Systematic Review:

The Therapeutic Effect of Zinc Sulfate in Iranian Neonates With Hyperbilirubinemia: A Systematic Review and Meta-Analysis

Gholamreza Kalvandi[1], Mehdi Shokri[2], Hamed Tavan[3*]

1. Department of Pediatrics Gastroenterology, School of Medicine, Ilam University of Medical Sciences, Ilam, Iran.
2. Department of Pediatrics, School of Medicine, Ilam University of Medical Sciences, Ilam, Iran.
3. Clinical Research Development Unit, Shahid Mostafa Khomeini Hospital, Ilam University of Medical Sciences, Ilam, Iran.

Use your device to scan and read the article online

Citation Kalvandi GR, Shokri M, Tavan H. The Therapeutic Effect of Zinc Sulfate in Iranian Neonates With Hyperbilirubinemia: A Systematic Review and Meta-Analysis. Journal of Pediatrics Review. 2020; 8(3):145-152. http://dx.doi.org/10.32598/jpr.8.3.834.1

http://dx.doi.org/10.32598/jpr.8.3.834.1

Article info:
Received: 25 May 2019
First Revision: 06 Jun 2019
Accepted: 18 Oct 2019
Published: 01 July 2020

Key Words:
Therapy, Infant, Treatment, Zinc sulfate

ABSTRACT

Background: Physiologic jaundice in neonates usually occurs during the first week of life. The main cause of this condition is increased serum bilirubin due to heme catabolism.

Objectives: This systematic review and meta-analysis study aimed to investigate the therapeutic effect of zinc sulfate in Iranian newborns with hyperbilirubinemia.

Methods: This review was performed based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocol. The databases of ISI, Cochrane Library, Google Scholar, PubMed, and Scopus were independently searched by two researchers using MeSH keywords. We included the studies published in different regions of Iran from 2015-2018. The obtained data were analyzed using the meta-analysis technique and STATA. To determine the heterogeneity across the studies, the Q and I square (I2) indices were used.

Results: A total of 40 articles were collected from which 5 studies with adequate quality entered the systematic review process. The collected results were assessed in the intervention (zinc sulfate recipients) and control (without zinc sulfate treatment) groups. After the first day of consumption, total serum bilirubin level decreased 4.46 mg/dL (I2=61.9%, P=0.049) and 4.08 mg/dL (I2=72.9%, P=0.011) in the intervention and comparison groups, respectively. In the second and third days, the mean values of decreases in serum bilirubin reached 7.64 mg/dL and 6.66 mg/dL in the intervention and comparison groups, respectively. From the third day onward, serum bilirubin dropped by 8.46 and 7.08 mg/dL in intervention and control groups, respectively. Meta-regression analysis data based on the sample size and year of the study indicated a significant growing trend in using zinc sulfate by increasing years and sample size.

Conclusions: Zinc sulfate is a safe and effective medication in reducing bilirubin level and its usage has increased in recent years. Therefore, this supplement could be used for the treatment of neonatal hyperbilirubinemia.

** Corresponding Author:*
Hamed Tavan, MSc.
Address: *Clinical Research Development Unit, Shahid Mostafa Khomeini Hospital, Ilam University of Medical Sciences, Ilam, Iran.*
Tel: *+98 (918) 7474221*
E-mail: *hamedtavan@gmail.com*

1. Introduction

The physiologic jaundice in neonates usually occurs within the first weeks of life (1). Its prevalence is estimated to be approximately 60% in term neonates and 80% in premature infants (2). The main cause of neonatal hyperbilirubinemia is the increased level of serum bilirubin due to heme catabolism (3). Direct bilirubin is produced by the destruction of erythrocytes. Erythrocytes are produced in the bone marrow and destructed in the spleen at the end of their lifespan. Hemoglobin is then broken down into hem and globin chains (4). Indirect hyperbilirubinemia occurs when non-conjugated bilirubin enhances. Increased non-conjugated bilirubin occurs in neonatal jaundice, Gilbert's syndrome, hemolytic anemia, and Crigler–Najjar syndrome (5, 6). Conjugated hyperbilirubinemia generates in liver and bile ducts conditions, including liver cirrhosis, liver tumors or abscesses, intrahepatic obstruction, hepatitis, congenital rotors syndromes, and Dubin–Johnson syndrome (7, 8).

