



Research Article

Effectiveness of conventional phototherapy, intensive phototherapy and exchange transfusion in treating neonatal jaundice at Fatima Al-Zahra Hospital for maternity and children in Baghdad

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Abstract

Background: Neonatal hyperbilirubinemia is a common disease in neonates especially in the early days of birth that requires a good and successful treatment for reducing the severity and its complications that can produce important and irreversible effects.

Objectives: To evaluate the effectiveness of conventional phototherapy, intensive phototherapy, and exchange transfusion on outcomes of neonatal jaundice at Fatima Al-Zahra Hospital for maternity and child care in Baghdad.

Patients & Methods: A retrospective study was carried out using medical records of neonates with a diagnosis of unconjugated jaundice, admitted in the septic neonatal care unit of Fatima Al-Zahra hospital over 6 months period between 1st May till 31st October 2018. The total serum bilirubin, fractionations, and blood group were done in all cases. They were treated with conventional phototherapy, intensive phototherapy, and exchange transfusion according to the severity of jaundice.

Results: Total neonates admitted from 1st May to 31st October 2018 in septic neonatal care unit were 1254, among them 432 (35%) were diagnosed as unconjugated neonatal jaundice "indirect hyperbilirubinemia". Male: Female ratio (1.4:1), males 256(59.3%), females 176(40.7%). Physiological jaundice was the most common cause in 129(29.9%) cases. Prematurity in 104(24.1%) and ABO incompatibility 59(13.7%) while Rh incompatibility 14(3.2%), sepsis 8(1.9%), and unknown causes of jaundice were 118(27.3%) because of lack of lab facilities. Conventional phototherapy was the most common kind of treatment in 237(55%) while intensive phototherapy was used in 175(40.3%) cases with a successful reduction in T.S.B level and the rate of improvement without the need for exchange transfusion (92%) (161/175). Only 20(4.5%) cases were treated with exchange transfusion especially for ABO incompatibility 8 (42.1%) cases and Rh incompatibility 4 (21.1%) cases. Most of the neonates 429 (99.3%) discharged with complete improvement and only 2 (0.5%) neonates suffered from kernicterus and one death (0.2%).

Conclusion: Conventional phototherapy is still the standard treatment of mild to moderate indirect hyperbilirubinemia. The use of intensive phototherapy in the treatment of unconjugated neonatal hyperbilirubinemia is effective in reducing T.S.B level, need for exchange transfusion, and hospital stays.

Recommendations: provide an aseptic neonatal care unit in the hospital with a further number of intensive phototherapy devices as it is so effective in treating unconjugated neonatal jaundice and reduces the need for exchange transfusion as it is proven in the study.

Introduction

Neonatal hyperbilirubinemia is common during the first week after birth in about 60% of term neonates and 80% of preterm neonates [1, 2]. In term infants, the serum bilirubin level reaches a clinically detectable level by day 3 or 4 mg/dl. This gradually falls over the next few days before reaching the normal childhood serum bilirubin level by the end of the second week of life. This is generally referred to as physiological jaundice [3].

In severe neonatal hyperbilirubinemia, unconjugated bilirubin can cross to the brain through the blood-brain barrier and can lead to bilirubin neurotoxicity. The most severe and permanent clinical manifestation of severe neonatal hyperbilirubinemia is Kernicterus [4].

In some developing countries, the incidence of severe neonatal hyperbilirubinemia may be as much as 100 times higher than in developed countries [5]. The main risk factors identified for neonatal jaundice include prematurity, ABO incompatibility, and neonatal sepsis [6].

Infants that are exclusively breastfed have an increased risk for severe hyperbilirubinemia in the first 2 to 5 days of life compared to formula-fed infants. It is, therefore, essential to provide good lactation support to all mothers at all levels of care to increase successful breastfeeding, at least 8-12 times a day, as breast-milk benefits outweigh the risk [7].

