ROLE OF HEAD COVERING AS A PROPHYLACTIC TOOL FOR PHOTOTHERAPY INDUCED HYPOCALCEMIA

Ehab Ibrahim I. Sorour, M.D; and Tarek El Sayyad

Pediatric Department Faculty of Medicine, Al-Azhar University Cairo

ABSTRACT

Background: Hyperbilirubinemia is the most common abnormal physical finding in the first week of life and is observed in approximately 60% of term infants and 80% of preterm infants **(Stoll and Piazza, 2007).**

Melatonin stimulates secretion of corticosterone which decreases calcium absorption by bones. Phototherapy leads to inhibition of pineal gland via transcranial illumination, resulting in a decline in melatonin level and as a result, hypocalcemia develops **(Karamifar et al., 2002).**

The aim of the study was to determine the effect of covering the head of infants during phototherapy on phototherapy induced hypocalcemia in jaundiced newborns.

Methodology: We conducted a comparative case control study at neonatal intensive care unit of Al Hussein hospital,(Al Azhar University in Cairo) starting from April 2014 to December 2014.This study included 100 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.

Calcium level was measured on admission and after 48 hours of phototherapy.

We designed a hat with a dark color that can cover all the head including the occipital area, ears and neck to prevent passage of light. The hat was used from admission and for 48 hours of treatment with phototherapy.

Neonates were randomized and divided into two groups: group (A) 50 infants under the routine phototherapy without hats and group (B) 50 infants using hats that cover occipital area. A comparative study was made between these groups to determine the effect of hat in prevention of phototherapy induced hypocalcemia.

Results: In this study, we found that 19 infants (19 %) of both groups developed hypocalcemia after 48 hours of starting phototherapy. There was significant statistical difference between the incidence of hypocalcemia in group A (without hats) which were 13 infants (26%) and group B (with hats) which were 6 infants (12 %)(p= 0.031).

Conclusion: We conclude that, phototherapy induced hypocalcaemia can be prevented by covering newborn head during phototherapy.

Recommendations: We recommend that neonates should be regularly evaluated for total serum calcium levels 48 hours after continuous exposure to phototherapy and should be managed accordingly; also all neonates with phototherapy should cover their heads using hats during treatment to prevent phototherapy induced hypocalcaemia.

INTRODUCTION

In Egypt about 20.4% of new-borns develop jaundice yearly. Incidence of jaundice was found to be higher in low birth weight infants (35.6%) compared to normal birth weight infants (16.9%) (**Mansour et al. , 2005).**

Features of pathologic jaundice include the appearance of jaundice within 24 hours after birth, a rapidly rising total serum bilirubin concentration (increase of more than 5 mg /dL / day), and a total serum bilirubin level higher than 17 mg / dL in a full-term newborn. Other features of concern include prolonged jaundice, evidence of underlying illness, and elevation of the serum conjugated bilirubin level to greater than 2 mg / dL or more than 20 % of the total serum bilirubin concentration **(Dennary et al., 2001).**

Phototherapy is the most widely used form of therapy for unconjugated hyperbilirubinernia **(Gathwala and Sharma, 2002)**.

Hypocalcemia is defined as total serum calcium of less than 8 mg/dL (2 mmol/L) or ionized calcium less than 4.8 mg/dl (1.2 mmol/L) in term neonates **(Jain et al., 2010).**

Physiological hypocalcemia occurs after birth as the transplacental calcium supply is cut, there is insufficient supply from the GI tract and insufficient release of PTH from the immature parathyroid gland. Total calcium levels drop to about 2 mmol/L and ionized to about 1 mmol/L. The nadir in calcium level occurs within the first 48 hours **(Stuart and Midgley, 2006).**

Hypocalcemia appears to be more common in premature infants under phototherapy lights. This may be due to higher penetration of light in premature infants. It has been suggested that this is mediated by altered melatonin metabolism **(Karamifar et al., 2002**).

