Double Phototherapy in Jaundiced Term Infants with Hemolysis

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Abstract

Objective : To compare the efficacy of double phototherapy and conventional phototherapy in term newborn infants with hemolytic jaundice.

Method : Full-term infants with evidence of severe hemolysis on the peripheral blood smear, whose serum bilirubin levels were between 15-21 mg/dl were divided into 2 groups, depending on the availability of the phototherapy bed. Group 1 infants received double phototherapy consisting of conventional (single) phototherapy plus an extra light source from a phototherapy bed (Medela Billibed™, Switzerland). Group 2 infants received only conventional phototherapy. Maternal and infants' blood groups and Rh, direct Coomb's test, G6PD screening test and hematocrit were determined on every infant. Phototherapy was given until the serum bilirubin level dropped to $\leq$ 13 mg/dl. Exchange transfusion was indicated when the serum bilirubin level was $\geq$ 21 mg/dl after phototherapy had been given for 4-6 hours.

Results : There were 110 infants included in this study, 62 and 48 in group1 and 2 respectively. There was no statistical difference in terms of birth weight, sex ratio, proportion of breast feeding infants and the initial hematocrit level. However, the initial mean $\pm$ SD of bilirubin level of group 1 infants was higher than that of group 2, (17.7 $\pm$ 1.6 mg/dl *vs* 16.2 $\pm$ 0.9 mg/dl, $p < 0.001$). Causes of hemolysis could be determined in 74 infants; 27 (24.5%), 39 (35.5%) and 8 (7.3%) infants had ABO incompatibility, G6PD deficiency and both ABO incompatibility and G6PD deficiency respectively. Rate of bilirubin reduction in group 1 infants was significantly faster, (3.3 $\pm$ 2.4 mg/dl/24 h *vs* 2.1 $\pm$ 1.1 mg/dl/24 h, $p < 0.01$). Duration of phototherapy was also shorter in group 1 infants, (45.8 $\pm$ 29.7 hours *vs* 58.5 $\pm$ 26.0 hours, $p < 0.05$).

Four infants failed to respond to the phototherapy that was assigned. Two infants in group 2 had to be switched to receive double phototherapy because of rapid rising of serum bilirubin. One in each group needed exchange transfusion.

Conclusion : The study demonstrated that double phototherapy is more efficient than conventional phototherapy in term infants with severe jaundice caused by hemolysis.

Key word : Full-Term Infant, Jaundice, Hemolysis, Bilirubin, Double Phototherapy, Single or Conventional Phototherapy

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J Med Assoc Thai 2002; 85: 1176-1181

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Phototherapy is effective in decreasing serum bilirubin levels of newborn infants and reducing the number of exchange transfusions particularly in full-term infants without hemolysis[1]. Several studies have shown a dose response relationship and faster decline in serum bilirubin levels in infants with more skin exposure to the light[2,3]. However, phototherapy in infants with hemolytic disease is less successful, although some trials have shown significant benefit [4-6]. Double phototherapy or intensive phototherapy is a special system providing simultaneous light exposure to both the anterior and posterior surface of the infant's body. It has been shown that double phototherapy is more effective in both pre-term and full-term infants without hemolysis compared with single phototherapy during the first 24 hours of treatment [7,8]. But studies comparing double phototherapy with single phototherapy on infants with hemolysis is still limited[9,10]. Therefore, the authors conducted a clinical trial on jaundiced full-term infants with hemolysis in order to compare the efficacy of double phototherapy with single phototherapy.

