Original Research

Effect of Intravenous Fluid Supplementation on Duration of Phototherapy in Term Babies with Severe Hyperbilirubinemia

Priyanka Tank[1], Rakesh Tank[2]

[1]Assistant Professor, Department of Pediatrics, SKHM Government Medical College, Nuh, Haryana, [2]Professor, Department of General Medicine, SKHM Government Medical College, Nuh, Haryana.

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Abstract

Background: Varied results emerging out of various studies have created a controversy about effect of intravenous fluid supplementation on duration of phototherapy required in term babies with severe hyperbilirubinemia. Phototherapy works by exposing the infant's skin to a specific wavelength of light (usually blue light in the range of 430–490 nm) that transforms bilirubin into water-soluble isomers that can be easily excreted via urine and bile thereby preventing severe complications like kernicterus. Paucity of literature warrants this study.

Objective: The objective of this study is to evaluate the probable effect, if any, of intravenous fluid supplementation in decreasing the duration of phototherapy requirement in healthy term babies with hyperbilirubinemia.

Methods: In this prospective study healthy term neonates (37-41 week gestation) from day 1 up to 28 days of life with serum bilirubin (>18 mg/dl and <25 mg/dl) for treatment with phototherapy were randomly allocated to two groups, study group received intravenous fluid for total 16 hours along with breast feed and control group given only breast feeds.

Results: Baseline variables like sex distribution, age at admission, gestation, birth weight, admission weight, appropriate for gestational age, mode of delivery, oxytocin use, breast feeding and serum bilirubin level at the time of inclusion in study, were comparable in both control and study group. Required duration of Phototherapy was 59.03 $\pm$ 11.79 hours in control group and in study group 32.43 $\pm$ 23.12 hrs (P <0.001). Duration of phototherapy was significantly less in study group than control group (P < 0.001). It was 27 hours shorter in extra fluid group.

Conclusions: Based on our findings it can be concluded that required duration of phototherapy significantly decreases with the use of extra fluid supplementation in neonates with hyperbilirubinemia

Keywords: Fluid supplementation, Hyperbilirubinemia, Phototherapy

Corresponding Author: Rakesh Tank, Professor, Department of General Medicine, SKHM Government Medical College, Nuh, Haryana.

E-mail: drrakeshtank24@gmail.com

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Introduction

Hyperbilirubinemia among newborns has a prevalence rate of 50-60% within the first week of life.[1,2] This condition is particularly common among preterm infants, with approximately 80% of preterm newborns and 60% of term newborns exhibiting bilirubin levels exceeding 5 mg/dl. A small percentage of term babies, around 6%, have bilirubin levels surpassing 15 mg/dl.[3,4.5] Severe hyperbilirubinemia is linked to the toxic effects of bilirubin on brain known as kernicterus.[6,7] Various factors have been identified as causes of pathological jaundice, including sepsis, Rh incompatibility, ABO incompatibility and idiopathic causes accounting for 50% of neonatal hyperbilirubinemia.[8,9] Out of this idiopathic group, studies have reported 65% to 82.7%, are solely nourished through breastfeeding.[8,10,11]

Augmenting fluid supplementation has the potential to enhance the elimination of water-soluble photoproducts of bilirubin through urine and bile, hence amplifying the efficacy of phototherapy. Furthermore, it is worth noting that fluid supplementation can potentially serve as a means of compensating for the insensible losses that occur during phototherapy.[13,14]

Numerous studies have been conducted in the past to examine the impact of oral water, dextrose, or artificial feed supplementation on term neonates. [15] These studies have yielded inconclusive findings. In contrast, other studies have demonstrated a faster reduction in serum bilirubin levels and a shorter duration of phototherapy following parenteral fluid supplementation.[16]

The controversy surrounding the utilization of parenteral fluid supplementation in the context of phototherapy for the purpose of reducing serum hyperbilirubinemia persists. Therefore, this study employed a randomized controlled trial design to assess the potential impact, if any, of intravenous fluid supplementation on duration of phototherapy during management of term infants with hyperbilirubinemia.

