The role of intensive phototherapy in decreasing the need for exchange transfusion in neonatal jaundice

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Abstract

Objectives: To assess the effectiveness of intensive phototherapy in reducing the need for exchange transfusion and the duration of phototherapy.
Methods: The prospective study with historical controls was conducted at Cairo University Paediatric Hospital, from February to July 2012, and comprised 360 newborns with indirect hyperbilirubinaemia. The 183 subjects were treated with Bilisphere 360 (Bilisphere group) compared with 177 who had been treated with conventional phototherapy (control group). Both groups were subjected to complete clinical evaluation and laboratory investigations.
Results: Bilisphere 360 decreased the need for exchange transfusion in 19 (10.4%) neonates of the Bilisphere group versus 130 (73.4%) of the control group ($p<0.001$); decreased the level of serum bilirubin as exchange transfusion (6.7 mg/dl [24.9%] in the subjects vs. 6.9 mg/dl [22.7%] in the controls); shortened the duration of phototherapy (2.7 days in the subjects, vs. 4.2 days in the controls; $p<0.001$).
Conclusion: The use of Bilisphere 360 in the treatment of indirect pathological hyperbilirubinaemia is as effective as exchange transfusion in lowering Total Serum Bilirubin when its level is within 2-3 mg/dl (34-51umol/l) of the exchange level. Bilisphere 360 is effective in reducing needs for exchange transfusion and duration of phototherapy.
Keywords: Intensive phototherapy, Exchange transfusion, Neonatal jaundice. (JPMA 64: 5; 2014).

Introduction

Neonatal jaundice is one of the most common diagnoses in the neonatal period; it is estimated to occur in 60% of term newborns in the first week of life. In rare instances, the Total Serum Bilirubin (TSB) reaches levels that can cause kernicterus, a condition characterized by bilirubin staining of neurons and neuronal necrosis involving primarily the basal ganglia of the brain and manifested in athetoid cerebral palsy, hearing loss, dental dysplasia, and paralysis of upward gaze.[1]
The most common cause of jaundice in the first 24 hours of life due to haemolytic disease of newborn (HDN) is rhesus (Rh) haemolytic disease[2] followed by ABO incompatibility that may cause elevated levels of bilirubin and anaemia but less severe than Rh haemolytic disease.[3]
For preventing the kernicterus and other complications of hyperbilirubinaemia, jaundice should be managed by phototherapy or exchange transfusion (ECT).[4] Phototherapy is a useful method because it is easily available and devoid of all complications of double volume ECT. The efficacy of phototherapy depends on the dose and wavelength of light used and the surface area exposed.[5] Despite ECT being an effective method in decreasing TSB level after failing phototherapy, ECT remains an invasive procedure with associated morbidity and mortality. ECT should be considered only when the benefit of decreasing TSB level to prevent kernicterus outweighs the complications associated with the procedure.[6]
Intensive phototherapy is a new modality that can rapidly decrease TSB below the threshold for ECT.[7]

The current study aimed at assessing the effectiveness of intensive phototherapy in lowering the level of bilirubin in neonates and reducing the need for ECT and the duration of phototherapy.

Patients and Methods

The prospective study with historical controls was conducted from February to July 2012 and comprised all term neonates with indirect hyperbilirubinaemia near the level of ECT who were admitted to the Neonatal Intensive Care Unit (NICU) of Cairo University Children Hospital (Abou El Rish El Mounira), Faculty of Medicine, Cairo University, Egypt, and treated with intensive phototherapy (Bilisphere 360). These neonates were compared with historical group who had been admitted between February and July 2011 and treated with conventional therapy before the use of Bilisphere 360. Premature newborns (gestational age <37 weeks), cases with direct hyperbilirubinaemia, critically-ill newborns, those with multiple congenital anomalies and inborn errors of metabolism were excluded. The study was approved by the Ethics Committee of Cairo University and verbal consent was obtained from each patient's guardian.

