exchange: The exchange transfusions were carried out with a two-port (isovolumetric) technique where an umbilical vein or umbilical artery or peripheral artery was used to withdraw blood (out port), while blood was simultaneously transfused using a peripheral intravenous catheter (in port). Compatible, cross-matched, fresh (<seven-day-old) Packed Red Blood Cells (pRBCs) suspended in plasma or whole blood, as per availability, was used for conducting the exchange transfusion.

With 120 mL/kg being the midpoint between a single volume and a double volume exchange, it was taken as a cut-off point for categorising patients into two groups. The analysis was separately done for the two groups: a) exchange blood volume 80 mL/kg to ≤120 mL/kg (group 1); b) exchange blood volume >120 mL/kg to ≤160 mL/kg (group 2). Percentage drop in bilirubin was calculated as (admission bilirubin-postexchange bilirubin)×100/admission bilirubin.

STATISTICAL ANALYSIS

Independent samples t-test was performed to determine the difference in the percentage drop of bilirubin between the groups. Paired sample t-tests and Mann-Whitney U tests were performed to check the significant difference between pre-exchange and postexchange serum haemoglobin, electrolytes and platelet values, as the data followed normality. Postexchange complications were analysed for both groups, and a Chi-square test was done to determine if there was a significant difference between the groups. A p-value <0.05 was considered statistically significant, and the entire statistical analysis was performed using R software (EZR).

RESULTS

A total of 131 neonates required exchange transfusion during the period of the study. Among these, 116 patients who underwent exchange transfusion for hyperbilirubinaemia were included in the present study, while 15 (11 with anaemia and 4 with sepsis) were excluded. There were 67 (57.78%) patients (group 1) who received exchange transfusion with a blood volume of 80-≤120 mL/kg and 49 (42.24%) patients (group 2) for whom exchange was done with >120-≤160 mL/kg blood.

The baseline analysis of the groups regarding gestational age, birth weight, gender, place of delivery, mode of delivery, maternal age, Rh incompatibility, ABO incompatibility, and Coombs test status showed no significant difference between the groups, except for birth weight [Table/Fig-1].

Variables	All subjects N=116	Group 1 n=67	Group 2 n=49	p-value
Gestational age (weeks)	37.6±1.57	37.79±1.49	37.41±1.67	0.197[t]
Gestational age distribution (in weeks)				
GA: 32-33+6	2 (1.72)	1 (1.49)	1 (2.04)	-
GA: 34-36+6	19 (16.37)	10 (14.92)	9 (18.37)	
GA: >37	95 (81.89)	56 (83.58)	39 (79.59)	
Birth weight (kg)	2.99±0.49	3.08±0.38	2.87±0.59	**0.028**[t]
Weight at admission (kg)	2.77±0.49	2.84±0.43	2.67±0.54	0.055[t]
Gender				
Male	59 (50.86)	37 (55.2)	22 (44.9)	0.272[c]
Female	57 (49.14)	30 (44.8)	27 (55.1)	
Place of delivery				
Outborn	98 (84.4)	57 (85.1)	41 (83.7)	0.837[c]
Inborn	18 (15.52)	10 (14.93)	8 (16.3)	
Mode of delivery				
LSCS	51 (43.97)	26 (38.8)	25 (51)	0.190[t]
VD	65 (56.03)	41 (61.2)	24 (49)	
Maternal age (years)	28.19±4.776	28.34±4.98	27.98±4.53	0.687[t]
Hour of life at admission	80 (45-120)	84 (48-120)	76 (45-120)	0.5[m]
Weight loss at admission				
≤10%	80 (69)	45 (67.2)	35 (71.4)	0.624[c]
>10%	36 (31)	22 (32.8)	14 (28.6)	
Etiology				
Rh incompatibility	30 (25.86)	20 (29.9)	10 (20.4)	0.251[c]
ABO incompatibility	34 (29.31)	19 (28.35)	15 (30.61)	0.792[c]
DCT negative	66 (56.89)	37 (55.2)	29 (59.2)	0.67[c]
DCT positive	50 (43.10)	30 (44.78)	20 (40.81)	
DCT weak positive	8 (6.89)	3 (4.5)	5 (10.2)	
DCT 1+	8 (6.89)	5 (7.5)	3 (6.1)	
DCT 2+	3 (2.58)	2 (3)	1 (2)	
DCT 3+	7 (6.03)	4 (6)	3 (6.1)	
DCT 4+	24 (20.69)	16 (23.9)	8 (16.3)	
Reticulocyte count (n=110)	7.02±5.3	7.22±5.5	6.76±5.15	0.661[t]
Reticulocyte count ≤7%	64 (58.18)	38 (59.38)	26 (56.52)	-
Reticulocyte count >7%	46 (41.81)	26 (40.62)	20 (43.47)	
Method of exchange	UV-PV: 114 (98.27)	UV-PV: 65 (97.01)	UV-PV: 49 (100)	-
	UA-UV: 1 (0.86)	UA-UV: 1 (1.49)		
	PA-PV: 1 (0.86)	PA-PV: 1 (1.49)		