Material and Methods

Study setting and Study design:

The study was conducted in the Level II Neonatal Unit at Government Multi Speciality Hospital Sector-16 Chandigarh, utilizing a randomized controlled trial design from August 2012 to May 2013. This work was approved by the Ethical Committee of the institute.

Study population and Enrolment:

The term neonates (37–4 wk gestation) from day 1 upto 28 days of life who exhibited severe hyperbilirubinemia (total serum bilirubin (TSB) > 18 mg/dl and < 25 mg/dl) were enrolled in the study.[17] Informed consent, obtained in writing, was provided by either one or both parents. The study was continued till desired samples size was achieved.

The neonates who did not exhibit overt symptoms of dehydration were assigned into study and control groups by a random allocation process using a computer-generated random number list. The allocation of groups was conducted by placing them in sequentially numbered sealed opaque envelopes, which were subsequently unsealed during the enrolment process. During the course of the trial, a patient who had previously been enrolled was not re-enrolled.

The study group participants were administered a calculated intravenous solution of N/5 saline with 5% dextrose over a period of 16 hours, in addition to breastfeeding. While control group received only breast feeding as they had been receiving before to the randomization process.

Sample Size:

The sample size was calculated using open epi software for comparison of means. Based on the assumption of a 1.5 difference in TSB at the endpoint between two groups, with a standard deviation of 2.2, our calculated sample size was 34 participants per group. This sample size was determined to achieve a 95% confidence interval and a statistical power of 80%. An additional 10% of participants were recruited to account for potential loss to follow-up. The ultimate sample size for each group was determined to be 37.

Inclusion and Exclusion Criterion:

The term neonates (37–41 wk gestation) from day 1 up to 28 days of life who exhibited severe hyperbilirubinemia (TSB > 18 mg/dl and < 25 mg/

dl) were enrolled in the study. The determination of gestational age was conducted by considering the date of the last menstrual cycle in conjunction with the utilization of the recently developed Ballard scoring system.[18]

The study excluded neonates who met the following criteria: TSB levels exceeding 25 mg/dl, presence of acute bilirubin encephalopathy, evidence of hemolysis such as ABO or Rh incompatibility, positive direct Coombs test, reticulocyte counts higher than the average for their age (greater than 6%), diagnosed G6PD deficiency, clinically observable signs of dehydration, and neonates who were either sick or receiving intravenous fluid treatment.

A cohort of 74 healthy infants, ranging in gestational age from 37 -41 weeks, were included in the study based on predetermined criteria for inclusion and exclusion. A total of 74 infants were included in the study, with 37 infants randomly assigned to the control group, which got just phototherapy, and 37 infants assigned to the experimental group, which received both phototherapy and intravenous fluid.

Study Strategy and Procedure:

The study group participants were administered a calculated intravenous solution of N/5 saline with 5% dextrose over a period of 16 hours, in addition to breastfeeding. The quantity of intravenous fluid administered during the initial 8-hour period was determined using the following calculation method:

1. 50 ml/kg of fluid equivalent to mild dehydration in newborn with no clinical signs of dehydration. Fluid deficit was calculated according to birth weight of each baby.
2. Half of daily fluid requirement for 8 hors was given intravenously that was calculated according to weight and postnatal day of newborn (60 ml/kg/day on day 1 of life, with daily increment of 15 ml/kg/day, maximum 150 ml/kg/day of fluid was given on day 7 of life and onwards).
3. Over all 20 ml/kg/day additional fluid support was given to the patients because of insensible fluid loss due to phototherapy. And this amount was calculated according to 8 hours of phototherapy and weight of the patient.

For next 8 hours

Half of daily fluid requirement for 8 hours was continued along with phototherapy losses for 8 hours (as calculated above).