All cases were subjected to detailed perinatal history, including maternal illness, mode of delivery, one and five minutes Apgar scores, history of cyanosis or convulsion, gestational age, weight, gender and age at admission. Comprehensive clinical examination was performed, with special emphasis on vital signs, anthropometric measures, presence of cephalohaematoma and neurological evaluation for neonatal reflexes, level of consciousness, sensory and motor functions.

The subject, received intensive phototherapy (Bilisphere 360 phototherapy system) which consisted of a chamber containing 16 blue TL 20W/52 fluorescent tubes arranged cylindrically. The baby was laid on a gauze hammock suspended along the centre of the chamber which was illuminated on all sides. The historical control group had received conventional phototherapy. It comprised of two phototherapy units with blue light and was placed 45 cm above the neonate. Hyperbilirubinaemia Guidelines of the American Academy of Paediatrics (AAP)[8] were applied at our NICU for the management of admitted newborns during the study period.

Total and direct serum bilirubin, complete blood count (CBC), reticulocyte count, blood group and Rh of mother and neonate and Direct Coombs test using antiglobulin reagent specific for IgG were measured for all cases on admission. All of the studied neonates received phototherapy immediately after admission and TSB was measured 6 hours after the initiation of phototherapy. Phototherapy was administered continuously, except during feeding, nursing care and blood sampling. The infants were treated naked except for diapers and eye pads. During phototherapy, total bilirubin was measured at variable intervals on the basis of days of life, gestational age and risk factors. Infants with unresponsive hyperbilirubinaemia underwent urgent ECT using fresh blood type O Rh negative, double the blood volume of the baby (2x85ml/kg).[8] The outcome was assessed and recorded.

The primary outcome measure was the frequency of ECT before and after using Bilisphere 360. Secondary outcome measures were: days of stay at NICU in cases under intensive phototherapy and rate of decline of serum bilirubin.

Data management and analyses were performed using Statistical Analysis Systems. The graphs were done using Microsoft Excel 2007. Numerical data was summarised using means and standard deviations or median and interquartile ranges (IQR). Categorical data was summarised as percentages. Comparisons between the two groups with respect to numeric variables were done by the Student's t test for parametric data and Mann-Whiteny test for non-parametric data. Comparisons between categorical data were done using the chi-square test. To measure the effect of time on bilirubin and differences between groups, a two-way analysis of variance (ANOVA) with repeated measures on one factor was done.[9] All p-values were two-sided. $P<0.05$ was considered significant.

Results

Of the 360 infants in the study, the Bilisphere group consisted of 183 (50.8%) newborns (104 (56.8%) males and 79 (43.2%) females) while the control group consisted of 177 (49.2%) newborns (91 (51.4%) males and 86 (48.6%) females). Both groups were comparable regarding their gender and positive family history of jaundice. The commonest cause for hyperbilirubinaemia in both groups was ABO incompatibility (89 (48.6%) cases vs. 90 (50.8%) controls p=0.49). There was no statistically significant difference between the two groups as regards gestational age, birth weight, onset of jaundice and age on admission. Regarding the baseline laboratory data, including TSB, haemoglobin level, haematocrit, total leucocytic count, platelet count and reticulocyte count, there were no significant statistical differences between the study and control groups (Table).

Table: Demographic, laboratory data, duration of phototherapy and frequency of exchange transfusion in both groups.

	Bilisphere group (N=183)		Control group (N=177)		P- value
	Median	IQR	Median	IQR	
Gestational age (wks)	38.0	37.0-38.0	38.0	37.0-38.0	0.877
Birth weight (g)	2970.0	2602.5-3250.0	2900.0	2550.0-3222.5	0.80
Onset of jaundice(days)	2.0	1.0-3.0	2.0	1.0-3.0	0.697
Age on admission(days)	4.0	3.0-6.0	4.0	3.0-6.0	0.606
Total serum bilirubin (mg/dl)	26.20	24.0-30.0	27.00	25.00-31.05	0.080
Haemoglobin (g/dl)	12.90	11.62-14.90	13.40	11.67-14.90	0.713
Haematocrit	37.50	33.92-43.77	38.00	33.62-43.00	0.976
Platelets	264.00	213.25-327.50	258.0	203.75-325.50	0.421
White blood cells	10.70	8.80-14.00	11.00	8.25-13.60	0.808
Reticulocytes	7.0	3-13.9	7.0	2.4-13.27	0.755
Duration of Phototherapy (days)(mean±SD)		2.7	1.5	4.2	1.4
<0.001*					
	No	(%)	No	(%)	
Exchange transfusion	19	(10.4)	130	(73.4)	<0.001*