Therapeutic methods in neonatal hyperbilirubinemia include phototherapy, blood exchange, and pharmaceutical treatments, like zinc sulfate supplementation (9). Each of these treatments is used considering the neonates' clinical conditions. Some studies have suggested that phototherapy during the neonatal period may increase the risk of melanoma at older ages (10, 11).

Mendez et al. found that zinc salts could dissociate almost all non-conjugated bilirubin from unsaturated bile salts in physiologic pH in hamster's intestine inhibiting its reuptake. Oral zinc supplements could suppress the biliary secretion of bilirubin in hamsters (12). A study evaluated the effect of zinc sulfate on patients with Gilbert's syndrome. The relevant data demonstrated that administrating oral zinc sulfate significantly reduced serum bilirubin levels in the studied subjects (13). Another study indicated that zinc sulfate administration on the second day after birth did not significantly reduce serum bilirubin level in the term and preterm healthy neonates; however, it reduced the duration of phototherapy (14).

Zinc sulfate has a great safety profile and is associated with no adverse complications. Besides, zinc is an essential mineral required for growth and development and participates in multiple metabolic pathways (15, 16). The purpose of meta-analysis surveys is to provide an integrated approach toward a specific issue (17, 18). Comprehensive data on the therapeutic effect of zinc sulfate in neonatal hyperbilirubinemia in Iran are scarce. Systematic review and meta-analysis of clinical trials regarding the therapeutic effect of zinc sulfates in neonatal jaundice have been disregarded.

Therefore, to validate the results of clinical trials on this issue, it seems necessary to perform a meta-analysis to provide precise and valid evidence for planners and researchers in this field. The present study aimed to investigate the therapeutic effect of zinc sulfate in neonatal hyperbilirubinemia in Iran. Accordingly, we performed a systematic review and meta-analysis on clinical trials in this regard.

2. Methods

This systematic review and meta-analysis study was conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The study involved 5 steps, including initial design, literature search, collection and review of articles for inclusion criteria, qualifying the articles, and finally the statistical analysis. To prevent publication bias, the search was independently performed by two researchers; then, the results of the studies were combined by a third person.

To obtain the studies related to the research question, a comprehensive search was conducted in the national and international scientific resources (Magiran, Iran Medex, Scopus, PubMed, Cochrane, and Web of Science), and Google Scholar. According to the research question, "bilirubin" and "zinc sulfate" were used as keywords. These keywords were initially searched individually following a combinational comprehensive search using Boolean operators. Eventually, to find relevant articles, the references of the recruited articles were checked. The full-texts of relevant and non-duplicated articles were finally provided to the researchers. Original research papers assessing the effect of zinc sulfate in the treatment of hyperbilirubinemia in Iranian newborns were included.

Low-quality and irrelevant articles, those with incomplete data, review articles, case reports, letters to editors, qualitative studies, the abstracts of articles presented in congresses without complete information were excluded from the study.

The Consolidated Standards of Reporting Trials (CONSORT) checklist [18-17] was used to qualify the listed articles. Two of the authors independently dedicated each part of the checklist with a score between 0-2. Based on the total scores obtained from the checklist, the ar-

ticles were categorized as weak (scores 1-15), moderate (scores 16-30), and good (scores 31-44). Articles that acquired ≥16 scores were entered into the meta-analysis.

In the final list of evaluated papers, those investigating the therapeutic effect of zinc sulfate in neonatal hyperbilirubinemia in Iran were analyzed. The recorded variables were the first author's name, publication date, research location, sample size, the characteristics of zinc sulfate treatment and control groups, as well as features related to the neonates with hyperbilirubinemia, comparisons between the intervention and comparison groups, and alternations in bilirubin levels in the intervention (i.e., zinc sulfate) and control groups. The information from the final papers was entered into a researcher-made checklist.

