

Original Article

Effect of Intravenous Fluid Supplementation on Serum Bilirubin Level in Jaundiced Healthy Neonates during Conventional Phototherapy

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Abstract

Background: Adequate hydration and good urine output improve the efficacy of phototherapy. The aim of this study was to evaluate the effect of intravenous fluid supplementation on decrease of serum bilirubin levels in jaundiced healthy term infants during conventional phototherapy.

Methods: Sixty healthy breast-fed neonates with non-hemolytic hyperbilirubinemia were assigned randomly to receive either breast milk exclusively (non-supplemented group; n=30) or intravenous fluid in addition to breast milk (supplemented group; n=30) during conventional phototherapy.

Results: The mean total serum bilirubin (TSB) levels at the time of enrollment and within 84 hours after phototherapy were not statistically different between two groups. Similarly, the mean rate of decrease in TSB levels during the first 12 h of phototherapy were 0.13 ± 0.06 and 0.10 ± 0.1 mg/dL/h in supplemented and non supplemented groups, respectively (P=0.13). Duration of phototherapy required in supplemented and non-supplemented groups was 58 ± 13.02 and 63.20 ± 13.71 hours, respectively (P=0.13).

Conclusion: These data show that administration of extra intravenous fluid in jaundiced healthy, term, breastfed neonates have no beneficial effect on the rate of serum bilirubin reduction during conventional phototherapy.

Keywords: Hyperbilirubinemia, Phototherapy, Neonates, Fluid Supplementation, Dehydration.

Hyperbilirubinemia is one of the most common problems in neonatal period and in sever circumstances may cause brain damage even in healthy term newborns¹. Phototherapy is a safe way which has remained the standard treatment in neonatal hyperbilirubinemia^{2,3}. During phototherapy, bilirubin is converted to less toxic water-soluble photoisomers⁴. Because the photoproducts responsible for the decline in serum bilirubin are excreted in both urine and bile, maintaining adequate hydration and good urine output should help improving the efficacy of phototherapy⁵. Phototherapy also increases the amount of body water loss, via insensible transepidermal⁶ and stool water loss⁷. Furthermore, some infants who are admitted with severe hyperbilirubinemia are relatively dehydrated⁸. For

these reasons, in some centers fluid supplementation is given to infants undergoing phototherapy. During phototherapy an increase of about 25% above the estimated maintenance fluids⁹ and even, in intensive phototherapy, administration of intravenous fluid as 1-1.5 times of maintenance, in addition to oral alimentation, has been suggested¹⁰. The American Academy of Pediatrics (AAP) states that supplementation (with dextrose water) of infants receiving phototherapy is not routinely indicated. However some infants with high bilirubin levels, who are also mildly dehydrated, may need supplemental fluid intake to correct their dehydration. When sever jaundice appears in breast-fed infants the recommendation of AAP includes s

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upplementing breast-feeding with formula in an attempt to increase the caloric intake and decrease the enterohepatic circulation¹¹. Since there are considerable center to center variations in the management of neonatal hyperbilirubinemia and provision of fluid supplementation¹², we decided to evaluate the effect of intravenous fluid supplementation on the treatment of the jaundiced healthy term neonates during conventional phototherapy.

Materials and Methods

During the period, March 2003 until October 2003, sixty jaundiced neonates who were admitted to the neonatal ward of Al-Zahra hospital, affiliated to Isfahan University of Medical Science, Isfahan, Iran, were selected. These neonates were all Iranian race, healthy, breast-fed, delivered between 38 and 41 weeks of gestation, following an uneventful pregnancy and had a total serum bilirubin (TSB) between 17 and 24.9 mg/dl.

The exclusion criterias were major congenital malformation, hemolytic disease (Rh or ABO incompatibility and a positive coombs' test), infection (congenital or acquired), G6PD deficiency, dehydration, conjugated hyperbilirubinemia > 15% of the total serum bilirubin levels, and prolonged jaundice persisting beyond 14 days of life. Neonates were diagnosed as being dehydrated when there were clinical evidences of dehydration (dryness of bucal mucosa, tongue and skin; loss of skin turgour; sunken eye; sunken anterior fontanel; and weight loss of more than 8% of birth weight).