On comparing the rate of decrement in TSB between the cases and the controls, no statistically significant difference was detected after 6 hours (6.7 mg/dl (24.9%) for cases vs. 6.9mg/dl (22.7%) for controls; p=0.05). Second assessment at 12 to 48 hours showed a statistically significant difference in the rate of decline (6.1mg/dl (21.4%) for cases vs. 3.6mg/dl (11.4%) for controls, p=0.05). The overall rate of decrement of bilirubin from admission to 48 hours was significantly greater in the cases than the controls (46.3% vs. 34.1%; p<0.05) (Figure).

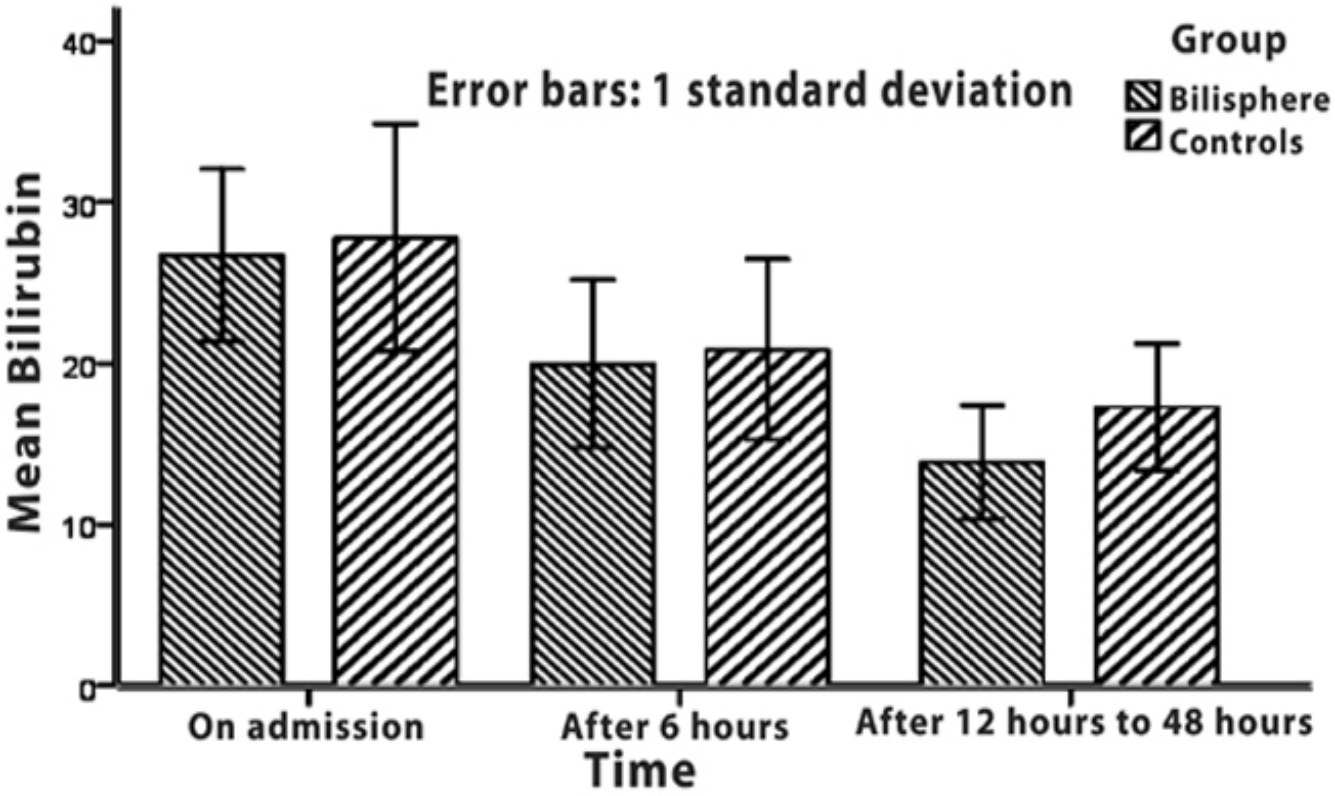

Figure: Bilirubin decline rate in both groups.

