

Effect of duration of phototherapy on serum calcium level in newborn with neonatal jaundice

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Abstract

Introduction: Hyperbilirubinemia (jaundice) is a common and in most cases, benign problem in neonates. Treatment options available for neonatal jaundice are phototherapy, exchange transfusion and pharmacological therapy. Hypocalcaemia is one of the know side effects of phototherapy. Objective: Effect of duration of phototherapy on serum calcium level in newborn with neonatal jaundice. **Methods:** Design: A prospective study Setting: A tertiary care center of Karnataka (SIMS, Shivamogga). Participants: 100 full term and 100 preterm neonates with gestational age between 34 to 42 weeks were included in study. Main outcome measures: Blood was drawn from these neonates to measure serum bilirubin and serum calcium at the time of initiation of phototherapy (0 hours) and at 24,36, 48 hours of phototherapy. **Results:** Incidence was 48% in preterm and 14% in term neonates. Incidence of hypocalcaemia according to duration of phototherapy being, 2 out of 24 (8%) at 24hrs of PT, 15 out of 73 (21%) at 36hrs of PT, 45out of 103 (44%) at 48hrs of phototherapy. Out of which incidence was more in preterm than in term neonates, more in SGA neonates then AGA. Incidence is not affected by sex of newborn and mode of delivery and parity of mother. **Conclusion:** These values show that incidence of hypocalcaemia is a significant side effect of phototherapy and more being in preterm and SGA neonates. So while starting phototherapy for neonatal jaundice, one need to be cautious about serum calcium status.

Key words: Hypocalcaemia, Neonates, SGA- small for gestational age, AGA- appropriate for gestational age TSB= total serum bilirubin, PT=phototherapy.

Introduction

Hyperbilirubinemia (jaundice) is a common and in most cases, benign problem in neonates. Jaundice is observed during first week of life in approximately 60% of term neonates and in 80% preterm neonates [1]. Jaundice is attributable to physiological immaturity of neonates to handle increased bilirubin production. Visible jaundice usually appears between 24-72 hours of age [2]. Treatment options available for neonatal jaundice are phototherapy, exchange transfusion and pharmacological therapy [2]. And out of which phototherapy is one of the routine and safest methods for management of hyperbilirubinemia [3]. Phototherapy can produce adverse effects such as dehydration, temperature instability, skin rashes, loose stool, retinal damage, hypocalcaemia, bronze baby syndrome, redistribution of blood flow and genotoxicity [3].

Hypocalcaemia is one of the know side effects of phototherapy. This effect is because of decrease secretion of melatonin from pineal gland, which is needed to inhibit hypocalcaemia action of serum cortisol [4,5]. Serum calcium is crucial for many biochemical processes, including blood coagulation, neuromuscular excitability, cell membrane integrity and function, and cellular enzymatic and secretory activity [6,7].

Most of the reports with regards to incidence of hypocalcaemia in phototherapy are from studies conducted at metropolitan cities in India and other countries and serum calcium level checked at the starting of phototherapy and at 48hours of phototherapy and no systematic studies have been carried out in relation to duration(at 24hrs,36hrs,48hrs) of phototherapy. Hence, it is the need of the hour to investigate the effect of duration of phototherapy on serum calcium level in neonates with hyperbilirubinemia and incidence of hypocalcaemia in those neonates.

Manuscript received: 8th October 2014
Reviewed: 17th October 2014
Author Corrected: 24th October 2014
Accepted for Publication: 31th October 2014

Research Article**Amis and objectives**

To assess the effect of duration of phototherapy on serum calcium level in newborn with neonatal jaundice

Materials and Method

Source of data: This study conducted in SIMS, Shivamogga. 200 neonates with neonatal jaundice were included in this study who is admitted to Neonatal Intensive Care Unit at SIMS, shivamogga. Study done over a period of 1 year from June 2013 to May 2014.

Blood screening

- Blood drawn from the peripheral hand or feet veins of each neonate. Sterile, disposable syringes and needles, and proper tubes were used.
- The blood samples were analyzed at SIMS, Shivamogga clinical laboratory for Serum TSB and serum calcium at the time of admission and every 12 hourly.
- Pretest and post-test counseling is given to parents. After written consent from the parents, those neonates fulfilling the above mentioned criteria are subjected to blood test.
- And "*hypocalcaemia defined as <7mg/dl*"[8]

Type of study: Hospital based prospective study.

Inclusion criteria

1. Full-term neonates (37 completed weeks to 41 weeks) with unconjugated hyperbilirubinemia requiring phototherapy.

Results

The study consisted of total 200 neonates (100 full term and 100 preterm). Study consisted of 115(57.5%) male and 85(42.5%) female neonates. 123(61.5%) neonates were born by normal vaginal delivery and 77(38.5%) were LSCS. 133(66.5%) neonates were born to primipara and 67(33.5%) neonates were born to multipara.