Phototherapy and exchange transfusion are well-established as the most effective treatments for severe hyperbilirubinemia [8]. Various phototherapy devices are using different light sources: fluorescent tubes, halogen lamps, and light-emitting diodes (LED). An effective phototherapy device should produce specific blue-light wavelengths (peak emission: 450 ± 20 nm), preferably in a narrow bandwidth to about 80% of an infant's body surface area. Conventional phototherapy (CPT) should have an irradiance of at least 8-10 $\mu\text{W}/\text{cm}^2/\text{nm}$ and intensive phototherapy should have an irradiance of $\geq 30 \mu\text{W}/\text{cm}^2/\text{nm}$ (from either a single or multiple phototherapy units) [9]. An Exchange transfusion was introduced initially in the 1970s as a specific treatment for Rhesus hemolytic diseases in the 1940s. It reduces serum bilirubin level and removes the antibody-coated neonatal erythrocytes and circulating maternal antibodies to reduce further erythrocyte destruction. Approximately 85% of the neonatal blood is replaced by irradiated donor blood double volume exchange transfusion [10].

Phototherapy causes photoisomerization of bilirubin in the skin to water-soluble isomers that can be excreted by the kidneys and stool. [11,12]. Intensive phototherapy using "special blue" fluorescent tubes, placing the lamps within 15-20 cm of the infant, and putting a fiber optic phototherapy blanket under the infant's back to increase the exposed surface area. Aggressive phototherapy may improve neurodevelopmental outcomes in infants <1.000 g [13]. Exchange transfusions are recommended when bilirubin levels remain above exchange transfusion thresholds despite intensive phototherapy, or if signs of acute bilirubin encephalopathy occur [14].

The current study was conducted aiming to evaluate the effectiveness of conventional phototherapy, intensive phototherapy, and exchange transfusion on outcomes of neonatal jaundice at Fatima Al-Zahra Hospital in Baghdad.

Subjects and methods

A retrospective study was carried out using the medical records of all cases of neonatal indirect hyperbilirubinemia admitted into the septic neonatal care unit of the Fatima Al-Zahra hospital over a 6 months period between 1st May and 31st October 2018

Data collected from the case records include patients' gender, age, total serum bilirubin and fractionation, maternal and neonatal blood group and Rh, weight, risk factors, type of feeding, type of delivery, type of treatment, and outcomes.

Total serum bilirubin and fractionation were done at the time of admission and indirect hyperbilirubinemia was the criteria of inclusion in the study. Monitoring is done by measuring total serum bilirubin (T.S.B) level each morning and evening and sometimes every 4 hours especially for severe neonatal hyperbilirubinemia.

After exclusion of 1st-day jaundice, mild neonatal hyperbilirubinemia was considered when T.S.B level of up to 10 mg/dl in preterm neonates and up to 12 mg/dl in full-term neonates. Level above 18

mg/dl in preterm neonates and above 20 mg/dl in full-term neonates were considered severe neonatal hyperbilirubinemia. Bilirubin levels between these values indicated moderate neonatal hyperbilirubinemia [12]. Kernicterus was diagnosed in severely jaundiced infants depending on clinical features as poor sucking, stupor, and hypotonia were symptoms in the early phase, while hypertonia and opisthotonos were symptoms in the late phase [15].

According to the guidelines charts for phototherapy and exchange transfusion in hospitalized patients, full-term neonates with indirect hyperbilirubinemia (<15 mg /dl) were treated with conventional phototherapy while infants with (>15 mg /dl) were treated with intensive phototherapy. Phototherapy is interrupted only during breastfeeding or nappy change. Severe indirect hyperbilirubinemia which did not respond to intensive phototherapy were treated with exchange transfusion and neonates who present with signs of Kernicterus on admission were treated with immediate exchange transfusion [1].

In preterm neonates, phototherapy is usually started at 50-70% of the maximal indirect serum bilirubin level. If values greatly exceed this level, if phototherapy is unsuccessful in reducing the maximal bilirubin level, or if signs of kernicterus are evident, exchange transfusion is indicated.

Neonates with blood group A or B of mothers with blood group O were defined as ABO incompatibility. Newborns with a positive Rh born from a mother with negative Rh were defined as Rh incompatibility [3].

Septicemia was diagnosed depending on positive blood culture and/or clinical features like poor activity, poor feeding, hypothermia, or hyperthermia, and neonate treated with antibiotics for 7 days or more. Tests for pyruvate kinase and gluronyl transferase could not be done because of a lack of lab. facilities.

