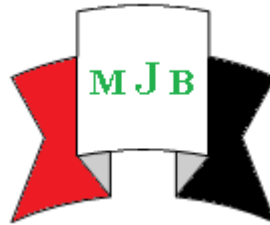


Adverse Effects and Rebound Increase in Bilirubin Level: Comparison between Conventional Versus Intensive Phototherapy

Shamil Abd-Alzahra Sharba

College of Medicine, Kufa University , Najaf , Iraq



Received 28 May 2014

Accepted 9 September 2014

Abstract

Phototherapy is the mainstay of treatment of hyperbilirubinemia. The efficacy of phototherapy depended on the light spectrum (wavelength), flux of light, and surface area of the infant exposed to phototherapy. A rebound in the total serum bilirubin level of 1 to 2 mg per deciliter and occasionally more, can occur after phototherapy is discontinued.

The aim of this study was to evaluate and compare the possible side effects and rebound increase in bilirubin level in the use of conventional and intensive phototherapy.

A total 80 neonates present with significant jaundice and need phototherapy were included in the study, they were term and near term. The patients are divided it tow group : - group 1 (40 patients) who receive intensive phototherapy and group 2 (40 patients) who receive conventional phototherapy. The side effects and rebound increase were observed in both groups.

It was found that the complications of conventional phototherapy compared with intensive phototherapy was dehydration (2.5%) for each, skin rash by intensive phototherapy 50%, while in conventional phototherapy 25% ($p=0.018$), frequent bowel motion by intensive phototherapy 20%, while in conventional phototherapy 7.5% that the rebound increase in the level of bilirubin was more in an intensive phototherapy group than the conventional phototherapy group.

This study concluded that increasing the surface area of phototherapy associated with the shorter term adverse effect and more rebound increase of bilirubin level than conventional phototherapy.

Keywords: Intensive phototherapy, conventional phototherapy, hyperbilirubinemia, phototherapy side effect, rebound increase

الخلاصة

العلاج بالضوء هو الدعامية الأساسية لعلاج فرط بيليروبيين الدم . فعالية العلاج بالضوء تعتمد على طيف الضوء (الطول الموجي) ، شدة تدفق الضوء ، و المساحة السطحية للرضع المتعرضة للعلاج بالضوء . عودة الزيادة في إجمالي مستوى البيليروبيين في المصل من ١-٢ ملغم لكل ديسيلتر ، وأحيانا أكثر من ذلك، يمكن أن تحدث بعد التوقف عن العلاج بالضوء .

الهدف من الدراسة هو تقييم و مقارنة الآثار الجانبية المحتملة و عودة الزيادة في مستوى البيليروبيين في استخدام العلاجات الضوئية التقليدية والمكثفة . تم تضمين ما مجموعه ٨٠ طفل رضيع مصاب بفرط بيليروبيين وولادي مهم و يحتاجون العلاج بالضوء في الدراسة ، كانوا مكتملي او تقريبا عمر حياة الرحم . تم تقسيمهم الى مجموعتين: - المجموعة ١ (٤٠ مريضا) الذين يتلقون العلاج بالضوء المكثف و المجموعة ٢ (٤٠ مريضا) الذين يتلقون العلاج بالضوء التقليدي . وقد لوحظت الآثار الجانبية و عودة زيادة في كلا المجموعتين .

واثبتت النتائج أن المضاعفات الناجمة عن العلاج بالضوء التقليدي مقارنة مع العلاج بالضوء المكثف كان الجفاف (٢.٥٪) لكل منهما، الطفح الجلدي بواسطة المكثفة ٥٠٪، بينما في التقليدية ٢٥٪ ($P = 0.018$)، الاسهال من قبل المكثف ٢٠٪ ، بينما في التقليدية ٧.٥٪ . أن عودة الزيادة في مستوى البيليروبيين كانت أكثر في مجموعة العلاج بالضوء المكثف من مجموعة العلاج بالضوء التقليدي .

