Effect of Head Covering on Phototherapy induced Hypocalcaemia in Icterus Newborns

Dr. Salah Abdrabbo Elsayed[1]; Dr. Hany Abdel Hady Elkhalegy[1], Dr. Amr Mohamed Elkhrsawy[2] and Dina Abdel Fattah Hassan[1]

[1] Pediatrics Department, Damietta Medicine Faculty of, Al-Azhar University, Egypt
[2] Clinical Pathology Department, Damietta Faculty of Medicine, Al-Azhar University, Egypt
dinalina2017@yahoo.com

Abstract: Background: Hyperbiliubinemia is one of the most common problems in newborns. Phototherapy is used to treat these patients. Hypocalcaemia is one important side effect of phototherapy. Phototherapy leads to inhibition of pineal gland by transcranial illumination resulting in a decline in melatonin level which leads to increased calcium absorption by bones. **Aim:** To assess that's head covering having protective effect on Hypocalcaemia induced by phototherapy? **Patients and Methods:** We conducted a randomized controlled study at the neonatal intensive care unit at Al azhar university hospital Damietta, during the period from September 2015 to September 2016. The study included 50 full term neonates with indirect hyperbilirubinemia treated with phototherapy. Neonates were divided into two equal groups: Group A without hats and Group B with hats. The hat covers all the head including the occipital area ears to prevent passage of light. The hat was used from admission and for 48 hours of treatment with phototherapy. Total and Ionized Ca levels were measured on admission and after 48 hours of phototherapy. **Results:** We found significant difference between Total and Ionized Ca levels on admission and after 48 hours in group A (P=0.049) and (P=0.048). Hypocalcaemia was detected in 6 neonates (24%) in Group A without hats and in 3 neonates (12%) in Group B with hats. The difference between two groups was statistically significant (P=0.030). **Conclusion:** Phototherapy induced hypocalcaemia is an important side effect can be prevented by covering the heads during phototherapy. This is an effective, safe, non-invasive and cheap method.
[Salah Abdrabbo Elsayed; Hany Abdel Hady Elkhalegy, Amr Mohamed Elkhrsawy and Dina Abdel Fattah Hassan. **Effect of Head Covering on Phototherapy induced Hypocalcaemia in Icterus Newborns.** *Nat Sci* 2017;15(12):165-171]. ISSN 1545-0740 (print); ISSN 2375-7167 (online). http://www.sciencepub.net/nature. 17. doi:10.7537/marsnsj151217.17.

Keywords: Neonates, Serum Calcium, Hat, Hyperbilirubinemia.

1-Introduction

Hyperbiliubinemia is one of the most common problems in newborns.

according to the latest global reports and statistics,60% of full-term newborns are afflicted with jaundice in the first week of their birth [(1)].

It is a cause of anxiety because high bilirubin level may be toxic to central nervous system and may cause neurological impairment even in term newborn [(2)].

Phototherapy plays a significant role in treatment ofHyperbiliubinemia in neonates. This therapy lowers the serum bilirubin level by transforming bilirubin into water-soluble isomers that can be eliminated without conjugation in the liver [(3)]. The actual effect of phototherapy on jaundice was proved by Black and his method has been used for icterus newborns until now [(4)].

Phototherapy has some complications such as insensible water loss, mutation and DNA strand break, hyperthermia, tremor, retinal damage, bronze baby syndrome, and affect maternal-infant interaction [(5)]

Hypocalcaemia has been reported as a reaction to phototherapy in premature and full term newborns [(6)].

Some complications of hypocalcaemia in newborns are apnea, convulsion, muscle cramp, tremor and tetany [(7)].

Hypocalcaemia may cause long-term complications such as mental retardation, physical disability, and educational failure [(8)].

Phototherapy leads to increased calcium absorption by the bones through radiating the pineal gland and reducing melatonin level [(6)]. Some studies have suggested the administration of calcium for this condition, but intravenous calcium therapy may lead to bradycardia, cardiac arrest and necrosis [(9)].