Conventional phototherapy units used were blue light fluorescent tubes, with the spectral irradiance of 10-30 mW/cm² /nm. The device which had been used for intensive phototherapy was Novos TIBBI CIHAZLAR SAN.TiC.iTtl.ve iHR.LTD.STi Mod: Bilisphere 360 SN:BS-12-01-208.It consists of 16 blue light fluorescent tubes with up and down double surfaces.

The exchange transfusion procedure was done through the umbilical vein using fresh whole blood taking about 45-60 minutes by repeatedly removing and replacing 20cc of blood and one ml of calcium gluconate 10% was given after exchange of every 100 ml of blood. For Rh incompatibility, Rh-negative and blood group that compatible with mother and baby, cross-matched with baby's blood was used; for ABO incompatibility, blood group and Rh compatible with mother and baby, cross-matched with baby's blood was used.

Outcomes were classified as discharged with improvement, kernicterus, or death.

Data analysis was performed using the SPSS program, version 20.

Results

The total number of neonates admitted from 1st of May to 31st October 2018 in the septic neonatal care unit was 1254, among them 432 (35%) were diagnosed with unconjugated neonatal jaundice (indirect hyperbilirubinemia). Males 256(59.3%) and females 176 (40.7%) with male to female ratio (1.4:1).The most common age group was 72 hs-1week in 266 cases (61.6%) and > 1 week in 132(30.6%) while the least age group was < 24 hours in 5 (1.2%) cases (mean=3.2 days).Bodyweight of newborns on admission was > 2.5 kg in the majority of patients 351 cases (81.3%) while 81 newborns (18.7%) < 2.5 kg. Most neonatal deliveries were by normal vaginal delivery 278 (64.3%) and cesarean section was 154 (35.6%). Breastfeeding was found in most neonates 334 (77.3%), mixed feeding 78 (18.1%), and only 20 (4.6%) neonates with bottle feeding. (Table 1).

Physiological jaundice was the most common cause of neonatal hyperbilirubinemia in 129 cases (29.9%). Prematurity 104(24.1%) and ABO incompatibility 59(13.7%) were also major causes of jaundice. On the other hand, there is a low rate of patients with Rh incompatibility 14(3.2%) and sepsis 8(1.9%). There was a high rate of patients

constituting 118 cases (27.3%) with unidentifiable cause labeled as "unknown" as shown in Table 2.

A relatively high rate of patients 237(55%) cases were treated with conventional phototherapy. Intensive phototherapy was used in the treatment of moderate and severe N.H in 175 (40.5%) cases with a successful reduction in T.S.B level and improvement without the need for exchange transfusion (92%) (161/175). Only 14 cases (8%) failed to respond to intensive phototherapy and exchange transfusion was done. The decision of immediate exchange transfusion was made in six cases, three of them because of patients age was < 1 day old with ABO incompatibility and the other three cases because of signs of kernicterus on admission so the total No. of cases with exchange transfusion was 20(4.5%) cases. Table 3.

Table 1.

Suggested maximal indirect serum bilirubin concentrations (in mg/dl) in preterm infants (1).

BIRTHWEIGHT (g)	UNCOMPLICATED*	COMPLICATED*
<1,000	12-13	10-12
1,000-1,250	12-14	10-12
1,251-1,499	14-16	12-14
1,500-1,999	16-20	15-17
2,000-2,500	20-22	18-20

*Complications include perinatal asphyxia, acidosis, hypoxia, hypothermia, hypoalbuminemia, meningitis, intraventricular hemorrhage, hemolysis, hypoglycemia, or signs of kernicterus.

Table (4) demonstrate the modes of treatment according to the T.S.B level. The higher percentage of patients including preterm and term neonates were with moderate N.H (10-19 mg /dl) in 360 cases (83.6 %) mostly treated with conventional phototherapy in 234 cases (65 %), intensive phototherapy in 124 cases (34.4 %) and only exchange transfusion in 2 cases (0.05%).

