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Original Article

Intravenous Fluid Therapy in neonates receiving phototherapy for Hyperbilirubinemia - A randomized control trial

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Abstract:

Background: Most newborn babies experience jaundice after birth. In most cases, jaundice is benign; however, infants must be supervised since bilirubin may be dangerous to their health. Acute bilirubin encephalopathy or kernicterus is the potentially fatal side effect of extreme hyperbilirubinemia. Therefore, the treatment of neonatal jaundice or hyperbilirubinemia is crucial.

Method: This randomized controlled study was conducted in the department of Pediatrics, Sylhet Women's Medical College, Hospital in order to determine the requirement of intravenous fluid therapy in neonatal jaundice. By simple random sampling, 300 neonates with non-hemolytic jaundice were enrolled. 134 neonates were allocated to Group A, and they received intravenous (IV) fluid along with phototherapy. Another 166 neonates were included in Group B who received phototherapy only. Total serum bilirubin (TSB) (Both direct and indirect) was measured initially and every 24 hours during treatment. All the neonates were allowed to breastfeed during the treatment. The hydration status of neonates was checked at the beginning of the study, then every 8 hours for the next 24-72 hours. All the data were processed and analyzed in SPSS version 26. Chi-square test and independent sample 't' test were used. p value < 0.05 was considered as significant.

Result: The serum total, direct and indirect bilirubin levels of the neonates were similar (p>0.05) in both groups. Upon discharge, total serum bilirubin levels were reduced earlier in infants who received intravenous supplementation in conjunction with phototherapy, but the result was not significant (p>0.05). The clinical outcome of the neonates was insignificant. The discharge period for neonates in both groups was comparable (p>0.05).

Conclusion: In healthy term neonates with hyperbilirubinemia, intravenous fluid therapy does not provide significant benefits during phototherapy.

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Introduction:

A newborn's skin and sclera turn yellowish in neonatal jaundice, which is caused by bilirubin.[1] Hyperbilirubinemia refers to an increase in the serum bilirubin level in a newborn greater than 5 mg/dl. Jaundice develops in about 60% of term babies and 80% of preterm infants during their first week of life.[2,3,4]

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A few of them develop serious health conditions. Jaundice occurs when unconjugated bilirubin accumulates in the skin and mucous membranes.[3] If the bilirubin level rises to dangerous levels, treatments and close observation are required to prevent the complications and fatal consequences.[5] Treatment of neonates with jaundice has been investigated using a number of different approaches. Phototherapy is the commonly used technique.[6] Itis the most frequently utilized treatment because it is safe, inexpensive, non-invasive, and widely accessible.[7] Phototherapy has various adverse effects. Dehydration is the most frequent of them. When phototherapy fails

to reduce total serum bilirubin (TSB) levels gradually, exchange transfusion is necessary. But, this may raise the risk of consequences such as sepsis, emboli, anemia, apnea, hypocalcemia, and transfusion reactions.[8] Therefore, the use of intravenous fluid (IV fluid) along with phototherapy to accelerate the treatment is recommended by some studies.[8-10] The researchers suggested that, IV fluids support the maintenance of ideal hydration levels. It increases blood flow and the liver's capacity to metabolize and eliminate bilirubin, therefore aiding in a shorter hospital stay.[8-10]

Lumirubin is an isomer of bilirubin, a water-soluble product that is produced during phototherapy. Lumirubin is excreted through bile and urine. Adding intravenous fluid corrects dehydration and also improves urine output and enhances the body's ability to eliminate lumirubin.[7] But there is rising concern regarding the use of IV fluid along with phototherapy. A study by Goyal et al., 2018 found the mean rate of decrease in serum total bilirubin (STB) levels did not decline significantly when IV fluid was given to the neonates. They stated that, IV fluid supplementation is an invasive procedure and causes several other complications. Dehydration of the neonates can be corrected by frequent breast feeding.[11]

Regarding the use of IV fluids, there is some disagreement among doctors. Therefore, the goal of the current study was to determine the necessity of intravenous fluid therapy in infants receiving phototherapy for non-hemolytic hyperbilirubinemia.

Methods:

This randomized controlled trial was conducted at the Department of Pediatrics, Sylhet Women's Medical College Hospital, Sylhet. This study was commenced after approval by Ethical Review Committee of Sylhet Women's Medical College and Hospital, and the duration of the study was 1 year after approval of the protocol. The targeted population of the study were neonates with hyperbilirubinemia who had bilirubin level at the phototherapy threshold according to the bilirubin chart. The investigation encompassed a total of 300 neonates.