نستنتج من هذه الدراسة زيادة مساحة سطح العلاج بالضوء مرتبطة بزيادة التأثيرات الجانبية و عودة الزيادة في مستوى البيليروبين مقارنة بالعلاج بالضوء التقليدي .

Introduction

Some sixty percent of normal newborns become clinically jaundiced sometime during the first week of life. Unconjugated (indirect) hyperbilirubinemia occurs as a result of excessive bilirubin formation and because the neonatal liver cannot clear bilirubin rapidly enough from the blood [1, 2]. Sufficiently elevated levels of bilirubin can lead to bilirubin encephalopathy and subsequently kernicterus, with devastating, permanent neurodevelopmental handicaps [3].

Because of the potential toxicity of bilirubin, newborn infants must be monitored to identify those who might develop severe hyperbilirubinemia and, in rare cases, acute bilirubin encephalopathy or kernicterus [4,5,6]. Phototherapy is the mainstay of treatment of hyperbilirubinemia [2], its clinical efficacy was confirmed in many studies [7,8,9]. The efficacy of phototherapy depended on the light spectrum (wavelength), flux of light, and surface area of the infant exposed to phototherapy [10,11,12].

The goal of therapy is to lower the concentration of circulating bilirubin or keep it from increasing. Phototherapy achieves this by using light energy to change the shape and structure of bilirubin, converting it to molecules that can be excreted even when the normal conjugation is deficient [13].

Since the only effective alternative to phototherapy in infants with severe jaundice is exchange transfusion, a measure of the efficacy of phototherapy is the dramatic reduction in the number of exchange transfusions being performed [14-17]. The dose and efficacy of phototherapy are affected by the type of light source. Commonly used phototherapy units contain daylight, white, or blue fluorescent tubes.

However, when total serum bilirubin levels approach the range at which intensive phototherapy is recommended [18]

A rebound in the total serum bilirubin level of 1 to 2 mg per deciliter and occasionally more, can occur after phototherapy is discontinued. Infants at increased risk of a clinically significant rebound are those born at less than 37 weeks gestation, those with hemolytic disease, and those treated with phototherapy during the birth hospitalization. It is usually unnecessary to keep an infant in the hospital to check for a rebound [19-22].

Reports of clinically significant toxicity from phototherapy are rare [23,24]. phototherapy can produce the bronze neonate syndrome, erythematous rash . Conventional phototherapy can produce an acute change in the infant's thermal environment, leading to an increase in peripheral blood flow and insensible water loss [25-27]. A recent study suggested that intensive phototherapy might increase the number of atypical Melanocytic nevi identified at school age, [28] although other research has not shown this association. [29] The aim of this study was to evaluate and compare the possible side effects and rebound increase in bilirubin level in the use of conventional and intensive phototherapy.

Patients and Methods

A prospective study was conducted in the Neonatal care unit in Al-Zahraa teaching hospital in Najaf city.

A total 80 neonates present with jaundice and need phototherapy were included in the study, they were term and near term (36 – 38) weeks. The patients are divided it two groups: - group 1; 40 patients who received intensive phototherapy (IPT) and group 2;

40 patients who received conventional phototherapy (CPT).

A capillary blood sample was taken from each newborn neonate by heparinized capillary tube by pricking the heel then put in the micro centrifuge for 5 minutes at 5000 rounds per minute then TSB measured by a (Bilirubin Meter, from EAMA B- 105N) at the start and at the end of phototherapy.

The conventional phototherapy consisting of 3 deep blue and 3 daylight (Philips TL 20W/52) fluorescent tube within 40 cm from the infant. The intensive 360 ° phototherapy provided by 16 (TL 20W/52) fluorescent tube at a 360 degree within 20 cm from the infant (CRADELE 360 device from Mediprema manufacturer).

Breast feeding was encouraged throughout the phototherapy period. The newborn in both groups wore eye patches and disposable diapers folded to allow maximum skin exposure to phototherapy. Phototherapy was administered continuously except for minor procedures such as feeding, physical examination and taking capillary blood samples. Phototherapy discontinued when the TSB reached below 50% of the maximal TSB level ⁽¹⁾ and at different time period in both groups.