Hooman and Honarpisheh, (2005) evaluated the effect of phototherapy on urinary calcium excretion in newborns. They founded that after exposure to phototherapy the urinary calcium

excretion is increased in 22% of icteric cases **(Hooman and Honarpisheh, 2005).**

Melatonin stimulates secretion of corticosterone which decreases calcium absorption by bones. Phototherapy leads to inhibition of pineal gland via transcranial illumination, resulting in a decline in melatonin level and as a result, hypocalcemia develops **(Eghbalian and Monsef, 2008).**

Light and dark alterations constitute the principal timing signal of melatonin secretion from the pineal gland, light influences melatonin synthesis in three ways. First, light exposure acutely suppresses elevated melatonin levels. Second, light is able to shift the melatonin rhythm. Third, changes in the photoperiod can alter the melatonin secretion, a single light pulse of moderate room illuminance induces an interruption of melatonin secretion and shifts the phase of the melatonin rhythm, thus, melatonin acts as a sensitive marker of environmental lighting in everyday conditions **(Hatonen, 2000).**

METHODS

This is a prospective study at the neonatal intensive care unit of Al Hussein hospital (Al-Azhar University in Cairo) starting from April 2014 to December 2014.

The study includes 100 full term neonates with symptoms, signs and laboratory findings of neonatal indirect hyperbilirubinemia treated with phototherapy. Apart from jaundice, their physical examination was apparently normal.

● Inclusion criteria:

1. Full term neonates.
2. Appropriate for gestational Age.
3. Neonates from 2 - 10 days old at the onset of indirect hyperbilirubinemia and will be managed by phototherapy.
4. Infants with normal vaginal delivery and Apgar score (7-10) at birth.

● Exclusion criteria:

1. The newborns with jaundice in the first 24 hours of life.
2. Premature newborns.
3. Infants with obstructed labor or Apgar score (<7) at birth.
4. Newborns of mothers taking anticonvulsants therapy (phenobarbital) during pregnancy.
5. Infants of mothers with thyroid or parathyroid disorders.

6- Cow milk fed newborns.

● Randomization:

Neonates were divided into two equal groups: group (A) 50 neonates under the routine phototherapy

without hats and group (B) 50 neonates using hats that covered their heads.

● **Procedure:**

We designed a hat from dark color clothes that can cover all the head including the occipital area, ears and neck to prevent passage of light. The hat was used from admission and for 48 hours of treatment with photo-therapy (figure 1) (Kargar et al: 2014).

(Kargar et al: 2014)

All neonates in the study were subjected to the following:

1. Full history taking:

With special emphasis on age, sex, onset of jaundice, maternal blood group and Rh, Apgar score and family history of jaundice.

2. Full clinical examination with special concern on:

A. Gestational age assessment using new Ballard score **(Ballard et al, 2012).**

B. detection of clinical signs of hypocalcemia: apnea, irritability, jitteriness and convulsions.

3. Laboratory investigations including:

A. Complete Blood Cell Count (CBC) with differential count and reticulocyte count.
B. Blood group and Rh.
C. CRP.
D. Serum calcium, total and ionized.
E. Total and direct bilirubin on admission.

A blood sample of 2 ml was obtained from all included neonates for measurement of serum calcium. Centrifugation system was used to obtain serum then calcium was measured using *Beckman CX9 PRO* (Mikolaenko et al., 2000).

We used a preset definition for hypocalcemia: Total serum calcium less than 8 mg/dl or ionized serum calcium less than 4.8 mg/dl in term neonates was considered hypocalcaemia **(Jain et al., 2010)**.

4. 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. **(Johnson et al., 2002).**

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. For comparing categorical data, Chi square ($\chi 2$) test was performed. *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 21 for Microsoft Windows **(Altman et al., 2005).**

RESULTS

The present study was carried out on 100 full term neonates with indirect hyperbilirubinemia treated with phototherapy. Their mean body weight was 3370 ± 334.14 grams (group A) and 3529.6 ± 277.6 (group B) and the difference between both groups was statistically significant. There is no statistical difference between both groups as regard sex difference.