There is some evidence that the use of a cap to cover the head prevents phototherapy induced hypocalcaemia [(10)].

In Our study we assessed the effect of head covering on total and ionized calcium levels in neonates with hyperbilirubinemia during phototherapy.

2. Patients and methods:

We conducted a study at the neonatal intensive care unit of AL-Azhar university hospital Damietta, starting from September 2015 to September 2016. The study included 50 full term neonates with symptoms, signs and laboratory findings of neonatal indirect hyperbilirubinemia treated with phototherapy. Apart from jaundice, their physical examination was completely normal.

Inclusion criteria: included full term newborns, weight 2500 g or more, in the first 7 days of life, who developed clinical symptoms and signs of neonatal indirect hyperbilirubinemia and have normal serum calcium level. Exclusion criteria: included newborns with jaundice in the first 24 hours of life or lasting more than 14 days, if they suffered from respiratory distress, ABO, RH incompatibility, sepsis, congenital anomalies, asphyxia, neonatal hypocalcaemia, or Infant of diabetic mother, or preterm and newborns who had undergone exchange transfusion.

Neonates were divided into two equal groups: group (A) 25 infants under the routine phototherapy without hats and group (B) 25 infants using hats that covered their heads.

2. Procedure:

We designed a hat that can cover all the head including the occipital area and ears to prevent passage of light. The hat was used from admission and for 48 hours of treatment with phototherapy. Phototherapy equipment containing four blue light fluorescent lamps with wave length of 410-470 nm, was placed at a distance of 30-40 cm.

All neonates in the study were subjected to the following**:**

1- Comprehensive history taking including**:** Antenatal history:- Maternal age, maternal diseases, Drugs. Natal history:- Gestational age, sex and mode of delivery, history of premature rupture of membranes. Family history:- Consanguinity, congenital anomalies, hyperbilirubinemia in previous sibling (onset, course and treatment method). onset of hperbilirubinemia in studied cases, Type of feeding, Assessment of gestational age through analysis of maternal dates, Record Apgar score at 1 and 5 minutes [11] if present.

2-Clinical examination for neonates: Complete examination including cardiac, chest, abdominal and neurological, Weight, length, Head circumference, Gestational age by Ballard scores [12], detection of clinical signs of hypocalcaemia: apnea, irritability, jitteriness and convulsions.

3- Laboratory investigations including: Complete Blood Cell Count (CBC) with differential count, reticulocyte count, C-reactive protein (CRP), Maternal and infant blood group and RH, Serum total and direct bilirubin on admission and 48 hours after starting phototherapy, Serum calcium (total and ionized) on admission and 48 hours after starting phototherapy.

Calcium level measurement needed 2 ml blood sample from peripheral vein. Centrifugation system was used to obtain serum then calcium was measured from serum using Bechman CX9 PRO.

We used a preset definition for hypocalcaemia: Total serum calcium less than 8 mg/dl was considered hypocalcaemia [13].

Statistical Methods

Data were statistically described in terms of mean ± standard deviation (± SD), median and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Student t test for independent samples and Paired t test for paired samples. For comparing categorical data, Chi square ($\chi 2$) test was performed. Exact test was used instead when the expected frequency is less than 5. p values less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 20 for Microsoft Windows.

3- Results:

We included in our study 50 full-term neonates with hyperbilirubinemia treated with phototherapy, their mean body weight was 3.235 ± 0.334 g (ranged from 2.600 to 3.800 grams) and their mean gestational age was 38.12 ± 0.824 weeks. The mean Length was 50.02 ± 0.820 cm, the mean Head Circumference was 34.90± 0.647 cm, the mean Heart Rate was 142.42 ± 8.347 beats/min and the mean Respiratory Rate was 49.66 ± 3.055 breath/min.

The Onset of jaundice was 2.62 ± 0.49 days. Their mean Age on admission was 4.00 ± 0.70 days.

