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The Comparison of Single and Double Phototherapy Effects in Blood Calcium Level in Neonates with Jaundice

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Abstract

Background: Given the high prevalence of infant's jaundice and the importance of rapid and timely diagnosis and treatment, selecting the appropriate treatment, such as the type of phototherapy is necessary which can be done in single and double phototherapy. The aim of this study is to compare the effect of single and double phototherapy in neonates with jaundice in Imam Hossain hospital of Shahroud.

Methods: A cross-sectional study was conducted on 130 infants with jaundice who had been referred to Bahar Hospital, Shahroud, between March 2020 and February 2021. The patients were randomly divided into two equal groups: A (double phototherapy) and B (single phototherapy), and calcium levels were measured 24, 48 and 72 hours later and compared with each other.

Results: The results showed that the groups were matched for demographic and clinical characteristics that there was no significant difference between the two groups. The calcium reduction after 72 hours in the double phototherapy group was 9.9± 0.5 to 8.3± 0.7 mg/dl and in the single phototherapy group it was 9.9± 0.4 to 8.6± 0.4 mg/dl, which did not differ significantly (p = 0.125).

Conclusion: This study showed that although single and standard phototherapy is an effective and common method to control hyperbilirubinemia, it seems that double phototherapy can accelerate the reduction of serum bilirubin and does not have significant changes in calcium levels, but according to the contradictory results of different studies, more studies and a larger sample size are needed for final confirmation.

Keywords: Jaundice; Phototherapy Single; Double Phototherapy; Calcium Level

Introduction

Jaundice refers to the yellow appearance of the skin that occurs with the deposition of bilirubin in the dermal and subcutaneous tissue [1]. Normally in the body, bilirubin is processed through the liver, where it is conjugated to glucuronic acid by the enzyme uridine diphosphate glucuronyl transferase (UGT). This conjugated form of bilirubin is then

excreted into the bile and removed from the body via the gut [2-3]. When this excretion process is low following birth, does not work efficiently, or is overwhelmed by the amount of endogenously produced bilirubin, the amount of bilirubin in the body increases, resulting in hyperbilirubinaemia and jaundice [4]. Over 60% of all term new-borns develop jaundice in their first days of life. A significant proportion of causes of hyperbilirubinaemia in the term newborn are benign and reversible [1]. However, considering the potentially irreversible toxicity of bilirubin on the central nervous system (kernicterus), new-borns must be evaluated to identify which ones will need treatment.

One of the most important treatments for controlling jaundice in babies is phototherapy. In cases of lack of response to phototherapy or very high and severe amounts of jaundice, blood exchange is used [5].

Since the 1950s, phototherapy has been the therapy of choice for the newborn with indirect hyperbilirubinemia [6]. The efficacy of phototherapy depends mainly on the intensity and wavelength of the light and also on the proportion of skin area exposed to light [1,4-6]. Single phototherapy (SP) is the most commonly used method, and when bilirubin levels are close to the threshold for exchange transfusion, intensive phototherapy is indicated [6]. This can be obtained by increasing the surface area of the newborn exposed to light and the intensity of phototherapy using lateral panels, reflecting objects and fiber-optic blankets. Among them, a second lateral panel, also known as double phototherapy (DP), is frequently used [7,8].

The possible adverse effects associated with phototherapy are skin rash, increased insensible losses, and retinal damage, hyperthermia, and deposition alterations due to increased intestinal flow. Phototherapy has very few effects. Sometimes it causes diarrhoea and dehydration of the baby [1]. In some cases, it also causes skin rashes on the baby's body. One of the most important disadvantages is the variation in the level of some of the electrolytes, such as calcium, which plays a role for many vital reactions [1,3-6]. Considering the high prevalence of jaundice in neonates and the low level of studies in Iran on the efficacy and complications of various phototherapy techniques, the aim of the present study was to comparatively evaluate the efficacy of DP and SP in changes of serum calcium levels in term newborns with hyperbilirubinaemia.

Methods

All newborns admitted to infants unit of Bahar hospital of Shahroud, between March 2020 and February 2021, for phototherapy with the diagnosis of hyperbilirubinaemia were included in the study if they met the following inclusion criteria: gestational age greater or equal to 36 weeks; nonhemolytic hyperbilirubinaemia (negative direct Coombs' test and no other sign of hemolysis); more than 24 hours and less than 9 days of life; no signs of sepsis or congenital malformations; indication for phototherapy following criteria recommended by the American Academy of Pediatrics [9] and consent of the parents. So, exit criteria include: the presence of symptoms of infections and neonatal sepsis; acute electrolyte impairment requiring rapid intervention; the presence of any underlying disease; seizure; direct hyperbilirubinaemia; high bilirubin requiring blood transfusion; non-oral feeding; diabetic mother; asphyxia; maternal anticonvulsant medications; IUGR; premature and less than 24 hours of birth [1]. The patients were randomly divided into two groups: A (double phototherapy) and B (single phototherapy), with the help of random quadrilateral blocks.

