Double-surface intensive phototherapy versus single-surface conventional phototherapy in treatment of neonatal hyperbilirubinemia

Nashwan M. Al-Hafidh, Ziad K. Ali, Ruthwan S. Saeed

From the "Department of Medicine, University of Mosul, "Ibn Al-Atheer Pediatric Hospital, Mosul.

Correspondence: Nashwan M. Al-Hafidh. Department of Medicine, University of Mosul, Mosul, Iraq. Email: nashwan_ped@yahoo.com.

(Ann. Coll. Med. Mosul 2013; 39 (1): 25-31).
Received: 18th Jan. 2012; Accepted: 15th Jul. 2012.

ABSTRACT

Objective: To compare the efficacy of double-surface intensive phototherapy (DSIPT) and single-surface conventional phototherapy (SSCPT) in treatment of neonatal jaundice.

Patients and methods: This is a case control study conducted in Ibn Al-Atheer Pediatric Hospital (Mosul) included 110 jaundiced neonates subjected to the newly used (DSIPT) during the period between 1st of Jan. 2011 to 30th of June 2011 compared to 142 jaundiced neonates underwent phototherapy using SSCPT during the period between 1st of July 2010 to 31st of December 2010. Patients with acute bilirubin encephalopathy, sepsis, meningitis and asphyxia were excluded from this study as well as those aged > 1 week. The medical files data of included infants were analyzed regarding their gestational age, body weight, sex, age, type of feeding and total serum bilirubin level (TSB) at initiation of phototherapy. Levels of TSB at intervals of approximately 6 hours during the first 24 hours of treatment, the need of exchange transfusion and duration of hospitalization were registered.

Results: Demographic characteristics apart from gestational age were similar in both groups. The initial mean serum bilirubin level had no statistically significant difference between DSIPT and the SSCPT group. DSIPT group had significantly greater TSB decline rates than SSCPT in term and preterm infants with hyperbilirubinemia. The mean percentages of TSB decline per hour was significantly higher within 6, 12, and 24 hours after starting DSIPT compared to SSCPT type. The mean percentages of TSB decline of DSIPT group within the second 12 hours after phototherapy was significantly higher and more than double the value of SSCPT type (43.45 ± 14.83 vs. 17.03 ± 14.22, p<0.001). Duration of hospitalization was significantly shorter in DSIPT subjected infants. At initial TSB level between 20-25 mg/dl exchange transfusion was avoided among intensively treated patients whereas it was inevitable in 86.36 % of patients in the SSCPT group. At TSB on exchange line 91.56% of infants received SSCPT type required an exchange transfusion whereas such intervention was eliminated in patients treated by DSIPT.

Conclusions: DSIPT was significantly more effective than SSCPT in treatment of neonatal hyperbilirubinemia. When initial TSB level is on and below exchange line on nomogram, exchange transfusion can be avoided with the use of DSIPT.

العلاج الضوئي ثنائي السطح المكثف مقارنة بالعلاج الضوئي أحادي السطح التقليدي في علاج اليرقان الولادي

الخلاصة

هدف الدراسة: لمقارنة فعالية العلاج الضوئي ثنائي السطح المكثف بالعلاج الضوئي أحادي السطح التقليدي في علاج اليرقان الولادي.

طريقة البحث والمشاركون: هذه دراسة لحالات أدخلت إلى مستشفى ابن الاتير للأطفال (الموصل) خلال الفترة بين الأول من كانون الثاني 2011 وفوج شملت 110 وليد مصاب باليرقان خضعوا للعلاج الضوئي ثنائي السطح المكثف.
Double-surface intensive phototherapy...

Nashwan M. Al-Halidh, et al

Audience is observed during the 1st wk of life in approximately 60% of term infants and 80% of preterm infants, 5-10% of all newborns require intervention for pathological jaundice. The sunlight fading effect on the yellow skin color of jaundiced newborns was discovered accidentally by Sister J. Ward an English nurse in 1956, an observation that led to the discovery that visible light could lower serum bilirubin levels in newborn infants. The very first phototherapy unit incorporating an artificial light source was devised and tested by Cremer et al at Rochford Hospital in 1958. Phototherapy is the most common therapeutic intervention used for the treatment of hyperbilirubinemia and it is used to prevent the neurotoxic effects of bilirubin.