They had a mean Total bilirubin level on admission of 17.619 ± 1.116mg/dl and a level of 10.082 ± 1.227mg/dl 48hours after phototherapy. Their mean Direct bilirubin level on admission of 0.731 ± 0.176mg/dl and a level of 0.798 ± 0.241mg/dl 48hours after phototherapy. Their mean Total Ca level on admission was9.195 ± 0.374 mg/dl (ranging from 8.5-10 mg/dl) and after 48 hours was 8.841 ± 1.003 mg/dl (ranging from 6.75-10 mg/dl). the mean Ionized calcium on admission was 4.889 ± 0.114 mg/dl (ranging from 4.80-5.40 mg/dl) and after 48 hours was 4.556 ± 0.759 mg/dl (ranging from 2.80-5.45 mg/dl).

There is no significant difference between the two groups as regard their clinical and laboratory characteristics of two groups .

(Table 1).

We found significant difference between mean total calcium level on admission and after 48 hours of phototherapy in group A (Table 2), (Figure 1).

We found significant difference between mean ionized calcium level on admission and after 48 hours of phototherapy in group A

(Table 3), (Figure 2).

We found a statistically significant difference between the two groups as regard the percentage of neonatal hypocalcaemia after phototherapy. Neonates with hypocalcaemia represented in group A 6 cases (24%) and in group B 3 cases (12 %) and neonates with normal calcium represented in group A 19 cases (76 %) and in group B 22 cases (88 %). (Table 4) (Figure 3).

There is no significant difference between the two groups in neonates as regard the development of jitteriness (P value = 0.186). (Table 5). (Figure 4).

Table 1: comparison of clinical and laboratory parameters between two groups

Variable	Group A Without hats Mean ± SD (N=25)	Group B Without hats Mean ± SD (N=25)	P-value
Body weight (g)	3,196 ± 0.326	3,274 ± 0.346	0.415
Gestational age (weeks)	38.08 ± 0.759	38.16 ± 0.898	0.735
Female (%)	13 (52%)	9 (36%)	0.387
Male (%)	12 (48%)	16 (64%)	
C.S (%)	17 (68%)	15 (60%)	0.868
N.V.D (%)	8 (32%)	10 (40%)	
Breast Feeding (%)	15 (60%)	16 (64%)	0.786
Artificial Feeding (%)	3 (12%)	2 (8%)	
Breast Feeding + Artificial Feeding (%)	7 (28%)	7(28%)	
Mean onset of jaundice (days)	2.56 ± 0.507	2.68 ± 0.476	0.392
Mean age on admission (days)	3.92± 0.702	4.08± 0.702	0.425
Mean Total Bilirubin on admission (mg/dl)	17.625 ± 1.191	17.612 ± 1.058	0.968
Mean Direct bilirubin on admission (mg/dl)	0.746 ± 0.223	0.715 ± 0.113	0.531
Mean Total Bilirubin after 48hours (mg/dl)	10.148 ± 1.213	10.015 ± 1.261	0.704
Mean Direct Bilirubin after 48hours (mg/dl)	0.8212 ± 0.273	0.0774 ± 0.206	0.501
Mean total Ca on admission (mg/dl)	9.157± 0.411	9.186± 0.892	0.479
Mean total Ca after 48hours (mg/dl)	8.596± 1.064	9.233± 0.337	0.084
Mean ionized Ca on admission (mg/dl)	4.881± 0.116	4.887± 0.655	0.626
Mean ionized Ca after 48hours (mg/dl)	4.418± 0.841	4.894± 0.114	0.203

Table 2: shows the change in total calcium level induced by phototherapy in each group

Variable	Mean Total Ca on admission	Mean Total Ca after 48 hours		P value
Group AMean ± SD	9.157± 0.411	8.596± 1.064	0.561	0.049
Group B Mean ± SD	9.186± 0.892	9.233± 0.337	-0.047	0.303

Table 3: shows the change in ionized calcium level induced by phototherapy in each group.

