

SERUM SODIUM CHANGES IN NEONATES RECEIVING PHOTOTHERAPY FOR NEONATAL HYPERBILIRUBINEMIA

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ABSTRACT: BACKGROUND: Neonates receiving phototherapy have side effects like hypocalcemia and electrolyte changes. Our study is hereby intended to study the serum sodium changes due to phototherapy. **AIMS:** To evaluate the serum sodium changes in neonates receiving phototherapy for neonatal hyperbilirubinemia. **SETTINGS AND DESIGN:** A prospective hospital based comparative study conducted on neonates admitted in the Neonatal Intensive Care Unit receiving phototherapy. **METHODS AND MATERIAL:** A predesigned proforma has aided the enrollment of 252 newborns into the study. Serum bilirubin and serum sodium were determined before and after termination of phototherapy. The first samples were considered as controls. A comparative study was made between before and after phototherapy groups to determine the incidence of serum sodium imbalances. **STATISTICAL ANALYSIS USED:** Proportions will be compared using chi-square test. All data of various groups will be tabulated and statistically analyzed using suitable statistical tests (Student's t test). **RESULTS:** Male to Female ratio was 1.45:1. Incidence of low birth weight babies was 23% and preterm was 20.2%. Mean birth weight and gestational age was 2.84±0.51 kg and 38.44±1.98 wks respectively. Mean duration of phototherapy was 37.65±11.06 hrs. The incidence of hyponatremia post phototherapy found to be 6% which was more in low birth weight (LBW) babies (17.2%, $p < 0.001$) and preterm neonates (17.6%, $p < 0.001$) than in normal weight babies (2.6%) and term neonates (3.1%) and in 17.4% babies when duration of phototherapy was >48 hrs ($p < 0.001$). Even the decline in mean serum sodium values after phototherapy found to be statistically significant. **CONCLUSION:** Our study shows that neonates under phototherapy are at higher risk of hyponatremia. This risk is greater in premature and LBW babies and hence this group of babies should be closely monitored for changes in serum sodium and should be managed accordingly.

KEYWORDS: Serum sodium, Neonatal Hyperbilirubinemia, Phototherapy.

INTRODUCTION: Neonatal hyperbilirubinemia (NH) is commonest abnormal physical finding during the first week of life. Over two third of newborn babies develop clinical jaundice. The physical finding like yellowish discoloration of the skin and sclera in newborns is due to accumulation of unconjugated bilirubin. In most infants, unconjugated hyperbilirubinemia reflects a normal physiological phenomenon.^[1] Neonatal hyperbilirubinemia nearly affects 60% of term and 80% of preterm neonates during first week of life. Nevertheless untreated, severe unconjugated hyperbilirubinemia is potentially neurotoxic and conjugated hyperbilirubinemia is a harbinger of underlying serious illness.^[2]

ORIGINAL ARTICLE

Neonatal hyperbilirubinemia is a reflection of liver immature excretory pathway for bilirubin and is the most common reason for readmission of neonates in first week of life in current era of postnatal discharge from hospital.^[3] Neonatal hyperbilirubinemia is a cause of concern for the parents as well as for the pediatricians.^[4] Premature babies have much higher incidence of neonatal jaundice requiring therapeutic intervention than term neonates. Hyperbilirubinemia was found to be the most common morbidity 65% among 137 extremely low birth weight neonates born over a period of 7 years in AIIMS.^[5]

Elevated levels of unconjugated bilirubin can lead to bilirubin encephalopathy and subsequently kernicterus, with devastating, permanent neurodevelopment handicaps. Hence appropriate management of neonatal hyperbilirubinemia is of paramount importance. Hyperbilirubinemia can be treated either by phototherapy or exchange transfusion or pharmacologic agents. Phototherapy plays a significant role in prevention and treatment of hyperbilirubinemia. The main demonstrated value of phototherapy is that it reduces the need for exchange transfusion. Phototherapy also have its adverse effects like hyperthermia, feed intolerance, loose stools, skin rashes, bronze baby syndrome, retinal changes, dehydration, hypocalcemia, redistribution of blood flow and genotoxicity.^[4-6]

Unlike other side effects a very few studies are currently available that depicts the adverse effects of phototherapy on serum sodium. One of the side effects of phototherapy is diarrhea. As diarrhea can lead to electrolyte changes, and as hypocalcemia is already a known fact, our study is hereby intended to study the serum sodium changes due to phototherapy.