The intravenous fluid administration was terminated after a duration of 16 hours. Neonates were consistently provided with breast milk according to their feeding needs.

The control group did not get any additional liquids. The participants were consistently provided with breast milk as they had been receiving before the randomization process.

Both groups were administered CFL double surface blue light phototherapy using the Osran Dulex L, 18W/865 FPL 15EXD device manufactured in Italy. Eyes and genitalia of neonates were properly covered during phototherapy. Standardizing phototherapy machines for neonatal hyperbilirubinemia involved ensuring consistent performance, safety, and efficacy. Key parameters included were emitting light in the blue-green spectrum (430–490 nm) at an irradiance of 30–40 μW/cm²/nm for standard therapy and >50 μW/cm²/nm for intensive therapy, with uniform coverage of at least 80% of the infant's body.

The levels of TSB were measured at the beginning of the study period and subsequently at 4, 8, 12, 24, 36, 48, 60, and 72 hours. The bilirubin levels were assessed using a blood sample obtained via a heel prick using a micro-capillary. The sample was then centrifuged, and the bilirubin measurement was obtained using a dual wavelength spectrophotometer manufactured by ERMA, Tokyo.

The administration of phototherapy was ceased once two consecutive blood bilirubin measurements, taken 12 hours apart, indicated levels below 14 mg/dl. Neonates who exhibited an increase in TSB levels over 1 mg/dl per hour, despite undergoing phototherapy, were subjected to exchange transfusion. Additionally, if the TSB level remained equal to or greater than 20 mg/dl after 8 hours into the trial period, exchange transfusion was administered. The measurement of the outcome variable was conducted by assessing the decrease in blood bilirubin concentration at four specific time points during the study: 4, 8, 12, and 24 hours.

Date Analysis:

The continuous data was reported in the form of mean ± standard deviation (SD). The normality of the quantitative data was assessed using Kolmogorov-Smirnov tests of normality. A Student's t-test was employed to compare the means of two groups, assuming that the data followed a normal distribution. The frequencies and proportions were utilized to characterize qualitative or category variables. The comparison of proportions was conducted using either the Chi square test or Fisher's exact test, depending on the appropriateness of each test. A P-value < 0.05 was considered to demonstrate statistical significance. All the computations were conducted using SPSS® version 17, Statistical Packages for the Social Sciences, Chicago, IL.

Results

Baseline Variables:

The baseline variables that have the potential to influence TSB levels, such as the distribution of sex, age at admission, gestation, birth weight, admission weight, appropriateness for gestational age, mode of delivery, oxytocin use, breastfeeding, and TSB levels at the time of inclusion in the study, were found to be similar in both the control and study groups, as indicated in Table 1.

There were no statistically significant differences seen between the two groups, as indicated by all P values > 0.05.

Table 1: Baseline Variables

Baseline variables	Study group (n=37)	Control group (n=37)	*P* value#
Sex Males No. (%)	24 (64.9%)	16 (43.2%)	0.0620
Females No. (%)	13 (35.1%)	21 (56.8 %)	
Age at admission (hours) (Mean ± SD)	114.73 ± 45.911	109.86 ± 37.937	0.6204
Gestation (wks) (Mean ± SD)	38.5 ± 0.81	38.11 ± 0.80	0.1407
Birth weight (gm) (Mean ± SD)	2818.65 ± 428.93	2772.57 ± 407.62	0.6372
Admission weight (gm) (Mean ± SD)	2682.27 ± 398.58	2637.19 ± 404.59	0.6307
AGA No. (%)	33 (89.2%)	29 (78.4%)	-
NVD No. (%)	23 (62.2%)	20 (54.1%)	-
Oxytocin Use No. (%)	18 (48.6%)	16 (43.2%)	-
Exclusive Breast feeding No. (%)	35 (94.6%)	32 (86.5%)	-
TSB (mg/dl) Mean ± SD	20.257 ± 1.7	19.689 ± 1.7	0.1550
Range	18 – 24.7	18 – 24.7	

Unpaired t test or Chi square test wherever applicable

Serum bilirubin levels:

The TSB levels of the two groups were found to be comparable at the beginning of the study (P = 0.182). However, at 4 hours, 8 hours, 12 hours, 24 hours, 36 hours, and 48 hours, the TSB values were considerably lower in the group of infants who received intravenous fluid supplementation compared to the control group, as indicated in Table 2.