The wave length of P.T light in both I.P.T. &C. P. T. Is within the wavelength of 430 - 490 nm which is the best absorbable wave length of the skin.

The Investigations which were done include : HB, PCV%, TSB (direct & indirect serum bilirubin), blood group &RH of mother & neonate, blood film, direct & indirect coombs test

The results were analyzed using the z score to compare between the two proportions and percentage using statistical 5 software. The p-value < 0.05 was defined as statistically significant.

Results

A total 80 neonates present with jaundice and need phototherapy were included in the study, they were term and near term (36 – 38) weeks . 40 neonates need intensive phototherapy and 40 neonates received conventional phototherapy.

It was found that blood groups and Rh for neonates was A+, B+, O+ (35%,50%,15%) respectively and the type of mother blood groups and Rh were A+, B+, O+ (25%,35%,40%) respectively (table 1).

Table 1: Blood group distribution in babies and their mothers

BLOOD GROUP	Neonate (No.%)	Mother (No.%)
A+	28(35%)	20(25%)
B+	40(50%)	28(35%)
O+	12(15%)	32(40%)
TOTAL	80(100%)	80(100%)

The male to female ratio in the intensive phototherapy group was 32/17 while it was

17/23 in conventional phototherapy group as showed in figure 1.

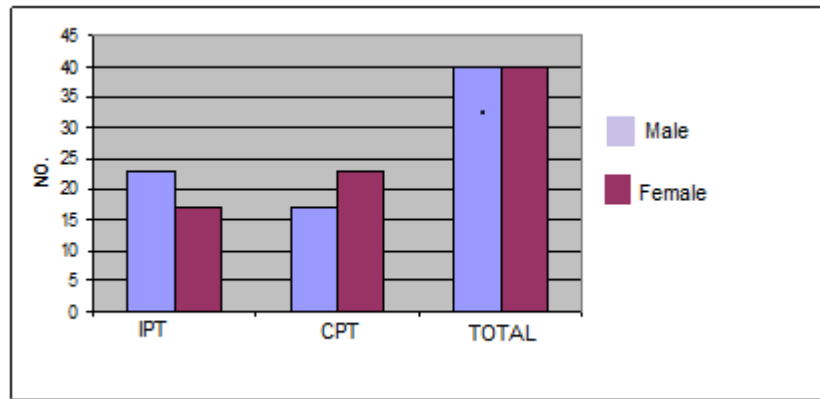


Figure 1: gender distribution of 80 neonates.

It was found that the complications of conventional phototherapy compared with intensive phototherapy was , skin rash by

intensive 50%, while in conventional 25% (p=0. 018), as shown in table 2 .

Table 2: comparison between IPT and CPT regarding the complications

COMPLICATIONS	DEHYDRATION	SKIN RASH	F.B.M	Total
IPT (no. =40)	1(2.5%)	20(50%)	8(20%)	29(72.5%)
CPT (no. =40)	1(2.5%)	10(25%)	3(7.5%)	14(35%)
P value	NS	0.018	NS	0.0003

IPT=intensive phototherapy, CPT= conventional phototherapy, NS not significant , F.B.M = frequent bowel motion .

It was found that the rebound increase in the level of phototherapy was more in an intensive phototherapy group than the

conventional phototherapy group but it was statistically not significant as showed in table 3

Table 3: rebound increase in IPT and CPT

REBOUND	FREQUENCY
IPT (no. =40)	6(15%)
CPT (no. =40)	2(5%)
P value	1.4 NS

IPT=intensive phototherapy, CPT= conventional phototherapy, NS= not significant

Discussion

In general, if the infants became significantly jaundiced, they were treated with single-surface phototherapy and if the

infants did not respond, the further treatments were increasing phototherapy unit beside or beneath the infant or exchange transfusion [30]. This is what had been used in our neonatal care unit until new intensive

360 degrees with special blue light fluorescent tube used.