Since the number of final studies <10 and given the type of data used, funnel plot and analyses on publication bias were not performed. Then I square (I2) index was used to calculate the data heterogeneity. The heterogeneity index between the studies was individually calculated for each study variable. Considering the significant heterogeneity between the studies (P<0.001), the random-effects model was used to combine the results of different studies. The obtained data were analyzed using STATA.

3. Results

Initially, a list of all the titles and abstracts of the collected articles was prepared. After hiding the specifications of the articles (including the names of the journals and authors), the articles' full-texts were provided to the researchers.

First, 40 related articles were obtained. Of these, 20 articles were excluded due to improper communication and incomplete results on the topic. After reviewing the articles' full-texts, 15 related papers were omitted due to the lack of necessary criteria. Finally, 5 papers were entered into the evaluation step. The selection protocol of the studies is shown in Figure 1. The total number of the samples was 364 neonates with hyperbilirubinemia rendering 73 subjects per study. The characteristics of the included articles are presented in Table 1 (19-23). All the variables studied in each intervention (zinc sulfate

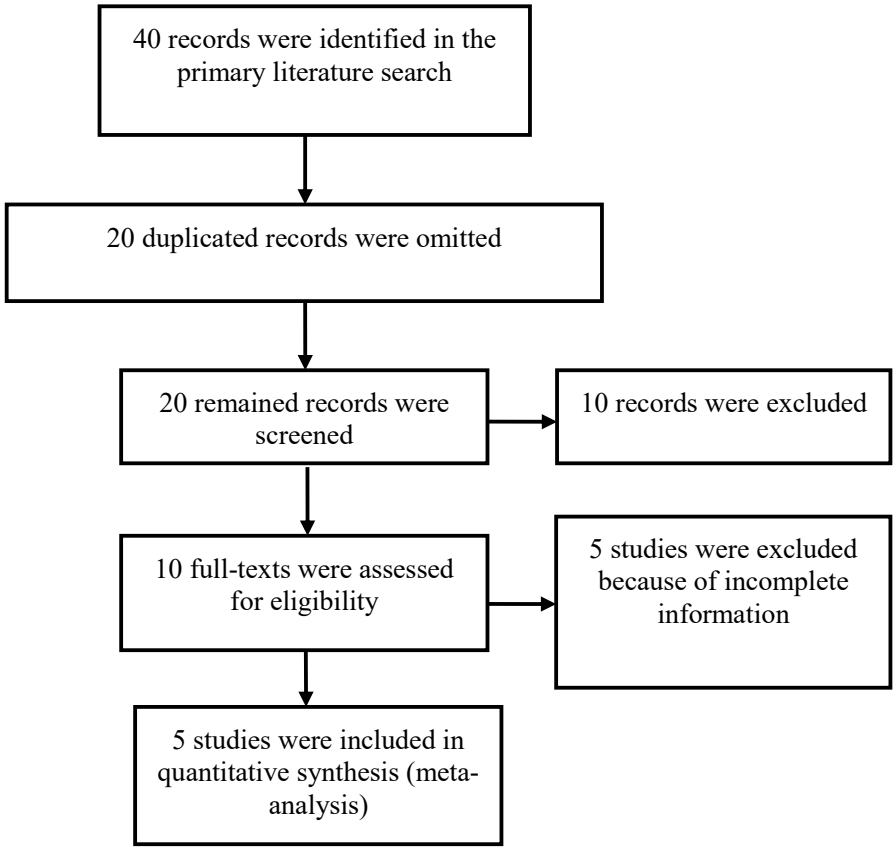


Figure 1. Flowchart of the studies in the systematic review and meta-analysis

Table 1. Specifications of the reviewed articles

References	Author	Year	Place	Total (No.)	Male (No.)	Female (No.)
19	Mafinezhad	2015	Khorasan	66	25	41
20	Nabavizadeh	2015	Yasooj	78	4	74
21	Mohammadzadeh	2016	Mashhad	60	20	40
22	Hashemian	2017	Mashhad	70	39	31
23	Beiravand	2018	Lorestan	90	-	-

