Role of intravenous extra fluid therapy in icteric neonates receiving phototherapy

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ABSTRACT

الأهداف: تقييم دور العلاج بالمزيد من السوائل داخل الوريد وبتسريع تخفيض اليرقان لدى المواليد الذين تلقوا العلاج الضوئي.

الطريقة: أجريت هذه الدراسة على 100 مولود مكتمل فترة الحمل وعلى مواليد مصابين باليرقان الذين تلقوا إجمالي 18mg/dl من البيلوروبلين أو أكثر من في جناح الأطفال – مستشفى غايم خلال الفترة من أكتوبر 2007م حتى ابريل 2008م مدينة مشهد – إيران. تم تقسيم المواليد عشوائياً إلى مجموعتين متساويتين حيث تلقت كل مجموعة واحدة فقط حليب الأم (مجموعة التحكم)، والمجموعة الأخرى تلقت سوائل زائدة بالإضافة إلى الرضاعة الطبيعية. (مجموعة الحالة). تمت مقارنة معدل تقليص البيلوروبلين وأيام البقاء في المستشفى ومعدل نقل الدم.

النتائج: بلغ انخفاض مصل البيلوروبلين في 12 ساعة الأولى بعد الدخول 95%CI: 0.1-0.41mg/dl، في مجموعة الحالة مقابل 0.0.3 95%CI: 0.38mg/dl في مجموعة التحكم (p=0.22). كانت 95%CI 0.0001 ـ 0.41mg/dl و 95%CI 0.06 ـ 0.21mg/dl في 12ساعة الثانية لمجموعة الحالة ومجموعة التحكم على التوالي. بعد 24 ساعةكانت 95%CI: 0.0001 لدى مجموعة الحالة تقدر 0.38mg/dl وعند 95%CI: 0.09 تقدر 0.29mg/dl لدى مجموعة التحكم، p=0.037. بلغت فترة البقاء في المستشفى 68.5 ساعة لدى مجموعة الحالة و67.4 لدى مجموعة التحكم (p=0.95).

خاتمة: العلاج الإضافي بالسوائل للمواليد يمكن أن يسرع من تخفيض مستويات مصل البيلوروبلين خلال 24 ساعة الأولى.

Objectives: To evaluate the role of intravenous extra fluid therapy in accelerating the reduction of jaundice in newborns who received phototherapy.

Methods: This study was performed on 100 terms, jaundiced neonates who had a total bilirubin of 18mg/dl or more in the Pediatrics Ward of Ghaem Hospital, Mashhad, Iran from October 2007 to April 2008. The patients were randomly divided into 2 equal groups; group I (case group) were given extra parenteral fluid besides breast feeding, and group II (control group) received only breast milk. The rate of bilirubin decrement, length of hospital stay, and rate of blood exchange were compared.

Results: The rate of serum bilirubin decrease per hour in the first 12 hours after admission in group I (0.41mg/dl [95%CI 0.1] versus 0.38mg/dl in group II [95% CI 0.3], [p=0.22]). It was 0.41mg/dl for group I (95% CI 0.0001), and 0.21mg/dl (95%CI 0.06) for group II in the second 12 hours (p=0.02). After 24 hours, it was 0.38mg/dl in group I (95% CI 0.0001), and 0.29mg/dl in group II (95% CI=0.09) (p=0.037). The mean hospital stay was 68.5 hours in group I, and 67.4 hours in group II (p=0.95).

Conclusion: Additional parenteral fluid therapy in icteric newborns can accelerate reduction in serum bilirubin levels in the first 24 hours.

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Severe neonatal jaundice can cause serious permanent side effect called kernicterus, in which the brain stem nuclei and basal ganglia are damaged. Its clinical features include lethargy, hypotonia, convulsion, opisthotonos, and mental delay.[1-5] In extreme neonatal jaundice, progressive reduction in the serum bilirubin levels using phototherapy and exchange transfusion may be necessary. Phototherapy has some side effects

such as diarrhea, skin rash, dehydration, overheating, mother-baby bonding, and feeding disruption.[6,7] On the other hand, exchange transfusion complications include infections, emboli, and anemia, apnea, and hypocalcemia transfusion reactions.[8-10] Keeping in mind these potential risks encourage us to find some ways consisting of extra fluid supplementation to reduce resorting to these measures. A study has shown that the administration of extra fluid to icteric baby can reduce the jaundice more rapidly.[11] However, other studies have revealed no relationship between extra fluid administration and bilirubin decrement.[12,13] Therefore, with regard to the opposite results of such few studies, we conducted this study to identify the probable role (if any) of the administration of additional intravenous (IV) fluid in promoting the reduction of hyperbilirubinemia in neonates who received phototherapy.