After obtaining the parental permission, neonates were assigned randomly to two groups, either the breast-fed on demand (non-supplemented group; n=30), or breast-fed in addition to intravenous fluid supplementation (supplemented group; n=30). Neonates in the fluid-supplemented group received an additional 25% of their maintenance fluid requirement. The daily maintenance fluid level considered 80 ml/ kg on day 2, 120 ml/kg on day 3 and 150 ml/kg on day 4 and thereafter. The supplementary fluid was given as continuous intravenous 1/5 normal saline and 5% dextrose infusion via a peripheral vein over 24h. All phototherapy units contained 4 special blue lamps (Philps TL18/54, Philips lighting, Rosendaal, Netherlands) and adjusted to be 20 cm above the

neonates cots. Lamps were changed regularly after 2000 hours of utilization.

Total and direct serum bilirubin levels were measured at the beginning, and then every 12 hours. Phototherapy and bilirubin measurement were continued until the TSB declined to less than 14 mg/dl. Laboratory investigations included complete blood count, blood group typing of neonates and their mothers, direct and indirect coombs tests, reticulocyte count, serum bilirubin level (total and direct) and erythrocyte G6PD level. TSB was measured by Unistate®Bilirubinometer (Reichert-Jung, Germany), and determination of direct bilirubin was made by the Colorimetric method of Lathe and Ruthven. Other tests were performed accordingly, by the standard laboratory methods.

Numeric variables were compared between two groups using the Independent Student test. The Chi-Square test was used to compare sex and type of delivery between the two groups. P values of less than 0.05 were considered statistically significant. Data were analyzed using the Statistical Package for Social Sciences (SPSS version 10.05).

Results

Table 1 shows the basic demographic data of the two groups. There were no significant differences between the two groups regarding the birth weight, gestational age, age on admission, weight on admission, gender distribution and mode of delivery. In addition, there were no statistically significant differences in the reticulocyte count, hematocrit, hemoglobin, and TSB levels at the time of enrollment between the groups (table 2). Thus, supplemented and non-supplemented groups were comparable. The age of admission ranged from 3 to 14 days in supplemented group and from 4 to 14 days in the non-supplemented group. The TSB levels on enrollment in supplemented and non-supplemented groups ranged from 18.5 to 24.8 mg/dl and 18 to 24.7 mg/dl, respectively.

As shown in table 2, the mean TSB levels in the two groups of neonates were not significantly different within 80 hours after treatment by conventional phototherapy.

There was no significant difference between the rates of TSB decrease in the two groups during the first 12 hours after phototherapy (0.13 ± 0.06 mg/dl/h in supplemented vs. 0.10 ± 0.1 mg/dl/h in

non-supplemented group; $P = 0.13$). Required duration for phototherapy in supplemented and non-supplemented groups were 58 ± 13.02 and 63.20 ± 13.71 hours, respectively ($P=0.13$).

No cases developed local or systemic infection, dehydration, need for exchange blood transfusion and long stay in hospital. All neonates discharged with good general condition.

Table 1. Demographic data of neonates in the supplemented and non-supplemented groups. Data are mean \pm SD or n (%) when appropriate.

	Supplemented (N=30)	Non-supplemented (N=30)	P Value
Birthweight (g)	3321 \pm 514	3258 \pm 502	0.63
Weight on admission (g)	3211 \pm 492	3176 \pm 482	0.77
Gestation (week)	39 \pm 1.01	38.9 \pm 0.93	0.59
Age on admission (days)	7.4 \pm 3.33	8.8 \pm 3.19	0.11
Sex	Male	13 (43.3)	0.35
	Female	17 (56.7)	
Delivery	Vaginal	18 (60)	0.39
	Cesarean	12 (40)	

Table 2. Laboratory characteristic of neonates in the supplemented and non-supplemented groups. Data are mean \pm SD .