The mean age at admission for group A was 4.56 ± 0.83 and 4.86±0.75 for group B with no significant statistical difference. The mean age of onset of jaundice in group A was 3.62±0.780 days and in group B was 3.40±0.495 and the difference between both groups was statistically insignificant (table 1).

Table (1): **Shows the baseline characters of the study population in both groups**.

Variable	Group A(50) Mean ± SD	Group B(50) Mean ± SD	P value
Body weight (gm)	3370±334.14	3529.6±277.6 *	**0.011**
Sex Female	25 (50%)	27 (54%)	**0.68**
Male	25(50%)	23 (46%)	**0.57**
Age of admission(days)	4.56±0.83	4.86±0.75	**0.063**
Age of onset of Hyperbilirubinemia (days)	3.62±0.780	3.40±0.495	**0.095**

*** Significant at p-value ≤ 0.05**

There was a significant decrease ($p \leq 0.05$) of total serum calcium 48 hours after phototherapy in group B compared to group A*. There was no significant difference among the studied groups in total serum calcium on admission, ionized calcium on admission, ionized calcium 48 hours after phototherapy and total serum bilirubin. (Table 2).

Table (2): Shows the descriptive data of biochemical parameters of both groups.

Variable	Group A Mean ± SD	Group B Mean ± SD	p value
Total Calcium on Admission (mg/dl)	**8.45±0.38**	**8.59±0.468**	**0.111**
Total calcium 48 hours After phototherapy (mg/dl)	**8.55±0.86**	**9.11±0.88 ***	**0.002 ***
Ionized Calcium on Admission (mg/dl)	**4.93±0.119**	**4.94±0.113**	**0.526**
Ionized Calcium48 hours After phototherapy (mg/dl)	**4.77±0.64**	**4.98±0.462**	**0.062**
Total serum bilirubin (mg/dl)	**17.5±1.07**	**17.72±0.87**	**0.471**

*** Significant at p-value ≤ 0.05**

Total number of studied newborn were 100 cases, 19 cases developed hypocalcemia after 48 hours of phototherapy (19%) and 81 of them showed normal calcium level (81%) (figure 2).

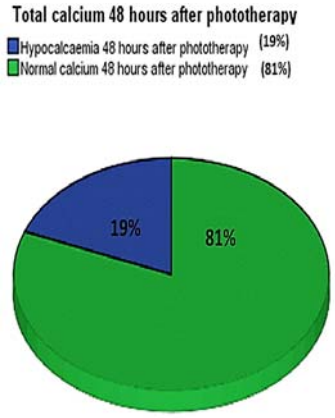

Figure (2): Shows the percentage of neonates with hypocalcaemia 48 hours after phototherapy.

Hypocalcemia was found in 19 patients of both groups(19%), 13 of them were in group A(26%) and 6 cases in group B(12%)while 81 cases were with normal calcium level in both groups, 37 of them was in group A (74%) and 44 were in group B(88%). The statistical difference between both groups was significant (p<0.01) (table 3).

Table (3): shows the percentage of neonates who developed hypocalcemia after 48 hours of phototherapy.

Variable	Group A N= 50	Group B N= 50	p value
Hypocalcemia	13 (26%)	6 (12%)	<0.01*
Normal calcium	37 (74%)	44 (88%)	

*p value <0.01 is significant

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

In this study, we found a significant statistical difference in the mean total calcium level on admission and after 48 hours of phototherapy in group B (p <0.01) , while in group A the statistical difference between results of mean total calcium were insignificant (table 4).

Table 4: Shows the change in the mean total serum calcium (mg/dl Mean ± SD) induced by phototherapy in both group.