[Table/Fig-1]: Baseline characteristics of study participants (N=116).
Values presented as Mean±SD/ n (%)/Median {Inter Quartile Range (IQR)};
[t]Independent samples t-test; [c]Chi-square test; [m]Mann-Whitney U test;
GA: Gestational age; LSCS: Lower segment caesarean section; VD: Vaginal delivery; DCT: Direct Coombs test; UV: Umbilical vein; UA: Umbilical artery, PA: Peripheral artery; PV: Peripheral vein; The p-value in bold font indicates statistically significant value

There was a statistically significant difference in postexchange bilirubin, the percentage drop in bilirubin, and the rebound bilirubin at six hours between the two groups. However, the duration of phototherapy, duration of admission and discharge bilirubin were similar in both groups. Six patients in group 1 required more than one exchange transfusion. They had Rh isoimmunisation and received an average blood volume of 86.4 mL/kg for the first exchange [Table/Fig-2].

Variables	All subjects (N=116)	Group 1 (n=67)	Group 2 (n=49)	p-value
Mean pre-exchange bilirubin (mg/dL)	22.569±5.24	22.493±5.505	22.673±4.917	0.855[t]
Volume of blood used for exchange (mL)	353.58±92.89	295.63±36.09	432.84±88.23	**<0.001[t]**
Volume of blood (mL/kg)	119.90±30.56	97.02±13.31	151.19±16.29	**<0.001[t]**
Duration of exchange (minutes)	80.07±28.39	74.75±28.89	87.37±26.26	**0.017[t]**
Postexchange bilirubin	11.9±3.7	13.12±3.85	10.26±2.78	**<0.001[t]**
Percentage drop in bilirubin	46.26±13.90	40.74±12.81	53.81±11.67	**<0.001[t]**
Rebound bilirubin at 6 hours (mg/dL)	12.34±3.71	13.15±4.32	11.23±2.30	**0.006[t]**
Percentage rise of bilirubin at 6 hours	6.31±22.08	1.23±19.92	13.25±23.2	**0.002[t]**
More than 1 exchange	6 (5.17)	6 (8.96)	0	
Duration of phototherapy (hours)	48 (36-78)	48 (36-96)	48 (42-72)	0.977[m]
Duration of admission (days)	5 (4-7)	5 (4-7) 6.090±3.73	5 (4-7) 6.55±4.38	0.711[m]
Discharge bilirubin (mg/dL)	8.47±2.32	8.38±2.41	8.60±2.20	0.616[t]

[Table/Fig-2]: Comparison of serum bilirubin levels, volume of blood used, duration of exchange, postexchange bilirubin levels and treatment duration in the two studied groups.
Values presented as Mean±SD/n (%)/Median (IQR); [t]Independent samples t-test; [m]Mann-Whitney U test

A positive correlation (r-value=0.548, p-value <0.001) was noted between the percentage drop in bilirubin and the volume of blood used for exchange transfusion. The positive significant correlation was seen only in group 1 (r=0.572, p-value <0.001). No significant correlation was seen in group 2 (r=0.031, p-value=0.83). While the rebound rise in bilirubin at six hours had a weak correlation with the volume of blood used for exchange, the other parameters like the total duration of phototherapy and duration of admission had no significant correlation [Table/Fig-3].