In the Bilisphere group, 69 (37.7%) neonates continued on intensive phototherapy till 6 hours; 65 (35.5%) continued till 12 hours; 4 (2.2%) till 18 hours; 1 (0.5%) till 20 hours; 29 (15.8%) till 24 hours; 5 (2.7%) till 30 hours; 5 (2.7%) till 36 hours; and 5 (2.7%) till 48 hours.
The Bilisphere group showed a shorter duration of phototherapy with a mean of 2.7±1.5 days when compared with the control group which showed a mean of 4.2±1.4 days, which in turn proved to be statistically highly significant ($p < 0.001$). Besides, 19 (10.4%) neonates in the Bilisphere group needed ECT versus 130 (73.4%) in the control group ($p=0.001$).

Discussion

Although jaundice in newborns is common and generally benign, very high TSB levels can injure the newborn's central nervous system. Phototherapy and/or ECT remain the main lines of treatment in jaundiced newborns if they are at risk of rising to or have already reached potentially dangerous levels.[10] Phototherapy is safer and less expensive than ECT. In addition, ECT requires more complex level of care and specific professional expertise. High-intensity phototherapy has been shown to be effective in rapidly decreasing TSB levels and reducing the need for ECT. Bilisphere 360 is a novel neonatal phototherapy device designed to maximise the irradiance and treatment area coverage.[11] The current study evaluated its effectiveness on 188 newborns with severe indirect hyperbilirubinaemia and compared it to a historical control group consisting of 177 neonates treated with conventional phototherapy. Both groups were comparable regarding all of the pre-treatment demographic, clinical and laboratory parameters.
Bilisphere 360 was more effective in decreasing bilirubin levels; the overall bilirubin decline rate from admission to 48 hours was significantly greater in Bilisphere group than the controls ($p<0.05$). The

results are in agreement with previous reports proving that serum bilirubin levels in newborns may be controlled more effectively with high-intensity phototherpy than with conventional modalities.[12]
In comparing the bilirubin decline rate between Bilisphere group and the control group, it was found that there was no statistically significant difference between them from admission to 6 hours. However, a statistically significant difference between the two groups regarding bilirubin decline rate from 6 hours to 48 hours was obvious. This may be explained by the high percentage of cases that underwent ECT in the control group during the 1st 6 hours of therapy.
Centre National de Reference en Haemobiologie Perinatale[13] studied the time effect of Bilisphere 360 intensive phototherapy on blood levels of TSB over 20 hours treatment in jaundiced newborn, concluding that this device allows an average decrease in TSB levels of 15%, 26% and 37% at hours 4, 10 and 20 exposure respectively. A study[14] reported decrease in the TSB levels after 6 hours of high-intensity phototherapy to be 23%, which was almost the same rate of reduction as in the present study (24.9% after 6 hours).
Bilisphere 360 phototherapy shortens the duration of hospital stay which reflects a higher cost-effect value as the shorter duration of treatment means that more patients can be treated with fewer phototherapy units. Secondly, decreasing the duration of phototherapy may lead to a shorter length of hospitalisation. This would also mean considerably less separation from the mother and less interruption of breastfeeding. Previous studies reported a higher rate of bilirubin decline and a shorter duration of action of intensive phototherapy devices when compared with conventional phototherapy.[15-17] In the current study, the Bilisphere group showed a significantly shorter period of hospital stay and duration of phototherapy compared with the control group ($p<0.001$).
Concerning the need for ECT in Bilisphere group, only 19 (10.4%) out of 188 cases required ECT and this was much lower than the control group (130 (73.4%) out of 177 cases). Our results confirmed the previous reports.[14,18]

Conclusion

The use of Bilisphere 360 in the treatment of indirect hyperbilirubinaemia is as effective as ECT in lowering TSB. Bilisphere 360 is effective in reducing needs for ECT and duration of phototherapy. Long-term follow-up trials should be performed to evaluate the long-term effects in newborn infants with severe indirect hyperbilirubinaemia who are treated with this therapeutic modality.