Variable	Mean Ca on admission	Mean Ca after 48 hours	Mean Difference	P value
Group A Mean ± SD	8.892±.48	8.146±.56	0.1	<0.01*
Group B Mean ± SD	9.284±.63	8.454±.57	0.53	0.08

*p value <0.01 is significant

DISCUSSION

Phototherapy plays a significant role in the treatment of hyper-bilirubinemia in neonates **(Stokowski, 2006).** However, this treatment modality may itself result in the development of some complications **(Ehsanipour et al., 2008).**

One of the important complications is the induction of hypocalcaemia, which can create serious adverse effects including convulsions, jitteriness and irritability **(Eghbalian and Monsef, 2008).**

There are several studies explain the effect of phototherapy on calcium, phototherapy decreases melatonin level and corticosterone secretion **(Karamifar et al., 2002).** Also urinary calcium excretion is increased after exposure to phototherapy **(Hooman and Honarpisheh, 2005).**

In order to prevent the development of hypocalcemia 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 hypocalcemia can be prevented **(Eghbalian and Monsef, 2008).**

In our study hypocalcaemia was found in 19 of our neonates (19 %), this is inconsistent with the previous studies which reported that the incidence of hypocalcaemia after 48 hours of photothera**py** was 14.4% **(Karamifar et al., 2002)**, and 15% **(Ehsanipour et al., 2008).**

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

Neonates with hypocalcemia were 13 cases (26%) in group A and 6 cases (12%) in group B . Neonates with normal calcium were 37 cases (74%)in group A and 54 cases (88%) in group B**.**

There was no significant difference in serum ionized calcium on admission compared to level 48 hours after phototherapy in the studied groups.

Our study was consistent with study done by ***Ehsanipour`s 2008***, where 23.3% full-term infants without covering their heads and 6.7% full-term after covering their heads developed phototherapy-induced hypocalcaemia**.**

Hypocalcaemia can be explained by the effect of phototherapy on melatonin secretion. Melatonin is a hormone (N-acetyl-5 methoxy-tryptamine) that is produced naturally in the human body by the pineal gland. It is produced especially at night **(Goni, 2003).**

Melatonin stimulates secretion of corticosterone which decreases calcium absorption by bones. Phototherapy leads to inhibition of pineal gland via transcranial illumination, resulting in a decline in melatonin level and as a result, hypocalcemia develops **(Karamifar et al., 2002).**

No side effects were detected from using hat during this study. Hat is 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 **(Pohanka, 2011).**

CONCLUSION/ RECOMMENDATIONS

From this study we conclude that, phototherapy induced hypo-calcaemia is an important side effect of phototherapy.

All neonates should be regularly evaluated for total and ionized serum calcium levels 48 hours after continuous exposure to phototherapy and should be managed accordingly.

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.

Further studies, including a big number of full term and preterm neonates are required to support our conclusion and to study the effects of head covering versus calcium supplementation in the prevention of phototherapy induced hypocalcemia.

REFERENCES

1. **Altman, Edward I., Brooks Brady, Andrea Resti and Andrea Sironi**, (2003): "The Link between Default and Recovery Rates: Theory, Empirical Evidence and Implica-tions", NYU Salomon Center Working Paper Series # S-03-4, Journal of Business, 78 (6), 2203-27.

2. **Ballard, JL; Khoury, JC; Wedig, K; Wang, L; Eilers-Walsman, BL;**

Lipp, R(1991): "New Ballard Score, expanded to include extremely premature infants.". The Journal of Pediatrics 119 (3): 417–23. doi:10.1016/s0022-3476(05)82056-6. PMID 1880657. Retrieved 13 August 2012.

3. **Dennery PA, Weng Yi-Hao, Stevenson DK, Yang Guang** (2001): The biology of bilirubin production. Journal of Perinatology; 21:17 – 20.

4. **Eghbalian F, Monsef A**(2008): Phototherapy-induced hypocalcemia in icteric newborns. IJMS; 27(4):162-171.