MATERIAL AND METHODS: A prospective hospital based comparative study conducted on 252 eligible neonates admitted in the Neonatal Intensive Care Unit receiving phototherapy at Adichunchanagiri Hospital and Research Center, B. G. Nagara from December 2013 to May 2014. Neonates receiving phototherapy for unconjugated hyperbilirubinemia without any co-morbidity like birth asphyxia, septicemia and renal failure were included in the study. Neonates with conjugated hyperbilirubinemia, with abnormal electrolyte status detected before start of phototherapy, whose mother had history of taking anti-convulsants, fed with cow's milk, who had exchange transfusion, with jaundice lasting more than 14 days of life were excluded in the study. Ethical clearance was sorted from institute ethical clearance committee. Written informed consent was taken from the subjects prior to enrollment of study. Data was collected by using pre-tested proforma meeting the objectives of the study.

Venous blood samples were collected from the neonates included in the study and sent for total bilirubin, direct bilirubin and serum sodium. Total and direct bilirubin was measured by Diazo method (Diazotized sulfanilic test). Serum sodium was measured by autoanalyser Erba EM 200 Machine.

Serum sodium was checked at 0 hour (first sample) and at 48 hours of phototherapy or at discontinuation of phototherapy (second sample) whichever is earlier. The first samples were considered as controls. Comparative study was made between these two sample groups to determine the changes in serum sodium.

Collected data were compared using chi-square test. All data of various groups were tabulated and statistically analyzed using suitable statistical tests (Student's t test).

ORIGINAL ARTICLE

RESULTS: 252 neonates were enrolled in study, out of which males and females were 59.1% (149) and 40.9% (103) respectively. Incidence of low birth weight babies was 23% and mean birth weight was 2.84±0.51 kg. The incidence of preterm babies were 20.2% (51), 77% (194) were in between 37-40 wks gestational age and 2.8%⁽⁶⁾ were >40 wks gestational age. Mean gestational age in the study group was 38.44±1.98 wks. 69.8% of the study group was born by normal vaginal route and 30.2% by caesarian section. In the study group, 47.6% neonates were born to primi mothers and 52.4% born to multigravida mothers.

| Serum sodium level (mEq/L) | Gender | | Total (n=252) | P value |
|----------------------------|--------------|----------------|---------------|---------|
| | Male (n=149) | Female (n=103) | | |
| <135 | 9(6%) | 6(5.8%) | 15(6%) | 0.806 |
| 135-145 | 137(91.9%) | 96(93.2%) | 233(92.5%) | |
| >145 | 3(2%) | 1(1%) | 4(1.6%) | |

Table 1: Sex ratio of serum sodium imbalance

Table 1 shows following phototherapy, 15 neonates out of the 252 in study group showed serum sodium levels of <135 mEq/L and only 4 neonates showed serum sodium >145mEq/L. 6%⁽⁷⁾ of the male babies in the study population and 5.8%⁽⁸⁾ of the female babies developed hyponatremia following phototherapy. P value found to be 0.806 (not significant) indicating that there is no sex difference in the occurrence of hyponatremia. Thus, the incidence of hyponatremia in our study group post phototherapy was found to be 6%.

| Serum sodium level (mEq/L) | Weight(kg) | | Total (n=252) | P value |
|----------------------------|------------|----------------|---------------|---------|
| | LBW (n=58) | Normal (n=194) | | |
| <135 | 10(17.2%) | 5(2.6%) | 15(6%) | <0.001 |
| 135-145 | 48(82.8%) | 185(95.4%) | 233(92.5%) | |
| >145 | 0(0%) | 4(2.1%) | 4(1.6%) | |

Table 2: Correlation of post phototherapy serum sodium with birth weight

Table 2 shows the incidence of hyponatremia following phototherapy was also more in low birth weight babies (17.2%) than in normal babies (2.6%). Thus it infers that low birth weight babies were at more risk of hyponatremia following phototherapy than term babies. The p value obtained was <0.001, which was considered to be statistically significant.

