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# Effect of phototherapy on serum electrolytes in neonatal hyperbilirubinemia

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## Abstract

**Introduction:** Neonatal hyperbilirubinemia is the most common clinical finding noted during the first seven days following birth. Amongst all the modalities available for management of neonatal hyperbilirubinemia, phototherapy is proven to be the safest. However, like any other intervention, phototherapy too has some of its own side effects.
**Aim & objectives:** To estimate and compare alterations in serum electrolytes of healthy term neonates before and after phototherapy.
**Material & methods:** A hospital based prospective observational comparative study was conducted over a period of 18 months in the department of Pediatrics on 110 healthy term neonates with unconjugated hyperbilirubinemia who were subjected to phototherapy as per American Academy Pediatrics guidelines. Electrolytes including sodium, potassium, chloride and calcium were analyzed from serum using standard laboratory techniques.
**Results:** The mean sodium, chloride, potassium and calcium levels before phototherapy was 141.3±2.69 meq/L, 102.2±2.98 meq/L, 4.43±0.52 meq/L, 9.14±0.46 mg/dl and after phototherapy was 140.5±2.70 meq/L, 102.0±2.93 meq/L, 4.23±0.48 meq/L and 8.09±0.55 mg/dl respectively. All were found to be statistically significant (p-value <0.05); although none were clinically significant and conveyed no symptom of dyselectrolytemia in this study.
**Conclusion:** This study shows that neonates exposed to phototherapy are at a risk of developing electrolyte imbalances and consequently their complications. Hence, close monitoring of such babies are needed to prevent imbalances and their untoward consequences.

**Keywords:** Electrolytes, jaundice, phototherapy

## Introduction

Neonatal hyperbilirubinemia (NH) is the most common clinical problem noted during the early neonatal period. NH occurs as a consequence of unconjugated bilirubin (UCB) accumulation due to ineffective erythropoiesis, deficient liver enzymes, excess production of bilirubin, deficient conjugation and immature bilirubin excretory pathway with increased enterohepatic circulation. It manifests as yellowish discoloration of sclera and skin and is clinically evident when total serum bilirubin (TSB) level is >5 mg/dL or more than 86 micromole/L [1]. NH affects around 80% pre-term and 60% term neonates [1]. The presence of raised levels of unconjugated bilirubin in most infants is of normal physiological occurrence. However, it may also be seen in association with infections, haemolytic disorders, anatomic anomalies of hepatobiliary system as well as endocrine and metabolic disorders [2].

Elevated levels of UCB can enter brain and may get deposited in the brain stem nuclei and basal ganglia leading to bilirubin encephalopathy with permanent neurodevelopment impairment. If left untreated, it can cause kernicterus (chronic stage). While severe conjugated hyperbilirubinemia reflects major systemic ailment, the raised levels of unconjugated bilirubin in blood is likely neurotoxic in neonatal period if it crosses blood-brain barrier. Thus, timely and judicious management of NH is of immense importance and presence of NH is alarming for both paediatricians as well as for parents.

NH is usually managed by phototherapy (PT) in which on exposure to blue-green light (wavelength=460-490nm), bilirubin molecule gets converted to soluble, non-toxic isomers that can be readily eliminated by kidneys through urine and via the gastrointestinal tract through faeces. Phototherapy is well tolerated and non-invasive modality of bilirubin reduction. Also, its sensible usage has reduced the need for Double volume exchange transfusion (DVET) in neonates which is indicated in indicated in emergency situation.

Phototherapy acts by the following mechanisms:

A) **Configurational isomerization:** immediate but reversible conversion of Z-isomer of bilirubin to E-isomer on exposure to light.
B) **Structural isomerization:** main mechanism of decline in TSB; irreversible conversion of bilirubin to lumirubin.
C) **Photo-oxidation:** Bilirubin is converted to photo-oxidants which are excreted through urine.

However, like any other intervention, phototherapy too has some of its own side effects. The major adverse effects include PT skin rash, intolerance to feed, hyperthermia, vomiting, watery diarrhea and reduced urine output leading to dehydration, insensible water losses, bronze baby syndrome, skin tanning, retinal damage, genotoxicity, increased cutaneous blood flow and electrolyte imbalance [3].