5. **Ehsanipour F, Khosravi N, Jalali S** (2008): The effect of hat on photo-therapy induced hypocalcaemia in icteric newborns. IUMS; 15(58):25-29.

6. **Gathwala G and Sharma S** (2002): Phototherapy induces oxidative stress in premature neonates. Indian J Gastroenterol.; 21(4):153-154.

7. **Goñi LA** (2003): Regulation of melatonin synthesis: sympathetic noradrenergic mechanisms. In: Human melatonin receptors: molecular mechanisms of action and their implication in cell proliferation. Faculty of Biology. University of Hamburg;.7- 9.

8. **Hannibal J** (2002): Neurotransmitter of the retino-hypothalamic tract. Cell Tissue Res; 309(1):73- 88.

9. **Hätönen T (**2000): Melatonin and the Pineal Gland. In: The Impact of Light on the Secretion of Melatonin in Humans. University of Helsinki. Helsinki, Finland;. 19- 27.

10. **Hooman N and Honarpisheh A** (2005): The effect of phototherapy on urinary calcium excretion in newborn. Pediatr Nephrol; 20:1363-4

11. **Jain A, Agarwal R, Sankar MJ, Deorari A, Paul VK** (2010): Hypocalcemia in the Newborn. Indian J Pediatr; 77: 1123– 1128.

12. **Johnson LH, Bhutani VK, Brown AK** (2002): System-based approach to management of neonatal jaundice and prevention of kernicterus. *J Pediatr.*;140 :396– 403

13. **Karamifar H, Pishva N, Amirhakimi GH (**2002): Prevalence of phototherapy induced hypocalce-mia. IJMS; 27(4):166-168.

14. **Kargar M, Jamshidi Z, Beheshtipour N, Pishva N, Jamali M** (2014): Effect of head covering on phototherapy-induced hypocalcaemia in icterus newborns; a randomized controlled trial. *Int J Community Based Nurs Midwifery*.;2(2):121–126.

15. **Mansour B, Eissa AN, Nofal LM, KhArboush I, Reda AA** (2005): Morbidity and Mortality of low birth weight infants in Egypt. East Mediterr Health J; 11(4):723-731.

16. **Mikolaenko I, Benson E, Konrad RJ, Chaffin C, Robinson CA, Hardy RW** (2000): Evaluation of the Beckman Coulter LX20 Clinical Chemistry Analyzer. Lab Med.; 31:387–93.

17. **Pohanka M** (2011). Alzheimer´s disease and related neurodegenerative

disorders: implication and counteracting of melatonin. Journal of Applied Biomedicine .; 9: 185–196.

18. Stokowski LA (2006)**.** Fundamentals of phototherapy for neonatal jaundice. Adv Neonatal Care; 6: 303-312.

19. Stoll BJ and Piazza AJ (2007)**.** Jaundice and hyperbilirubinemia in the newborn. In: Behrman RE, Kliegman RM, Jenson HB. Nelson Textbook of Pediatrics. 18th ed. Philadelphia: WB Saunders Co;. 756-761.

20. Stuart AO and Midgley P (2006). Hypocalcaemia. In: Practical Neonatal Endocrinology. 1st ed. Cambridge: Cambridge University Press;. 133- 142.

دور غطاء الرأس كوسيلة حماية من انخفاض مستوى الكالسيوم بالدم المصاحب للعلاج الضوئي لحديثي الولادة الذين يعانون من اليرقان

إيهاب إبراهيم سرور - طارق السيد
قسم طب الأطفال - كلية الطب - جامعة الأزهر - القاهرة

اليرقان من اشهر المشاكل التى يتعرض لها الأطفال حديثى الولادة. وتصل نسبة حدوث اليرقان الى حوالى 60% فى الأطفال مكتملى النمو والى حوالى 80% فى الأطفال ناقصى النمو أثناء الأسبوع الأول لحياة الطفل. يحدث اليرقان نتيجة ترسب صبغة الصفراء غير المرتبطة فى الجلد والأغشية المخاطية ويصعب تشخيصه بالفحص الطبى فقط.

