

Effect of Intravenous Fluid Adjuvant Therapy on Decreasing Serum Bilirubin during Intensive Phototherapy in Healthy Term Neonate with Severe Nonhemolytic Hyperbilirubinemia

Abstract

Background: Phototherapy is the most common form of treatment and prevention of neonatal nonconjugated hyperbilirubinemia. It seems that intravenous fluid therapy as a complementary method of phototherapy can accelerate the healing process in affected infants. This study aimed at investigating intravenous fluid therapy's effect in decreasing serum bilirubin in healthy term neonates with nonhemolytic hyperbilirubinemia under intensive phototherapy. **Methods:** As many as 160 healthy term infants with severe nonhemolytic hyperbilirubinemia and without exclusion criteria were enrolled. Infants were randomized to the two treatment groups (phototherapy alone and combination with intravenous fluid therapy). Serum bilirubin at admission time, 6, 12, 24, and 48 h later were measured. We evaluated decreasing serum bilirubin levels and duration of hospitalization in both groups. **Results:** In this study, the mean levels of serum bilirubin on admission time, 6, 12, 24, and 48 h after treatment gradually reduced in both groups; still, the decrease was not statistically significant between the two groups. **Conclusions:** Intravenous fluids therapy does not have a significant advantage in the process of phototherapy in healthy term neonates with severe nonhemolytic hyperbilirubinemia.

Keywords: Hyperbilirubinemia, neonatal, phototherapy

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Introduction

An increase in serum bilirubin level greater than 5 mg/dl in neonatal is called hyperbilirubinemia. Although 60% of term infants are born with jaundice, there are a few of them with severe conditions.^[1,2] Jaundice typically appears due to nonconjugated bilirubin deposition in the skin and mucous membranes.^[2] Indirect hyperbilirubinemia is usually benign; however, severe cases can lead to kernicterus. Thus, if the bilirubin level appears at dangerous levels, it requires treatment and careful monitoring.^[3] Several methods have been studied in the treatment of jaundice. The most common practice is phototherapy, and in severe cases, exchange transfusion is recommended.^[4,5] Each of these treatments has side effects. For example, phototherapy in open settings increases evaporation from skin infants.^[6] On the other hand, low-calorie intake due to insufficient breast milk is listed as one of the jaundice causes. Therefore, hydration therapy is discussed as an active agent in

reducing jaundice.^[7-12] The phototherapy mechanism is the bilirubin transformation to lumirubin; therefore, fluid supplementation can increase urine flow and facilitate lumirubin disposal.^[12-14]

However, there have been limited studies of the usefulness of intravenous fluid supplementation in reducing hospitalization duration and the rate of neonatal serum bilirubin with icterus. The suitability or efficacy of routine use in the treatment of severe jaundice requires intense phototherapy. In this study, we investigated the effect of intravenous fluid supplementation on decreasing serum bilirubin during intensive phototherapy in healthy term neonates with severe nonhemolytic hyperbilirubinemia. We compared the reduction rate in serum bilirubin and duration of hospitalization with the control group. This study aimed at investigating intravenous fluid therapy's effect in decreasing serum bilirubin in healthy term neonates with nonhemolytic hyperbilirubinemia under intensive phototherapy.

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Methods

Study design

In this case-control study, over 1 year, 160 neonates were admitted to Besat Hospital with severe hyperbilirubinemia (total bilirubin serum levels between 17 and 25 mg/dl) who were candidates for intensive phototherapy and fulfilled the inclusion criteria. Cases were divided into two equal case and control groups. The authors matched two groups in terms of number, sex, age, gestational age, birth weight, weight at admission time, and delivery mode. Inclusion criteria were the following: term neonates, lack of clinical and laboratory symptoms in favor of hemolysis, total bilirubin serum levels between 17 and 25 mg/dl, infant weight between 2500 and 4000 g, routine clinical examination, and the absence of any signs of systemic disease, such as anemia, etc.