Methods. This is a randomized-controlled study that was performed at the Pediatric Ward of Ghaem Hospital in Mashhad, Iran from October 2007 to April 2008. Informed consent was obtained from parents. Terms newborn that has no other problem such as congenital abnormalities, sepsis, dehydration symptoms were randomly placed into 2 groups. The sample size was chosen, more than in other similar studies.[11-13] By using a random number table, simple randomization was performed. We included in our study those neonates who had non-hemolytic jaundice. The neonates were feed breast milk adlib before, and after admission. The first serum bilirubin level was taken upon admission. Other blood tests including mother and neonate blood group and Rh factor, complete blood count, reticulocyte count, Coomb's test, G6PD, and peripheral blood smear were also simultaneously taken. Since they were well hydrated, no serum urea and electrolytes were obtained. Those with hemolysis were excluded. Further serum bilirubin level evaluation was performed after 12, and 24 hours of admission. Extra fluid administration in the first 24 hours was our interruption. Other blood samples including serum bilirubin levels, and measures such as, discontinuation of phototherapy and exchange transfusion, and discharge was in accordance to the routine protocol of the pediatric ward. When bilirubin decreased to 14 mg/dl, phototherapy was discontinued. Then, 24 hours later, serum bilirubin level was evaluated again. In the absence of rising bilirubin, patients were discharged. In the case group (group I) that includes 50 patients, breast milk and extra IV fluid including 1/5 normal saline in 5% dextrose at a rate of 80 cc/kg for a 2-day-old neonate, and an additional 10 cc/kg each day thereafter, to a maximum of 120 cc/kg was administered through the peripheral vein during the first 24 hours after admission to the hospital. The control group (group II) consists of 50 patients that were fed only with breast milk. The serum bilirubin levels were evaluated upon admission, and 12 hours. A third sample was taken at the end of the 24th hour after admission. Both groups received the same type of phototherapy, including fluorescent lamps radiating from a 25 cm distance. We included all term, healthy neonate from 2-28 days old, who had serum total bilirubin of 18 mg/dl or more in our study.

We excluded those patients with any of following: jaundice in first day after birth, any manifestations of kernicterus, any form of hemolysis, dehydration, any congenital malformation, antibiotics taken, direct bilirubin above 15% of the total bilirubin, exchange transfusion if it was performed soon after admission. This study was approved by the Committee of Ethics of Mashhad University of Medical Sciences.

Data was analyzed with SPSS version 11.5 (SPSS Inc., Chicago, IL, USA). The t test, Chi-square, Fisher's, and Mann-Whitney tests were also used. A p-value <0.05 was considered significant. The 95% confidence interval (CI) was also calculated.

Results. There were 27 (54%) males, and 23 (46%) females in group I. In group II, there were 24 males (48%), and 26 females (52%) (p=0.69, Chi-square test). The mean age of patients in group I was 7.7 days (standard deviation - 5.12), and 7.9 days in group II (standard deviation - 6.8) (p=0.69, Mann-Whitney test). The mean birth weight was 3,031.4 g (standard deviation - 484.36) in group I, and 3,072.00 g (standard deviation - 430.6) in group II (p=0.52, t test). At admission, the mean bilirubin levels was 21.2 mg/dl in group I (p=0.19, t test [95% CI: 0.11]), and 21.00 mg/dl in group II (p=0.19, t test [95% CI: 0.34]). At discharge, the mean serum bilirubin levels was 11.20 mg/dl in group I (p=0.26, t test [95% CI: 0.14]), and 11.70 mg/dl in group II (p=0.26, t test [95% CI: 0.38]). As shown in **Figure 1**, the serum bilirubin decrement rate in both groups has decreased. However, it has a statistically significant decrement in group I in the first 24 hours. There was no significant differences between the mean age of patients, mean birth weight and gender, weight loss rate from birth, and serum bilirubin levels at admission in both groups. Maternal characteristics were not evaluated in this study. Also, the number of blood tests to evaluate serum bilirubin levels during the hospital stay had no significant differences in both groups. The mean hospital stay was 68.6 hours in group I, and 67.4 hours in group II (p=0.85, Mann-Whitney test). There was no significant difference in exchange transfusion rate in both groups. (p=0.09, Fisher's exact