Umran et al. proved the effectiveness of the intensive phototherapy in our neonatal care unit to decrease bilirubin levels by 1.3 mg/dl [31]. In this study we try to show the possible adverse effect of using this increased surface area of the phototherapy.

We found that the skin rash was the most common adverse effect of intensive phototherapy in compare with conventional phototherapy ($P=0.018$), and increased frequency of the bowel motion, although it is statistically not significant but it was more in IPT. Conventional phototherapy can produce an acute change in the infant's thermal environment, leading to an increase in peripheral blood flow and insensible water loss [26, 27]. This finding has not been studied with LED lights, which, because of their relatively low heat output, should be much less likely to cause insensible water loss. In term infants who are nursing or feeding adequately, additional intravenous fluids are usually not required.

There is a common belief that the discontinuation of phototherapy is associated with rebound hyperbilirubinemia. In a recent study, 264 healthy newborns who weighed 1800 g or more had lower serum bilirubin concentrations as long as 30 hours after the discontinuation of phototherapy than they did immediately after discontinuation, suggesting that rebound hyperbilirubinemia is rare [22]. In this study although the difference in rebound increases in bilirubin was statistically not significant but it is more with the use of IPT than the conventional.

The increase in the rebound level of bilirubin with those patients exposed to intensive phototherapy, the cause behind these is the large area of the skin which exposed to the light or those patients has higher level of bilirubin (could be due-to hemolytic cause) than those patient on conventional phototherapy.

References

- 1- Kaplan M, Muraca M, Hammerman C, et al. Imbalance between production and conjugation of bilirubin: a fundamental concept in the mechanism of neonatal jaundice. *Pediatrics* 2002; 110 (4): e47.
- 2- Maisels MJ, Kring E. The contribution of hemolysis to early jaundice in normal newborns. *Pediatrics* 2006; 118:276-9.
- 3- AAP Subcommittee on Neonatal Hyperbilirubinemia. Neonatal jaundice and kernicterus. *Pediatrics* 2001; 108:763-5.
- 4- AAP Subcommittee on Hyperbilirubinemia, Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation. *Pediatrics* 2004; 114:297-316.
- 5- Krista A Jangaard, Michael J Vincer, Alexander C Allen. A randomized trial of aggressive versus conservative phototherapy for hyperbilirubinemia in infants weighing less than 1500 g: Short- and long-term outcomes. *Paediatr Child Health* Vol 12 No 10 December 2007.
- 6- Bratlid D. Criteria for treatment of neonatal jaundice. *J Perinatol* 2001; 21 (Suppl 1): S88-92; S104-7.
- 7- Tan KL, Lim GC, Boey KW. Efficacy of "high-intensity" bluelight and "standard" daylight phototherapy for non-hemolytic hyperbilirubinemia. *Acta Paediatr* 1992; 81: 870-4.
- 8- Akman İ, Arıkan C, Bilgen H, Kalaca S, Ozek E. Transcutaneous measurement of bilirubin by icterometer during phototherapy on a bilibed. *Turk J Med Sci* 2002; 32:165-8.
- 9- Nurdan URAŞ, Ahmet KARADAĞ, Alparslan TONBUL, Musemma KARABEL, Guzide DOĞAN2, M. Mansur TATLI. Comparison of light emitting diode phototherapy and double standard conventional phototherapy for nonhemolytic neonatal hyperbilirubinemia. *Turk J Med Sci* 2009; 39 (3): 337-341. 12.