Variable	Mean Ionized Ca on admission	Mean Ionized Ca after 48 hours		P value
Group A Mean ± SD	4.881± 0.116	4.418± 0.841	0.463	0.048
Group B Mean ± SD	4.887± 0.655	4.894± 0.114	-0.007	0.116

Table 4: shows the percentage of neonates who developed hypocalcaemia after 48 hours of phototherapy

Variable	Group A N= 25	Group B N= 25	P value
Hypocalcaemia	6 (24%)	3 (12%)	0.030
Normal calcium	19 (76%)	22 (88%)	

Table 5: shows the percentage of neonates who developed jitteriness after 48 hours of phototherapy

Variable	Group A N= 25	Group B N= 25	P value
Jitteriness	4 (16%)	2 (8%)	0.186
NO	21 (84%)	23 (92%)	

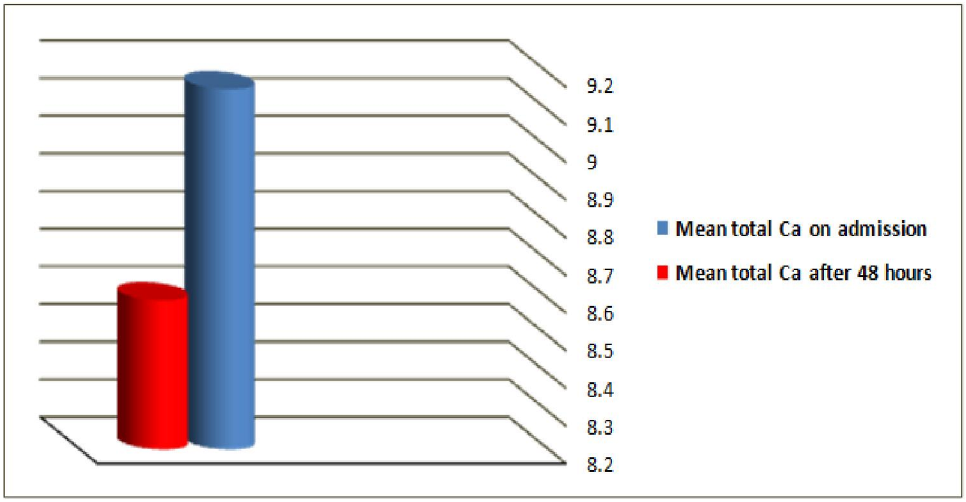

Figure 1: shows the change in total calcium level induced by phototherapy in group A.

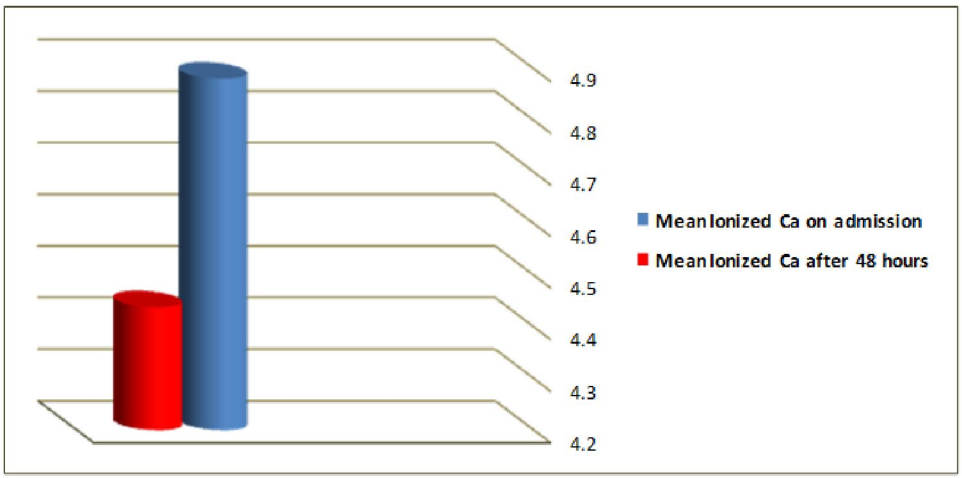

Figure 2: shows the change in ionized calcium level induced by phototherapy in group A.

