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Original Research Article

Impact of Phototherapy Duration on Hypocalcemia in Neonatal Hyperbilirubinemia

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Abstract

Background: Phototherapy is a standard treatment for neonatal hyperbilirubinemia. While effective, it is associated with adverse effects, including hypocalcemia. Understanding the incidence of phototherapy-induced hypocalcemia and its correlation with phototherapy duration is crucial for mitigating potential complications.

Objective: To determine the prevalence of hypocalcemia in neonates undergoing phototherapy for hyperbilirubinemia and evaluate its correlation with the duration of phototherapy.

Methods: This prospective observational study included 100 neonates receiving phototherapy for hyperbilirubinemia in Department of Pediatrics, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India for one year . Serum calcium levels were measured before, during, and after phototherapy. Data were analyzed to assess the prevalence of hypocalcemia and its correlation with phototherapy duration.

Results: Hypocalcemia was observed in 38% of neonates after phototherapy, with a statistically significant decrease in mean serum calcium levels ($p < 0.01$). The incidence of hypocalcemia increased with prolonged phototherapy, particularly beyond 48 hours. A strong negative correlation ($r = -0.65$) was observed between serum calcium levels and phototherapy duration.

Conclusion: Phototherapy-induced hypocalcemia is a common complication in neonates undergoing treatment for hyperbilirubinemia, especially with prolonged phototherapy. Regular monitoring of calcium levels and timely supplementation can mitigate adverse effects.

Keywords: Phototherapy, Hypocalcemia, Neonatal, Hyperbilirubinemia, Calcium, Bilirubin, Correlation

Introduction

Neonatal hyperbilirubinemia is a common condition affecting newborns, characterized by elevated levels of serum bilirubin. This condition occurs due to the immature liver's limited ability to conjugate and excrete bilirubin [1]. While most cases are physiological and resolve spontaneously, some neonates develop pathological hyperbilirubinemia, which necessitates medical intervention to prevent complications such as kernicterus and bilirubin-induced neurological dysfunction [2].

Phototherapy is the cornerstone treatment for neonatal hyperbilirubinemia. By converting bilirubin into water-soluble isomers that can be excreted via urine and bile, phototherapy effectively reduces serum bilirubin levels. However, despite its widespread efficacy and safety, phototherapy is not devoid of adverse effects [3]. Known complications include dehydration, diarrhea, skin rash, hyperthermia, and, notably, hypocalcemia. Hypocalcemia, defined as total serum calcium levels below 7 mg/dL in term neonates and 6 mg/dL in preterm neonates, is an often-overlooked consequence of phototherapy that can lead to neuromuscular and cardiovascular complications if not promptly identified and managed [4].

The mechanism of phototherapy-induced hypocalcemia is multifactorial. It is hypothesized that phototherapy suppresses melatonin secretion, which in turn reduces parathyroid hormone (PTH) levels. PTH plays a critical role in calcium homeostasis by stimulating calcium reabsorption in the renal tubules and mobilizing calcium from bone [5]. The suppression of PTH by phototherapy disrupts this balance, leading to hypocalcemia. Additionally, neonates with lower baseline calcium levels, such as preterm infants and those with poor

nutritional status, are particularly susceptible [6].

Although the relationship between phototherapy and hypocalcemia is well-documented, there is limited data on the extent to which the duration of phototherapy influences the development and severity of hypocalcemia [7]. Prolonged exposure to phototherapy may exacerbate calcium depletion, posing a greater risk of complications. However, this correlation remains underexplored, particularly in resource-limited settings where routine monitoring of serum calcium levels during phototherapy is not always feasible [8].

This study aims to determine the prevalence of phototherapy-induced hypocalcemia in neonates with hyperbilirubinemia and to evaluate the correlation between hypocalcemia and the duration of phototherapy. By addressing these gaps, the findings can guide clinicians in implementing preventive strategies, such as routine calcium monitoring and supplementation, to enhance the safety and efficacy of phototherapy in neonatal care.

Materials and Methods

Study Design and Setting: This prospective observational study was conducted in the neonatal unit at Department of Pediatrics, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, in India, over a duration of one year. The aim was to evaluate the incidence of phototherapy-induced hypocalcemia and its correlation with the duration of phototherapy in neonates with hyperbilirubinemia.

Study Population: A total of 100 neonates diagnosed with neonatal hyperbilirubinemia and requiring phototherapy were recruited for the study.

Inclusion Criteria:

- Neonates aged ≤14 days.
- Total serum bilirubin levels exceeding phototherapy thresholds based on gestational age and weight.
- Parental consent for participation.

Exclusion Criteria:

- Neonates with pre-existing hypocalcemia or hypercalcemia.
- Neonates with congenital anomalies, metabolic disorders, or sepsis.
- Neonates already receiving calcium supplementation or medications affecting calcium metabolism.