A challenging group of patients with severe N.H (> 20 mg /dl) without signs of kernicterus constituting 63 (14.5 %) cases; treated with intensive phototherapy with a successful outcome in 49/63 cases (77.8 %) while only 14/63 cases (22.2 %) with exchange transfusion after they had been given a chance of intensive phototherapy for 4-6 hours.

Regarding gender and its relationship to the modes of treatment, the results show that the response of male to intensive phototherapy (109/107) (98.2%) was much higher than female (67/79) (84.8%) while the occurrence of complications e.g signs of kernicterus on admission or 1st-day jaundice with immediate exchange transfusion was only seen in male neonates (6/265) (2.3%) and one male died after exchange transfusion.

Stay at hospital < 4 days in 402 (92.8%) of cases, while only 31(7.2%) cases stay > 4 days. Outcomes of neonatal jaundice revealed that 429 neonates (99.3%) were discharged with complete improvement and only 2 neonates (0.5%) suffered from kernicterus and one death (0.2%).

Discussion

The rate of neonatal jaundice reported in the study is (35%) in agreement with Dantas et al 31%, [16] while it is lower than Siromani et al 42.03% [17] and Thielemans et al 53% [18].

The results revealed a higher rate of male predominance with male to female ratio of 1.4:1 is comparable to Sharma et al [19] (60%), Thielemans et al [18] (58.4%), and Siromani et al 64% [17].

Table 2.

The patients' criteria.

Criteria	Total No.	%	
Age at time of admission (days)	<1 day	6	1.2
	1---2	28	6.7
	3---6	266	61.6
	=>7	132	30.6
Gender	Male	256	59.3
	Female	176	40.7
Weight (Kg)	=>2.5 Kg	351	81.3
	<2.5 kg	81	18.7%
Type of delivery	CS	154	35.6
	NVD	278	64.4
Feeding	Bottle feeding	20	4.6
	Breast feeding	334	77.3
	Mixed	78	18.1
	Physiological	129	29.9
Causes	Prematurity	104	24.1
	ABO- Incompatibility	59	13.7
	Rh- Incompatibility	14	3.2
	Sepsis	8	1.9
	Unknown	118	27.3

Table 3.

Kinds of treatment and Outcome

Type of treatment	Total	%	Improved	% of improved	Not improved
Conventional phototherapy	237	55	237	100	0
Intensive Phototherapy	175	40.5	161	92	14
Exchange transfusion after a trial of intensive phototherapy	14	3.2	14	100	0
Immediate exchange transfusion	6	1.3	5	83.3	1
Outcome	432	100	429	99.3	3*

*2 cases kernicterus and 1 case died after exchange transfusion.

Table 4.

Modes of treatment in relation to T.S.B level

TSB level (mg/dl)	Total No.	%	Phototherapy	Intensive phototherapy	Exchange transfusion
<10	6	1.4%	3	2	1*
10-19	360	83.6%	234	124	2*
=>20 without Kernicterus	63	14.5%	0	49	14**
=>20 & Kernicterus	3	0.5%	0	0	3*
Total No.	432	100%	237	175	20

*Immediate exchange transfusion

The results showed that the most common age group was 72 hs-1week in (61.6%), similar findings reported in the Sharma et al 57.9% [19], while (1.2%) of neonates admitted within the first 24 hours of age which is lower as compared to Sharma et al 7.6% [19]. Depending on the popular beliefs and the use of some traditional medicine made people late to bring the neonate to the hospital for treatment which leads to poor prognosis in some neonates with severe jaundice.

The majority of patients (81.3%) were > 2.5 kg which is in contrast to Siromani et al work which revealed that 66% with low birth weight

which is considered as one of the contributing factors for hyperbilirubinemia [17].

There was a higher rate of Breastfeeding jaundice (77.3%) which usually occurs in the first week of life while the baby and mother are in the early stages of learning how to breastfeed. Breastfeeding jaundice is the result of inadequate milk intake by the baby. This causes a delay in the passage of meconium and reabsorption of bilirubin into the intestines and keeps the elevated levels of bilirubin [1]. This finding is somewhat higher than the findings of Siromani et al 67% [17] and to Singhal et al 65.6% [20].