Journal of Pediatrics Review

Table 2. The effect of zinc sulfate supplementation in hyperbilirubinemia newborns by subgroups

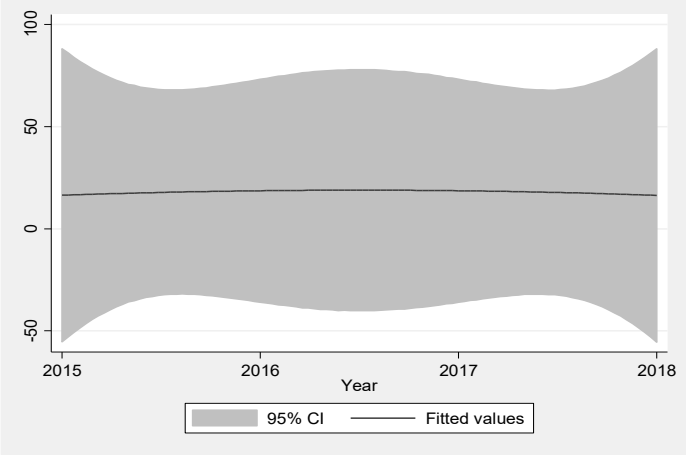
Subgroup	Articles No. (%)	CI/95	I2	P
Age of infants (d)	4 (5.87)	3.41.-8.33	99.8	0.000
Weight of infants (gr)	6 (1837.4)	1603-2071	87.9	0.000
Pregnancy birthday	3 (37.38)	35.82-38.94	79.7	0.007
Amount of hemoglobin in the intervention group	3 (15.74)	12.94.-18.55	99.2	0.000
Amount of hemoglobin in the control group	2 (B16.53)	13.51-19.55	-	-
Amount of reticulocyte in the intervention group	3 (1.34)	-0.04-2.72	0	0.926
Amount of reticulocyte in the controls	3 (0.86)	0.45.-1.27	0	0.739
Total bilirubin value in intervention group (baseline)	4 (17.12)	15.08.-19.16	61.9	0.049
Total bilirubin value in the controls (baseline)	4 (17.15)	15.47.-18.82	72.9	0.011
Total bilirubin in intervention group (day one)	4 (12.66)	10.9-14.42	0	0.887

Journal of Pediatrics Review

supplementation) and control (no zinc sulfate supplementation) group are noted in Table 2.

Meta-regression analysis, in terms of the year of the study, suggested a significant result (P<0.001); it indicated a growing trend in using zinc sulfate by the increasing year of study conduction and sample size (Figure 2).

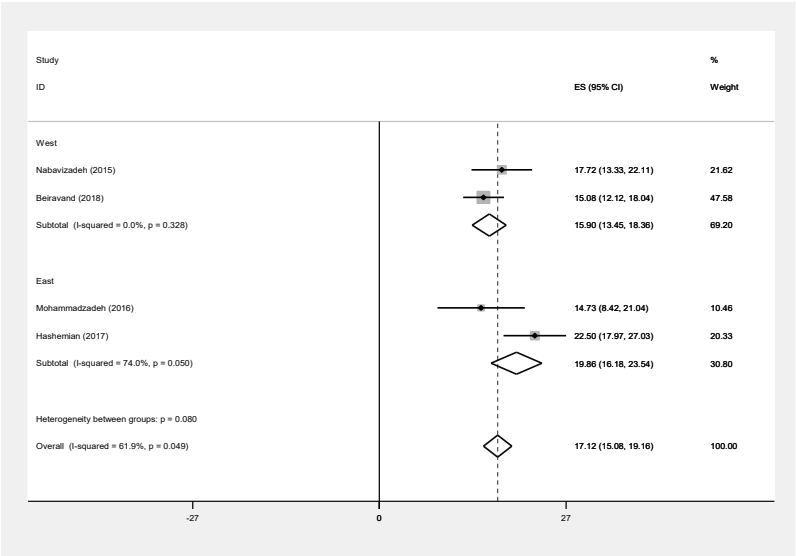
Forest plot 3a) shows the total bilirubin value in the case group (baseline) 17.12 (95% CI: 15.08. -19.16, I2=61.9), and Forest plot 3b) demonstrates the total bilirubin value in the control group (baseline) 17.15(95% CI:15.47.-18.82, I2=72.9) (Figure 3).