- 10- Donzelli GP, Moroni M, Pratesi S, Rapisardi G, Agati G, Fusi F. Fiberoptic phototherapy in the management of jaundice in low birthweight neonates. *Acta Paediatr* 1996; 85: 366-70.
- 11- Holtrop PC, Ruedisueli K, Maisels MJ. Double versus single phototherapy in low birth weight newborns. *Pediatrics* 1992; 90: 674-7.
- 12- Tan KL. Comparison of the efficacy of fiberoptic and conventional phototherapy for neonatal hyperbilirubinemia. *J Pediatr* 1994; 125: 607-12.
- 13- Lightner DA, McDonagh AF. Molecular mechanisms of phototherapy for neonatal jaundice. *Accts Chem Res* 1984;17: 417-24.
- 14- Maisels MJ. Phototherapy — traditional and nontraditional. *J Perinatol* 2001;21: Suppl 1:S93-7.
- 15- Steiner LA, Bizzarro MJ, Ehrenkranz RA, Gallagher PG. A decline in the frequency of neonatal exchange transfusions and its effect on exchange-related morbidity and mortality. *Pediatrics* 2007;120: 27-32.
- 16- Patra K, Storfer-Isser A, Siner B, Moore J, Hack M. Adverse events associated with neonatal exchange transfusion in the 1990s. *J Pediatr* 2004;144: 626-31.
- 17- O'Shea TM, Dillard RG, Klinepeter KD, Goldstein DJ. Serum bilirubin levels, intracranial hemorrhage, and the risk of developmental problems in very low birth weight neonates. *Pediatrics* 1992; 90:888-92.
- 18- American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. *Pediatrics* 2004;114: 297-316.
- 19- Maisels MJ, Kring E. Rebound in serum bilirubin level following intensive phototherapy. *Arch Pediatr Adolesc Med* 2002; 156: 669-72.
- 20- Kaplan M, Kaplan E, Hammerman C, et al. Post-phototherapy neonatal bilirubin rebound: a potential cause of significant hyperbilirubinaemia. *Arch Dis Child* 2006; 91: 31-4.
- 21- Sarici SU, Alpay F, Unay B, Ozcan O, Gokcay E. Double versus single phototherapy in term newborns with significant hyperbilirubinemia. *J Trop Pediatr*. 2000; 46: 36-9.
- 22- Yetman RJ, Parks DK, Huseby V, Mistry K, Garcia J. Rebound bilirubin levels in infants receiving phototherapy. *J Pediatr* 1998;133: 705-7.
- 23- Maisels MJ. Phototherapy. In: Maisels MJ, Watchko JF, eds. *Neonatal jaundice*. Amsterdam: Harwood Academic Publishers, 2000:177-203.
- 24- Jährig K, Jährig D, Meisel P, eds. *Phototherapy: treating neonatal jaundice with visible light*. Munich, Germany: Quintessence Verlags-GmbH, 1993.
- 25- Tönz O, Vogt J, Filippini L, Simmler F, Wachsmuth ED, Winterhalter KH. Severe light dermatosis following photo therapy in a newborn infant with congenital erythropoietic uroporphyrria. *Helv Paediatr Acta* 1975; 30:47-56. (In German.)
- 26- Dollberg S, Atherton HD, Hoath SB. Effect of different phototherapy lights on incubator characteristics and dynamics under three modes of servocontrol. *Am J Perinatol* 1995; 12:55-60.
- 27- Maayan-Metzger A, Yosipovitch G, Hadad E, Sirota L. Transepidermal water loss and skin hydration in preterm infants during phototherapy. *Am J Perinatol* 2001; 18:393-6.
- 28- Csoma Z, Hencz P, Orvos H, et al. Neonatal blue-light phototherapy could increase the risk of dysplastic nevus development. *Pediatrics* 2007; 119:1036-7.
- 29- Bauer J, Büttner P, Luther H, Wiecker TS, Möhrle M, Garbe C. Blue light phototherapy of neonatal jaundice does not increase the risk for melanocytic nevus development. *Arch Dermatol* 2004; 140:493-4.

30- Payon B, Warawut Kr, Kannikar B, Effectiveness of Double-Surface Intensive Phototherapy versus Single-Surface Intensive Phototherapy for Neonatal Hyperbilirubinemia. J Med Assoc Thai 2008; 91 (1): 50-5.

31- Raid M R Umran. Effectiveness of 360° Intensive Phototherapy versus Conventional Phototherapy for Neonatal Hyperbilirubinemia. Kufa Med. J. 2012. Vol.15.No.1:204-210.