Conventional or standard daylight phototherapy units should deliver a spectral irradiance (measured at the level of the infant) of 8 to 10 μW per square centimeter per nanometer in the 430-490 nm band. The American Academy of Pediatrics (AAP) defines intensive phototherapy as irradiance in the blue-green spectrum (wavelengths of approximately 430-490 nm) of at least 30 μW per square centimeter per nanometer. This may be achieved by using light sources placed above and beneath the infant. Hyperbilirubinemia may lead to encephalopathy at any time during the neonatal period. Lethargy, poor feeding, and loss of the Moro reflex are common initial manifestations. Immediate exchange transfusion is recommended in any infant who is jaundiced and has the manifestation of acute bilirubin encephalopathy even if the TSB is falling. Exchange transfusion should also be considered if the TSB remains above the indicated exchange level after 6 hours of intensive phototherapy.

This study was done for the purpose of comparing the efficacy of recently introduced intensive phototherapy device with the already in use conventional phototherapy type.

PATIENTS AND METHODS

This study analyzed the medical case files of all newborn infants aged ≤1 week with neonatal hyperbilirubinemia and the TSB ≥12 mg/dL. A double-surface phototherapy device was used for all patients in this study. The device consisted of two groups of phototherapy lights placed above and beneath the infant. Hyperbilirubinemia was defined as a serum bilirubin level ≥12 mg/dL measured at the level of the infant. Newborns were classified as high-risk (HR) if they were either premature (<37 wk of gestation) and had a birth weight ≤2500 g or were >37 wk of gestation and had a birth weight ≤10th percentile. The primary end point was the efficacy of phototherapy in reducing the TSB level in both the HR and nonHR groups.

The study was done for the purpose of comparing the efficacy of recently introduced intensive phototherapy device with the already in use conventional phototherapy type.
Double-surface intensive phototherapy... Nashwan M. Al-Hafidh, et al

Hyperbilirubinemia requiring phototherapy who were admitted to Neonatal Care Unit (NCU) in Ibn Al Atteer pediatric hospital (Mosul), between 1st of July 2010 to 30th of June 2011. Patients with acute bilirubin encephalopathy, sepsis, meningitis, asphyxia, were excluded from this study.

During the period between 1st of July 2010 to 31st of December 2010 only conventional phototherapy type was available. The first studied group (142 patients) was selected from this period and was compared to the second group (110 patients) who was treated by intensive phototherapy during the period between 1st of Jan 2011 to 30th of June 2011. All infants’ gestational age, body weight, sex, ages at phototherapy, type of feeding, total serum bilirubin level at initiation of phototherapy and duration of hospitalization were registered.

Blood examination for all admitted infants included blood group, total serum bilirubin (TSB) concentration, complete blood picture, reticulocyte count as well as blood group of the infant’s mother. Non hemolytic cause was labeled if isolated hyperbilirubinemia was reported with normal hemoglobin and reticulocyte count.

Levels of TSB were plotted on appropriate guidelines charts recommended by the American Academy of Pediatrics Subcommittee on Hyperbilirubinemia which indicate the need of phototherapy or exchange transfusion. Standard AAP guidelines were used to start and stop phototherapy. If the initial TSB level was high (≥ 20 mg/dl) or the TSB level is on exchange line on chart according to gestational age and post conceptual age in hours, phototherapy was applied and the patient companion is immediately contacted to provide compatible blood for possible exchange transfusion.