The postexchange values of haemoglobin and electrolytes were significantly different from the pre-exchange values, except for haemoglobin and sodium in group 2 patients [Table/Fig-4]. The post-transfusion platelet values were available only for 65 patients, and among them, 53.8% had thrombocytopenia. No significant difference in complications was seen between the two groups [Table/Fig-5]. Postexchange thrombocytopenia and electrolyte imbalances are well-documented in the literature. None of the patients had complications warranting active management. There was no mortality related to exchange transfusion in the present study.

Correlation of exchange blood volume with:	Total participants	Group 1	Group 2
Percentage drop of bilirubin	r=0.548; p**<0.001**	r=0.572; p**<0.001**	r=0.031; p=0.834
Rebound rise in bilirubin at 6 hours	r=0.274; p=**0.003**	r=-0.026; p=0.84	r=0.182; p=0.21
Duration of phototherapy	r_s=-0.04; p=0.667	r_s=-0.136; p=0.274	r_s=0.51; p=0.730
Duration of admission	r_s=0.033; 0.725	r=0.1; p=0.423	r=0.102; 0.487

[Table/Fig-3]: Correlation of exchange blood volume with treatment effects.
r: r-value; p: p-value

Parameters		Normal range	Pre-exchange	Postexchange	p-value
Haemoglobin (n=111)	Group 1 (n=64)	15-24 gm/dL	14.19±3.20	17.69±2.47	**<0.001[p]**
	Group 2 (n=47)		16.10±2.98	15.345±3.70	0.330[p]
Sodium (N=116)	Group 1 (n=67)	133-146 mEq/L	143.24±5.35	141.37±4.41	**<0.001[p]**
	Group 2 (n=49)		143.10±5.91	143.04±4.38	0.92[p]
Potassium (N=116)	Group 1 (n=67)	3.2-6 mEq/L	4.70±0.72	4.06±0.72	**<0.001[p]**
	Group 2 (n=49)		4.76±0.802	3.786±0.595	**<0.001[p]**
Calcium (N=116)	Group 1 (n=67)	7-10.9 mg/dL	9.33±1.35	8.40±1.04	**<0.001[p]**
	Group 2 (n=49)		9.44±1.14	8.82±1.05	**<0.001[p]**

[Table/Fig-4]: Pre and postexchange laboratory parameters.
[p]Paired t-test

Adverse effects	Affected participants, n (%)	Group 1 (n=67), n (%)	Group 2 (n=49), n (%)	p-value
Hyponatraemia (<130 mEq/L) (N=116)	0	0	0	-
Hypokalaemia (<3.5 mEq/L) (N=116)	26 (22.4)	12 (17.91)	14 (28.57)	0.174[c]
Hypocalcaemia (<7.5 mg/dL) (N=116)	21 (18.10)	16 (23.88)	5 (10.20)	0.059[c]
Thrombocytopenia (<1.5 L) (n=65)	35 (53.8)	23/41 (56.09)	12/24 (50)	0.634[c]
Sepsis (N=116)	9 (7.76)	6 (8.95)	3 (6.12)	0.723[c]

[Table/Fig-5]: Adverse effects related to exchange transfusion.
[c]Chi-square test

DISCUSSION

Exchange transfusion is the only available treatment for infants at risk of bilirubin encephalopathy, who are unresponsive to intensive phototherapy. The recommended double volume exchange treatment, as practiced in various parts of the world [12-15], typically results in a reduction of serum bilirubin by 40-60% [13,14,16].

In the current study, the average volume of blood used per patient is around 353.58±92.89 mL, translating to approximately 120 mL/kg, markedly less than current treatment guidelines. The mean drop in observed serum bilirubin was 47.27%. The drop in bilirubin showed a positive correlation with the volume of blood used. Serum bilirubin reduction in group 2 was 53%, consistent with earlier findings. Group 1, which had a significantly smaller exchange volume, also displayed a 40% drop in bilirubin. A recent study from China claims to have achieved a 50% reduction in bilirubin with a single volume exchange [17]. Previous studies have documented a rebound rise of bilirubin at six hours postexchange period to be around 60% [13,18]. In the present study, the six hours postexchange bilirubin had risen in group 1 and 2 to 58.42% and 49.53% of pre-exchange levels, respectively. There were 6 (8.95%) patients in group 1 who required repeat exchange transfusion, indicating that patients who received lower volume exchange must be kept under monitoring to detect further rise in bilirubin.