ويعتبر العلاج الضوئى من أشهر وسائل العلاج وأكثرها استخداما.

وقد يعانى بعض الأطفال الذين يخضعون للعلاج الضوئى من بعض الأعراض الجانبية مثل الطفح الجلدى وفقدان لسوائل الجسم اذا لم يأخذ الطفل السوائل المناسبة وتدمير الأعصاب فى شبكية العين وتأثير ضار على الأعضاء التناسلية. كما يعانون من الاسهال وارتفاع درجة الحرارة.كما يعتبر انخفاض نسبة الكالسيوم بالدم الناشئ عن استخدام العلاج الضوئى من المضاعفات التى يجب ان تؤخذ فى الاعتبار.

ويعزى انخفاض الكالسيوم الى تأثير الضوء على افراز هرمون الميلاتونين بحيث يقل الميلاتونين ونتيجة لذلك يقل افراز الكورتيزون مما يؤدى الى زيادة ترسيب الكالسيوم فى العظام أكثر من اللازم وبالتالى انخفاض نسبة الكالسيوم بالدم.

وقد كان الهدف من هذه الدراسة تقييم فائدة استخدام غطاء لرأس الطفل حديث الولادة اثناء العلاج الضوئى.

وشملت الدراسة 100 حالة من حديثي الولادة كاملي النمو مقسمين الي مجموعتين: المجموعة الأولى وتضم 50 من حديثى الولادة الذين تعرضوا للعلاج الضوئى دون تغطية الرأس والمجموعة الثانية وتضم 50 من حديثى الولادة الذين استخدم معهم غطاء للرأس أثناء العلاج الضوئى.

وقد تم استبعاد حالات نقص النمو والعمر الرحمى و الحالات التى تحتاج الى تغيير الدم وحالات العدوى الميكروبية والذين عانوا من اختناق اثناء الولادة والأطفال من أمهات مرضى بالسكر.

وقد اسفرت نتائج هذه الدراسة عن ظهور انخفاض فى مستوى الكالسيوم الكلي بالدم بعد مرور 48 ساعة من بداية العلاج الضوئى وذلك فى 19 حالة من ال100 حالة موضوع الدراسة (19%) مما يعضد نظريه انخفاض نسبه الكالسيوم بالدم نتيجة للعلاج الضوئي .

اما عند قياس نسبه الكالسيوم بالدم في الاطفال حديثي الولادة الذين تمت تغطية رؤوسهم بغطاء الرأس (المجموعه الثانيه) فقد وجد ان نقص نسبه الكالسيوم لديهم اقل من الاطفال بدون غطاء الرأس (المجموعه الاولي) 12 % مقارنة ب 26 % علي الترتيب .

ونستنبط من هذه الدراسة اتضح ان نقص مستوى الكالسيوم بالدم يمكن ان ينتج عن العلاج الضوئى اثناء علاج حالات ارتفاع الصفراء بالدم إلا انه يمكن تقليص فرص حدوثه عن طريق تغطية رأس الطفل اثناء استخدام العلاج الضوئى.

وتوصى هذه الدراسة باستخدام غطاء للرأس اثناء تعرض الطفل الى العلاج الضوئى للحد من حدوث نقص الكالسيوم بالدم وإن هذه الطريقة أمنه ومتاحة وغير مكلفة.

كما توصي هذه الدراسة بعمل دراسات أخرى باستخدام أعداد أكبر من حديثي الولادة من مكتملي العمر الرحمي وكذلك اللأطفال المبتسرين والمقارنة بين تغطية الرأس أثناء العلاج الضوئي وبين العلاج بالكالسيوم لمنع حدوث تلك الظاهرة.