SUBJECTS AND METHOD

Full-term, jaundiced infants with evidence of hemolysis on the peripheral blood smear were recruited at the neonatal unit of King Chulalongkorn Memorial Hospital in Bangkok from April 1998 to December 1999. Eligible infants had to meet the following criteria: (I) no congenital anomalies, (II) no intravenous fluid treatment, (III) no dehydration or weight loss more than 5 per cent of birth weight and (IV) no extra-vascular blood such as skin ecchymosis, subgaleal hematoma or cephalhematoma. Phototherapy was initiated at the serum bilirubin levels between 15 and 21 mg/dl. After entry into the study the infants were assigned to receive either double or single phototherapy depending on the availability of the phototherapy bed. Group 1 infants received double phototherapy which consisted of conventional or single phototherapy plus an extra blue light source from a commercial phototherapy bed (Medela Bilibed™, Switzerland), (Fig. 1). Group 2 infants received single phototherapy. A single phototherpy unit consisting of 8 white fluorescent lamps (Toshiba FL18W/T8/D) was placed 30 cm above the infant, (Fig. 2). Light intensity in the range of 425-475 nm was measured at the level of the infant's abdomen and at the surface of the phototherapy bed where the infant lay. It was measured with a standard photometer (Joey Dosimeter, The Wallaby® Phototherapy System, PA). Maternal and infant's blood group and Rh, direct Coomb's test, G6PD screening using methemoglobin reduction test and hematocrit were performed on every infant. Capillary blood, approximately 20 µl was collected for serum bilirubin measurement just prior to the initiation of phototherapy (0 hour), 6 hours later and then every 12 or 24 hours until phototherapy had been discontinued. Serum bilirubin levels were measured by direct spectrophotometer (Leica Unistat® Bilirubinometer, Buffalo, NY). Exchange transfusion was performed when the serum bilirubin level was $\geq$ 21 mg/dl after phototherapy for 4-6 hours. Phototherapy was discontinued when the serum bilirubin level dropped to $\leq$ 13 mg/dl. The infants were removed from phototherapy during feed-

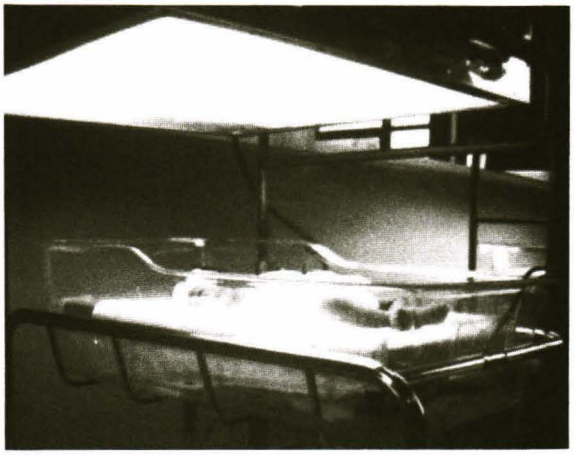

Fig. 1. Infant under double phototherapy.

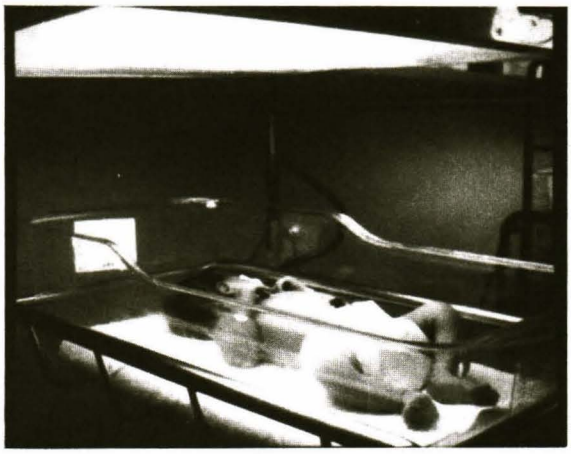

Fig. 2. Infant under single or conventional phototherapy.

ing and blood drawing. They wore only a small disposable diaper and an eye pad while having phototherapy. The infant's skin temperature was recorded every 4 hours until phototherapy was discontinued. Decline in the serum bilirubin at 6 and 24 hours after initiation of treatment and total bilirubin reduction were compared between the two groups. Unpaired *t*-test was used for continuous variables and Chi square test was used for categorical variables.

Written informed consent obtained from the mothers prior to treatment.