Since fluid losses and hyperthermia are well known to cause electrolyte imbalances, very few evidences are presently available that can precisely depict the undesired effects of PT on electrolytes. Although, some studies have reported changes in levels of calcium, magnesium, sodium, potassium & chloride but most of them are from developed countries and there is paucity of data from the developing world like our country India who have their own limitation of resources in terms of funds, sophisticated tools, trained personnel's and lack of awareness among parents. Therefore, in this study we intend to study the alterations in serum electrolyte levels of sodium, potassium, chloride & calcium after PT.

## Materials and Methods

### Study design and recruitment

The present study was a prospective before and after observational study undertaken in the Department of Paediatrics in collaboration with Department of Biochemistry, Maharishi Markandeshwar Medical College and Hospital, Kumarhatti, Solan.

This study included live healthy term neonate born ≥ 37 completed weeks of gestation, requiring phototherapy for ≥24 hours as per hospital policy using American Academy of Pediatrics (AAP) guidelines as reference.

### Inclusion criteria

115 healthy term neonates with unconjugated hyperbilirubinemia who are ≥ 37 weeks of gestation requiring phototherapy for ≥24 h.

## Exclusion criteria

1) Gestation age < 37 completed weeks.
2) Major congenital malformation.
3) Conjugated hyperbilirubinemia.
4) Infant undergoing exchange transfusion.
5) Those requiring resuscitation >3 minute at birth.
6) Those meeting sepsis criteria.
7) Neonates on intravenous (i/v) fluids.
8) Neonates with deranged electrolytes at the time of initiation of phototherapy.

## Collection and processing of sample

The study was conducted after approval and an informed consent (written) from the parents of all neonates enrolled.

Details including gestational age, mode of delivery, baby blood group with Rh status, maternal blood group with Rh status and age of appearance of icterus was noted in a pre-designed proforma along with the electrolyte levels.

Healthy term neonates were further classified based on the mode of delivery as lower segment Caesarean section (LSCS) and normal vaginal delivery (NVD) and weeks of gestation (37 weeks to 42 completed weeks of gestation). Gestation was further categorised as early term, full term and late term. Early term was defined as newborns born between gestational age 37 0/7 to 38 6/7 weeks while full term were those born between 39 0/7 to 40 6/7 weeks and late term between 41 0/7 and 41 6/7 completed weeks of gestation.

Anthropometric indicators were also used in the study to assess basic growth which includes weight, length and occipitofrontal circumference.

Under all aseptic precautions taken, first venous blood sample of around 2-3ml. was taken before commencement of phototherapy and another sample following 24 hrs. of phototherapy and whenever possible at the time of termination of phototherapy if >24 hrs. First sample taken served as a control while second sample determined the study group. Comparative study between the two samples was done to assess for changes in the levels of serum electrolytes.

Total & direct bilirubin was measured by diazo method [4]. Electrolyte levels (sodium, potassium and chloride) were determined using electrolytes-ion selective electrode. An ion-selective electrode (ISE), also known as a specific ion electrode (SIE), is a transducer (or sensor) that converts the activity of a specific ion dissolved in a solution into an electrical potential. The voltage is theoretically dependent on the logarithm of the ionic activity, according to the Nernst equation [5]. Calcium estimation was done using OCPC (O-Cresolphthalein Complexone) method. Calcium is precipitated as calcium oxalate and after decomposition of the oxalate by heat, estimated calorimetrically with o-Cresolphthalein Complexone [6]. Processing of the sample was done following quality checks of above parameters.

## Phototherapy

Before initiating PT, clinical estimation of bilirubin levels was done by applying digital pressure and noting the color of underlying skin and subcutaneous tissue. Further grading was done as per the extent of skin stained based on the Kramer zones.

Neonates were put on PT if indicated. All neonates included in the study group were exposed to PT using Medicaid Neo Bili-300 LED PT unit. The unit comprise of 15 high power LED (blue + white) of wavelength 420-480nm. and irradiance of >42 mcW/cm2/nm. The whole body of the baby was kept exposed in the radiant warmer except for eyes and genitals which were covered by eye bandage and diaper respectively. Discontinuation of PT was done when serum bilirubin levels fell below the recommended range as per AAP guidelines. In between the study, if the serum bilirubin elevated to an extent where DVET was required, the neonate was excluded from the study.