Many adverse events related to exchange transfusions, including life-threatening ones, have been documented in the literature. Hypocalcaemia and thrombocytopenia in the postexchange period are documented in many studies [13,14,19,20]. It is thought that the volume of exchange, duration and route are major factors affecting the incidence of complications [7,10]. In the present study, although authors observed hypokalaemia, hypocalcaemia, thrombocytopenia and sepsis, there was no statistical difference in the incidence of complications on group-wise analysis. Postexchange thrombocytopenia is a well-known complication of exchange transfusion. The authors observed that repeat examinations after 24 hours usually show a rise in platelets. Electrolyte changes also usually self-correct.

Postexchange transfusion, the patients continued on phototherapy for a median duration of 48 hours in both group 1 and group 2. Documentation regarding the duration of phototherapy that the subjects received in the postexchange phase is scarce in the literature. Many have reported hospital stays ranging from 9-10 days [16,17]. In the current study, the patients were admitted for a median duration of five days in both groups.

The duration of phototherapy, the length of hospital stay, or the bilirubin levels at discharge were not affected by the low volume exchange, despite the fact that the initial decline in serum bilirubin was 13% lower in group 1. Predischarge bilirubin levels were 8.38 and 8.60 mg/dL in group 1 and group 2, respectively, which were below treatment thresholds.

The appropriate use of phototherapy has contributed to a reduction in the number of exchange transfusions worldwide [21,22]. All patients in the present study underwent double surface phototherapy in the postexchange transfusion period. This may be the reason why, despite the use of a reduced volume of exchange, group 1 patients did not require a prolonged duration of treatment. A comparison of previously published literature with current study is shown in [Table/Fig-6] [12-17,20,23].

Author	Place and year of the study	Number of patients	Volume of blood	Mean pre-exchange bilirubin (mg/dL)	Mean postexchange bilirubin (mg/dL)	Duration of admission (days)	Duration of phototherapy (hours)
Hakan N et al., [12]	Turkey, 2015	306	NA	25.8±6.6	NA	NA	NA
Bujandric N and Grujic J, [23]	Serbia, 2016	398	660 mL	NA	NA	NA	NA
Kakkar B et al., [14]	India, 2019	14	422 mL	16.5±6.5	9.2±3.6	NA	NA
Wolf MF et al., [20]	USA, 2020	1252	NA	20	15	NA	NA
Duan L et al., [16]	China, 2021	120	NA	25.72±5.4	13.56±3.15	9.28±3.3	NA
Okulu E et al., [15]	Turkey, 2021	132	160-180 mL/kg	24.9±9.1	NA	NA	NA
Boskabadi H et al., [13]	Iran, 2022	379	180 mL/kg	22.99±4.04	12.57±3.83	NA	NA
Xiong Z et al., [17]	China, 2023	48	80-110 mL/kg	24.61±3.55	11.92±1.50	9.14±3.78	56.43±21.89
		48	150-180 mL/kg	25.37±3.34	11.13±1.37	9.75±4.05	49.40±18.91
Present study	India, 2023	67	80-≤120 mL/kg	22.493±5.505	13.12±3.85	5	48(36-96)
		49	120-<160 mL/kg	22.673±4.917	10.26±2.78	5	48(42-72)

[Table/Fig-6]: Comparison of the present study with published literature [12-17,20,23].

Limitation(s)

The study is retrospective in nature. The postexchange platelet values of many patients were not available, and there is no control population. The authors were not sure whether they can extrapolate the same results to a push-pull technique of exchange transfusion or to preterm patients.

CONCLUSION(S)

Exchange transfusion with a lower volume of blood, followed by phototherapy, can lead to a clinically acceptable reduction in serum bilirubin. Patients who have received a lower volume exchange must continue to receive phototherapy, and their bilirubin levels should be monitored for any subsequent rise. Proceeding with exchange, even when the blood volume is less than 160 mL/kg, is therefore advantageous for the patient.

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Authors contribution: Krishna Kumar Diwakar conceptualised the paper. Manu Rajan Idicula planned and developed the protocol, completed the ethics application, collected the data and analysed the results. Leela Sudhakaran Kamath and Manu Rajan Idicula edited and revised the manuscript. All authors were responsible for

interpreting the results, drafting and revising the manuscript and its final approval.