Table 2: Serum bilirubin levels at regular intervals

Hours of study	Study group (mean±SD) mg/dl	Control group (mean ± SD) mg/dl	*P* value
At Inclusion	20.25 ± 1.7	19.716 ± 1.69	0.182
4hrs	17.46 ± 1.4	18.8 ± 1.78	0.001
8hrs	15.74 ± 1.7	17.88 ± 1.25	0.001
12hrs	14.12 ± 1.9	16.88 ± 1.19	0.001
24hrs	12.83 ± 1.57	15.82 ± 1.39	0.001
36hrs	12.57 ± 1.1	14.86 ± 1.28	0.001
48hrs	12.24 ± 0.73	13.85 ± 1.1	0.002
60hrs	12.5 ± 0.70	13.03 ± 1.07	0.498

Drop of Serum Bilirubin

Drop of TSB were found to be considerably significant in the study group at 4 hours, 8 hours, 12 hours, 24 hours, 36 hours, and 48 hours, as indicated in Table 3. There was no statistically significant difference observed in the decrease in TSB levels at the 60-hour mark between the two groups.

Table 3: Drop of Total Serum Bilirubin

Hours of study	Study group (Mean ± SD) mg/dl	Control group (Mean ± SD) mg/dl	*P* value
4hrs	2.8 ± 1.34	1.316 ± 1.19	<0.001
8hrs	4.51 ± 1.6	2.04 ± 1.12	<0.001
12hrs	6.13 ± 1.99	2.862 ± 1.36	<0.001
24hrs	7.66 ± 2.15	3.89 ± 1.56	<0.001
36hrs	8 ± 1.78	4.08 ± 1.59	<0.001
48hrs	8.84 ± 2.2	5.87 ± 1.64	<0.001
60hrs	9.15 ± 5	6.81 ± 1.63	0.093

Duration of phototherapy:

The duration of phototherapy after inclusion in study was determined. In the control group, the total duration of time spent was 59.03 ± 11.79 hours. In contrast, the study group had a total duration of 32.43 ± 23.12 hours. This difference between the two groups was found to be statistically significant, with a p-value < 0.001. The duration was 27 hours shorter in the group administered with more fluids. (Table 4)

Table 4: Duration of phototherapy

Parameter Compared	Study group (Mean ± SD) hrs	Control group (Mean ± SD) hrs	P value
Duration of Phototherapy (hours)	32.43 ± 23.12	59.03 ± 11.79	< 0.001

Discussion

The primary concern around neonatal hyperbilirubinemia is to the potential danger of short-term neurological sequelae and long-term neurodevelopment abnormalities. Phototherapy is a well-established therapeutic modality that has been utilized since long. In circumstances where phototherapy proves ineffective, exchange transfusion has been implemented as an alternative approach. The efficacy of fluid supplementation, whether either orally or intravenously, in reducing serum bilirubin

levels to prevent the need for exchange transfusion and minimise associated consequences, as well as shorten the time of phototherapy, has been a topic of controversy.