Simple random sampling method was adopted for the selection of the subjects. All the patients were enrolled from department of Pediatrics, Sylhet Women's Medical College Hospital, Sylhet. Premature infants with gestational age of less than 37 weeks, presence of any congenital malformations, presence of any systemic disease, sepsis, evidence of hemolysis, patients who required blood transfusion at the beginning of hospitalization, infants received intravenous (IV) fluids previously for any reason and neonates with signs of bilirubin encephalopathy (kernicterus) were excluded.

After selection, the objectives, nature, purpose, benefits of the study and likely risks of all the procedures was explained to each guardian of neonates. After enrollment, informed written consent was obtained from the guardians. The patient's level of dehydration was evaluated by a pediatrician (researcher) at the bedside. Total, direct and indirect serum bilirubin level were measured initially. Two envelopes, one labeled with phototherapy and another labeled with phototherapy with intravenous fluid was given to each guardian to pick up. Based on the envelope they selected, the neonates were allocated to either Group A or Group B. 134 neonates were enrolled in group A, and 166 neonates were enrolled in group B. Group A neonates received intravenous fluid supplementation along with phototherapy and group B received only phototherapy during the study. The extra fluids group (Group A) were given IV fluid supplementation with Quarter strength normal saline (0.225%) in 10% dextrose for a period of 24 hours via a peripheral vein during phototherapy. The volume of the fluid supplement was 50 mL/kg presumed deficit (corresponding to mild dehydration), half of the daily maintenance requirements for a period of 24 hours. Group B patients received only phototherapy. Both group of neonates were also permitted to breastfeed. The hydration status was evaluated and I/V fluid was stopped at the end of 24-hours period in neonates of Group-A.

Each phototherapy device were included four unique blue lamps that were positioned 20 cm above the babies' cribs. Serum bilirubin levels, both total and direct, were assessed initially and

then every 24 hours. The total serum bilirubin (TSB) were monitored and phototherapy was continued until it dropped to less than 14 mg/dl. Kramer scale was be used to determine the clinical outcome of the jaundice. Heart rate, respiratory rate, capillary filling time, anterior fontanelle, skin turgor, oral mucosa, weight, and urine output all were monitored to look for clinical indicators of dehydration. These were noted at the beginning of the study, then every 8 hours for the next 24-72 hours. Data were recorded in a predesignated checklist and analyzed by SPSS version 26.

Results:

The mean age of group A was 7.03±2.177 days and group B was 7.07±035 days. The mean age difference of supplement group and phototherapy group showed no significant differences (p=0.721) (Table 1). Majority of both groups belonged to rural area (p>0.05) (Table 2). There were no significant difference observed in terms of gestational age, prenatal checkups, place of delivery and birth attendants (p>0.05) (Table 3).

The mean weight and length of both groups of neonates were similar (p>0.05) (Table 4).

The onset of jaundice among neonates also showed no significant difference (p>0.05) (Table 5).

Results showed no significant difference (p>0.05) in the serum total, direct and indirect bilirubin levels of neonates of both groups (Table 6). Total serum bilirubin levels were similar in both the study groups when they were discharged (p>0.05) (Figure 1). The clinical outcome of the patients were similar in both groups (p>0.05) (Table 7). The time of discharge of the neonates were also similar in both groups (p>0.05) (Figure 2).

Table 1: Mean age of the study subjects (N=300).

Variable	Group A	Group B	p value
Age (Days)	7.03±2.177	7.07±035	0.721
Range	3-13	4-13	

Statistical analysis was done by unpaired 't' test; values in the parenthesis indicate range; N= total number of the subjects.

Table 2: Demographic variables of the patients (N=300)

Variables		Group A (n=134) Frequency (%)	Group B (n=166) (Frequency %)	*p* value
Residence	Rural	76 (56.72)	106 (63.85)	0.417
	Urban	58 (43.23)	60 (36.14)	
Socioeconomic status	Lower	40 (29.85)	46 (27.71)	0.108
	Middle	94 (70.15)	120 (72.29)	

Statistical analysis was done by chi-square (χ^2) test.; values in the parenthesis indicate percentages; n=number of the subject in each group; N= total number of the subjects.