test). The rate of serum bilirubin level reduction in the first 24 hours, weight changes, and bilirubin levels at admission and discharge are shown in **Table 1**.

Discussion. Based on our findings, additional IV fluid administration during the first 24 hours can significantly decrease serum bilirubin levels in very icteric neonates. It is opposite to one study in Isfahan.[13] This difference may be in some extent due to the amount of given fluid, in which 25% additional IV fluid is taken in that study, that is 1/4 in our study. In another report,[12] extra oral fluids versus extra oral and IV fluids are compared without any significant difference between groups in the reduction of serum bilirubin levels. However, there was no control group in that study to compare the reduction in the bilirubin levels in the receiving fluid groups versus non-receiving group. But our findings is similar to another report,[11] with a different rate of fluid supplementation in that study, in which extra IV fluids were given for 8 hours at a rate half of the maintenance. Besides, the patients were given another 20 ml/kg in 24 hours. After 8 hours, IV therapy was discontinued, and an extra oral fluid at a rate of 30 ml/kg in 24 hours was started. This extra fluid treatment have resulted in the reduction of serum bilirubin levels significantly. The combination of oral feeding and extra IV fluid therapy may result in the decrease in enterohepatic circulation, and then a lower rate of bilirubin reabsorption from the bowel. Also, it seems that additional fluids therapy can cause dilution of serum bilirubin, and also increases blood circulation in the kidneys, and rising urine output, and subsequently improves excretion of water soluble photo isomers in urine.[14] On the other hand, it was suggested that high serum bilirubin levels can cause sleepiness in icteric newborns.[15] Hence, inadequate oral feeding in such sleepy cases can, along with increased insensible water loss during phototherapy predispose to the worsening of hyper-bilirubinemia in newborns not receiving extra fluid. And also due to this sleepiness of very icteric babies, the intake of breast feeding of a newborn's auto regulatory mechanisms may be influenced. The mean hospital stay in both groups had no significant differences. Also, exchange transfusion rates did not detect any statistically significant differences in both groups. These findings may be related to the limitation of extra fluid treatment to the first 24 hours of admission.

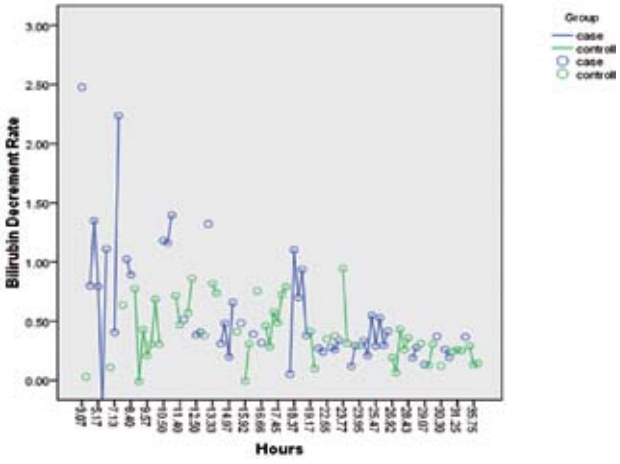

Figure 1 - Bilirubin decrement rate in both groups.

Table 1 - The rate of bilirubin reduction in the first 24 hours, weight changes, and bilirubin levels upon admission, and at discharge.

