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ORIGINAL ARTICLE

To investigate the electrolyte alterations in newborns ≥ 35 weeks gestation and undergoing phototherapy for neonatal jaundice

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ABSTRACT:
Aim: To investigate the electrolyte alterations in newborns ≥ 35 weeks gestation and undergoing phototherapy for neonatal jaundice. **Material and methods:** Neonates who were born or admitted to a tertiary care centre , receiving Light Emitting Diode(LED) phototherapy for unconjugated hyperbilirubinemia after 24 hrs of life without any co-morbidities were involved in the study. Neonates receiving phototherapy for unconjugated hyperbilirubinemia after 24 hrs of life without any co-morbidities were included in the study. Venous blood samples were collected from the neonates during the course of phototherapy and sent for total bilirubin, direct bilirubin, electrolytes, and blood group. **Results:** Mean bilirubin at the time admission was 17.65±2.58 and after phototherapy there were significant decrease in bilirubin 13.06±1.96. Mean urea at the time admission was 36.78± 4.63 and after phototherapy there were significant decrease in urea 29.96±4.37, and, mean creatinine at the time admission was 0.91±0.11 and after phototherapy there were significant decrease in creatinine 0.77±0.11. The mean sodium, potassium and calcium level before therapy were 148.50±3.96, 5.11±0.77, and 9.58±0.96 respectively. After phototherapy the mean sodium, potassium and calcium level were 141.36±3.47, 4.36±0.78 and 8.36±0.55 respectively. There was significant difference in sodium level before and after phototherapy with p-value= 0.03. But, in level of Potassium there But, in level of Potassium there was no significant difference (p=0.41) due to phototherapy before and after. **Conclusion:** Neonatal hyperbilirubinemia can easily pickup on clinical examination however require quick and on the spot treatment. If not treated properly, it leads to many complications. Currently the best treatment option for jaundice is photo therapy. Phototherapy is not a treatment free of side effects and further studies need to be conducted to elucidate its harmful effects on neonates.
Keywords: Electrolyte Changes, Phototherapy , Neonatal Jaundice

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INTRODUCTION

Neonatal hyperbilirubinemia is a common clinical problem encountered during the neonatal period. High serum bilirubin levels can be toxic for central nervous system development and may cause behavioral and neurological impairment (Kernicterus) even in term newborns[1]. Pathological jaundice may also lead to deafness, cerebral palsy and/or mental retardation[2]. Several risk factors have been identified for the occurrence of exaggerated or severe unconjugated hyperbilirubinemia out of which low birth weight and preterm birth are the major risk factors for exaggerated jaundice warranting intervention[3]. Neonatal hyperbilirubinemia nearly affects 60% of term and 80% of preterm neonates during first week of life[4].The treatment options for jaundice include phototherapy further subdivided to conventional, intensive and exchange transfusion, and pharmacological treatment subdivided to phenobarbitone, intravenous immunoglobulins (IVIG), metallo-porphyrins and follow-up remedies[5]. Phototherapy is one of the most effective way available in preventing the neurotoxic complications of indirect hyperbilirubinemia[6]. It leads to changes in the structure of bilirubin, and the resulting isomers, lumirubin which is radially excreted in bile and urine[7]. Phototherapy is safe, but is only used when needed (usually for two to three days after which the baby's liver takes over). The commonly known side effects of phototherapy are loose stools, hyperthermia, dehydration fluid loss, skin burn, photo retinitis, low platelet count, increased red cell osmotic fragility, bronze baby syndrome, riboflavin deficiency and DNA damage. A lesser known side effect, but potential complication of phototherapy is electrolyte imbalance specially hypocalcaemia[8].

MATERIAL AND METHODS

It is a prospective interventional study. Ethical clearance was obtained from institutional ethical committee. Neonates who were born or admitted to a tertiary care centre, receiving Light Emitting Diode(LED) phototherapy for unconjugated hyperbilirubinemia after 24 hrs of life without any co-morbidities were involved in the study.

Neonates receiving phototherapy for unconjugated hyperbilirubinemia after 24 hrs of life without any co-morbidities were included in the study.

Neonates with evidence of Hemolysis, Onset of jaundice < 24 hrs. & received exchange transfusion, Neonates with Conjugated Hyperbilirubinemia , Neonates who receive I.V. fluid and intensive care, Neonates with formula feeding and Neonates with co-morbidities like birth asphyxia, septicaemia, acute renal failure and others were excluded from the study.