Table 3: Obstetrical history of the patients (N=300)

Variables		Group A(n=134) (Frequency %)	Group B(n=166) (Frequency %)	*p* value
Gestational age	38	56 (41.79)	68 (40.96)	
	39	70 (52.23)	90 (54.22)	0.889
	40	08 (5.97)	08 (4.82)	
Antenatal checkup	Yes	34 (25.37)	56 (33.73)	0.129
	No	100 (7.46)	110 (66.27)	
Mode of delivery	VD	74 (55.22)	86 (51.80)	0.568
	LUCS	60 (44.78)	80 (84.19)	
Place of delivery	Home	30 (22.39)	30 (18.07)	
	SWMC	50 (37.31)	82 (49.39)	0.111
	Other hospital	54 (40.29)	54 (32.53)	
Delivered by	Doctors	104 (77.61)	134 (80.72)	
	Nurse	08 (5.97)	02 (1.02)	0.150
	Dai	14 (10.45)	20 (12.04)	
	Relatives	08 (5.94)	10 (6.02)	

Statistical analysis was done by chi-square (χ^2) test.; values in the parenthesis indicate percentages; n=number of the subject in each group; N= total number of the subjects.

Table 4: Mean weight and length of the patients (N=300)

	Group A (n=134) (Mean ± SD)	Group B (n=166) (Mean ± SD)	*p* value
Weight (Kg)	2.99±0.28 (2.50-3.70)	2.93±0.27 (2.50-3.70)	0.911
Length (cm)	49.89±0.95 (47-52)	49.84±2.57 (30-60)	0.824

Statistical analysis was done by unpaired 't' test; values in the parenthesis indicate range; n=number of the subject in each group; N= total number of the subjects.

Table 5: Day of onset of jaundice among study patients (N=300)

	Group A (n=134) Frequency (%)	Group B (n=166) (Mean ± SD)	*p* value
Day 2	41(30.59)	61 (27.75)	0.509
Day 3	85(63.43)	97(58.43)	
Day 4	06(4.48)	10 (6.02)	

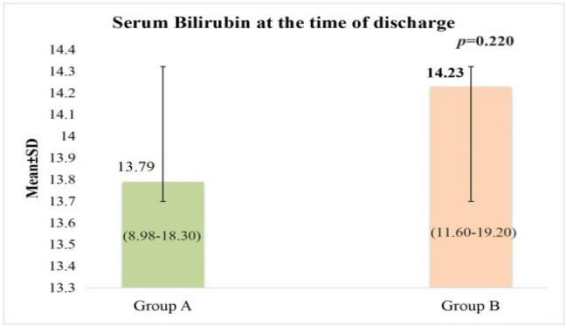
Statistical analysis was done by chi-square (χ^2) test.; values in the parenthesis indicate percentages; n=number of the subject in each group; N= total number of the subjects.

Table 6: Bilirubin levels of the patients at the time of admission (N=300)

Variables	Group A (n=134) (Mean ± SD)	Group B (n=166) (Mean ± SD)	*p* value
S. total bilirubin	18.79±2.06 (15-25.40)	18.32±2.15 (15-27.50)	0.51
S. direct bilirubin	0.43±0.14 (0.20-0.80)	0.68±1.88 (0.20-0.82)	0.074
S. indirect bilirubin	18.43±1.95 (15.00-25.00)	17.63±2.81 (12.52-27.20)	0.566

Statistical analysis was done by unpaired 't' test; values in the parenthesis indicate range; n=number of the subject in each group; N= total number of the subjects.

Figure 1: Serum bilirubin at the time of discharge of the patients (N=300)



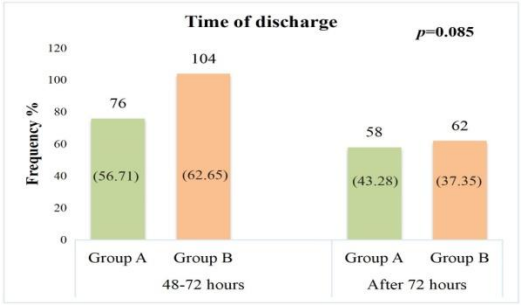
Statistical analysis was done by unpaired 't' test; values in the parenthesis indicate range;
N= total number of the subjects.

Table 7: Clinical outcome of the patients (N=300)

Clinical outcome	Group A (n=134) (Frequency %)	Group B (n=166) (Frequency %)	*p* value improvement
Within 24-48 hours	20(14.92)	29 (17.47)	
Within 48-72 hours	50(37.31)	70 (42.17)	0.417
After 72 hours	64(47.67)	67 (40.36)	

Statistical analysis was done by chi-square (χ^2) test.; values in the parenthesis indicate percentages; n=number of the subject in each group; N= total number of the subjects.

Figure 2: Time of discharge after treatment (N=300



Statistical analysis was done by chi-square (χ^2) test.; values in the parenthesis indicate percentages; N= total number of the subjects.