Level of TSB was measured by Bilirubin meter (photomech 301-A/D, Optima Inc, Tokyo, Japan), assessed and calibrated regularly by laboratory technician or trained pediatric permanent resident. After initiating phototherapy TSB concentration was again determined at intervals of approximately 6 hours during the first 24 hours of treatment. After this period, TSB concentration is checked approximately every 24 hours until phototherapy is discontinued. If after the initial 6 hours of phototherapy TSB level remained above the indicated exchange level or the patient developed manifestations compatible with diagnosis of acute bilirubin encephalopathy an exchange transfusion was performed.

Conventional overhead phototherapy used in this study was of Micro-Lite® PTS68-1 phototherapy system type (Germany) which have been equipped with three lamps of EXZ quartz halogen emitting a white light of 400 -520 nanometer wavelength having an intensity of at least 10 µw/cm²/nm placed at 43 cm from the center of mattress. Lamps were replaced before the recommended replacement usage time of 1000 hours.

Intensive phototherapy used was Bilisphere 360° which is registered trademarks of Novos Ltd. (Ankara/Turkey) consisting of 16 pieces of blue light fluorescent tubes with spectral irradiance 420 nm to 500 nm and intensity of 30 µW/cm2 / nm, encircling the patient throughout 360° and located at distance of 25 centimeter from the center of the bed which consist of a hammock made from fabric network overlying glassy bed through which the light in the lower surface of the bed is transmitted to the infant. At the end of this study the lamp usage time displayed by each of the two used intensive phototherapy units were 1180 hours and 896 hours respectively which were less than recommended replacement lamp usage time of 1980 hours.

During both types of phototherapy all infants were exposed, completely unclothed with their eyes and genital regions covered. Phototherapy was administered continuously except during feeding, diapering, physical examination and capillary blood sampling.

Routine nursing care was similarly applied to all infants; feeding on demand was encouraged and if the patient showed clinical signs of dehydration, intravenous fluids were initiated.

Results are expressed in terms of the mean ± standard deviation and in numbers and percentages (for categorical variables). Data were computed through using Statistical Package for Social Sciences (SPSS, version 11.5). Independent sample T test was used to test the different between means. A p-value of less than 0.05 was defined as statistically significant.

The study was approved by the local ethical committee in Nineveh College of Medicine and Local Health Authority.
RESULTS

During the period of this study, 142 neonates subjected to SSCPT, whereas 110 neonates underwent DSIPT type. Apart from significant gestational age difference there were no significant demographic differences in term of age at phototherapy, birth weight, sex, and feeding type between the compared groups (Table 1).

Both groups had no significant difference regarding their initial TSB level. Mean TSB Percentages decline rate per hour within first 6 and second 6 and 12 hours after phototherapy were significantly greater in DSIPT group compared to SSCPT group. The mean TSB percentages decline within the second 12 hours after phototherapy among DSIPT treated infants was significantly higher and more than double the value of SSCPT type (43.45 ± 14.83 vs. 17.03 ± 14.22; p<0.001) respectively. The mean TSB decline rate in term of mg/dl/hour within second 6 hours after starting DSIPT was significantly higher than SSCPT group. That rate was approximately twice the value of SSCPT group (0.61 ± 0.34 vs. 0.31 ± 0.31; p < 0.046), likewise in the second 12 hours after therapy the mean TSB decline rate in patients using DSIPT type was > four folded the value of SSCPT group (0.49 ± 0.24 vs. 0.11 ± 0.10; p<0.001) respectively (Table 2). Duration of hospitalization was significantly shorter in DSIPT than SSCPT subjected infants (2.10 ± 1.29 vs. 3.01 ± 1.49; p<0.001) respectively.

The main TSB decline rate in term of mg/dl/hour within the second 12 hours after initiating DSIPT was significantly higher than SSCPT group in both hemolytic and non hemolytic categorical causes of hyperbilirubinemia among studied infants. The same rate was also significantly higher in DSIPT group compared to SSCPT group among the enrolled full term and preterm infants (p<0.001) (Table 3).

