In healthy baby with severe jaundice do we need to give fluid supplementation during phototherapy?

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 هل هناك حاجة لإعطاء الأطفال البالغين الذين يعانون من اليرقة الودية المزمنة في الوريد أثناء العلاج بالضوء؟

 الدكتور حازم عطالة المصري.إخصائي أطفال وحديثي الولادة
 الخدمات الطبية الملكية،الأردن،عمان

خلفية الدراسة:

الهدف: دراسة مدى فائدة إعطاء الأطفال الطبيعيين الذين يعانون من اليرقة الودية المزمنة أثناء العلاج بالضوء. وهل هناك من ضرر أو لائحة
 طرق البحث: هذه الدراسة تحتل أولى لعام 2008 وشسرت ثانياً لعام 2009 في مستشفى الأمير هاشم ومدينته الحسين الطبي، 80 طفلاً رضيعاً سيلما
 يعانون من اليرقة تم شملهم عشوائيا في مجموعتين: المجموعة الأولى التي تم إعطاؤها العلاج بالضوء. والثانية التي تم إعطاؤها محلول ورديي
 بالإلقاء على البطن (د. 40). لا يوجد فرق بين المجموعتين بالنسبة لعمر الحمل ولا في معدل الوزن على الولادة أو في نسبة معدل اليرقة الودية غير المباشر عند النخول، المجموعة
 فقط العلاج بالضوء المضاعف تم استخدامه للمجموعتين. تم استكشاف الدلائل: أعراض تحمل الدم (عدم توافق زمر الدم)
 والإيجابي. محسوب الالقاع. الوردي الودي بالسمن والملف.

النتائج: معدل اليرقة الودي على النخول لم يكن مختلفًا إيجابيًا بين المجموعتين (18 مغم/ملتر) في مجموعه عدم إعطاء محلول الوردي. و (2.5 مغم/ملتر)
 مغمول السائل في مجموعة المضاعف البيا محلول ورديي ملال الهيبرو في نسبة اليرقة خلال 6 ساعات من العلاج بالضوء كان كان (1.5 مغم/ملتر) و (1.3 مغم/ملتر) في المجموعة المضاعف البيا محلول ورديي المجموعين الذين لم ينصحوا البيا محلول وردي على التوالي. معدل اليرقة بعد 72 ساعة من العلاج بالضوء لم
 يكن مختلفًا إيجابيًا بين المجموعتين.

الخلاصة: إن الأطفال المرضانيون الذين يعانون من اليرقة الودية، لا حاجة لإعطاؤهم محلول ورديي المضاعف خلال العلاج بالضوء. باستخدام الرضاعة
 بالفم فقط لتجنب الإعراض الجانبى لضفرة الوردي.

Abstract

Objective
Evaluation of the effectiveness of fluid supplementation in jaundiced healthy infants during phototherapy and if it is necessary to supplement healthy infants with fluid during phototherapy?

Methods
This prospective study was conducted between September 2008 and November 2009 at Prince Hashim Hospital and King Hussein Medical Centre (KHMC). A total of 80 healthy term breast-fed and formula fed infants with hyperbilirubinemia were assigned randomly into two groups: the first group have received oral fed only (n=40) and the other group received intravenous fluid in addition to oral fed (n=40). There were no significant differences in the mean gestational age, the mean weight and in the mean indirect serum bilirubin (ISB) level at the time of admission to the hospital between the two groups. Only double standard phototherapy was used in both groups. The exclusion criteria included the following: hemolytic disease (ABO or Rh incompatibility with positive comb’s test), G6PD deficiency, direct hyperbilirubinemia, sepsis and dehydration.

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Results
The mean total serum bilirubin (TSB) level on admission was not statistically different between two groups (18.3mg/dl [312.9µmol/L] in non supplemented group and 18.5mg/dl [316.4µmol/L] in supplemented group). The mean rate of decrease in TSB levels during the first 6 hours of phototherapy were 22.2µmol/L (1.3mg/dl) and 20.5µmol/L (1.2mg/dl) in supplemented and non-supplemented groups, respectively. The mean TSB levels within 72 hours after phototherapy were not statistically different between two groups.

Conclusion
In healthy term neonates presenting with hyperbilirubinemia, there is no need to add an extra fluid during phototherapy, by only using oral feeding, we avoid the side-effect of intravenous cannulation.

Keywords: Jaundice, phototherapy, infant.