RESULTS

There were 110 infants enrolled in the study. Sixty-two infants were in group 1 and 48 were in group 2. There was no statistical difference in terms of birth weight, sex ratio, proportion of breast feeding infants and the initial hematocrit levels between the two groups. Group 1 infants had higher serum bilirubin levels when phototherapy was initiated. (Table 1). The mean $\pm$ SD of the initial serum bilirubin levels of both groups were 17.7 ± 1.6 and 16.2 ± 0.9 mg/dl respectively, $p < 0.001$. Cause of hemolysis could be determined in 74 infants; 27 (24.5%), 39 (35.5%) and 8 infants (7.3%) were ABO incompatibility, G6PD deficiency and both ABO incompatibility and G6PD deficiency respectively. There was no Rh or minor blood group incompatibility. Ten out of 35 infants with ABO incompatibility had positive Coomb's test (27%). G6PD deficiency was noted in 17 of 42 girls (40.5%) and 30 of 68 boys (44.1%). Rate of bilirubin reduction was faster in group 1 infants at both 6 and 24 hours of treatment, (Table 2). The mean $\pm$ SD of total serum bilirubin reduction of group 1 infants was significantly higher (5.4 ± 2.2 mg/dl *vs* 4.3 ± 1.2 mg/dl, $p < 0.01$) or (3.3 ± 2.4 mg/dl/24 h *vs* 2.1 ± 1.1 mg/dl/24 h, $p < 0.01$) and the duration of phototherapy was also shorter (45.8 ± 29.7 *vs* 58.5 ± 26.0 hours, $p < 0.05$). Drop of hematocrit was not different between the two groups ($6.9 \pm 5.0\%$ *vs* $7.4 \pm 5.1\%$, $p > 0.05$), (Table 3). Mean $\pm$ SD of light intensity on the infant's abdomen of both groups was not statistically different, (7.9 ± 1.4 $\mu w/cm^2/nm$ *vs* 8.0 ± 1.2 $\mu w/cm^2/nm$, $p > 0.05$). However, group 1 infants received more light energy from the phototherapy bed with the mean $\pm$ SD intensity of 36.6 ± 11.5 $\mu w/cm^2/nm$. Four infants failed to respond to the treatment. Two infants of group 2 had to be switched to receive double phototherapy because of the rapid rising of serum bilirubin level. These 2 infants were successfully treated with double phototherapy and were not included in group1. Another 2 infants needed an exchange transfusion, one in each group, within 6 hours after initiation of phototherapy. Side effects such as nausea and eye pain caused by the blue light from the phototherapy bed were noted in only one nurse and were resolved after discontinuing the nursing care. There was no side effect noted on the infants.

DISCUSSION

This study demonstrated that double phototherapy was more effective than single phototherapy in newborn infants with hemolysis. It was consistent

Table 1. Clinical and laboratory characteristics.

	Group 1 n = 62	Group 2 n = 48	P-value
B.W. (g)	3121 ± 339	3142 ± 366	ns
M : F	42 : 20	26 : 22	ns
At phototherapy initiation age (d)	2.7 ± 0.7	3.0 ± 0.9	ns
Serum bilirubin (mg/dl)	17.7 ± 1.6	16.2 ± 0.9	< 0.001
Hct (%)	59.9 ± 8.7	62.4 ± 7.0	ns

Table 2. Serum bilirubin reduction during phototherapy (mg/dl).

	Group 1 n = 62	Group 2 n = 48	P-value
6 hours after phototherapy	1.6 ± 1.4	0.3 ± 2.0	< 0.0001
24 hours after phototherapy	3.4 ± 2.0	1.5 ± 1.6	< 0.001
Total reduction	5.4 ± 2.2	4.3 ± 1.2	< 0.01
Average rate of bilirubin reduction/d	3.3 ± 2.4	2.1 ± 1.1	< 0.01

Table 3. Outcome of phototherapy of the study group.

	Group 1 n = 62	Group 2 n = 48	P-value
Duration of phototherapy (h)	45.8 ± 29.7	58.5 ± 26.0	< 0.5
Total bilirubin reduction (mg/dl)	5.4 ± 2.2	4.3 ± 1.2	< 0.005
Total Hct droups (%)	6.9 ± 5.0	7.4 ± 5.1	ns
B.W. at the end of phototherapy (g)	3,117 ± 350	3,153 ± 376	ns
Discontinued treatment	0	2	
Exchange transfusion	1	1	

with previous studies in infants with ABO incompatibility[10] and Rh incompatibility[9]. It was also more effective in infants with G6PD deficiency as shown in the present study. The authors found G6PD deficiency was the most common cause of hemolysis that occurred in both male and female infants. However, causes of hemolysis in 36 infants (32.7%) could not be identified. One of the two infants who needed an exchange transfusion had unknown etiology. G6PD deficiency could still be one of the causes of hemolysis among these infants. Because, during acute hemolytic episodes, false negative results for G6PD deficiency were common with the screening test[11]. The authors used the methemoglobin reduction test as the screening test for G6PD deficiency. This test is adequate for diagnostic purposes in patients who are in the steady state but not for patients in the hemolytic state with reticulocytosis; also, it cannot be expected to identify all heterozygotes[12]. Therefore, it might be necessary to re-evaluate these infants' repopulated red blood cells when the hemolytic crisis is over (approximately 8-12 weeks later)[11].