Table 1. Demographic characteristics of neonates subjected to two types of phototherapy.

|                | SSCPT type  | DSIPT type  | P-value |
|----------------|-------------|-------------|---------|
|                | (N=142)     | (N=110)     |         |
| No. %          | No. %       |             |         |
| Gestation      |             |             |         |
| Full term      | 116 81.70   | 100 90.90   | 0.038*  |
| Premature      | 26 11.30    | 10 9.10     |         |
| Gender         |             |             |         |
| Male           | 82 57.75    | 69 62.73    | 0.424*  |
| Female         | 60 42.25    | 41 37.27    |         |
| Feeding        |             |             |         |
| Breast feeding | 103 72.53   | 86 78.18    | 0.258*  |
| Bottle feeding | 26 18.31    | 12 10.91    |         |
| Mixed feeding  | 13 9.155    | 12 10.91    |         |
| Mean± SD       | Mean± SD    |             |         |
| Age at phototherapy (hours) | 108.09 ± 41.48 | 110.60 ± 38.48 | 0.652** |
| Body weight    | 3.02 ± 0.63 | 3.18 ± 0.64 | 0.068** |

*Chi–square test used. **Independent sample T test was used.

Table 2. Total serum bilirubin decline after starting 2 different phototherapy types, in relation to duration of phototherapy (Mean ± SD).

|                | SSCPT type  | DSIPT type  | P-value* |
|----------------|-------------|-------------|----------|
|                | (N=142)     | (N=110)     |          |
| No. %          | No. %       |             |          |
| Initial TSB level (mg/dl) | 19.56 ± 5.35 | 18.85 ± 4.57 | 0.253    |
| After phototherapy |             |             |          |
| Mean TSB decline rate within first 6 hour (%/hour) | 1.51±1.55 | 4.23±2.02 | 0.012    |
| Mean TSB decline rate within second 6 hours (%/hour) | 1.26±0.79 | 3.28±1.67 | 0.007    |
| Mean TSB decline rate within second 12 hours (%/hour) | 0.77±0.66 | 2.39±1.1 | <0.001   |
| Mean TSB percentages decline within first 6 hour | 14.72 ± 10.22 | 21.89±10.03 | 0.164    |
| Mean TSB percentages decline within second 6 hours | 15.10 ± 9.46 | 27.74±12.26 | 0.070    |
| Mean TSB percentages decline within second 12 hours | 17.03±14.22 | 43.45±14.83 | <0.001   |
| Mean TSB decline rate within first 6 hours,(mg/dl/hour) | 0.73 ± 0.51 | 0.81±0.38 | 0.746    |
| Mean TSB decline within second 6 hours,(mg/dl/hour) | 0.31±0.31 | 0.61±0.34 | 0.046    |
| Mean TSB decline within second 12 hours,(mg/dl/hour) | 0.11±0.10 | 0.49±0.24 | <0.001   |

*Independent samples T test was used.
Among neonates not required an exchange transfusion, although there was no statistically significant difference between the compared types of phototherapy among neonates who had initial TSB level between 10-15 mg/dl, the main TSB decline rate at initial bilirubin level between 15-25 mg/dl was significantly higher in DSIPT group compared to SSCPT group levels within the second 12 hours post therapy. At initial TSB level of 20-25 mg/dl the bilirubin decline rate in this study was approximately 1 mg/dl/hour in DSIPT group compared to 0.36 ± 0.13 mg/dl/hour in SSCPT group \( (p =0.029) \) (Table 4).

Failure of phototherapy treatment was the only indication for an exchange transfusion in this study given that manifestation of acute bilirubin encephalopathy was not reported in both groups. With initial TSB level between 20-25 mg/dl exchange transfusion was avoidable among intensively treated patients whereas it was inevitable in 86.36\% of patients in the SSCPT group. Level of TSB higher than 25 mg/dl was totally not responding to SSCPT compared to failure of DSIPT in only 1.81\% of comparable studied patients. Over all nearly half of patients 67 (47, 18\%) were urged to underwent exchange transfusion in the SSCPT group compared to 2 (1.81\%) patients in DSIPT group. With high TSB levels on exchange line exchange transfusion was required in 91.56\% of neonates treated by SSCPT compared to total prevention of the exchange transfusion need in those subjected to DSIPT (Table 5).