These babies were put on phototherapy (PT) and blood was drawn from these neonates for serum bilirubin and serum calcium at the time of starting of phototherapy and every 12hourly.

At 12 hours of PT no neonates completed PT. At 24hours of PT 24 neonates , at 36hours 73 neonates and at 48 hours 103 neonates completed phototherapy as shown in table1. Neonates who completed PT at 24hours were grouped as group A , at 36hours were grouped as group B and at 48hours were grouped as group C and TSB and serum calcium level were taken at their respective completion period.

Table-1: Distribution of neonates depending on duration of phototherapy

| | Pre term | Term | Total |
|-----------------|----------|------|-------|
| 24hrs (group A) | 9 | 15 | 24 |
| 36hrs (group B) | 37 | 36 | 73 |
| 48hrs (group C) | 54 | 49 | 103 |

So most of neonates (>50%) needed phototherapy for \geq 48hours.

2. Preterm neonates (34 weeks to less than 37 completed weeks) with unconjugated hyperbilirubinemia requiring phototherapy.

Requirement of phototherapy decided according to guidelines of phototherapy graph by American academy of pediatrics⁶.

Exclusion criteria

Newborn,

1. With jaundice in first 24 hours of life.
2. Born To a diabetic mother, hypothyroid mother, hyperparathyroidism mother
3. With APGAR score of less than 7 at 5 minutes of birth.
4. Whose mother had history of taking anti-convulsants.
5. Fed with Cow's milk.
6. Who had exchange transfusion.
7. With jaundice lasting more than 14 days of life.
8. With sepsis.
9. Hypocalcaemia before starting of phototherapy
10. Preterm<34 weeks

Stastical methods: Data analysis was performed using statistical package of social science (SPSS) version 16.0 for windows.

- 1) Proportions will be compared using chi-square test and student t test.
- 2) Mean between the groups will be compared using T-test or ANNOVA.

Table-2: Average TSB and serum calcium level in each group

| | Average TSB(mg/dl) | | Difference (mg/dl) | Average s. ca(mg/dl) | | Difference (mg/dl) |
|-----------------|--------------------|---------|--------------------|----------------------|---------|--------------------|
| | Pre PT | Post PT | | Pre PT | Post PT | |
| 24hrs (group A) | 17.22 | 11.92 | 5.3 | 9.08 | 8.33 | 0.75 |
| 36hrs (group B) | 17.78 | 13.12 | 4.66 | 9.45 | 8.25 | 1.2 |
| 48hrs (group C) | 18.84 | 11.12 | 7.72 | 9.34 | 7.53 | 1.81 |

From table it's clear that reduction of calcium is more with increasing duration of phototherapy and chances of developing hypocalcaemia increases with increasing duration.

Table-3: Incidence of phototherapy induced hypocalcaemia depending on duration of phototherapy

| | Preterm | Term | total | P value |
|-----------------|-----------------------|-----------------------|-----------------------|-----------------|
| 24hrs (group A) | 1 out of 9 (11%) | 1out of 15(6%) | 2out of 24 (8%) | <0.05 |
| 36hrs (group B) | 10 out of 37 (27%) | 5 out of 36(14%) | 15out of 73(21%) | <0.05 |
| 48hrs (group C) | 37 out of 54 (68.5%) | 8 out of 49(16%) | 45out of 103(44%) | <0.05 |
| Total | 48(out of 100) | 14(out of 100) | 62(out of 200) | <0.05 |

From above table it is seen that p value (<0.05) is significant at 24, 36 and 48 hours.

And number of neonates developing hypocalcaemia increases with increasing duration of PT and effect of duration of phototherapy more in preterm compared to term.

Discussion

This study is undertaken to confirm effect of duration of phototherapy on serum calcium level and incidence of hypocalcaemia in neonates with jaundice and recommendation to prevent it. Study is conducted in newborn unit SIMS, Shivamogga over a year from June 2013 to May 2014.

Jaundice is a well-known clinical entity in Indian medicine. And phototherapy is one of the best and safe method as a treatment option in neonatal jaundice as described by cremer et al in 1953, Every safe method has its own side effects and even the phototherapy [3]. One of the known side effects of phototherapy is hypocalcaemia².

Neonatal jaundice is a common clinical condition. There is a high prevalence of neonatal hyperbilirubinemia which might be attributed to the high frequency of glucose-6-phosphate dehydrogenase (G6PD) enzyme deficiency. Phototherapy is amongst common therapeutic modalities used in the treatment of uncomplicated neonatal jaundice. So far, several investigations have been conducted to determine the safety of phototherapy in the treatment of neonatal hyperbilirubinemia. Very soon, detrimental effects of phototherapy on eyes and genitalia have been shown. Nonetheless, no change in blood ions/ metabolites has been reported except for calcium concentration; a drop in serum calcium has been noticed in patients undergoing phototherapy.