The authors agreed that double phototherapy should not be used as a substitute for exchange transfusion if the latter was indicated. But double phototherapy could play an important role in decreasing serum bilirubin level better than single or conventional phototherapy in infants with severe hyperbilirubinemia. The authors believed that with the early notice of jaundice in every infant, close monitoring of serum bilirubin levels and using double phototherapy, the rate of exchange transfusion should be decreased significantly. Blue light from the phototherapy bed might have some disadvantages, for instance, it made the infants appear blue and reduced the ability to recognize the onset of true cyanosis

or disturbance of the nursing staff. However, these adverse effects seemed to be minimal and temporary. The phototherapy bed might be more superior than the fiber-optic pad or blanket. For active infants, in spite of moving off the light source as they did with the fiber-optic pad or blanket, they still remained on the phototherapy bed and received continuous light exposure. This phototherapy bed was easy to use and well tolerated. Heat emission to the infant's skin was negligible because an aluminium frame covered with a transparent plastic foil and a thin cloth sheet was placed on top of the irradiation unit. Although the authors did not measure the insensible water loss secondary to phototherapy, the mean body weight of the infants in both groups during phototherapy were not statistically different and there was no significant weight loss. There was no hyperthermia or burn noted on the studied infants.

SUMMARY

Double phototherapy is a safe and effective method for lowering serum bilirubin levels in full-term infants with active hemolysis. The phototherapy bed (Medela Bilibed™), one of the commercial devices, provides an extra irradiance to skin at the back of the infants in addition to the conventional or single phototherapy with minimal and temporary side effects. It is a kind of intensive phototherapy that could benefit infants with hemolysis by reducing the duration of phototherapy and the frequency of exchange transfusion.

ACKNOWLEDGEMENTS

The authors wish to thank the nurses and residents in the neonatal unit of King Chulalongkorn Memorial Hospital. Their extra effort and co-operation are gratefully acknowledged.

(Received for publication on May 26, 2002)

REFERENCES

1. Brown AK, Kim MH, Wu PYK, Bryla DA. Efficacy of phototherapy in prevention and management of neonatal hyperbilirubinemia. Pediatrics 1985; 75 (Suppl): 393-400.
2. Sisson TRC, Kendall N, Shaw E, Kechavarz-Oliai L. Phototherapy of jaundice in the newborn infants. II Effect of various light intensities. J Pediatr 1972; 81: 35-8.
3. Mim LC, Estrada M, Gooden DS, Caldwell RR, Kotas RV. Phototherapy for neonatal hyperbilirubinemia - a dose response relationship. J Pediatr 1973; 83: 658-62.
4. Sisson TRC, Kendall N, Glauser SC, Knutson S, Bunyaviroch E. Phototherapy of jaundice in newborn infants. I: ABO blood group incompatibility. J Pediatr 1971; 79: 904-9.
5. Meloni T, Costa S, Dore A, Cutillo S. Phototherapy for neonatal hyperbilirubinemia in mature newborn infants with erythrocyte G6PD deficiency. J Pediatr 1974; 85: 560-2.
6. Maurer HM, Kirkpatrick BV, McWilliams NB, Draper DA, Bryla DA. Phototherapy for hyperbilirubinemia of hemolytic disease of the newborn. Pediatrics 1985; 75 (Suppl): 407-12.
7. Tan KL. Comparison of the effectiveness of single direction and double direction phototherapy of neonatal jaundice. Pediatrics 1975; 56: 550-3.
8. Holtrop PC, Ruedisueli K, Regan R, Maisels MJ. Double *vs* single phototherapy in low birth weight infants. Pediatr Res 1991 ; 29: 218A.
9. Ebbesen F, Moller J. Blue double light improved method of phototherapy. Arch of Dis Child 1976; 51: 476-8.
10. Amato M, Von Muratt G. Efficacy of intensive blue double-lamp phototherapy in treament of ABO incompatibility and idiopathic severe hemolytic jaundice. Pediatr Med Chir 1984; 6: 95-8.
11. Glader BE, Naiman JL. Erythrocyte disorders in infancy. In: Taeusch HW, Ballard RA, Avery ME, eds. Schaffer and Avery's Diseases of the Newborn. 6th ed, Philadelphia: WB. Saunders Co., 1991; 811-3.
12. Luzzatto L. Glucose-6-phosphate dehydrogenase deficiency and Hemolytic Anemia. In: Nathan DG, Orkin SH, eds. Hematology of infancy and childhood. 5th ed, Philadelphia: WB. Saunders Co., 1998; 704-26.