### Table 3. Total serum bilirubin decline rate (mg/dl/hour) within the second 12 hour after starting 2 different phototherapy types.

| Gestational age | Total serum bilirubin decline rate (mg/dl/hour) | P-value* |
|-----------------|-----------------------------------------------|----------|
|                 | SSCPT type (N=142) | DSIPT type (N=110) |          |
| No.             | Mean ± SD | % | Mean ± SD | % |        |
| Full term       | 116 | 81.70 | 0.13 ± 0.10 | 100 | 90.90 | 0.48 ± 0.23 | <0.001 |
| Premature       | 26 | 18.30 | 0.06 ± 0.027 | 10 | 9.10 | 0.59 ± 0.28 | 0.006 |

* Independent sample T test was used.

### Table 4. Total serum bilirubin decline rate (mg/dl/hour) within the second 12 hour after starting 2 different phototherapy types, among neonates not required an exchange transfusion.

| Initial TSB level (mg/dl) | Total serum bilirubin decline rate (mg/dl/hour) | P-value* |
|---------------------------|-----------------------------------------------|----------|
|                            | SSCPT type (N=75) | DSIPT type (N=108) |          |
| No. | Mean ± SD | % | Mean ± SD | % |        |
| 10-15 | 32 | 42.66 | 0.17 ± 0.25 | 14 | 12.96 | 0.29 ± 0.21 | 0.134 |
| 15-20 | 37 | 49.33 | 0.21 ± 0.10 | 65 | 60.19 | 0.53 ± 0.30 | <0.001 |
| 20-25 | 6 | 8 | 0.36 ± 0.13 | 19 | 17.59 | 0.93 ± 0.303 | 0.029 |

*Independent samples T test was used.

### Table 5. Percentages of neonates subjected to exchange transfusion after using two types of phototherapy.

| Initial TSB level on nomogram | Exchange transfusion was required | SSCPT type (N=142) | DSIPT type (N=110) | P-value* |
|-----------------------------|----------------------------------|-------------------|-------------------|----------|
|                            | SSCPT type | DSIPT type |          |
| Total | Exchange transfusion was required | % | Exchange transfusion was required | % |        |
| No. | % | Mean ± SD | No. | % | Mean ± SD |        |
| 5-10 mg above exchange line | 2 | 2 | 100 | 3 | 2 | 66.66 | 0.361 |
| ≤5 mg above exchange line  | 7 | 7 | 100 | 1 | 0 | 0 | 0.005 |
| On exchange line            | 24 | 22 | 91.66 | 15 | 0 | 0 | <0.001 |
| Between phototherapy and exchange lines | 109 | 36 | 33.03 | 91 | 0 | 0 | <0.001 |
| Initial TSB level (mg/dl)   |                        |                   |                   |        |
| Above 30                    | 5 | 5 | 100 | 1 | 1 | 100 | ** |
| >25-30                      | 14 | 14 | 100 | 11 | 1 | 9.09 | <0.001 |
| >20-25                      | 44 | 38 | 86.36 | 19 | 0 | 0 | <0.001 |
| >15-20                      | 46 | 9 | 19.56 | 65 | 0 | 0 | <0.001 |
| 10-15                       | 33 | 1 | 3.03 | 14 | 0 | 0 | 0.510 |

* Chi-square test used. ** No statistics can be computed because exchange transfusion application was constant in both groups.
DISCUSSION

The efficacy of phototherapy is dependent on the color (wavelength), intensity (irradiance) of the light emitted during phototherapy, the exposed body surface area and the infant’s distance from the light. Blue lamps are most effective in reducing hyperbilirubinemia. The nearer the lights source to the infant, the greater the irradiance. In general the demonstrated significant differences between the compared studied groups in favor of DSIP type are collectively attributed to these factors. These factors were responsible for the significantly higher percentages of bilirubin decline in studied DSIP group compared to SSCPT group within 6, 12, 24 hours after commencing phototherapy. Those differences reflected the significant effectiveness of the used DSIP type in TSB reduction regardless the cause of neonatal hyperbilirubinemia.