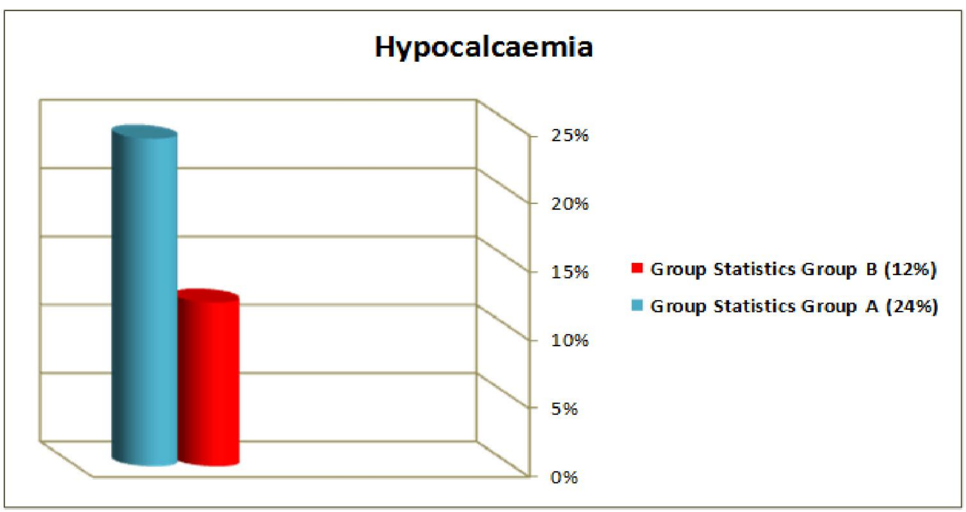

Figure 3: Comparison between both groups concerning hypocalcaemia after 48 hours of phototherapy.

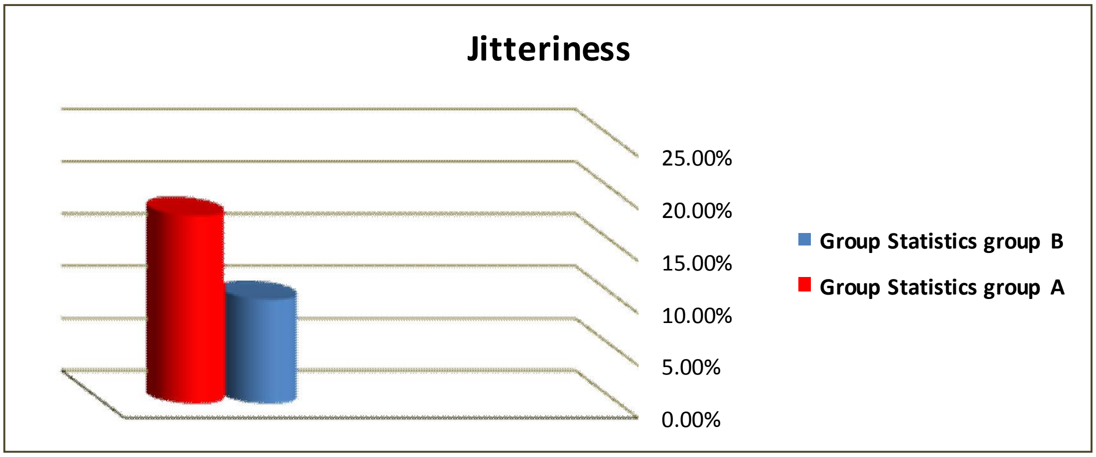

Figure 4: Comparison between both groups concerning jitteriness.

4. Discussion:

Phototherapy has a significant role in the treatment of hyperbilirubinemia in neonates [(14)]. However, this method may result in the development of some complications [(15)].