การรักษาทารกแรกเกิดครบกำหนดตัวเหลืองที่มีสาเหตุจากการแตกสลายของเม็ดเลือดแดง (hemolysis) ด้วยแสงบำบัด 2 ด้าน

พิมลรัตน์ ไทยธรรมยานนท์, พ.บ., ไชยะ วิสุทธิรัตนมณี, พ.บ.**

ทำการศึกษาเปรียบเทียบผลของการรักษาทารกแรกเกิดครบกำหนดตัวเหลือง ที่มีการแตกสลายของเม็ดเลือดแดงอย่างรุนแรง (severe hemolysis) จำนวน 110 คนที่โรงพยาบาลจุฬาลงกรณ์ ด้วยการให้แสงบำบัด 2 ด้าน (double phototherapy) กับการให้แสงบำบัดด้านเดียวตามปกติ (single or conventional phototherapy) แบ่งทารกออกเป็น 2 กลุ่มตามวิธีให้แสงบำบัดขึ้นกับความพร้อมของเครื่องให้แสงบำบัด ทารกทั้ง 2 กลุ่มได้รับแสงด้านบนจากเครื่องให้แสงตามปกติ (single phototherapy) แต่กลุ่ม 1 ได้รับแสงเพิ่มจากเครื่องให้แสงที่เป็นเตียงที่ทารกนอนอยู่ (Medela Billibed^{TM}, Switzerland) ทารกทุกคนได้รับการตรวจรูปร่างเม็ดเลือดแดงบนแผ่นฟิล์มเลือด หมู่เลือดและ Rh, direct Coomb's test ตรวจกรองเอนไซม์ G6PD ในเลือด ระดับบิลิรูบินในซีรั่มและฮีมาโตคริต หยุดให้แสงบำบัดเมื่อระดับบิลิรูบิน $\leq$ 13 มก/ดล จะทำการถ่ายเปลี่ยนเลือดเมื่อระดับบิลิรูบิน $\geq$ 21มก/ดล หลังให้แสงบำบัดแล้ว 4–6 ชม จำนวนทารกในกลุ่ม 1และ 2 เท่ากับ 62 และ 48 คน ตามลำดับ เมื่อเริ่มให้การรักษาทั้ง 2 กลุ่มไม่มีความแตกต่างกันทางสถิติในเรื่องเกี่ยวกับน้ำหนักแรกเกิด เพศ สัดส่วนการเลี้ยงด้วยนมแม่และระดับฮีมาโตคริต แต่ทารกกลุ่ม 1 มีค่าเฉลี่ยระดับบิลิรูบินสูงกว่ากลุ่ม 2 (17.7 $\pm$ 1.6 มก/ดล ต่อ 16.2 $\pm$ 0.9 มก/ดล, $p<0.001$) พบสาเหตุของ hemolysis ในทารกเพียง 74 คน เป็น ABO incompatibility 27 คน (24.5%) เอนไซม์ G6PD พร่อง 39 คน (35.5%) และเป็นทั้ง 2 สาเหตุนี้ 8 คน (7.3%) ระดับบิลิรูบินของทารกกลุ่ม 1 ลดลงโดยเฉลี่ยในอัตราเร็วกว่า (3.3 $\pm$ 2.4 มก/ดล/24 ชม ต่อ 2.1 $\pm$ 1.1 มก/ดล/24 ชม, $p<0.01$) และใช้เวลารักษาด้วยแสงบำบัดน้อยกว่าทารกในกลุ่ม 2 (45.8 $\pm$ 29.7 ชม ต่อ 58.5 $\pm$ 26.0 ชม, $p<0.05$) อย่างมีนัยสำคัญทางสถิติ ทารก 2 คนในกลุ่ม 2 ต้องเปลี่ยนมาให้แสงบำบัด 2 ด้านเนื่องจากระดับบิลิรูบินสูงขึ้นเร็วมาก ทารก 2 คน (กลุ่มละ 1 คน) ได้รับการถ่ายเปลี่ยนเลือด ห

คำสำคัญ : ทารกแรกเกิดครบกำหนด, ตัวเหลือง, เม็ดเลือดแดงแตกสลาย, บิลิรูบิน, แสงบำบัด 2 ด้าน, แสงบำบัดด้านเดียวหรือแสงบำบัดตามปกติ

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