Nuntnarumit P et al in Thailand, found that with intensity of 9-10 µw/cm²/nm the bilirubin reduction rate after therapy was 0.14 ± 0.1 mg/dl/h on day 1 of therapy, which was comparable to 0.11 ± 0.10 mg/dl/h rate of SSCPT studied group. With the same intensity of 9 -10 µw/cm²/nm Nuntnarumit P et al observed that the bilirubin reduction rate was 0.22 ± 0.12 mg/dl/h on day 1 of therapy with adapted double phototherapy placing daylight fluorescent lamps 38 cm above and 32 cm below the crib, a greater value of bilirubin reduction of 0.49 ± 0.24 mg/dl/h within second 12 hour of the DSIP was recorded in our study probably attributed to difference in light intensity and shorter distance from the light. There is a direct relationship between the irradiance used and the rate at which the level of total serum bilirubin declines.

When single-surface intensive phototherapy compared to double-surface intensive phototherapy equipped with a mixture of deep blue and day light phototherapy cumulative percent 48 hour decline (%) was 43.1 ± 12.4 among single-surface intensive phototherapy shown in the study of Boonyarittipong P et al in Bangkok, almost equivalent percentage was achieved 24 hour earlier in DSIP studied group, this difference probably because of type of light used and more surface area exposed to phototherapy in this study. Cumulative percent 24 hour decline (%) was 34.1 ± 11.1 among double-surface intensive phototherapy used in the same Bangkok study, which is also less than the mentioned value of the enrolled DSIP group, these differences may be attributed to type of light used. Intensive phototherapy can result in a bilirubin decrement of 30 to 40% in the first 24 hours. The level of serum bilirubin immediately after the exchange transfusion declines to levels that are about half of those before the exchange, a level which is achieved within the second 12 hour in this study using DSIP type.

Although there was no significant difference in the TSB decline rate in term of mg/dl/ h in the first 6 hour between the studied group, the cumulative bilirubin decline rate (mg/dl/h) after first 6 hour in DSIP cases was not only significantly higher (p = 0.046) than SSCPT group but more importantly it decreased the need for exchange transfusion to 1.81% in DSIP group versus 47.18% of compared SSCPT group. On other hand this result supports the accurate time selection of 6 hours recommended by AAP to determine exchange transfusion requirement.

Similar to this study other investigators confirmed that double surface phototherapy is more efficient than single surface phototherapy in term as well as in preterm infants. Duration of phototherapy was shorter in DSIP group compared to SSCPT group in this study likewise in other studies. Significant bilirubin decline rate (mg/dl/h) difference was verified between DSIP and SSCPT in both hemolytic and none a hemolytic category which was comparable to the finding of other researchers.

Because phototherapy works on bilirubin present in the skin and superficial subcutaneous tissue, the more bilirubin present at those sites (i.e., the higher the total serum bilirubin level), the more effective phototherapy will be. This may explain the non significant difference between the two studied groups at initial TSB level of 10 -15 mg/dl whereas it supported our findings of direct relationship of bilirubin decline rate to initial TSB level in both studied groups.

Among DSIP studied group no patient required exchange transfusion when TSB level was on exchange line or was ≤ 25 mg/dl, this is in concordance with AAP recommendations that if the TSB is at a level at which exchange transfusion is recommended or if the TSB level is 25 mg/dl or
higher at any time, it is a medical emergency and the infant should be admitted for intensive phototherapy (9) and it is particularly important to use lamps with blue emission (8). The use of phototherapy has decreased the need for exchange transfusion in term and preterm infants with hemolytic and nonhemolytic jaundice(11). Intensive phototherapy may eliminate the need for exchange transfusion (12).