Based on the results of our study, it was noticed that the administration of additional intravenous fluid supplementation led to a considerable reduction in TSB in the study group as compared to the control group. Similar findings have been documented in the study conducted by Saiedi et al.[16], a total of 100 newborns were randomly assigned to study group or the control group. The study group was administered with similar fluid as our study, however for an extended duration of 24 hours, in contrast to our study whereas the control group exclusively got breast milk. In the study group, a statistically significant decrease in serum bilirubin levels was observed at the 24-hour mark. In study by Mehta et al.[19] 74 neonates were randomly assigned to control group that received only breast milk and an experimental group that received intravenous fluid (of the same type) for 8 hours, followed by oral supplementation with breast milk during the phototherapy period. Study found a statistically significant decrease in blood bilirubin levels in the group receiving additional fluid compared to the control group. In contrast to these findings, several studies have not reported any decrease in serum bilirubin levels.[15,20,21] Iranpour et al. [20] specifically observed no reduction in serum bilirubin following intravenous fluid administration. This lack of effect may be attributed to the relatively low volume of intravenous maintenance fluid (25%) administered over a 24-hour period. In a further study conducted by Boo et al.[15], a comparison was made between extra oral fluid and oral and intravenous fluids, revealing no discernible differences between the two groups. Tan et al.[13] found that effectiveness of phototherapy was enhanced when formula feed was added in breastfeeding infants.

In present study, the levels of TSB were evaluated at regular intervals of 4 hours, 8 hours, 12 hours, 24 hours, 36 hours, and 48 hours in both the groups. The study conducted by Mehta et al.[19] revealed that the percentage drop in TSB levels at 24-hours was considerably greater in the group receiving additional fluid intake.

The duration of phototherapy was substantially shorter in the group receiving fluid therapy compared to the control group. The mean duration of phototherapy was found to be 27 hours shorter in the group receiving additional fluid compared to the control group (59.03 ± 11.79 hours versus 32.43 ± 23.12 hours, $P < 0.001$). Mehta et al.[19] reported a comparable finding, demonstrating a notable disparity in the duration of phototherapy between the study and control groups [52 ± 18 hours versus 73 ± 31 hours ($P = 0.004$)]. The studies conducted by Boo NY et al.[18], Iranpour et al. [20], did not provide information regarding the duration of phototherapy in groups that got additional fluid, whether either orally or intravenously.

One notable quality of our study is in its design as a randomized controlled trial, which allowed us to rigorously examine the impact of additional fluid therapy on neonatal hyperbilirubinemia. Furthermore, we diligently monitored serum bilirubin levels at regular intervals following enrolment, thereby enabling us to assess the potential effects of this intervention. Both groups continued with the administration of phototherapy and breastfeeding. Given that exchange transfusion services are typically limited to tertiary level hospitals rather than district level hospitals, our study aimed to assess the decrease in duration of phototherapy with intravenous fluids and the necessity for exchange transfusion in two distinct groups. Therefore, the administration of more fluid to infants with hyperbilirubinemia may serve as a preventative measure to circumvent the need for exchange transfusion.

One of the limitations of this study is that all neonates underwent phototherapy using the same type of phototherapy system. Another is smaller sample size. Further large-scale studies are needed to validate these results and establish standardized protocols for the combined use of IV fluids and phototherapy in neonatal hyperbilirubinemia management.

Conclusion

This study demonstrates that the administration of intravenous (IV) fluid therapy in term neonates with severe hyperbilirubinemia undergoing phototherapy can significantly influence the duration of phototherapy. IV fluid therapy appears to enhance the effectiveness of phototherapy by

improving hydration, promoting bilirubin excretion, and potentially accelerating the reduction of serum bilirubin levels. These findings suggest that IV fluid therapy could be considered as an adjunct to phototherapy in managing severe hyperbilirubinemia in term neonates, particularly in cases where hydration is a concern.

Ethical Approval: This work has been approved by the Ethical Committee of the Govt Multi Speciality Hospital Sector-16 Chandigarh. The trial has been duly registered at the Clinical Trial Registry of India, National Institute of Medical Statistics, New Delhi vide REF/2013/10/005799.