One of these complications is the induction of hypocalcaemia, which can create serious adverse effects including convulsions, jitteriness and irritability [(16)].

Karamifar et al. [(17)] found that only 22.6% of preterm and 8.7% of full-term infants developed hypocalcaemia.

Yadav et al. [(16)] observed that 66% of term and 80% of preterms developed hypocalcaemia after phototherapy. In his study 80% of hypocalcaemic term neonates became symptomatic, the most common sign was jitteriness.

Sameer Kumar Jain [(18)] found that 35% of preterm and 39% of full-term infants developed hypocalcaemia.

Hunter [(19)] hypothesized that phototherapy inhibits pineal secretion of melatonin blocks the effect of cortisol on bone calcium. Cortisol unchecked exerts a direct hypocalcaemic effect an increases bone uptake of calcium as well. It has been shown that by covering the heads of neonate during phototherapy, its effect on calcium level is prevented significantly proving the effect of phototherapy on pineal gland eventually causing hypocalcaemia. Neonates requiring phototherapy are at a higher risk of developing hypocalcaemia. Therefore, it is suggested that newborn requiring phototherapy administration of calcium may be considered in them.

There are several studies explain the effect of phototherapy on calcium. Phototherapy decreases melatonin level and corticosterone secretion [(19)]. Also urinary calcium excretion is increased after exposure to phototherapy [(20)].

To prevent the development of hypocalcaemia in phototherapy treated newborns, a previous study had recommended: either giving them oral calcium as prophylaxis or covering their heads and occipital area using a special hat during phototherapy, so that light effect from phototherapy on newborns' pineal gland and consequently melatonin decrease and hypocalcaemia can be prevented [(21)].

We detected hypocalcaemia after 48 hours of phototherapy in 6 neonates (24%) in group without hats and in 3 neonates (12%) in group with hats. The difference between groups was statistically significant (P value = 0.030).

Comparison between total and ionized calcium levels before and after 48 hours phototherapy in each group were done to detect the change in total and ionized serum calcium level induced by phototherapy.

In group A, the difference between total calcium level before and after 48 hours phototherapy (9.157 ± 0.411 and 8.596± 1.064 mg/dl) was statistically significant (P value = 0.049).

In group A, the difference between ionized calcium level before and after 48 hours phototherapy (4.881 ± 0.116 and 4.418± 0.841 mg/dl) was statistically significant (P value = 0.048).

In group B, the difference between total calcium level before and after 48 hours phototherapy (9.186 ± 0.892 and 9.233± 0.337 mg/dl) was not statistically significant (P value = 0.303).

In group B, the difference between ionized calcium level before and after 48 hours phototherapy (4.887 ± 0.655and 4.894± 0.114 mg/dl) was not statistically significant (P value = 0.116).

Our results are in agreement with the following studies:

Ehsanipour et al. [(9)], study: there were 14 (23.3%) full-term infants without covering their heads and 4 (6.7%) full-term after covering their heads developed phototherapy-induced hypocalcaemia, A significant difference was found between the incidence of hypocalcaemia in these two groups (P=0.000).

Also **Kargar M et al.** [22], study is in agreement with us: 14 (38.3%) full-term infants without covering their heads and 5(13.8%) full-term after covering their heads developed phototherapy-induced hypocalcaemia, A significant difference was found between the incidence of hypocalcemia in these two groups (P=0.03).

Our results are in consistent with **Ezzeldin Z et al.** [23], study, there was no difference in the mean Ca levels in the two groups on admission. However, after 48 hours of phototherapy, there was a trend toward an increased Ca level in the group with the hat; 8.74±0.95 mg/dLvs 8.51±0.24 mg/dL in the control group without hat. Moreover, there was a statistically significant decrease in the incidence of neonates with hypocalcaemia in Group B (with hat) in only six cases (9.7%), compared to 15 cases (24.2%) in Group A (without hat; P = 0.031).