| Serum sodium level (mEq/L) | Gestational age | | | Total (n=252) | P value |
|----------------------------|-----------------|-------------------|---------------|---------------|---------|
| | <37 wks (n=51) | 37-40 wks (n=194) | >40 wks (n=7) | | |
| <135 | 9(17.6%) | 6(3.1%) | 0(0%) | 15(6%) | <0.001 |
| 135-145 | 42(82.4%) | 185(95.4%) | 6(85.7%) | 233(92.5%) | |
| >145 | 0(0%) | 3(1.5%) | 1(14.3%) | 4(1.6%) | |

Table 3: Correlation of post phototherapy serum sodium with gestational age

ORIGINAL ARTICLE

Table 3 shows the Incidence of hyponatremia following phototherapy was more in preterm neonates (17.6%) than in term neonates (3.1%). Thus it infers that preterm babies were at more risk of hyponatremia following phototherapy than term babies. The p value obtained was <0.001, which was considered to be statistically significant.

| Serum sodium level (mEq/L) | Duration of phototherapy | | | Total (n=252) | P value |
|----------------------------|--------------------------|-------------------|----------------|---------------|---------|
| | <24 hrs (n=7) | 24-48 hrs (n=176) | >48 hrs (n=69) | | |
| <135 | 0(0%) | 3(1.7%) | 12(17.4%) | 15(6%) | <0.001 |
| 135-145 | 7(100%) | 171(97.2%) | 55(79.7%) | 233(92.5%) | |
| >145 | 0(0%) | 2(1.1%) | 2(2.9%) | 4(1.6%) | |

Table 4: Correlation of post phototherapy serum sodium with duration of phototherapy

Table 4 shows the mean duration of phototherapy was 37.65±11.06 hrs. The Incidence of hyponatremia was 17.4% when duration of phototherapy was >48 hrs as compared to duration <48 hrs (1.6%). Thus it infers that babies were at higher risk of hyponatremia if kept under phototherapy for more than 48 hrs. The p value obtained was <0.001, which was considered to be statistically significant.

| Variables | Before phototherapy | After Phototherapy | Difference | t value | P value |
|-----------------------------|---------------------|--------------------|------------|---------|---------|
| GA <37 wks (n=51) | | | | | |
| Total bilirubin | 16.98±1.78 | 11.43±1.74 | 5.553 | 20.084 | <0.001 |
| S. Sodium | 138.35±3.03 | 136.37±3.40 | 1.980 | 4.114 | <0.001 |
| GA 37-40 wks (n=194) | | | | | |
| Total bilirubin | 17.52±1.91 | 12.03±1.69 | 5.492 | 34.185 | <0.001 |
| S. Sodium | 139.26±3.14 | 138.56±3.18 | 0.701 | 3.062 | 0.003 |
| GA >40 wks (n=7) | | | | | |
| Total bilirubin | 16.84±1.47 | 12.63±1.32 | 4.214 | 8.136 | <0.001 |
| S. Sodium | 137.29±2.14 | 140.14±3.85 | 2.857 | 1.964 | 0.097 |

Table 5: Comparison of mean total bilirubin and serum sodium before and after phototherapy with gestational age (GA)

Table 5 shows in our study the decline in the mean serum sodium was noted in <37 wks and 37-40 wks gestational age groups and an incremental trend in >40 wks. However the decline was found to be more statistically significant in <37 wks gestation (p<0.001) than in 37-40 wks (p=0.003). The incremental trend in >40 wks gestation was found to be non-significant (p=0.097).

ORIGINAL ARTICLE

| Variables | Before phototherapy | After Phototherapy | Difference | t value | P value |
|-----------------------|---------------------|--------------------|------------|---------|---------|
| LBW (n=58) | | | | | |
| Total bilirubin | 16.72±1.80 | 11.17±2.00 | 5.553 | 18.910 | <0.001 |
| S. Sodium | 138.47±3.00 | 136.86±3.58 | 1.603 | 3.691 | 0.001 |
| Normal (n=194) | | | | | |
| Total bilirubin | 17.60±1.86 | 12.15±1.54 | 5.443 | 35.143 | <0.001 |
| S. Sodium | 139.19±3.14 | 138.55±3.21 | 0.639 | 2.672 | 0.008 |