Phototherapy leads to inhibition of pineal gland via transcranial illumination, resulting in a decline in melatonin level and, in turn, diminishing corticosteron to finally decrease calcium resorption from bones, producing hypocalcemia. This hypothesis, based on studies on rabbit suggests that melatonin, by stimulating corticosteron release, lowers calcium absorption in bones, thus decreasing secretion of melatonin which is secondary to phototherapy causes, bone calcium uptake increases and as a result, hypocalcemia develops

There are many studies conducted to prove that hypocalcaemia is a side of phototherapy. But there are no studies about effect of duration of phototherapy. We conducted the study to observe the effect of duration of phototherapy on serum calcium level and incidence of hypocalcaemia. The study group includes 200 neonates admitted in NICU for neonatal jaundice considering inclusion and exclusion criteria.

We took a cut value of serum calcium of <7mg/dl. which is similar to cut of value taken by Arora et al[9], karamifer el al[10], Taheri et al[11]. Our study variables are comparable to karamifer el al, Taheri et al, Therani et al, Egbalian et al[7] and Kumar et al[12].

After subjecting 200 neonates with jaundice for phototherapy total incidence of hypocalcaemia was 31%. In which incidence was 48% in preterm and 14% in term neonates. Incidence of hypocalcaemia according to duration of phototherapy being, 2 out of 24 (8%) at 24hrs of PT, 15 out of 73 (21%) at 36hrs of PT, 45 out of 103 (44%) at 48hrs of phototherapy. Indicating that not only phototherapy per say even the duration also affects incidence of hypocalcaemia. All the previous studies they measured serum calcium at the onset of PT and at the end of PT (commonly at 48hrs). No previous studies done serum calcium measurement at different interval.

Table-4: Showing comparison of present study variables and results with other studies

| P value | | <0.01 | <0.05 | <0.05 | | <0.01 | |
|------------------------------|---------|------------------------------|------------------------------|---------------------------|-----------------------------|------------------------------|-------------|
| % incidence of hypocalcaemia | | 43 | 22 | | | | 46 |
| Pre and post PT S.Ca (mg/dl) | Perm | 9.48±0.97 to 8.04±0.88 | 9.53±0.92 to 9.30±1.11 | 9.8±0.8 to 9.5±0.92 | 9.46±0.8 to 9.12±0.83 | 9.85±1.23 to 9.09±0.93 | |
| | Preterm | 9.21±0.9 to 7.08±0.7 | 8.73±1.3 to 8.40±1.7 | | | | |
| Average birth weight (kg) | Term | 2.98 | 2.88 | | | | |
| | Preterm | 2.003 | 2.077 | | | | |
| Gender | Female | 78 | 65 | 73 | | | |
| | Male | 122 | 88 | 74 | | | |
| Study population | Term | 100 | 91 | 147 | | | 55 |
| | Preterm | 100 | 62 | | | | 45 |
| | Total | 200 | 153 | 147 | | | 100 |
| Study | | Present study | Karamifar et al | Taheri et al | Therani et al | Egbalian et al | Kumar et al |

There was a direct relationship between duration of phototherapy and development hypocalcemia. It is recommended that in order to prevent development of hypocalcemia in phototherapy-treated newborns, one of two following measures be carried out.

1. Newborns under phototherapy should be given oral calcium as prophylaxis.
2. Parallel to the covering of the eyes that is routinely done to prevent retinal damage, measures be taken for covering head and occipital area of these newborns using a special hat during phototherapy, so that light effect from phototherapy on newborns' pineal gland and consequently melatonin decrease and hypocalcemia is prevented[7].

In one study, it was observed that by administration of melatonin to the newborn rat, it is possible to prevent phototherapy-induced hypocalcemia. It can also be prevented by covering and protection of occipital region of rats.6 In a study by Dutte, et al,[13] considerable decrease in serum calcium level was observed particularly into premature newborns, and prophylactic administration of calcium for newborns under phototherapy was recommended.

Conclusion

So in conclusion we need to be careful about calcium status while starting phototherapy for neonatal jaundice. More specifically when duration is >24hours and that to in preterm neonates. And it's better to monitor serum calcium level every 6 to 12 hourly after 24hrs of phototherapy and supplement calcium in preterm neonates and when duration of phototherapy is more than 24hours.

Acknowledgements: No

Funding: No funding sources

Conflict of Interest: The author declare no conflicts of interest

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Research Article

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How to cite this article?

Chandrashekar B. Prevalence of microcytic hypochromic anemia in children with LRTI in the age group of 3 months to 5year: Is iron deficiency anemia a risk factor for LRTI?. *Pediatr Rev: Int J Pediatr Res* 2014;1(3):93-97.doi:10.17511/ijpr.2014.i03.06

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