METHODOLOGY

All enrolled neonates were subjected for the test of serum level of sodium potassium and calcium at the time of admission along with serum bilirubin levels at the start of phototherapy and at the intervals of 24 hours, 48 hours or at the discontinuation of phototherapy whichever earlier. Informed and written consent were obtained from the parents of all enrolled neonates blood samples of neonate withdraw for regular biochemical examination were used for analysis of electrolytes before phototherapy. Venous blood samples were collected from the neonates during the course of phototherapy and sent for total bilirubin, direct bilirubin, electrolytes, and blood group. Total direct bilirubin is measured by Diazo method: electrolytes (Na, K,) by auto analyser Erba EM 200 machine and calcium by Arsenazo method. Blood group of new-borns was analysed by antisera method. Electrolytes were checked at 0 hour (first sample) at the start of phototherapy and at after 24 hours, 48 hours and at the discontinuation of phototherapy (second sample). The first sample was considered as control. Comparative study was made between these two sample groups to determine the changes in electrolytes.

Data was entered in Microsoft Excel sheet and analysed using SPSS v 23.0 for frequencies, mean, standard deviation, Chi square test and Paired T test.

RESULTS

A total of 120 neonates were involved of which 70 were males and 50 were. Mean bilirubin at the time admission was 17.65±2.58 and after phototherapy there were significant decrease in bilirubin 13.06±1.96. Mean urea at the time admission was 36.78± 4.63 and after phototherapy there were significant decrease in urea 29.96±4.37, and, mean creatinine at the time admission was 0.91±0.11 and after phototherapy there were significant decrease in creatinine 0.77±0.11. The mean sodium, potassium and calcium level before therapy were 148.50±3.96, 5.11±0.77, and 9.58±0.96 respectively. After phototherapy the mean sodium, potassium and calcium level were 141.36±3.47, 4.36±0.78 and 8.36±0.55 respectively. There was significant difference in sodium level before and after phototherapy with p-value= 0.03. But, in level of Potassium there But, in level of Potassium there was no significant difference (p=0.41) due to phototherapy before and after. Before phototherapy none of baby had hyponatremia while after phototherapy 8.33% cases had hyponatremia. Similarly, hypocalcaemic was present in 5% cases before phototherapy and after phototherapy 30% cases had hypocalcaemic which was found significant statistically. However, serum potassium was almost normal before and after phototherapy. Sodium and calcium were found statistically significant with p-value=0.03 and 0.02 respectively.

There was a significant difference in mean bilirubin, sodium and calcium after therapy as compared to before therapy (p-value=0.001, 0.03, and 0.02 respectively). But the difference was statistically non-significant in potassium, urea and creatinine after and before therapy (p-value=0.41, 0.07 and 0.24) (Table 1).

Hypocalcemia was found more in cases (12.86%) below 3 days old as compared above 3 days old cases (8%) as shown in Table 2. The difference was not statistically significant. In low birth weight group before phototherapy (12.5%) patients had hypocalcaemic and in normal birth weight (10%) patients had hypocalcaemic before therapy. But after phototherapy (14.55%) patients in low birth weight group and (7.69%) in normal weight group had hypocalcaemic respectively. Incidence of hypocalcaemic increases after phototherapy in low weight babies as compared to normal weight. Similarly, there is a hyponatremia in low birth weight babies after phototherapy as compared to patients before phototherapy. The difference was statistically significant (p-value=0.04). (Table 3)

Table 1: Mean serum parameters before and after phototherapy

Variables	Before phototherapy		After phototherapy		P value
	Mean	SD	Mean	SD	
Bilirubin (mg/dl)	17.65	2.58	13.06	1.96	0.001
Urea (mg/dl)	36.78	4.63	29.96	4.37	0.07
Creatinine (mg/dl)	0.91	0.11	0.77	0.11	0.24
Sodium (mEq/L)	148.5	3.96	141.36	3.47	0.03
Potassium (mEq/L)	5.11	0.77	4.36	0.78	0.41
Calcium (mEq/L)	9.58	0.96	8.36	0.55	0.02

Table 2: Prevalence of Hypocalcemia according to their age

Calcium level	≤3 days old=70	>3 days old=50	Total	P value
<8.0 mg/dl	9 (12.86%)	4 (8%)	13 (10.83%)	0.65
≥8.0 mg/dl	61 (87.14%)	46 (92%)	107 (89.17%)	

Table 3: Association of post phototherapy serum electrolytes with birth weight

	Electrolytes	Low birth weight=55	Normal birth weight=65	Total	P value
Sodium	<135 mEq/L	40	30	70	0.04
	>135 mEq/L	15	35	50	
Potassium	3.5-5.5 (mEq/L)	39	51	90	0.32
	>5.5 (mEq/L)	16	14	30	
Calcium	<8.0 (mg/dl)	8	5	13	0.41
	≥8.0 mg/dl	47	60	107	

DISCUSSION

Neonatal jaundice is one of the leading causes of NICU admission, and phototherapy is one of the best and safe methods as a treatment option in neonatal jaundice as described by Cremer et al[9]. Every safe method has its own side effects. One of the known side effects of phototherapy is the disturbance in serum electrolytes specially the changes in serum calcium level. Romagnoli was the first to observe the association of hypocalcemia as an effect of phototherapy among the preterm neonates[9]. Hakinson and Hunter have hypothesized that phototherapy inhibits the pineal secretion of melatonin, which blocks the effect of cortisol on bone calcium[11,12]. So, cortisol increases the bone uptake of calcium and induces hypocalcemia. A total of 120 neonates were involved of which 70 were males and 50 were.