Variables	Group I			Group II			*P*-value
	n	Median	CI	n	Median	CI	
Age	50	6.5	0.57	50	6	0.83	0.7
Weight upon admission	50	3075	0.03	50	3125	0.21	0.12
Weight at birth	50	3000	0.24	50	3075	0.52	0.38
Rate of serum bilirubin decrement/hour in the first 12 hours after admission*	50	0.41	0.1	50	0.38	0.3	0.22
Rate of serum bilirubin decrement/hour in the second 12 hours after admission*	31	0.41	0.0001	40	0.21	0.06	0.02
Mean of serum bilirubin decrement/hour in the first 24 hours after admission*	50	0.38	0.0001	50	0.29	0.09	0.037
Weight changes at admission (from birth weight)	50	0.0001	0.22	50	0.45	0.49	0.32
Bilirubin levels upon admission*	50	21.2	0.11	50	21	0.34	0.19
Serum bilirubin levels at discharge*	37	11.2	0.14	50	11.7	0.38	0.26
Exchange transfusion	6			1			

* - in mg/dl, 95% confidence interval (CI)

It may be taken into account as a limitation that one more group who received oral extra fluid is not included in our study. Also in our study, extra fluid administration was limited to the first 24 hours of admission.

In conclusion, extra fluid treatment in the first 24 hours in neonates with severe hyperbilirubinemia can significantly reduce the serum bilirubin levels in term newborns with no hemolytic disorder. Further study in which taking extra oral fluid in one more group during hospitalization is suggested.

References

1. Dennery PA, Seidman DS, Stevenson DK. Neonatal hyperbilirubinemia. ***N Engl J Med*** 2001; 344: 581-590.
2. Wong RJ, Desandre GH, Sibley E, Stevenson DK. Neonatal jaundice and liver diseases. In: Martin RJ, Fanaroff AA, Walsh MC, eds. Neonatal-perinatal medicine disease of the fetus and infants. 8th ed. Philadelphia (PA): Mosby; 2006. p. 1419-1465.
3. Watchko JF. Neonatal hyperbilirubinemia--what are the risks? ***N Engl J Med*** 2006; 354: 1947-1949.
4. AAP Subcommittee on Neonatal Hyperbilirubinemia. Neonatal jaundice and kernicterus. ***Pediatrics*** 2001; 108: 763-765.
5. Schwoebel A, Gennaro S. Neonatal hyperbilirubinemia. ***J Perinat Neonatal Nurs*** 2006; 20: 103-107.
6. Wananukul S, Praisuwanna P. Transepidermal water loss during conventional phototherapy in nonhemolytic hyperbilirubinemia term infants. ***J Med Assoc Thai*** 2001; 84 (Suppl 1): S46-S50.
7. Sivanandan S, Chawla D, Misra S, Agarwal R, Deorari AK. Effect of sling application on efficacy of phototherapy in healthy term neonates with nonhemolytic jaundice: a randomized conrolled trial. ***Indian Pediatr*** 2009; 46: 23-28.
8. Ip S, Chung M, Kulig J, O'Brien R, Sege R, Glicken S, et al. An evidence-based review of important issues concerning neonatal hyperbilirubinemia. ***Pediatrics*** 2004; 114: e130-e153.
9. Sanpavat S. Exchange transfusion and its morbidity in ten-year period at King Chulalongkorn Hospital. ***J Med Assoc Thai*** 2005; 88: 588-592.
10. Badiee Z. Exchange transfusion in neonatal hyperbilirubinaemia: experience in Isfahan, Iran. ***Singapore Med J*** 2007; 48: 421-423.
11. Mehta S, Kumar P, Narang A. A randomized controlled trial of fluid supplementation in term neonates with severe hyperbilirubinemia. ***J Pediatr*** 2005; 147: 781-785.
12. Boo NY, Lee HT. Randomized controlled trial of oral versus intravenous fluid supplementation on serum bilirubin level during phototherapy of term infants with severe hyperbilirubinaemia. ***J Paediatr Child Health*** 2002; 38: 151-155.
13. Iranpour RR, Nohekhan R, Haghshenas I. Effect of intravenous fluid supplementation on serum bilirubin level in jaundiced healthy neonates during conventional phototherapy. ***Journal of Research in Medical Sciences*** 2004; 4: 186-190.
14. Porter ML, Dennis BL. Hyperbilirubinemia in the term newborn. ***Am Fam Physician*** 2002; 65: 599-606.
15. Dittrichová J, Paul K, Hodr R. [Behavior of neonates with hyperbilirubinemia treated with blue light] ***Cesk Pediatr*** 1993; 48: 252-256. Czech.