## Statistical analysis

Levels of serum electrolytes before and after phototherapy with the baseline data of all study subjects was recorded in a predesigned Proforma and master chart was prepared in Microsoft Excel sheet.
Analysis of the data was done using SPSS 20 (Statistical Package for Social Sciences).
Each electrolyte (sodium, potassium, chloride and calcium) was analyzed separately.
Paired-t-test was used to compare pre and post patients electrolyte levels.
P-value of <0.05 was considered statistically significant.

## Ethical consideration

The proposed study was approved by Institutional Ethical Committee.

## Results

Total of 115 subjects were included in the study.
The median age of the recruited subject was 48 hrs. with the minimum age of 24 h and maximum of 6 days. The number of male patients was higher compared to the number of female patients with a male to female sex ratio of 1: 1.21. The mean birth weight, body length and occipitofrontal circumference was 2850±460 g, 49.84 ± 1.0 cm and 33.77 ± 0.69 cm respectively. The neonates born via lower segment cesarean section (52.17%) were slightly higher than those born via normal vaginal delivery (47.8%).
Baseline characteristics of all the subjects are represented in tabulated form (Table 1).

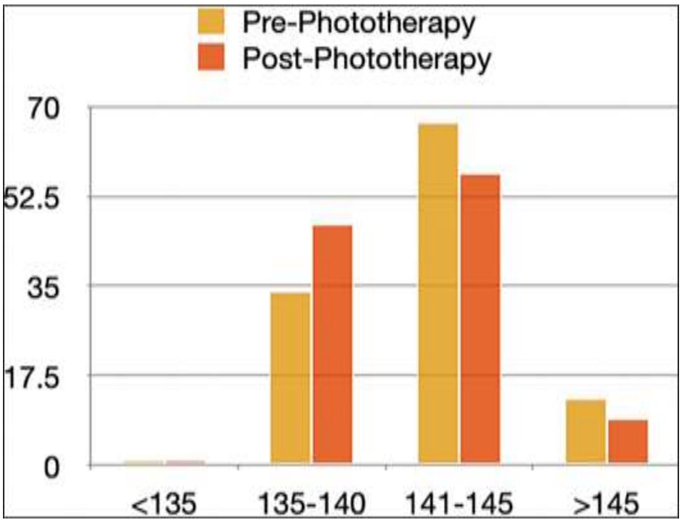
**Table 1:** Baseline neonatal characteristics

| Parameters | n=115 |
|---|---|
| Age (at start of phototherapy in hours), Median | 48 |
| Gender, n (%) | |
| Females | 52 (45.22%) |
| Males | 63 (54.78%) |
| Birth Weight(g), mean ± SD | 2850 ± 460 |
| Body Length (cms), mean ± SD | 49.84 ± 1.0 |
| Occipitofrontal circumference (cms), mean ± SD | 33.77 ± 0.69 |
| Mode of delivery, n (%) | |
| Lower segment caesarean section (LSCS) | 60 (52.17%) |
| Normal Vaginal delivery (NVD) | 55 (47.8%) |
| Category of gestation, n (%) | |
| Early term | 66 (57.3%) |
| Full term | 46 (40%) |
| Late term | 3 (2.6%) |
| Weight-for-gestational age | |
| AGA (Appropriate for gestational age) | 83 (72.17%) |
| SGA (Small for gestational age) | 29 (25.2%) |
| LGA (Large for gestational age) | 3 (2.6%) |