Introduction
An elevation in serum bilirubin above 5.0 mg/dL (85.5µmol/L) occurs in about 75% of all infants, 70% will have physiologic jaundice, 2% exceed a total serum bilirubin concentration of 20 mg/dl (342µmol/L). Unconjugated hyperbilirubinemia occurs due to the excessive bilirubin production and because decreased hepatic excretion of bilirubin, the immature liver of the newborn can not clear bilirubin rapidly enough from the blood circulation\(^{(1,2)}\).

Genetic disorders of bilirubin conjugation, like Gilbert's syndrome, can also contribute to neonatal hyperbilirubinemia\(^{(3)}\). The largest groups of otherwise healthy infants at increased risk for hyperbilirubinemia are those who are late- preterm infants who are exclusively breast-fed\(^{(4,5,6)}\) (particularly if breast-feeding is not going well). Breast-feeding and the poor caloric intake associated with breast-feeding difficulties are both thought to cause jaundice by increasing the enterohepatic circulation of bilirubin\(^{(7)}\). Phototherapy converted bilirubin to the less toxic water-soluble bilirubin\(^{(7)}\). Also, during phototherapy the amount of body water loss increases, due to increase loss via insensible transepidermal\(^{(9)}\). For these reasons, in many centers, fluid supplementation is given routinely to infants undergoing phototherapy.

During phototherapy, there is an increase of nearly 25% above the estimated maintenance fluid and even, in intensive phototherapy, administration of intravenous fluid as 1-1.5 times of maintenance, in addition to oral feeding, has always been suggested\(^{(10)}\).

Since there is considerable center to center variation in the management of neonatal hyperbilirubinemia and provision of fluid supplementation\(^{(11)}\), we decided to evaluate the effect of extra fluid during conventional phototherapy in healthy term neonates.

Patients & Methods
This randomized controlled study was conducted between September 2008 and October 2009. Eighty healthy term breast-fed infants with severe hyperbilirubinemia at both Neonatal Intensive Care - NICU in King Hussein Medical Center (KHMC) and Prince Hashim Hospital were enrolled into the study. From this study, we excluded hemolytic disease (ABO or Rh incompatibility and a positive comb’s test), G6PD deficiency, direct hyperbilirubinemia, infection, dehydration, and prolonged jaundice persisting beyond 14 days of life. Infants were divided randomly into two groups, either the breast or formula-fed on demand (non-supplemented group; n=40), or milk-fed in addition to intravenous fluid supplementation (supplemented group; n=40). The amount of extra fluid which was given to the supplemented group was 20% of the maintenance. The daily maintenance fluid level considered 80 ml/kg on day 2, 100 ml/kg on day 3 and 120 ml/kg on day 4, 140 ml/kg on day 5,150 ml on day 6,160 on day 7 and thereafter. The extra fluids were given as intravenous 10% dextrose in the second day of
life, 1/5 normal saline 10% dextrose in day 3 of life and thereafter. Laboratory investigations included complete blood count, blood group of neonates and their mothers, reticulocyte count, serum bilirubin level (total and direct), direct and indirect coomb’s tests and G6PD level. Total and direct serum bilirubin levels were measured at the beginning of phototherapy, and then only indirect bilirubin was measured every 6 hours on the first 24 hours of admission, after that bilirubin was measured every 12 hours. Phototherapy and bilirubin measurements were discontinued when the TSB declined to less than 12 mg/dl (205.2µmol/L).

**Results**

Of the 80 infants 45 were males and 35 were females. In group 1 (non supplemented group) 22 infants were males and 18 were females, in group two (supplemented group) 23 infants were males and 17 were females. The demographic characteristics of the two groups are shown in Table 1. The only type of phototherapy we have used was double phototherapy. There were no significant differences in the mean gestational age; mean weight and gender distribution between the two groups. The two groups were comparable, and statistically there was no significant difference in the reticulocyte count, hematocrit and TSB levels at the time of starting phototherapy between the two groups. The mean rates of decrease in TSB during the first 6 hours of phototherapy were also not significantly different between the non-supplemented group 20.5 µmol/L (1.2mg/dl) and intravenous group 22.2µmol/L (1.3mg/dl). There was no significant difference in the median duration of hospitalization between the two groups. The mean TSB levels in the two groups of neonates were not significantly different within 72 hours after treatment by conventional phototherapy (Table 2).