The results show that physiological jaundice was the most common cause of neonatal hyperbilirubinemia (29.9%), the same conclusion reached by Rasul et al 26.7% [21] and Singhal et al 34.6% [20]. Prematurity which is one of contributing factors for the development of neonatal hyperbilirubinemia consist (24.1%) of results which is lower than the findings of Rasul et al 37% [21] but higher than those of Singhal et al 16.7% [20].

The rate of ABO incompatibility was (13.7%) born to O group mothers similar to Siromani et al 12% [17] study results but it is lower than Thielemans et al 17.9% [18] study.

Rh incompatibility was (3.2%), in line with Bhutani et al 2% [4] but it is different from Siromani et al 10% [17]. The use of anti D for RH -ve mothers with RH +ve neonate reduced the risk of RH incompatibility and most mothers at marriage time will know their blood group so the mother will be more careful especially when her blood group negative and her baby blood group positive.

Sepsis was found in (1.9%) as a minor cause, this disagrees with the findings of Sharma et al 43% [19], Siromani et al 43% [17], and Thielemans et al 18.7% [18] which showed that sepsis being the major cause of neonatal jaundice. This is maybe due to more number of home deliveries, poor socio-economic conditions, or living in rural places while most deliveries in our study occurred in the hospital and urban areas.

The cause of neonatal hyperbilirubinemia could not be determined unfortunately in a relatively high percentage of patients (27.3%) because the use of the retrospective design in the study has limited information and lack of some special analysis such as lack of extensive investigations to determine the causes of jaundice.

Regarding gender to types of treatment. It seems that the response of males to intensive phototherapy (98.2%) is much higher than female (84.8%), in contrast to the study done in Baghdad by Al-Momen H.H et al [22] which showed an equal success rate (72%) in both sex groups. The occurrence of complications e.g kernicterus on admission and death after exchange transfusion was higher in males than females. This is in agreement with the scientific fact that the risk of developing significant neonatal jaundice is higher in male infants [1].

Different modes of treatment were used according to the bilirubin level. A relatively higher rate of patients 237 cases (55%) was treated with conventional phototherapy, the same finding (62-2%) was reported by Rasul C H study [21].

Intensive phototherapy was used in 175 cases (40.5%) with successful improvement (92%) (161/175) inconsistent with Al-Momen H.H et al 72% [22], and Abdelazeem KS et al study 68% [23] in Assiut university children hospital, Egypt. Intensive phototherapy played an important role in the treatment of severe N.H (> 20 mg /dl) and reduction of the need to exchange transfusion and this was approved in 63 (14.5 %) cases with severe N.H (> 20 mg /dl) without signs of kernicterus on admission with success rate 49/63 cases (77.8%).

Exchange transfusion in 20(4.5%) cases which are the same finding(5.2%) reported by Rasul et al [21] and lower as compared to Siromani et al 26% [17]. In our hospital, intensive phototherapy is used to treat moderate and severe jaundice as early as possible to reduce treatment with exchange transfusion.

Length of stay in hospital was < 4 days in (92.8%) mean 2.5± 1.5 days, same as Abdelazeem KS et al 23 study and > 4 days in (7.2%) because of sepsis and neonates treated with exchange transfusion; both conditions need cover antibiotics and close follow up. While in Sharma et al [19] (67.6%) of neonates stay < 4 days and those who are stay> 4 days (32.4%). This is maybe due to the use of intensive phototherapy in our study for the treatment of neonatal hyperbilirubinemia is effective in

reducing hospital staying and reducing needs for exchange transfusion and has a good effect on outcomes of jaundice.

There were 429 (99.3%) babies with neonatal hyperbilirubinemia discharged with improvement. It is comparable (96%) with Siromani et al findings [17].

Conclusion

Conventional phototherapy is still the standard treatment of mild to moderate indirect hyperbilirubinemia. Use of intensive phototherapy in the treatment of unconjugated neonatal hyperbilirubinemia is effective in reducing T.S.B level, need for exchange transfusion and reduce duration of hospital staying.

Recommendation

Provide an aseptic neonatal care unit in the hospital with a further number of intensive phototherapy devices as it is so effective in treating unconjugated neonatal jaundice and reduces the need for exchange transfusion as it is proven in the study.

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Conflicting Interest

No conflict of interest.

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