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References

1. Zabeen B, Nahar J, Nabi N, Baki A, Tayyeb S, Azad K, et al. Risk factors and outcome of neonatal jaundice in a tertiary hospital. Ibrahim Med Coll J 2010; 4: 70-3.
2. McIntosh N, Stenson B. The newborn. In: McIntosh N, Helms PJ, Symth RL (eds.) Forfar & Arneil's Textbook of Pediatrics. 6th ed. Edinburgh: Churchil Living Stone; 2003; pp 177-391.
3. Drabik-Clary K, Reddy VV, Benjamin WH, Boctor FN. Severe hemolytic disease of the newborn in a group B African-American infant delivered by a group O mother. Ann Clin Lab Sci 2006; 36: 205-7.
4. Behjati SH, Sagheb S, Aryasepehr S , Yaghmai B. Adverse events associated with neonatal exchange transfusion for hyperbilirubinemia. Indian J Pediatr 2009; 76: 83-5.
5. Sarin M, Dutta S, Narang A. Randomized controlled trial of compact fluorescent lamp versus

standard phototherapy for the treatment of neonatal hyperbilirubinemia. Indian Pediatri 2006; 43: 583-90.
6. Sanpavat S. Exchange transfusion and its morbidity in ten-year period at King Chulalongkorn hospital. J Med Assoc Thai 2005; 88: 588-92.
7. Bansal A, Jain S, Parmar VR , Chawla D. Bilirubin rebound after intensive phototherapy for neonatal jaundice. Indian Pediatri 2009; 47: 607-9.
8. 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.
9. Dawson B, Trapp GT. Basic and Clinical Biostatistics. 3rd edition. Norwalk, Connecticut: Appleton & Lange; 2001.
10. Newman TB, Vittinghoff E, McCulloch CE. Efficacy of phototherapy for newborns with hyperbilirubinemia: a cautionary example of an instrumental variable analysis. Med Decis Making 2012; 32: 83-92.
11. Mreihil K, McDonagh AF, Nakstad B, Hansen TW. Early isomerization of bilirubin in phototherapy of neonatal jaundice. Paeditr Res 2010; 67: 656-9.
12. Amato M, Von Muralt G. [Efficacy of intensive blue double-lamp phototherapy in the treatment of ABO incompatibility and idiopathic severe hemolytic jaundice]. Pediatr Med Chir 1984; 6: 95-8.
13. Centre National de Reference en Hemobiologie Perinatale (CNRHP 2009). (Online) (Cited 2013 October 11). Avalaible from URL: www.mediprema.com/uploadfile/Docs/1289320856.PDF.
14. De Carvalho M, Mochdece CC, Sa CA, Moreira ME. High-intensity phototherapy for the treatment of severe nonhaemolytic neonatal hyperbilirubinemia. Acta Paediatr 2011; 100: 620-3.
15. 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.
16. Nuntnarumit P, Naka C. Comparison of the effectiveness between the adapted-double phototherapy versus conventional-single phototherapy. J Med Assoc Thai 2002; 85(Suppl 4): 1159-66.
17. Karadaga A, Yesilyurtb A, Unalc S, Keskinb I, Demirind H, Urasa N, et al. A chromosomal-effect study of intensive phototherapy versus conventional phototherapy in newborns with jaundice. Mutat Res 2009; 676: 17-20.
18. Raghubir KV, Fox GF, Inwood S, Kelly EN. Follow up of term neonates with extremely high unconjugated bilirubin. Pediatr Res 1996; 39: 276-276.