In the same way **Zangoei et al.** [24], study also agree with us: Results of their study showed that the average of calcium level was significantly higher in the infants of test group with hat 48 hours after starting phototherapy compared to the control group without hat [P<0.001]. In other words, the incidence of hypocalcaemia in infants with phototherapy with hat was significantly lower than infants with routine phototherapy.

Also our study is in consistent with **Maha A. Nouh et al.** [25], study: Hypocalcaemia accounted for 11% and 24.4% in term neonates with covered heads and uncovered heads, respectively with significant difference (p0.02).

Our results are in agreement with **Abd-Elmagid M et al.** [26], study: in their study Hypocalcaemia was in12 neonate (34.3%) in group without hats and in 6 neonates 17.1%) in group with hats. The difference between groups was statistically significant (p=0.035). In group I without hats, the difference between total calcium level before and after 48 hours phototherapy (9.15±1.00 and 8.45±1.08) was statistically significant (p value<0.001). In group II with hats, the difference between total calcium level before and after 48 hours phototherapy (9.39±0.86 and 9.28±0.84) was statistically insignificant (p value = 0.265). In group I, the difference between ionized calcium level before and after 48 hours phototherapy (1.32±0.17 and 1.16±0.17) was statistically significant (p value<0.001). In group II, the difference between ionized calcium level before and after 48hours phototherapy (1.34±0.14 and 1.34±0.15) was statistically insignificant (p value=0.863).

Our results are not in agreement with **Afshin et al.** [27] where in 80 newborn cases under phototherapy, the mean serum Ca levels before and after phototherapy were 9.37 ± 0.86 and 9.25 ± 0.61 mg/dL, respectively (P = 0.171). They found no significant difference between serum Ca levels before and after phototherapy. Therefore, they do not suggest Ca prophylaxis before and during phototherapy.

According to our results the hat reduced incidence of hypocalcaemia but there was no statistically significant reduction in clinical signs of hypocalcaemia in the form of jitteriness.

Jitteriness is not pathognomonic for hypocalcaemia. More often it is non-specific and not related to the severity of hypocalcaemia and hypoglycamia [13].

So, it is hard to assess hypocalcaemia clinically and clinical signs cannot be evaluated properly.

No side effects were detected from using hat during this study. Hat was the safest method in prevention of phototherapy induced hypocalcaemia as it is non-invasive method and keeps the normal and physiological pattern of melatonin secretion.

Using prophylactic calcium supplementation can cause some side effects such as Constipation, belching and gas. Some possible side effects of calcium are more serious and include kidney stones, excessive drowsiness, muscle weakness, nausea, vomiting, frequent urination, changes in heart rate, confusion and allergic reactions [13].

Some limitations met us during this study. These limitations included the need for close contact with cases during phototherapy to be sure that hat was used all the time except during feeding. Also close follow up of clinical signs of hypocalcaemia that may appear during phototherapy.

5. Conclusion

We conclude that, phototherapy induced hypocalcaemia is an important side effect of phototherapy. Covering the head of infants under phototherapy using a hat was an effective, safe, non-invasive and cheap method for prevention of phototherapy induced hypocalcaemia.

References

1. Khosravi N, Samaie H, Mozhdehiazar K. Percentage of serum albumin in full term newborns in Shahid Akbar Abadi Hospital. Razi Journal of Medical Sciences. 2001;7:23-15.
2. Maisles MJ. Neonatal jaundice. *Pediatr Rev.* 2006;27(12):443-454.
3. Stokowski LA. Fundamentals of phototherapy for neonatal jaundice. *Adv Neonatal Care.* 2006;6(6):303-312.
4. Black S. The bright side of phototherapy. MCN Am J Matern Child Nurs. 1983;8:23.