Table 6: Comparison of mean total bilirubin and serum sodium before and after phototherapy with birth weight

Table 6 shows in our study the decline in the mean serum sodium was noted in both the groups. However the decline was found to be more statistically significant in LBW babies (p=0.001) than in normal weight. (p=0.008)

| | Pre phototherapy | Post phototherapy | Difference | t value | P value |
|-----------------|------------------|-------------------|------------|---------|---------|
| Total bilirubin | 17.39±1.88 | 11.93±1.71 | 5.469 | 39.972 | <0.001 |
| S. Sodium | 139.02±3.12 | 138.16±3.36 | 0.861 | 4.087 | <0.001 |

Table 7: Conclusive comparative evaluation of study variables pre and post phototherapy in neonates

Table - 7 shows overall there was significant decline in serum sodium along with total bilirubin following phototherapy.

DISCUSSION: Neonatal Hyperbilirubinemia (NH) is the commonest abnormal physical finding during the first week of life. Early discharge of healthy term newborns from the hospital after delivery has recently become a common practice for medical, social and economic reasons. However, it has been shown that newborns whose post-delivery hospital stay <72 hrs are at a significantly greater risk for readmissions than those whose stay is >72 hrs. There is concern regarding early discharge of healthy term newborns due to reports of bilirubin induced brain damage resulting in sequelae like kernicterus. The need for early detection of hyperbilirubinemia in the early discharged newborns from the hospital is therefore important. It is crucial to catalogue the babies who are at risk for significant jaundice before they are sent away from the hands of the pediatricians, and to prevent the potential bilirubin neurotoxicity so that, many of the significantly jaundiced neonates could see the light of the day from the nightmare of bilirubin encephalopathy. 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.

As any treatment has its side effects, phototherapy also has. Unlike other side effects a very few studies are currently available that depicts the adverse effects of phototherapy on serum electrolytes. A few studies in the recent past, have stressed on the incidence of hypocalcemia following phototherapy and very few studies till date regarding the effect of phototherapy on all electrolytes.

ORIGINAL ARTICLE

Hyponatremia, a very common electrolyte abnormality, is a serum sodium level <135 mEq/L. Both total body sodium and total body water determine the serum sodium concentration. Hyponatremia exists when the ratio of water to sodium is increased. This condition can occur with low, normal, or high levels of body sodium. Similarly, body water can be low, normal, or high.

Curtis MD et al studied diarrhea in jaundiced neonates treated with phototherapy. Study showed that absorption of sodium, chloride and potassium was significantly impaired in the patients receiving phototherapy.^[7] Dee Beresford and Glenys Conolly stated that babies under phototherapy can have sodium imbalances due to insufficient fluid replacements.^[9]

The differential effect of other electrolytes with phototherapy has not been studied by other workers except that for Curtis MD et al (1981).⁽⁷⁾ There are very few studies regarding phototherapy induced other electrolyte changes. Hence our study was designed to determine the serum sodium changes in neonates receiving phototherapy for neonatal jaundice.

Incidence of hyponatremia in our study group was 6% and found to be higher in <37 wks group (17.6%) and LBW babies (17.2%) than in >37 wks group (3.1%) and normal weight babies (2.6%). Mean Serum sodium levels were significantly decreased after phototherapy. As the p value <0.001, this difference is considered to be statistically significant. It is evident that in the present study phototherapy induced hyponatremia was more in preterm and LBW babies but the actual relationship in these babies with phototherapy has to be evaluated with larger sample studies for estimation of the incidence as the metabolic side effects are more common in preterm and LBW babies.

CONCLUSION: Phototherapy induced hypocalcemia is a known fact. Our study shows that neonates under phototherapy are even at higher risk of hyponatremia. Incidence of hyponatremia in our study is higher in preterm and low birth weight babies and also in babies when the duration of phototherapy is more than 48 hours. Mean Serum sodium levels were significantly decreased after phototherapy. Hence serum sodium should be checked periodically in newborn babies receiving phototherapy to detect sodium imbalances. Proper monitoring of electrolytes after phototherapy in the neonates can prevent dyselectrolytemia, in turn prevent its complications.

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ORIGINAL ARTICLE

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