	Supplemented (N=30)	Non-supplemented (N=30)	P values	
Hematocrit (%)	42.38 \pm 5.85	44.83 \pm 6.87	0.14	
Hemoglobin (mg/dl)	15.9 \pm 1.88	15.75 \pm 2.04	0.2	
Reticulocyte count (%)	2.32 \pm 1.25	2.39 \pm 1.15	0.82	
TSB (mg/dl) admission	21.60 \pm 2.02	22.33 \pm 2.09	0.17	
	12 h	20 \pm 1.96	21.02 \pm 2.11	0.06
	24 h	18.43 \pm 2.04	19.28 \pm 2.09	0.11
	36 h	16.46 \pm 2.09	17.29 \pm 2.10	0.13
	48 h	14.87 \pm 2.06	15.78 \pm 1.83	0.08
	60 h	13.93 \pm 1.53	14.45 \pm 1.56	0.29
	72 h	13.21 \pm 0.93	13.22 \pm 0.96	0.98
	84 h	13.15 \pm 0.35	12.72 \pm 0.27	0.17

TSB = Total Serum Bilirubin

Discussion

In this study, the rate of the decrease in bilirubin concentration in fluid-supplemented group was comparable with in the non-supplemented group. In addition, the duration of exposure to phototherapy was not significantly different in two groups.

In a controlled study on the effect of water supplementation in normal term breast-fed babies who have physiologic jaundice, water supplementation was given to 120 babies, while 55 babies

received no extra fluid. There was no significant difference between the two groups when peak serum bilirubin levels and incidence of phototherapy were compared¹³. Furthermore, nicoll's study has demonstrated that supplementation of water or dextrose during the first few days of life in breast-fed neonates who may take a little amount of breast milk, did not reduce hyperbilirubinemia¹⁴. The use of fluid supplementation for limited days was the problem of nicoll's study. Since breast milk

increases after few days of delivery, therefore continuing fluid supplementation may reduce bilirubin by decreasing enterohepatic cycle of bilirubin and increasing urine output. Although a review of the literature by AAP found no strong evidence that excess fluid administration affects the serum bilirubin concentration¹¹, Boo et al⁹ has shown the beneficial effect of additional fluid in reducing serum concentration of bilirubin⁹. They have compared the rates of decrease in serum bilirubin levels in well hydrated healthy and severely jaundiced term neonates during intensive phototherapy when given 10% extra oral, versus intravenous fluid supplementation. Although the mean rates of decrease in TSB were not significantly different between the extra oral and extra intravenous fluid supplementation groups but the rate of decrease in TSB were greater than that recommended by the AAP. The AAP proposed that an effective intensive phototherapy should reduce the serum bilirubin levels by 1-2 mg/dl within 4h of treatment (or at a rate of 0.25-0.48 mg/h), while in study of Boo et al⁹, the rate of decrease in serum bilirubin during the first 4h after admission was between 0.6 and 0.65 mg/h in oral and intravenous fluid supplemented groups, respectively. They concluded that these rates of decrease in TSB could be due to fluid supplementation⁹. In addition, some studies have shown evidence of decreased response to phototherapy in breast-fed compared with formula-fed neonates^{15, 16}. Tan et al¹⁵ have observed that in exclusively breast-fed neonates with severe jaundice who require conventional phototherapy, the addition of formula feeding might enhance the response to phototherapy. They have speculated that even a mild relative dehydration might be a contributing factor in reducing response to phototherapy. The AAP Work Group on Breast Feeding indicates that if supplementation is deemed

necessary as in cases of ineffective breast-feeding or mild dehydration, human milk is preferred feeding supplement in all infants¹⁷. In this situation mother must be helped with breast-pumping to maintain a generous milk supply. Furthermore, Tan et al² reported that neonates fed on demand during phototherapy, will increase their fluid intake by 20-40% compared to control.

As far as oral supplementation is dependent on mother or nurse accompany: ment, and consequently not accurate enough to rely on, we have to select intravenous supplementation instead.