Exclusion criteria include premature infants with the gestational age of fewer than 37 weeks, presence of any congenital malformations or systemic disease or evidence of hemolysis, requiring blood exchange at the beginning of hospitalization. Infants in the control group were treated with breastfeeding and serum therapy at the onset of hospitalization on admission; they were treated with breastfeeding and intensive phototherapy alone. In the case group, in addition to intensive phototherapy, serum/2 normal saline in dextrose water 5% of 70 cc/kg was given to infants. In both groups, infants were weighted on admission time, and their birth weight, age, gender, gestational age, mode of delivery, duration of hospitalization, and the need for blood exchange were recorded in the designed checklist. In both groups, total serum bilirubin (TSB) and direct bilirubin levels were measured at admission time, 6, and 12 h after treatment, and daily. Phototherapy and measurement of TSB level continued in infants until the TSB level below 12 mg/dl. When serum bilirubin levels reached below 17 mg/dl, standard intensive phototherapy (the devices available in Iran deliver four lamps from above and four lamps from below to the baby) was terminated, and conventional single phototherapy (4 lights) started. In the case group, fluid therapy was discontinued when bilirubin levels reached below 17 mg/dl. Blood exchange was performed when blood bilirubin levels reached blood exchange levels. When the bilirubin level appeared below 12 mg/dl, the neonate was discharged from the hospital. Laboratory procedures including complete blood sample, blood group, mother and infant Rh, and total and direct bilirubin measurement were performed in a single laboratory with results recorded in checklists. During the study, both groups were similar in phototherapy conditions. In the course of the study, none of the neonates under phototherapy met any exclusion criteria, such as the need for blood exchange appearance of sepsis symptoms.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Hamadan University of Medical Sciences approved this study. The institutional ethical committee at Hamadan University of Medical Sciences approved all study protocols (IR.UMSHA.REC.1390.2831 and IRCT COD:IRCT201012295497N1). Accordingly, written informed consent was taken from all participants before any intervention. This study was extracted from the MD Thesis of Abas Moein at this university (Thesis No. 2831).

Results

In this study, 160 healthy term infants with severe hyperbilirubinemia were compared in two groups of 80 each as intensive phototherapy subjects. The two groups were matched in terms of number, sex, age, gestational age, birth weight, weight at admission time, and mode of delivery [Table 1]. In this study, the duration of hospitalization in infants with combination therapy (phototherapy and intravenous therapy) was 4.21 ± 1.32 days, and in infants undergoing phototherapy, alone it was 5.68 ± 2.17 days. However, hospitalization duration was shorter in the case group, but the difference was not significant ($P = 0.178$).

However, in this study, the mean levels of serum bilirubin on admission time, 6, 12, 24, and 48 h after treatment gradually reduced in both groups; still, the decrease was not statistically significant between the two groups.

At the end of the first day, only 28 cases needed continued treatment due to higher than 12 mg/dl of serum bilirubin levels. The other infants with certain levels of serum bilirubin were discharged from the hospital. Also, the average loss of bilirubin was measured at 6, 12, and first and second 24 h in both case and control groups, and the most significant rate of decline was found to be at the end of the first 24 h of treatment [Table 2].

Although bilirubin level drops in the group treated with intravenous fluids were higher than the control group in all intervals, none of these differences were significant. The closest P value to a statistically significant level, at review intervals, belongs to the early 24 h of treatment. None of the infants in the case and control groups needed blood exchange.

Discussion

Fluid therapy did not have an overwhelming superiority in the phototherapy process of healthy term neonates with severe nonhemolytic hyperbilirubinemia, which is consistent with the results of other studies such as Boo *et al.* and Al-Masri.^[12,15-18] Boo *et al.*^[12] found no significant difference in hospitalization duration, bilirubin levels between infants with hyperbilirubinemia in case

Table 1: Distribution of necessary variables in both case and control groups

Properties	Case group (fluid supplementation)	Control group	P
Number of infants	80	80	-
Male-to-female ratio	50-30	60-20	-
Age on admission day	6.10±4.49	6.31±4.42	0.750
Gestational age (weeks)	38.89±0.9	38.96±0.68	0.554
Birth weight (g)	3184.62±396.44	3218.12±353.22	0.573
Weight on admission day (g)	3085.62±492.22	3146.75±370.84	0.376
Mode of delivery (normal delivery to cesarean)	43-37	49-31	-