<table>
<thead>
<tr>
<th>Table 1: Demographic characteristics of the neonates in the two groups.</th>
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<tbody>
<tr>
<td><strong>Non- Supplemented (Group 1) (N=40)</strong></td>
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<tr>
<td>Mean weight on admission (g) (Mean±SD)</td>
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<td>Mean gestational age (weeks) (Mean±SD)</td>
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<td>Mean age on admission (hours) (Mean±SD)</td>
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<td>Delivery mode</td>
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<tr>
<td>Vaginal</td>
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<td>Caesarian</td>
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<th>Table 2: Laboratory characteristic of neonates in the supplemented and non-supplemented groups.</th>
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<tr>
<td><strong>Non- Supplemented (Group 1) (N=40)</strong></td>
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<tr>
<td>Hematocrit (%) (Mean± Sd)</td>
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<tr>
<td>Mean Reticulocyte count (%) (Mean± Sd)</td>
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<td>Mean TSB (mg/dl)admission(%) (Mean± Sd)</td>
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<tr>
<td>6h (Mean± Sd)</td>
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<td>12h (Mean± Sd)</td>
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<td>18h (Mean± Sd)</td>
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<td>24h (Mean± Sd)</td>
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<td>36h (Mean± Sd)</td>
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<td>48h (Mean± Sd)</td>
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<td>60h (Mean± Sd)</td>
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<td>72h (Mean± Sd)</td>
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TSB = Total Serum Bilirubin
No cases developed infection, dehydration, need for exchange blood transfusion and long stay in hospital. All neonates were discharged with good general condition.

**Discussion**

In recent years, fluid supplementation has been studied in the treatment of babies with jaundice. Our results showed that the administration of intravenous fluid supplementation during phototherapy on healthy full-term jaundiced infants, has no benefit on reducing the serum bilirubin during phototherapy, and they had similar rates of decrease in TSB levels comparing with newborns given only oral feeding. Also, we found that supplementation fluid had no effect on the duration of phototherapy. However, by using the oral route only, we avoided the need for intravenous cannulation and their attendant complications. The best fluid therapy is breast milk or formula because it inhibits the enterohepatic circulation of bilirubin (12). Intravenous fluid therapy should be reserved only for jaundiced infants with moderate or severe dehydration, or to those with mild dehydration who are not able to feed well.

Giving extra oral fluids or sugar water to reduce bilirubin levels has been shown to be of no benefit, it even may be aggravate the jaundice. Infants may have been filling up on glucose water, so they may be lactating less effectively, reducing their milk intake and the opportunities for bilirubin to be excreted in stools (13).

In other study (14), datas from two randomized controlled studies were used, 121 newborn with severe jaundice, who were given fluid supply in one group, and the other group only received oral feeding. They found that fluid supplementation for severe non-hemolytic hyperbilirubinemia is less likely to be beneficial in newborns delivered by cesarean/instrumental delivery in comparing to normal vaginal delivery.

A study (15) was carried out in the neonatal intensive care unit of Zeynep Kamil Maternity and Children Hospital (Istanbul, Turkey) over a period of four months. Two hundred fifty healthy term infants with hyperbilirubinemia were randomized to receive either solely breastmilk (n=125) or both breastmilk and intravenous fluid (n=125) during phototherapy. Based on the results of this study, intravenous fluid support had shown no beneficial effect on the rate of decrease in serum bilirubin and decrease in duration of phototherapy treatment in healthy term infants.

In study done by Boo (16) and others, they studied the effect of supplemented fluid in reducing serum concentration of bilirubin, they have compared the rates of decrease in serum bilirubin levels in normal healthy and well hydrated jaundiced infants, during intensive phototherapy, when given 10% of the maintenance as extra oral feeding, 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 American Academy of Pediatrics (AAP). They concluded that these rates of decrease in TSB may be due to fluid supplementation.

In recent study done at University of Jena (17), 60 preterm newborns (GA ≤ 32 week) were assigned randomly to receive either a fluid supplementation due to short term demand (control group, n=30;) or a 20% extra fluid supplementation (study group, n=30) during intermediate phototherapy. Unfortunately we could not compare their result to our study because in their sample they included only premature infants. Sixty healthy breast-fed neonates with non-hemolytic hyperbilirubinemia were assigned randomly to receive either breast milk exclusively or intravenous fluid in addition to breast milk during conventional phototherapy,
in study done by Iranpour\(^{(18)}\). This study showed that, the mean total serum bilirubin levels at the time of enrollment and within 84 hours after phototherapy were not statistically different between two groups.

In summary, we have shown that the use of supplemented fluid in healthy full-term infant admitted with neonatal jaundice has no significant effect in reducing the level of bilirubin. In fact, by only using the oral route we avoid the side effect and the complication of cannulation like infection, pain and others.

References