Journal of Pediatrics Review

Figure 2. Meta-regression analysis of the therapeutic effect of zinc sulfate in neonatal hyperbilirubinemia by the year of study

A



B

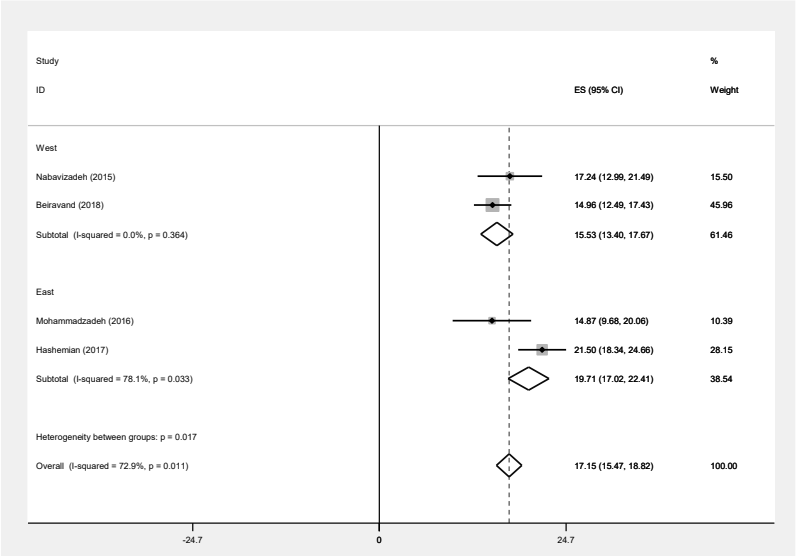


Figure 3. Forest plot related to the total bilirubin value

a) in the intervention group (baseline) with a 95% confidence interval; b) in the control group (baseline) with a 95% confidence interval

4. Discussion

The present study investigated the therapeutic effect of zinc sulfate in neonatal hyperbilirubinemia in Iran. A systematic review and meta-analysis were conducted on the related clinical trials. Our results suggested that hemoglobin levels were lower in the neonates treated with zinc sulfate, compared to those of the placebo group. Studies have also revealed that a high hemoglobin level is a prerequisite for neonatal jaundice and hyperbilirubinemia (24-26). Zinc sulfate supplementation could decompose and reduce blood hemoglobin; however, care should be taken to prevent anemia or other hematologic disorders in this condition.

The achieved results indicated that the reticulocyte percentage was higher in neonates administrated with zinc sulfate, compared to the controls. Hermanson et al. argued that elevated Nucleated Red Blood Cells (NRBCs) and reticulocytes could be related to either oxytocin-induced stress in labor, acute and chronic asphyxia, preeclampsia, maternal diabetes, smoking, and various types of anemia, or hemolytic during the embryonic period (27). Christianson et al. documented a significant

association between the increased levels of NRBCs and reticulocytes and the incidence of intracranial hemorrhage in preterm labor (28). Samiei et al. also suggested that elevated NRBCs and reticulocytes could predict the incidence of jaundice (29).