Study Procedures

1. **Baseline Assessments:** At the time of enrollment, detailed demographic and clinical information were collected, including gestational age, birth weight, feeding practices, and baseline serum calcium levels.
2. **Phototherapy Administration:** Phototherapy was delivered using blue light-emitting diode (LED) units with an intensity of 430–490 nm, as per standard neonatal care protocols. Duration and intensity of phototherapy were recorded.
3. **Serum Calcium Monitoring:** Serum calcium levels were measured at three time points:
    - **Before phototherapy:** To establish baseline levels.
    - **During phototherapy:** After 24 hours of exposure.
    - **After phototherapy:** Within 6 hours of discontinuing phototherapy.

    Total serum calcium levels were measured using an automated biochemical analyzer. Hypocalcemia was defined as total serum calcium levels <7 mg/dL for term neonates and <6 mg/dL for preterm neonates.
4. **Monitoring and Management:** Neonates were closely monitored for clinical signs of hypocalcemia, such as jitteriness, irritability, apnea, or seizures. Calcium gluconate supplementation was provided for symptomatic hypocalcemia, following neonatal resuscitation guidelines.

Data Collection

Data collected included:

- Demographic and clinical variables: gestational age, birth weight, mode of delivery, and feeding practices.
- Phototherapy parameters: duration of phototherapy, type of phototherapy unit, and intensity.
- Biochemical variables: baseline, during-treatment, and post-treatment serum calcium levels.

Statistical Analysis: Data were analyzed using statistical software.

- **Descriptive Statistics:** Used to summarize demographic, clinical, and biochemical variables.
- **Correlation Analysis:** Pearson's correlation coefficient was calculated to assess the relationship between phototherapy duration and changes in serum calcium levels.
- **Comparative Analysis:** Paired t-tests were performed to compare serum calcium levels before, during, and after phototherapy.
- **Regression Analysis:** Multivariate regression was used to identify predictors of hypocalcemia, adjusting for potential confounders such as gestational age and birth weight.

Results

This study analyzed the prevalence of phototherapy-induced hypocalcemia in neonates with hyperbilirubinemia and its correlation with the duration of phototherapy. A total of 100 neonates were included, and detailed data are presented in the tables below.

Table 1 shows the demographic and clinical characteristics of the study population, including gestational age, birth weight, and mode of delivery.

Table 1: Demographic and Clinical Characteristics of Neonates

Characteristic	Frequency (n = 100)	Percentage (%)
Gestational Age (Term)	70	70.0
Gestational Age (Preterm)	30	30.0
Birth Weight (<2.5 kg)	28	28.0
Birth Weight (≥2.5 kg)	72	72.0
Mode of Delivery (Normal)	65	65.0
Mode of Delivery (Cesarean)	35	35.0

Table 2: Feeding Practices of Neonates

Feeding Practice	Frequency (n = 100)	Percentage (%)
Exclusive Breastfeeding	85	85.0
Mixed Feeding	10	10.0
Formula Feeding	5	5.0

Table 3: Baseline Serum Calcium Levels

Serum Calcium Level (mg/dL)	Frequency (n = 100)	Percentage (%)
≥8.0	90	90.0
7.0–7.9	8	8.0
<7.0	2	2.0

Table 4: Prevalence of Hypocalcemia

Time Point	Frequency (n = 100)	Percentage (%)
During Phototherapy	36	36.0
After Phototherapy	38	38.0

Table 5: Duration of Phototherapy and Serum Calcium Levels

Duration of Phototherapy (Hours)	Mean Serum Calcium (mg/dL) ± SD
≤24	7.8 ± 0.6
25–48	7.2 ± 0.5
>48	6.8 ± 0.4

Table 6: Correlation Analysis Between Duration and Calcium Levels

Parameter	Correlation Coefficient (r)	p-Value
Duration vs. Serum Calcium	-0.65	<0.01

Table 7: Serum Calcium Levels Over Time

Time Point	Mean Serum Calcium (mg/dL) ± SD	p-Value
Before Phototherapy	8.2 ± 0.7	-
During Phototherapy	7.4 ± 0.6	<0.01
After Phototherapy	7.2 ± 0.5	<0.01

Table 8: Symptomatic Hypocalcemia

Symptoms	Frequency (n = 38)	Percentage (%)
Jitteriness	20	52.6
Irritability	12	31.6
Seizures	6	15.8

Table 9: Management of Hypocalcemia

Intervention	Frequency (n = 38)	Percentage (%)
Calcium Gluconate	38	100.0
No Additional Measures	0	0.0

Table 10: Predictors of Hypocalcemia

Predictor	Odds Ratio (95% CI)	p-Value
Phototherapy Duration >48 Hours	3.8 (2.1–6.7)	<0.01
Preterm Birth	2.5 (1.3–4.6)	<0.05
Exclusive Breastfeeding	1.1 (0.5–2.4)	0.75

The results demonstrate a significant correlation between phototherapy duration and hypocalcemia, emphasizing the importance of monitoring serum calcium levels during treatment.