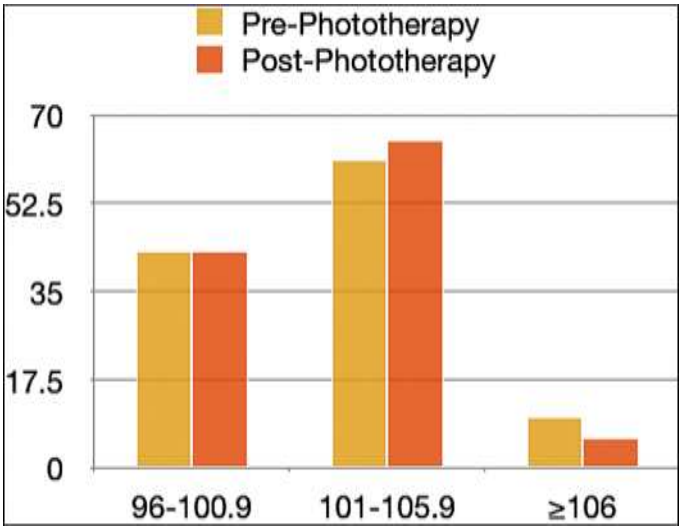
All the electrolytes included in my study (sodium, chloride, potassium and calcium) were further sub-grouped based on their levels and eventually comparison was done.

**Table 2:** Description of serum electrolyte levels before and after phototherapy

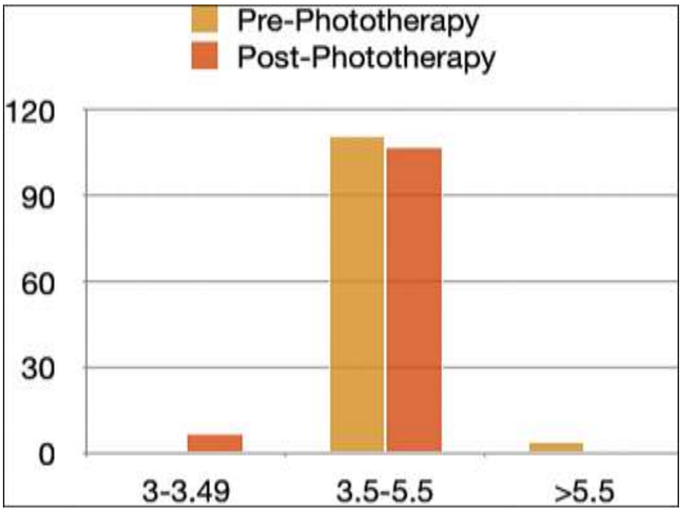
| Variable | Subgroups | Before Phototherapy Number (percentage) | After Phototherapy Number (percentage) |
|---|---|---|---|
| Sodium | <135 mmol/L | 1 (0.87%) | 1 (0.87%) |
| | 135-140 mmol/L | 34 (29.56%) | 47 (40.87%) |
| | 141-145 mmol/L | 67 (58.26%) | 58 (50.43%) |
| | >145 mmol/L | 13 (11.30%) | 9 (7.82%) |
| Calcium | <8 mg/dL | 0 | 53 (46.08%) |
| | 8-11 mg/dL | 115 (100%) | 62 (53.91%) |
| Potassium | 3-3.49 mEq/L | 0 | 7 (6.08%) |
| | 3.50-5.50 mEq/L | 111 (96.52%) | 107 (93.04%) |
| | >5.50 mEq/L | 4 (3.47%) | 1 (0.87%) |
| Chloride | <96 mEq/L | 1 (0.87%) | 1 (0.87%) |
| | 96-100.90 mEq/L | 43 (37.39%) | 43 (37.39%) |
| | 101-105.90 mEq/L | 61 (53.04%) | 65 (56.52%) |
| | >=106 mEq/L | 10 (8.69%) | 6 (5.21%) |



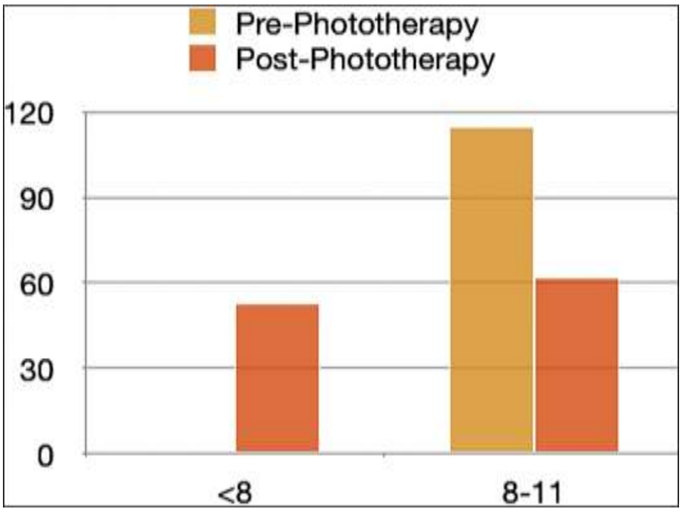

**Graph 1:** Compound bar diagram depicting levels of serum sodium levels based on subgroup before and after phototherapy