In the present report, the mean age of the infants was approximately 5 days. The obtained data revealed that the incidence of neonatal hyperbilirubinemia is common during the first week of life (30, 31). We investigated the total serum bilirubin level in two groups of neonates (zinc sulfate treated vs. non-treated). After the first day of life, the total bilirubin level declined 4.46 mg/dL and 4.08 mg/dL in the intervention and placebo groups, respectively. During the second and third days, there were 7.64 mg/dL and 6.66 mg/dL decreases of the same unit in the intervention and control groups, respectively. After the third day, the serum bilirubin level declined by 8.46 mg/dL and 7.08 mg/dL in the test and placebo groups, respectively.

In similar studies, Rana et al. described that an early administration of zinc sulfate failed to reduce the incidence of neonatal jaundice; nevertheless; it shortened the duration of hospitalization for phototherapy (14). Mendez et al. (32) reported that oral zinc sulfate supplementation could suppress the intestinal-hepatic cycle of bilirubin; therefore, it could be administered for treating neonatal physiologic jaundice. In individuals who are prone to bile ducts stones secondary to dietary regimens, diseases, or medications, oral zinc salts could reduce the risk of biliary stones by increasing the excretion of indirect bilirubin (12). Mendes et al. assessed the impacts of daily administration of oral zinc sulfate (100 mg) for 7 days on serum indirect bilirubin levels in patients with Gilbert syndrome (13). They concluded that administrating zinc sulfate reduced the bilirubin level in the studied patients, i.e., possibly due to suppressing the intestinal-hepatic cycle (13). Another study conducted on healthy-term and near-term neonates revealed that zinc sulfate supplementation failed to significantly reduce serum bilirubin levels; however, this method reduced the duration of phototherapy. The reason why zinc had no effect son bilirubin level in the recent study may be due to the late onset of treatment (i.e., day 2 after birth) (14). Zinc sulfate is a safe supplement without unwanted complications and is among the minerals required for proper growth and development. Zinc deficiency interferes with the main metabolic pathways (15). According to the results of the above-mentioned studies, zinc sulfate could be an effective supplement to treat neonatal hyperbilirubinemia; however, more studies are required to support this conclusion.

The meta-regression analysis data indicated that numerous studies explored the therapeutic roles of zinc sulfate with moving toward 2018. Therefore, the focus on zinc sulfate introduces it as an appropriate and safe supplement in neonatal hyperbilirubinemia (15).

The studied variables were very limited. There were differences in the days of treatments and the doses of zinc sulfate in some studies. Additionally, some studies merely reported the overall alternations in the serum bilirubin level without specified comparisons between genders, age groups, and risk factors.

5. Conclusion

Because of its excellent safety profile, zinc sulfate has been used more frequently in recent years to reduce serum bilirubin levels in neonatal hyperbilirubinemia.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles are considered in this article. The participants were informed about the purpose of the research and its implementation stages; they were also assured about the confidentiality of their information; moreover, they were free to leave the study whenever they wished, and if desired, the research results would be available to them.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or non-profit sectors.

Authors' contributions

All authors contributed in designing, running, and writing all parts of the research.

Conflicts of interest

The authors declared no conflicts of interest.

References

1. Daunhawer I, Kasser S, Koch G, Sieber L, Cakal H, Tütsch J, et al. Enhanced early prediction of clinically relevant neonatal hyperbilirubinemia with machine learning. Clinical

Research Article. 2019; 86(1):122-7. [DOI:10.1038/s41390-019-0384-x] [PMID]

2. Michael K, Ronald JW, Eric Sibley DK. Neonatal jaundice and liver disease. In: RJ Martin, AA Fanaroff, MC Walsh. Neonatal-Perinatal Medicine Diseases of the Fetus and Infant Medicine. 9th edition. Philadelphia: Mosby Elsevier. 2011; 1443-81. [DOI:10.1016/B978-0-323-06545-0.00057-1]

3. Castillo A, Grogan TR, Wegrzyn GH, Ly KV, Walker VP, Calkins KL. Umbilical cord blood bilirubins, gestational age, and maternal race predict neonatal hyperbilirubinemia. PLoS One. 2018; 13(6):e0197888. [DOI:10.1371/journal.pone.0197888] [PMID] [PMCID]

4. Duman H, Özyurt S, Erdoğan T, Kara BY, Durakoğlugil ME. The role of serum bilirubin levels in determining venous thromboembolism. Journal of Vascular Surgery: Venous and Lymphatic Disorders. 2019; 7(5):635-9. [DOI:10.1016/j.jvsv.2019.02.002].