Discussion

This study evaluated the prevalence of phototherapy-induced hypocalcemia in neonates with hyperbilirubinemia and its correlation with the duration of phototherapy. The findings provide valuable insights into the biochemical effects of phototherapy and the potential risk factors for developing hypocalcemia, a critical complication in neonatal care.

Prevalence and Timing of Hypocalcemia

Hypocalcemia was observed in 38% of neonates after phototherapy, with a significant drop in mean serum calcium levels during and after treatment. This prevalence aligns with previous studies, highlighting hypocalcemia as a common yet under-recognized complication of phototherapy. The increase in hypocalcemia cases during and after phototherapy underscores the necessity of routine calcium monitoring throughout the treatment period [9].

Mechanisms Underlying Phototherapy-Induced Hypocalcemia

The development of hypocalcemia during phototherapy can be attributed to multiple mechanisms. Phototherapy suppresses melatonin secretion, which indirectly affects parathyroid hormone (PTH) levels. The resultant decrease in PTH activity impairs calcium reabsorption in the kidneys and calcium mobilization from bones, leading to hypocalcemia. Additionally, the immature calcium-regulating mechanisms in neonates, especially preterm infants, further exacerbate this effect. The findings of this study reinforce the need for vigilance in managing calcium homeostasis in neonates receiving phototherapy [10].

Correlation Between Hypocalcemia and Phototherapy Duration

A strong negative correlation ($r = -0.65$, $p < 0.01$) was observed between phototherapy duration and serum calcium levels. Neonates exposed to phototherapy for more than 48 hours exhibited the lowest calcium levels and the highest risk of symptomatic hypocalcemia. Multivariate regression analysis identified prolonged phototherapy duration as the strongest predictor of hypocalcemia, with an odds ratio of 3.8 (95% CI: 2.1–6.7). These findings suggest that the duration of phototherapy is a critical factor influencing calcium depletion and necessitate careful monitoring in neonates undergoing extended treatment [11].

Clinical Implications and Management

The study highlights the clinical manifestations of hypocalcemia, including jitteriness, irritability, and, in severe cases, seizures. These symptoms, if unrecognized, can lead to significant morbidity. The universal administration of calcium gluconate effectively corrected hypocalcemia in all affected neonates, demonstrating its importance in the management protocol for phototherapy-induced hypocalcemia [12].

Public Health and Clinical Practice Implications

The results of this study have several implications for neonatal care:

1. **Routine Monitoring of Calcium Levels:** Serum calcium levels should be routinely monitored before, during, and after phototherapy to facilitate early detection and management of hypocalcemia [13].
2. **Duration-Specific Risk Assessment:** Neonates requiring phototherapy for more than 48 hours should be closely monitored for hypocalcemia, with a proactive approach to supplementation.
3. **Calcium Supplementation as a Preventive Measure:** For high-risk neonates, prophylactic calcium supplementation may be considered to prevent hypocalcemia and its complications [14].

Limitations and Strengths

This study has some limitations. The focus on a single tertiary care hospital may limit the generalizability of the findings to other settings.

Additionally, the relatively small sample size of 100 neonates restricts the ability to analyze rare outcomes. However, the study's strengths include its prospective design, systematic monitoring of calcium levels, and robust statistical analysis, which collectively provide reliable insights into the relationship between phototherapy and hypocalcemia.

Future Directions

Future studies should explore larger, multi-centric populations to validate these findings and investigate the long-term outcomes of phototherapy-induced hypocalcemia. Moreover, studies focusing on the efficacy and safety of routine prophylactic calcium supplementation during phototherapy can provide actionable evidence for clinical guidelines.

Conclusion

This study highlights the significant prevalence of phototherapy-induced hypocalcemia in neonates with hyperbilirubinemia and its strong correlation with the duration of phototherapy. Hypocalcemia was observed in 38% of neonates after phototherapy, with a significant decline in serum calcium levels during and after treatment. Neonates exposed to prolonged phototherapy, particularly beyond 48 hours, were at the highest risk, emphasizing the need for careful monitoring.

The findings underscore the critical importance of routine serum calcium monitoring in neonates undergoing phototherapy, especially in preterm infants and those requiring extended treatment durations. Early detection and timely management of hypocalcemia through calcium supplementation can prevent potential complications, including neuromuscular and cardiovascular symptoms. The study also supports the consideration of prophylactic calcium supplementation in high-risk neonates as a preventive measure.

Integrating these findings into clinical practice can enhance the safety and efficacy of phototherapy, ensuring optimal outcomes for neonates with hyperbilirubinemia. Further research is recommended to validate these findings in larger, multi-centric studies and to explore the long-term effects of phototherapy-induced hypocalcemia on neonatal development.

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