Discussion:

Jaundice is the most common clinical problem among neonates.[9] Phototherapy is the most common approach for the treatment of neonatal hyperbilirubinemia.[12] Fluid treatment is regarded as an effective technique to reduce bilirubin level.[12] The aim of this study was to ascertain the need of intravenous fluid therapy among infants undergoing phototherapy.

The mean age, accommodation types, socioeconomic status, gestational age, prenatal checkups, birth methods, place of delivery, and attendants were comparable in both groups ($p>0.05$) (Table: 1,2,3). Similar results were observed in a study conducted by Eghbalian et al. in 2022.[9] The two groups in their study were comparable regarding number, sex, age, gestational age, birth weight, weight at admission, and mode of delivery. Similar findings were also observed by Enad, Imran and Hussein, 2018.[13] The mean weight and length showed no difference between the groups. The weight of newborns upon admission was not significantly different between the intravenous supplement group and the phototherapy group, as noted by Morshed et al., 2017.[14] Most of the neonates developed jaundice at the third day of their life (Table: 5). Although the result was not significant. This finding was well supported by Hansen, 2021.[15] He stated that TSB eventually manifests with detectable bilirubin, typically on the second–third day of life.

The serum total, direct and indirect bilirubin levels of the newborns showed similar variation ($p>0.05$) (Table: 6). At the time of discharge, total serum bilirubin level were lower in IV supplement group neonates (Figure: 1). Although, the result was nonsignificant in both groups ($p>0.05$). This study was consistent with other study.[5,10] Eghbalian et al., 2022 observed that, the mean levels of serum bilirubin on admission, 6, 12, 24, and 48 hours after treatment decreased progressively in both groups; however, the difference was not statistically significant between the two groups.[5] In a study in Iran, the mean rate of decrease in TSB levels during the first 12 hours of phototherapy was not statistically significant in either the supplemented or non-supplemented groups ($p=0.13$).The duration of phototherapy required in the supplemented and non supplemented groups was also comparable ($p=0.13$).[10] Different outcomes were observed in certain investigations.[13,14] Total blood bilirubin (TSB) levels before treatment were found to be comparable in both groups in a study conducted by Enad, Imran, and Hussein, 2018.[13] But, after 24 hours of IV fluid supplementation, TSB level was significantly reduced in neonates who received IV fluid along with phototherapy in their study. The rate of bilirubin reduction was also statistically significant in the study group. Morshed et al., 2017 observed that, at 48 hours, the serum total bilirubin levels were significantly lowered in the IV supplement group ($p<0.001$).[14]

The clinical outcomes of the majority of newborns improved after 72 hours. Even yet, the findings were insignificant ($p>0.05$). Kaur et al., 2018 observed that the administration of additional intravenous fluids during the initial eight hours can substantially reduce TSB levels in severe non-hemolytic neonatal hyperbilirubinemia.[16] A study conducted by Eghbalian et al. in 2022 revealed similar findings with our study. The mean serum bilirubin level in their study groups showed no significant difference after 24 hours of phototherapy and phototherapy with IV supplementation in neonates.[9]

Although, the discharge time for neonates in the IV supplement group earlier, but the result was non-significant. In the intravenous supplement group, 56.71% were discharged between 48 to 72 hours, and 43.28% were discharged after 72 hours. Conversely, neonates who underwent only phototherapy had 62.657% discharged within 48 to 72 hours, while 37.35% were discharged beyond 72 hours. Comparable results were noted by Eghbalian et al., 2022. They found that, the duration of hospitalization was reduced in the fluid supplementation group; however, the results were also not significant in their study.[9]

Maintaining hydration with IV fluids is important for treating newborn jaundice because dehydration can make it challenging for the

body to get rid of bilirubin. Study observed that, IV supplementation keeps the patient hydrated and may speed up the drop in bilirubin levels, which makes neonates easier to eliminate bilirubin and reduce hospital duration. When neonates with mild to severe jaundice get phototherapy with IV fluid supplementation and drink breast milk, these may reduce the duration of hospital stays.[17,18]Butintra-venous fluid supplementation during phototherapy in newborns with hyper bilirubinemia did not have a meaningful effect in the present study.

Conclusion:

The current study suggests that the serum bilirubin level reduction, hospital duration, and clinical outcome during conventional phototherapy are not affected by the administration of additional intravenous fluid to healthy, term neonates with jaundice. So whenever phototherapy is sufficient to lower the serum bilirubin, we should avoid intravenous fluid therapy and promote frequent breast feeding to maintain hydration. Further study is suggested to assess the impact of intravenous supplementation in neonatal Hyperbilirubinemia with a larger sample size.

Ethical clearance: Taken from institutional ethics committee.

Conflict of interest: Nil.

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