Phototherapy and bilirubin measurements: SP was administered using standard phototherapy apparatus (Air-Shields Clinic Equip or ICR), with six fluorescent tubes (two blue and four white 20-watt lamps in each tube with a life span of at least 2500 hours at a frequency of 420 to 470 nm). To DP patients a second lateral panel with similar characteristics was placed at 90 degrees to the first panel. The panels were positioned at 30-40 cm from the patients, who were unclothed but with diapers [9].

For both groups nursing care was similar, with special emphasis on eye protection and temperature control. Phototherapy was administered continuously, being interrupted only for infant feeding and weighing, physical examination, and bilirubin and calcium measurements by with standard laboratory method. In both groups, weight, bilirubin and calcium levels were controlled at admission and at 24-hour intervals and temperature were controlled at admission and at 8-hour intervals for 72 hours. All babies were fed breastfeeding during phototherapy and used breast milk. Hypocalcemia was considered to be less than 7.5 mg/dl in the term neonates [1]. Hyperthermia, weight loss (in two or more control examinations) or significant skin rashes were considered as adverse effects of therapy. In this kind of circumstances, cut off phototherapy and the baby were excluded from the study. The data were recorded in a computer and analyzed by SPSS software version 16 and related statistical tests such as student's t-test and chi-square and Repeated measure test for comparing the two groups. Also, $p<0.05$ was considered significant in this study. In doing this research, were observed all the ethical requirements of the research, and oral satisfaction were obtained from all parents of infants. The patients who fit the inclusion criteria of our study were approached by the all authors that described the study in details. The all parents of patients were assured of the confidentiality of the data and were told they could withdraw from the study at any

time. The parents were also assured that not participating, or withdrawing after giving consent, would not affect the quality of care provided.

This study has an ethics code number from research deputy of Shahroud University of Medical Sciences. The essential information and the objectives of the study were explained to the parents of all babies, and written consent was obtained for participation in the plan.

Results

Between March 2020 and February 2021, 65 patients were randomized for SP and 65 for DP. Of the 130 neonates, 73 neonates (56.2%) were male and the rest were female, that no difference was seen between the two groups. So, the groups were matched for demographic and clinical characteristics that there was no significant difference between the two groups. The results of the demographic, clinical and laboratory findings of the two groups are shown in Table 1.

Demographic & characteristics Clinical	Double photother Number/Mean (%/SD)apy	Single photother Number/ Mean (%/SD)apy	Total Number/Mean (%/SD)	P-value
Sex				
Male	36 (55.4)	37 (56.9)	73 (56.2)	0.129
Female	29 (44.6)	28 (43.1)	57 (43.8)	
Nutrition				
Breast milk	61 (93.8)	59 (90.7)	120 (92.3)	0.069
Milk powder	4 (6.2)	6 (9.3)	10 (7.7)	
Type of delivery				
Normal	47 (72.3)	49 (75.4)	96 (73.8)	0.103
Cesarean section	18 (27.7)	16 (24.6)	34 (26.2)	
Average fetal age (week)	37.5 ± 1.5	37.9 ± 1.1	37.6 ± 1.8	0.085
Average age (day)	6.1 ± 2.3	5.3 ± 2.8	5.7 ± 2.7	0.055
Average weight (gram)	2683.5 ± 460.7	2591.7 ± 510.5	2628.6 ± 485.3	0.112
Average calcium Beginning of the study (mg/dl)	9.9 ± 0.5	9.9 ± 0.4	9.9 ± 0.3	0.183
Average indirect bilirubin Beginning of the study (mg/dl)	18.5 ± 2.8	18.8 ± 3.1	18.6 ± 2.9	0.123
Average indirect bilirubin End of the study (mg/dl)	10.4 ± 0.8	14.3 ± 1.3	12.2 ± 1.1	0.002

Table1: Comparison of Demographic and Clinical Data in Two Groups.

Also, the calcium reduction after 72 hours in the DP group was 9.9± 0.5 to 8.3± 0.7 mg/dl and in the SP group it was 9.9± 0.4 to 8.6± 0.4 mg/dl, which did not differ significantly (p = 0.125). The results of the study showed that there was no significant difference between the mean values of calcium in the two groups. Also, the results showed that with time, the amount of calcium in both groups was decreased, but the effect of interaction between time and group was not significant; there was no significant difference between the groups over time. Changes in calcium levels in two groups' infants in different hours of intervention (phototherapy) are shown in Table 2.