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Conflict of Interest: None

References

1. Daniele De Luca. NICE guidelines on neonatal jaundice : at risk of being too nice. The Lancet 2010Sep;375:771.
2. Schwartz HP, Harberman BE, Ruddy RM. Hyperbilirubinemia: current guidelines and emerging therapies. Pediatr Emerg care 2001 Sep;27(9):884-9.
3. Practice Parameter: Management of hyperbilirubinemia in the healthy term new born. American Academy of Pediatrics Provisional committee for quality improvement and subcommittee on Hyperbilirubinemia. Pediatrics 2004;94:558-68.
4. Tikmani S, Warraich H, Abbasi F, Rizvi A, Darmstadt G, Zaidi A. Incidence of neonatal Hyperbilirubinemia : a population based prospective study in Pakistan. Trop Med Int Health 2010May;15(5):502-7.
5. National Neonatal Perinatal Database [Internet]. Deoraro AK : Indian Council of Medical Reaserch New Delhi. Report 2002 – 2003 – [cited 2006 Aug]. Available from : www.newbornwhocc.org
6. Gregory MLP, Martin CR, Cloherty JP. Neonatal Hyperbilirubinemia. In, Cloherty JP (ed). Manual of Neonatal care, 7th edition. Philadelphia, Wolters Kluwer, 2011;317.
7. Gazzin S, Tiribelli C.J. Bilirubin induced neurological damage. J Matern fetal Neonatal Med 2011oct24suppl1:154-5.
8. Narnag A, Gathwala G, Kumar P. Neonatal jaundice. An analysis of 551 case. Indian pediatrics 1997;34:429-32.
9. Tiker F, Gulcan H, Kilicdaq H, Tarcan A, Gurakan B. Extreme Hyperbilirubinemia in newborn infants. Clin Pediatr (Phila) 2006Apr;45(3):257-61.
10. Maisel J, Gifford K. Normal serum bilirubin levels in the newborn and the effect of breast feeding. Pediatrics 1986;78:837-43.
11. Base K, Das PK, Bhattacharya R, Bhowmik PK. A new look on neonatal jaundice. J Indian Med Assoc 2002Sep;100(9):556-60.
12. Tan K L. Decreased response to phototherapy for neonatal jaundice in breast fed infants. Arch Pediatr Adolesc Med 1998;142:1187-90.
13. Nicoll A, Ginsburg R, Tripp J H. Supplementary feeding and jaundice in newborns. Acta Pediatr Scand 1982;71:759-61.
14. Wu PYK, Mossa A. Effect of phototherapy on nitrogen and electrolyte levels and water balance in jaundice preterm infants. Pediatrics 1978;61:193-8.
15. Boo NY, Lee HT. Randomized controlled trail of oral versus intravenous fluid supplementation on serum bilirubin levels during phototherapy of term infants with severe Hyperbilirubinemia. J Pediatr child Health 2002;38:151-5.
16. Saeidi R, Heydarian F, Fakehi V. Role of intravenous extra fluid therapy in icteric neonates receiving phototherapy. Saudi Medical Journal 2009;vol.30(9):1176-9.
17. Porter ML, Dennis BL. Hyperbilirubinemia in the term newborn. American family physician. 2002 Feb 15;65(4):599-607.
18. Ballard JL, Khoury JC, Wedig KL, Wang L, Eilers-Walsman BL, Lipp R. New Ballard Score, expanded to include extremely premature infants. The Journal of pediatrics. 1991 Sep 1;119(3):417-23.
19. Mehta S,Kumar P, Narang A. Fluid supplementation in term neonates with severe Hyperbilirubinemia. Journal of Pediatrics 2005;147:781-5.
20. R. Iranpour MD, R. Nohekhan MD, I. Haghshenas MD. Effect of intravenous fluid supplementation on serum bilirubin level in jaundiced healthy neonates during conventional phototherapy. Journal of research in Medical science 2004;4:186-90.
21. Demisroy U, Nalbantoglu B, Nalbantoglu A. Effect of fluid supplementation on serum bilirubin level during phototherapy of exclusively breastfed term infants with Hyperbilirubinemia. Breast feed Med 2011;1-5.