However, in our study we did not measure or estimate the volume of breast milk taken by the breast-fed neonates, and did not weigh them daily but since there was no significant difference in the rate of decrease of TSB, it seems that the exclusively breast-fed neonates compensated their fluid loss by increases in their breast milk intake during phototherapy. A study by Maisels et al⁸ identified a strong relationship between the frequency of breastfeeding and a decreased incidence of significant elevated bilirubin levels. Thus, based on our results, we recommend that all healthy term infants with significant hyperbilirubinemia requiring conventional phototherapy should not be given supplemental intravenous fluid. Furthermore administration of intravenous fluid may be accompanied by such problems as painful veinpuncture, and potential risks of extravasation of fluid and infection. In addition, setting up an intravenous drip is not cost effective.

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References

1. Maisels MJ, Newman TB. Kernicterus in otherwise healthy, breast-fed term newborns. *Pediatrics* 1995; 96(4 Pt 1): 730-3.
2. Tan KL. Phototherapy for neonatal jaundice. *Clin Perinatal* 1991; 18(3): 423-39.
3. Tan KL, Boey KW. Efficacy of phototherapy in non-haemolytic hyperbilirubinaemia. *Br Med J (Clin Res Ed)*. 1986;293(6558):1361-3.
4. Halamek LP, Stevenson DK. Neonatal jaundice and liver disease. In: Fanaroff AA, Martin RJ, editors. *Neonatal-perinatal medicine: disease of the fetus and infant*. Saint Louis: Mosby; 2002.p.1309-50.
5. Wu PY, Hodgman JE, Kirkpatrick BV, White NB Jr, Bryla DA. Metabolic aspects of phototherapy. *Pediatrics* 1985;75(2 Pt 2): 427-33.
6. Wananukul S, Praisuwanna P. Transepidermal water loss during conventional phototherapy in nonhemolytic hyperbilirubinemia term infants. *J Med Assoc Thai* 2001; 84 (1): 46-50.
7. Berant M, Diamond E, Brik R, Yurman S. Phototherapy associated diarrhea. The role of bile salts. *Acta Paediatr Scand* 1983; 72(6): 853-5.
8. Maisels MJ, Gifford K. Normal serum bilirubin levels in the newborn and the effects of breast feeding. *Pediatrics* 1986; 78: 837-43.
9. Boo NY, Lee HT. Randomized controlled trial of oral versus intravenous fluid supplementation on serum bilirubin level during phototherapy of term infants with severe hyperbilirubinemia. *J Pediatr Child Health* 2002; 38(2): 151-5.
10. Stoll BJ, Kliegman RM. Digestive system disorder. In: Behrman RE, Kliegman RM, Jenson HB, editors. *Nelson Textbook of pediatrics*. Philadelphia: Saunders;2004.p. 588-599.
11. Practice parameter: management of hyperbilirubinemia in the healthy term newborn. American Academy of Pediatrics. Provisional Committee for Quality Improvement and Subcommittee on Hyperbilirubinemia. *Pediatrics* 1994; 94(4 Pt 1): 58-65
12. Hanson TW. Therapeutic approaches to neonatal jaundice: an international survey. *Clin Pediatr (Phila)* 1996; 35(6): 309-16.
13. De Carvalho M, Holl M, Harvey D. Effects of water supplementation on physiological jaundice in breast-fed babies. *Arch Dis Child* 1981; 56(7): 568-69.
14. Nicoll A, Ginsburg R, Tripp JH. Supplementary feeding and jaundice in newborns. *Acta Paediatr Scand* 1982; 71(5): 759-61.
15. Tan KL. Decreased response to phototherapy for neonatal jaundice in breast-fed infants. *Arch Pediatr Adolesc Med* 1998; 152(12): 1187-90.
16. Porter ML, Dennis BL. Hyperbilirubinemia in the term newborn. *Am Fam Physician* 2002; 65(4): 599-606.
17. American Academy of Pediatrics Work Group on Breast-feeding. Breast-feeding and the use of human milk. *Pediatrics* 1997; 100:1035-1039.