**Graph 2:** Compound bar diagram depicting levels of serum chloride levels based on subgroup before and after phototherapy




**Graph 3:** Compound bar diagram depicting levels of serum potassium levels based on subgroup before and after phototherapy




**Graph 4:** Compound bar diagram depicting levels of serum calcium levels based on subgroup before and after phototherapy

Before PT, the mean serum sodium was 141.3 ± 2.69 mmol/L and after PT, the mean serum sodium was 140.5 ± 2.70 mmol/L. Serum sodium level was found to decrease significantly after PT (p=0.0001).

Before PT, the mean serum chloride was 102.2 ± 2.98 mEq/L and after PT, the mean serum chloride was 102.0 ± 2.93 mEq/L. Serum chloride level was found to decreased significantly after PT (p=0.0219).

In our study, mean serum potassium was 4.43 ± 0.52 mEq/L before PT and was 4.23 ± 0.48 mEq/L after PT. Serum potassium level was found to decreased significantly after PT (p=0.0001).

The serum calcium level before PT was 9.14 ± 0.46 mg/dL and was 8.09 ± 0.55 mg/dL after PT (Figure 4). Serum calcium level was found to decreased significantly after PT (p=0.0001) (Table 2).

**Table 3:** Comparative analysis of electrolytes before and after phototherapy

| Electrolyte | Before Phototherapy | After Phototherapy | P value |
|---|---|---|---|
| Sodium (mEq/L), mean ± SD | 141.3 ± 2.69 | 140.5 ± 2.70 | *0.0001 |
| Chloride (mEq/L), mean ± SD | 102.2 ± 2.98 | 102.0 ± 2.93 | *0.0219 |
| Potassium (mEq/L), mean ± SD | 4.43 ± 0.52 | 4.23 ± 0.48 | *0.0001 |
| Calcium (mg/dL), mean ± SD | 9.14 ± 0.46 | 8.09 ± 0.55 | *0.0001 |

*Statistical significance.

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## Discussion

Neonatal hyperbilirubinemia is an unusual physical finding observed by clinicians during the initial week of life noted in around 60-80% live births. Healthy term infants are frequently discharged from the hospital relatively earlier after delivery for medical, social, and economic reasons. According to a study, neonates with a post-delivery hospital stay of less than 72 hours had a much higher risk of readmission than newborns with a stay of more than 72 hours. Early discharge of healthy term newborns is generating concern due to reports of bilirubin-induced brain damage leading in complications such as kernicterus. The importance of early diagnosis of hyperbilirubinemia in prematurely discharged newborns cannot be overstated. Phototherapy has become the most commonly utilized therapeutic method. This is the most current treatment of choice for reducing the severity of newborn unconjugated hyperbilirubinemia. Phototherapy, like any other treatment, has adverse effects. Unlike other side effects, there are currently just a few studies that depict the negative impact of phototherapy on serum electrolytes. A few recent researches have focused on the occurrence of hypocalcemia as a result of phototherapy. The goal of this research was to determine the changes in serum electrolytes in newborns that were undergoing PT for neonatal jaundice in NICU. The study measured serum electrolytes in 115 jaundiced term newborns before and after PT in this study. The study compared how often PT-induced electrolyte abnormalities occurred in each one of them.

The majority of the newborns were between the ages of 24 hours to 6 days with the median age of 48 hours, which is comparable to Taheri PA *et al*. [7]. In context of gender distribution, males accounted for 63 percent of the total with male to female sex ratio of 1:1.21 which was similar to that seen in Purohit A et al study [8].

Anthropometric measurement revealed the average weight of 2850±460 g as opposed to 3182±430 g seen in a study conducted by Taheri PA et al [9] while it was comparable to the Karamifar et al study where mean birth weight of term neonates was 2889±474g [10].