CONCLUSIONS
This study demonstrated that DS IPT was more effective than SSCPT in treatment of neonatal hyperbilirubinemia in the first week of life. It clearly showed that DS IPT significantly reduced the exchange transfusion requirement among infants with high TSB level compared to SSCPT type.

RECOMMENDATION
We recommend DS IPT use when initial TSB level is on and below exchange line on nomogram, to reduce the need for exchange transfusion.

REFERENCES
1. Ambalavanan N, Carlo WA. Jaundice and Hyperbilirubinemia in the Newborn, kernicterus. In: Kliegman R M, Stanton BF, St Gome III J W, Schor N F Behrman R E, editors. Nelson Textbook of Pediatrics. 19th ed. Philadelphia: Saunders Elsevier; 2011:p.603-612.
2. Mishra S, Agarwal R, Deorari A K, Paul V K. Jaundice in the newborns. Indian J Pediatr. 2008 Feb; 75(2):157-163.
3. Maisels MJ. Phototherapy-traditional and nontraditional. Journal of Perinatology 2001; 21(Suppl 1):93-97.
4. Dobbs R H, Cremer R J. Phototherapy. Archives of Disease in Childhood.1975; 50, 833-836.
5. Cremer R J, Perryman P W, Richards D H. Influence of light on the hyperbilirubinemia of infants. Lancet 1958; 24(1):1094-1097.
6. Vreman H J, Wong R J, Stevenson D K. Phototherapy: current methods and future directions. Semin Perinatol. 2004 Oct; 28(5):326-333.
7. Ruud H T W. Phototherapy for neonatal jaundice—therapeutic effects on more than one level. Semin Perinatol. 2010 Jun; 34(3):231-234.
8. Maisels MJ, McDonagh AF. Phototherapy for Neonatal Jaundice. N Engl J Med. 2008; 358:920-928.
9. 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.
10. Chang YS, Hwang JH, Kwon HN, Choi CW, Ko SY, Park WS, et al. In vitro and in vivo efficacy of new blue light emitting diode phototherapy compared to conventional halogen quartz phototherapy for neonatal jaundice. J Korean Med Sci. 2005 Feb; 20(1):61-64.
11. Sisson T R C, Kendall N, Shaw E, Kechavarz-Oliai L. Phototherapy of jaundice in the newborn infant. II. Effect of various light intensities. The Journal of Pediatrics. 1972 July; 81(1): 35-38.
12. Wood A J J, Dennery P A, Seidman D S, Stevenson D K. Neonatal hyperbilirubinemia. N Engl J Med. 2001; 344(8): 581-590.
13. Nuintraumriti P, Naka C. Comparison of the effectiveness between the adapted-double phototherapy versus conventional-single phototherapy. J Med Assoc Thai. 2002 Nov; 85(Suppl 4):S1159-S1166.
14. Boonyarittipong P, Kriangburapa W, Booranavanich K. Effectiveness of double-surface intensive phototherapy versus single-surface intensive phototherapy for neonatal hyperbilirubinemia. J Med Assoc Thai 2008; 91(1):50-55.
15. Clarence W, Gowen J. Hyperbilirubinemia. In: Marcdante K J, Kliegman R M, Jensen H B, Behrman R E, editors. Nelson essential of pediatrics. 6th ed. Saunders Elsevier; 2010:p. 247-250.
16. Sarici SU, Alpay F, Unay B, Ozcan O, Gökçay E. Double versus single phototherapy in term newborns with significant hyperbilirubinemia. J Trop Pediatr. 2000 Feb; 46(1):36-39.
17. Thaithumyanon P, Visutiratmanee C. Double phototherapy in jaundiced term infants with hemolysis. J Med Assoc Thai. 2002; 85(11):1176-1781.
18. Kang J H, Shankaran S. Double phototherapy with high irradiance compared with single phototherapy in neonates with hyperbilirubinemia. Amer J Perinatol 1995; 12(3): 178-180.