REFERENCES

[1] Smith NJ. Management of erythroblastosis fetalis. Calif Med. 1956;84(5):313-17.
[2] Diamond LK. Erythroblastosis fetalis-now a preventable disease. Calif Med. 1969;110(2):170-72.
[3] Pugni L, Ronchi A, Bizzarri B, Consonni D, Pietrasanta C, Ghirardi B, et al. Exchange transfusion in the treatment of neonatal septic shock: A ten-year experience in a neonatal intensive care unit. Int J Mol Sci. 2016;17(5):695.
[4] Werner EJ. Neonatal polycythemia and hyperviscosity. Clin Perinatol. 1995;22(3):693-710.
[5] Wirth FH, Goldberg KE, Lubchenco LO. Neonatal hyperviscosity: I. Incidence. Pediatrics. 1979;63(6):833-36.
[6] Forfar JO, Keay AJ, Elliott WD, Cumming RA. Exchange transfusion in neonatal hyperbilirubinaemia. Lancet. 1958;2(7057):1131-37.
[7] Murki S, Kumar P. Blood exchange transfusion for infants with severe neonatal hyperbilirubinemia. Semin Perinatol. 2011;35(3):175-84.
[8] Arya RC, Wander G, Gupta P. Blood component therapy: Which, when and how much. J Anaesthesiol Clin Pharmacol. 2011;27(2):278-84.
[9] Lotterman S, Sharma S. Blood Transfusion. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022. Available from: http://www.ncbi.nlm.nih.gov/books/NBK499824/.
[10] Thayyil S, Milligan DWA. Single versus double volume exchange transfusion in jaundiced newborn infants. Cochrane Database Syst Rev. 2006;(4):CD004592.
[11] Theis SR, Hashmi MF. Coombs Test. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023. Available from: http://www.ncbi.nlm.nih.gov/books/NBK547707/.
[12] Hakan N, Zenciroglu A, Aydin M, Okumus N, Dursun A, Dilli D. Exchange transfusion for neonatal hyperbilirubinemia: An 8-year single center experience at a tertiary neonatal intensive care unit in Turkey. J Matern Fetal Neonatal Med. 2015;28(13):1537-41.
[13] Boskabadi H, Khodashenas E, Bagheri F, Behgam N, Zakerihamidi M. Evaluation of hematologic factors and bilirubin following exchange transfusion in neonatal hyperbilirubinemia. Transfus Apher Sci. 2022;61(5):103451.
[14] Kakkar B, Agrawal S, Chowdhry M, Muthukumaravel PJ, Makroo RN, Thakur UK. Exchange transfusion in neonatal hyperbilirubinemia: A single Centre experience from Northern India. Transfus Apher Sci 2019;58(6):102655.
[15] Okulu E, Erdeve Ö, Tuncer O, Ertuğrul S, Özdemir H, Çiftdemir NA, et al. Exchange transfusion for neonatal hyperbilirubinemia: A multicenter, prospective study of Turkish Neonatal Society. Turk Arch Pediatr. 2021;56(2):121-26.
[16] Duan L, Gan S, Hu H. A single-center experience on exchange transfusion therapy in 123 full-term cases of severe neonatal hyperbilirubinemia in Wuhan. J Matern-Fetal Neonatal Med. 2021;34(3):466-72.
[17] Xiong Z, Liu X, Li X. Efficacy of single-and double-volume exchange transfusion for neonatal hyperbilirubinemia. J Med Biochem. 2023;42(3):484-91.
[18] Falciglia HS, Greenwood C. Double volume exchange transfusion: A review of the "ins and outs." NeoReviews. 2013;14:e513-20.
[19] Patra K, Storfer-Isser A, Siner B, Moore J, Hack M. Adverse events associated with neonatal exchange transfusion in the 1990s. J Pediatr. 2004;144(5):626-31.
[20] Wolf MF, Childers J, Gray KD, Chivily C, Glenn M, Jones L, et al. Exchange transfusion safety and outcomes in neonatal hyperbilirubinemia. J Perinatol. 2020;40(10):1506-12.
[21] 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.
[22] Woodgate P, Jardine LA. Neonatal jaundice: phototherapy. BMJ Clin Evid. 2015;2015:0319.
[23] Bujandric N, Grujic J. Exchange transfusion for severe neonatal hyperbilirubinemia: 17 years' experience from Vojvodina, Serbia. Indian J Hematol Blood Transfus. 2016;32(2):208-14.

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