Table 2: Comparison of decreased bilirubin level in both case and control groups

Properties	Case group (fluid supplementation)	Control group	P
The mean bilirubin decrease in the first 6 h (mg/dl)	3.62±0.25	3.23±0.11	0.435
The mean bilirubin decrease in the second 6 h (mg/dl)	2.57±0.42	2.49±0.31	0.571
The mean bilirubin decrease in The first 12 h (mg/dl)	6.09±0.29	5.82±0.21	0.463
The mean bilirubin decrease in the second 12 h (mg/dl)	3.1±0.31	3.04±0.45	0.583
The mean bilirubin decrease in The first 24 h (mg/dl)	9.29±0.6	8.76±0.66	0.198
The mean bilirubin decrease in The second 24 h (mg/dl)	0.84±0.61	0.81±0.43	0.412

and control groups. The study by Demirsoy showed no difference in the mean duration of phototherapy and bilirubin levels at admission time, 4, 8, 12, 24, and 48 h after admission between infants with hyperbilirubinemia in case and control groups.^[15] Saini also found no significant difference in the required average time for phototherapy.^[16] However, in our study, the duration of hospitalization in the intravenous fluid therapy group was less than the control group. However, the difference was not significant which is in line with Patel which showed a significant reduction in hospitalization duration favoring the intravenous fluid therapy group.^[17] In our study, differences between the decreases of serum bilirubin levels in both case and control groups at the same intervals were not significant. It is in line with Al-Masri that reported serum bilirubin at 6, 12, 18, 36, and 60 h after admission; there was no significant difference in serum bilirubin between infants with hyperbilirubinemia in case and control groups.^[18]

This result can be because more intra venous (IV) fluid therapies may decrease enterohepatic circulation, and then a lower rate of bilirubin reabsorption from the bowel.

Meanwhile, some studies, such as the studies by Mehta *et al.*^[19] and Patel,^[17] concluded that serum therapy could be sound in the treatment of severe jaundice.

Metha found that infants who received IV fluid supplementation had a more significant percentage drop in serum bilirubin in 4.8 h after admission compared to control groups.^[19]

Also, Üit Sarici *et al.*^[20] showed that serum therapy is an effective treatment for severe jaundice cases and reduces the need for blood exchange. Balasubramanian also claimed that using fluid therapy reduces the need for blood exchange.^[20] As one of the mechanisms of phototherapy is the conversion of bilirubin into lumirubin from urine,

fluid therapy can shorten infant admission by increasing urine flow and facilitating excretion. This heterogeneity in our research results with others on the usefulness of serum therapy can be due to various causes. The volume of additional fluid and possibly type of fluid given and the severity of jaundice might have contributed to the difference in the results' estimates. Overall, no single factor can be accounted for the degree of heterogeneity, although the volume or type (or both) of additional fluid might have played a role. To achieve more reliable results, further randomised controlled trial (RCTs) with large sample volumes should be performed to indicate intravenous fluid administration in the process of phototherapy in infants with healthy jaundice has no significant advantage. And a larger sample is needed to evaluate all the influential factors in the treatment of neonatal nonhemolytic hyperbilirubinemia.

Conclusions

Intravenous fluid therapy does not have an advantage in the process of phototherapy in healthy term neonates with severe nonhemolytic hyperbilirubinemia. There was no significant relationship between serum therapy and reduction in jaundice and length of hospitalization. Designed and implemented with a larger sample size and considering all maternal and neonatal factors affecting hyperbilirubinemia, further studies can achieve more accurate and comprehensive results.

Limitations of the study

Our study's limitation was that phototherapy lamp radiation was not measurable in all infants, but we attempted to replace phototherapy lamps after 2000 h of operation. The study was single center and conducted on relatively small sample size.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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Conflicts of interest

There are no conflicts of interest.

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