	Double Phototherapy Mean±SD	Single Phototherapy Mean±SD	Intervention	Time	Intervention on Time
24 hours after phototherapy	9.3 ± 0.4	9.4 ± 0.3	f=0.023	f=10.3	f= 15.8
48 hours after phototherapy	8.9 ± 0.3	8.9 ± 0.4	p=0.999	p=0.473	p=0.125
72 hours after phototherapy	8.7 ± 0.3	8.6 ± 0.4			

Table 2: Comparison of Calcium in Two Groups at Different Times of Intervention.

Discussion

In the present study, the average amount of calcium in both groups decreased by 72 hours after phototherapy, but there was no significant difference between the two groups at different times. Also, double phototherapy with an additional lateral panel produced a greater decrease in the bilirubin level at 72 hours of treatment in term new-borns with nonhemolytic hyperbilirubinaemia. Neonatal jaundice is one of the diseases that have long been the subject of a wide range of opinions about the treatment of the general population, like the blade to the forehead or baby's ears, feeding with sugar juice, bathing and giving plants such as clay milk that has recently been considered by the researchers and is an important point that mothers' knowledge and attitude about neonatal jaundice will play an important role in the outcome of the illness [10,11]. On the other hand, the time of delivery of new-born babies in the hospital was shortened due to the early discharge of mothers. Diagnosis and timely treatment of jaundice in early life can prevent serious complications [12].

Problems with admission and hospitalization are one of the barriers to timely action in these patients [11]. The results of various studies show that double phototherapy is more secure and effective of standard phototherapy due to prolonged hospitalization, repeated blood sampling, physical and mental stress inflicted on parents and problems such as high cost of long-term stay in children, on the other hand, some studies do not have a definite opinion in this field and do not consider double phototherapy as an ideal method to reduce jaundice in new-borns [13-15].

In Shoris et al.'s study, it was stated that although phototherapy is usually the preferred option to reduce neonatal hyperbilirubinemia and is considered safe, evidence in recent years has shown that this treatment may be not free of side effects and adverse short-term and long term outcomes. It is necessary to shorten the duration of exposure to phototherapy, and therefore the use of double phototherapy should be done with more precision and control [14] Wang et al., showed that although phototherapy is recognized as the first choice for the treatment of neonatal jaundice worldwide due to its unique efficacy and safety in reducing high levels of free serum bilirubin and limiting its neurotoxic effects, it may cause creating a series of adverse short-term and long-term complications related to children's diseases such as hemolysis, allergic diseases, DNA damage or even cancer, so it is necessary to consider a standard phototherapy program with minimum duration and light intensity in neonatal clinics [15].

Various complications were mentioned for phototherapy, such as increased body temperature and ambient temperature, increased immersion of water and loose stools, are associated with increased secretion of non-conjugated bilirubin in the intestine. One of the important complications of phototherapy is hypocalcaemia, whose mechanism is not known correctly [12]. Hypocalcemia is one of the side effects of phototherapy, the prevalence of which is about 14%. It was also found that the prevalence of this complication is higher in premature babies than in term or full-term babies. One of the most common causes of hypocalcemia in these babies is hypercalciuria [16]. It may be because of the decrease in melatonin due to phototherapy or increased intestinal peristaltism and its absorption impairment [11-13] Ebbesen et al., stated that reducing the concentration of bilirubin in infants should be done carefully and relatively slowly because a very low concentration of serum bilirubin can cause neurodevelopmental disorders in very low birth weight infants (EBWL) and even their death. The intensity and duration of phototherapy (single or double) can be very important in this field [17]. In Nuntnarumit et al.'s study, 25% of preterm infants and 10% of term neonates experienced hypocalcaemia after phototherapy [18].

However, in the present study, although the mean amount of calcium in the duration of phototherapy was decreased in both groups, none of the newborns had hypocalcemia that may be because of repeated breastfeeding and sufficient fluid intake. This finding is consistent with the results of Zarinkob and Javadi studies [19,20]. Even in some studies, it has

been shown that electrolyte changes in babies undergoing phototherapy are not limited to calcium, but also occur in other electrolytes, including magnesium [21]. Phototherapy has little adverse effects with an appropriate nursing care. Consequently, it was not surprising that no adverse effects were observed in our patients.

Limitation

The limitation of the present study is that most patients had only moderate hyperbilirubinemia. However, the strength of this study is that it is based on common clinical practice with little evidence in clinical trials.

Conclusion

Finally, this study showed that although single and standard phototherapy is an effective and common method to control hyperbilirubinemia, it seems that double phototherapy can accelerate the reduction of serum bilirubin and does not have significant changes in calcium levels, but according to the contradictory results of different studies, more studies and a larger sample size are needed for final confirmation.

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