5. Cloherty JP, Eichenwald EC, Stark AR. Manual of neonatal care.6th ed. Tehran (Iran). 2008; p.181.
6. Hakaason DO, Penny R, Bergstrom WH. Calcemic response to photic and pharmacologic manipulation of serum melatonin. Pediatr Res.1981;22:414-416.
7. Velayati AA, Rahmati M, Khorgami MR. Nelson essentials of pediatrice. In Faranoosh M, editor. 2006;1st ed:341-344.
8. Pezeshki N. Effect of calcium injection on prevalence of hypocalcemia in preterm newborns. Scientific Journal of Hamadan University of Medical Sciences & Health Services. 2005;3:9-16.
9. Ehsanipour F, Khosravi N, Jalali S. The effect of hat on phototherapy induced hypocalcaemia in icteric newborns. Razi J Med Sci. 2008;15(58):25-29.
10. Whaley L, Wong D. Text book of infantand pediatric nursing care. 2004;4th ed.
11. Apgar V. A proposal for a new method of evaluation of the newborn infant. Cure Res Anesth Analg. 1953;32:260-267.
12. Ballard JL, Khoury JC, Wedig K. New Ballard Score, expanded to include extremely premature infants. Pediatrics. 1991;119:417-423.
13. Jain A, Agarwal R, Sankar MJ, Deorari A, Paul VK. Hypocalcemia in the Newborn. Indian J Pediatr. 2010;77:1123–1128.
14. Barrington KJ, Sankaran K, Canadian Paediatric Society, Fetus and Newborn Committee. Guidelines for detection, management and prevention of hyperbilirubinemia in term and late preterm newborn infants. Pediatrics. 2014;114(4):917-924.
15. Basiglio CL, Arriaga SM, Pelusa F. Complement activation and disease: protective effects of hyperbilirubinemia. Clin Sci (Lond). 2010;118:99-113.
16. Yadav RK, Sethi RS, Sethi AS. The Evaluation of Effect of Phototherapy on Serum Calcium Level. People's Journal of Scientific Research. 2012;5:51-54.
17. Karamifar H, Pishva N, Amirhakimi GH. Prevalence of phototherapy-induced hypocalcemia. Iran J Med Sci. 2002;27(4):166–168.
18. Sameer Kumar Jain. Evaluation of effect of phototherapy on serum calcium level Medical Journal. 2015;2(6):316-318.
19. Hunter KM. Hypocalcaemia. In: Manual of Neonatal Care. JP Cloherty, EC Eichenwald, AR Stark (eds.): 5th Edn.: Lippincott Williams and Wilkins, Philadelphia. 2004;5:579-588.
20. Hooman N, Honarpisheh A. The effect of phototherapy on urinary calcium excretion in newborns. Pediatr Nephrol. 2005;20(9):1363-4.
21. Eghbalian F, Monsef A. Phototherapy-induced hypocalcemia in icteric newborns. IJMS.2002;27(4):162-171.
22. Kargar M, Zahra Jamshidi, Nooshin, Beheshtipour, Narjes Pishva, Maryam Jamali. School of Nursing and Midwifery, Nemazee Square, Shiraz, Iran. 2013;71936-13119.
23. Ezzeldin Z, Mansi Y, Abdelhamid TA, Sabry M. Dovepress Research and Reports in Neonatology. 2015; Volume 5.
24. Zangoei, Dovvom, Samane, Mottaghi Minoo. International Journal of Medical Research & Health Sciences. 2016;5(S):138-142.
25. Maha A. Nouh, Wafaa F. El-Saeed, Amaal E. Shehata, Sanaa M. Mostafa. Med.1 Cairo Univ. 2013;81(2):219-222.
26. Abd-Elmagid M. Bayomy, Ahmed Mahmoud Solaiman, Mohamed amr. American Journal of Medicine and Medical Sciences. 2017;7(2):55-60.
27. Afshin Safaei Asl, Marjaneh Zarkeshl, Abtin Heidarzadeh, Shohreh Maleknejad, Kaveh Hagikhani. Saudi Journal of kidney diseases and transplantation. 2016;27(3):486-492.

12/20/2017