In this study there was significant decrease in total and direct bilirubin at the time of admission and after 24-hour phototherapy. Mean bilirubin at the time admission was 17.65±2.58 and after phototherapy there were significant decrease in bilirubin 13.06±1.96. Mean urea at the time admission was 36.78± 4.63 and after phototherapy there were significant decrease in urea 29.96±4.37, and, mean creatinine at the time admission was 0.91±0.11 and after phototherapy there were significant decrease in creatinine 0.77±0.11, which are similar to study done by Watchko JF et al[13].In a study by Kaini NR et al, observed that there were marked alterations were observed in levels of bilirubin profile markers, in patients of Neonatal hyperbilirubinemia after receiving phototherapy[14]. There occurred significant decrease in Serum creatinine levels following phototherapy whereas decrease in urea levels were insignificant. In this study the mean sodium, potassium and calcium level before therapy were 148.50±3.96, 5.11±0.77, and 9.58±0.96 respectively. After phototherapy the mean sodium, potassium and calcium level were 141.36±3.47, 4.36±0.78 and 8.36±0.55 respectively. There was significant difference in sodium level before and after phototherapy with p-value= 0.03. But, in level of Potassium there But, in level of Potassium there was no significant difference (p=0.41) due to phototherapy before and after. But, in level of potassium there was no significant difference due to phototherapy[12]. The p-value is 0.31. Study by Reddy et al found similar results[15]. They found that the frequency of potassium and chloride imbalances was found to be non- significant (p value of potassium vs chloride was 0.967 versus 0.085 respectively) with duration of phototherapy. Overall, there was significant decline in serum calcium and sodium along with total bilirubin following phototherapy.

Huang MJ et al were found following phototherapy the mean values of all the electrolytes were significantly decreased[16]. Kumral A et al, found that there was significant decline in serum sodium and potassium along with total bilirubin following 48 hours of phototherapy[17]. Narayan S et al, found that after phototherapy about 67% babies had a decrease in serum calcium level from the initial value[18]. Out of these 30% babies had a 5-9% reduction and 20% babies had >10% reduction in serum calcium value. This reduction in serum calcium level was found to be statistically significant (p value - <0.001). Even though 65% babies had a reduction in calcium value only 5% babies developed hypocalcemia after phototherapy. These results are comparable with an Iranian study done by Eghbalian F et al, reported that out of 147 term babies about 56% babies had a reduction in serum calcium level after phototherapy and 7% newborns developed hypocalcemia after 48 hours of phototherapy[19].In the present study there were hyponatremia and hypocalcemia after phototherapy. Hypocalcemia was found more in cases (12.86%) below 3 days old as compared above 3 days old cases (8%). Level of Potassium was almost normal before and after phototherapy. In this study authors found hypocalcemia in cases below 3 days old as compared above 3 days old patients. It is found that Phototherapy has emerged as the most widely used form of treatment and is the current therapy of choice to reduce severity of neonatal unconjugated hyperbilirubinemia. In study by Reddy et al, also found that the frequency of hypocalcemia following phototherapy was more in preterm neonates (41.2%) than in term neonates (6.2%)[15].

In study by Huang MJ et al were found similar results with 41.3% cases had hypocalcemia after phototherapy[16]. They found that the incidences of hypocalcemia are also more in LBW (26.25%, 10% respectively) than in normal neonates (7.94%, 4.76%). Based on this study it is suggested that, even though the prevalence of hypocalcemia is less there is significant reduction in serum calcium level in term newborns undergoing phototherapy, so it is better to monitor S. calcium level in newborns treated with phototherapy for 48 hours or more. Authors recommend further and larger studies needed for

estimation of prevalence of hypocalcemia in phototherapy.

CONCLUSION

Neonatal hyperbilirubinemia can easily pickup on clinical examination however require quick and on the spot treatment. If not treated properly, it leads to many complications. Currently the best treatment option for jaundice is photo therapy. The use of neonatal phototherapy must be judicious and aimed only at neonates who really need it, following the recommended guidelines and always weighing the risks and benefits of the treatment for neonates. It has proved to cause electrolyte imbalance especially hyponatremia and hypocalcemia. Phototherapy is not a treatment free of side effects and further studies need to be conducted to elucidate its harmful effects on neonates.

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