In my study, subjects born via LSCS were slightly higher than those born via NVD correlating with the study conducted by Vigneshwar NKV et [11]. This may be attributed to our institute being a tertiary care centre where large number of high risk deliveries is being conducted and significant patients are being referred from far flung areas due to scarcity of medical healthcare facility.

Before PT, the mean serum sodium was 141.3±2.69 mmol/L and after PT, the mean serum sodium was 140.5 ± 2.70 mmol/L. Serum sodium level was found to decreased significantly after PT (p=0.0001) in the study. This decline was proposed to be as a result of diarrhea causing reduced gastrointestinal absorption of sodium and also generous frequent feeding ensured in our institution. Similar results were recorded by Jena PK et al [12] and Shilpa S et al [13].

In the study, mean serum potassium was 4.43 ± 0.52 mEq/L before PT and was 4.23 ± 0.48 mEq/L after PT. The decline in serum potassium level was found to be statistically significant after PT (p=0.0001). However, this decline was marginal with levels close to near normal range in all the cases. The results are in accordance with Krishna P et al study (p- value <0.001) [14]. However, Tan KL et al conducted a study on healthy term newborns undergoing PT and observed a significant rise in levels of serum potassium which was in contrast to our observation [15].

Before PT, the mean serum chloride was 102.2 ± 2.98 mEq/L and after PT, the mean serum chloride was 102.0 ± 2.93 mEq/L. Serum chloride level was found to decreased significantly after PT (p=0.0219).

The serum calcium level before PT was 9.14 ± 0.46 mg/dL and was 8.09 ± 0.55 mg/dL after PT with p-value=0.0001 (statistically significant). In this study, notable decline in the serum calcium was appreciated following completion of phototherapy with 53 neonates (46.08%) showing hypocalcemia in contrast to no neonate at the time of start of study. However, none exhibited any clinical evidence of hypocalcemia with only trivial deflection of levels hovering around the lower limit of normal range in majority of the cases. In their study, Eghbalian et colleagues (2008) discovered that blood calcium levels in newborns with hyperbilirubinemia

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treated with PT decreased significantly [16]. Calcium is required for a variety of biochemical processes, including cell enzymatic and secretory activity, blood coagulation, cell membrane integrity and function and neuromuscular excitability [17]. In hypocalcemia, the cell's sodium permeability is increased and the cell membrane's excitability is increased. Hyperreflexia, apnea, cyanosis, vomiting, seizures, tachypnea, stridor or laryngospasm, increased extensor tone, jitteriness, and clonus are common non-specific symptoms. However, some may also present with tachycardia, prolongation of $QT_c$ interval (>0.45 s), and even heart failure but these symptoms suggestive of cardiac involvement are relatively less observed [18]. According to Sethi et al. in 1990, following PT, 75% of term newborns had hypocalcemia [19]. After PT, 66.6 percent of term newborns had a substantial decrease in calcium levels, according to Yadav RK and Rajesh KY in 2011 [20]. After 48 hours of PT, 56 percent of infants had lower blood calcium levels, according to Taheri PA et al (2013) [21].

PT inhibits melatonin production by the pineal gland [1]. As a result, corticosterone's impact on bone calcium is reduced. Because melatonin levels drop during PT, the level of corticosterone in the blood also drops. As a result, reduced corticosterone reduces bone resorption, resulting in hypocalcemia. Hypocalcemia was produced by a decrease in parathormone production in jaundiced newborns treated with PT [22].

In all the studies described above, statistical significant decline in the levels of total serum calcium was asserted but this decline is of little clinical importance in majority.

## Conclusion

- The findings of the current study revealed a decline in the levels of serum sodium, potassium, chloride and calcium levels in infants exposed to PT. However, these changes were not clinically significant.
- Statistically significant decline was noted in all the electrolytes included in the study but none of the baby exhibited any clinical manifestation since only marginal change was observed.
- Even though the exact mechanism for this decline could not be understood clearly, further large sample studies are needed to elucidate the same.
- We must not forget that these imbalances might have an adverse effect on the neonates and must remain keen eyed.
- Although, we do not recommend measurement of serum electrolytes routinely; we suggest one to remain vigilant regarding the same.

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