5. Saylam Kurtipek G, Sarı N, Tuncez Akyurek F. Significant Reduction in Bilirubin Levels in a patient with Gilbert Syndrome under Isotretinoin treatment for Acne Vulgaris: A new area of use for Isotretinoin? Dermatologic Therapy. 2019; 32(3):e12884 [DOI:10.1111/dth.12884] [PMID]

6. Liang TQ, Tang LJ, Huang WM. Effects of Yinzhihuang oral liquid and Lonicera japonica extract on hemolysis and hyperbilirubinemia in rats with glucose-6-phosphate dehydrogenase deficiency. Zhongguo Dang Dai ErKeZaZhi. 2018; 20(9):769-74.

7. Chiou FK, Ong C, Phua KB, Chedid F, Kader A. Conjugated hyperbilirubinemia presenting in first fourteen days in term neonates. World Journal of Gastroenterology. 2017; 9(26):1108-14. [DOI:10.4254/wjh.v9.i26.1108] [PMID] [PMCID]

8. Brumbaugh D, Mack C. Conjugated hyperbilirubinemia in children. Journal of Pediatrics Review. 2012; 33(7):291-302. [DOI:10.1542/pir.33-7-291] [PMID]

9. Quidde J, Azémar M, Bokemeyer C, Arnold D, Stein A. Treatment approach in patients with hyperbilirubinemia secondary to liver metastases in gastrointestinal malignancies: A case series and review of literature. Therapeutic Advances in Medical Oncology. 2016; 8(3):144-52. [DOI:10.1177/1758834016637585] [PMID] [PMCID]

10. Ennery PA, Lorch S. Neonatal blue-light phototherapy could increase the risk of dysplastic nevus development. Pediatrics. 2007; 120(1):247-8. [DOI:10.1542/peds.2007-0844] [PMID]

11. Newman TB, Maisels MJ. Evidence insufficient to recommend melanoma surveillance following phototherapy for jaundice. Archives of Dermatological Research. 2007; 143(9):1216. [DOI:10.1001/archderm.143.9.1216-a] [PMID]

12. Mendez-Sanchez N, Roldan-Valadez E, Flores MA, Cardenas-Vazquez R, Uribe M. Zinc salts precipitate unconjugated bilirubin in vitro and inhibit enterohepatic cycling of bilirubin in hamsters. European Journal of Clinical Investigation. 2001; 31(9):773-80. [DOI:10.1046/j.1365-2362.2001.00879.x]

13. Mendez-Sanchez N, Martinez M, Gonzalez V, Roldan-Valadez E, Flores MA, Cardenas-Vazquez R, et al. Zinc sulfate inhibits the enterohepatic cycling of unconjungated bilirubin in subjects with Gilbert's Syndrome. Annals of Hepatology. 2002; 1(1):40-3.

14. Rana N, Mishra S, Bhatnagar S, Paul V, Deorari AK, Agarwal R. Efficacy of zinc in reducing hyperbilirubinemia among at risk neonates: A randomized, double- blind, placebo- controlled trial. Indian Journal of Pediatrics. 2011; 78(9):1073-8. [DOI:10.1007/s12098-011-0407-z] [PMID]

15. Lamberti LM, Walker CL, Chan KY, Jian WY, Black RE .Oral zinc supplementation for the treatment of acute diarrhea in children: A systematic review and meta-analysis. Nutrients. 2013; 5(11):4715-40. [DOI:10.3390/nu5114715] [PMID] [PMCID]

16. Babaei H, Hemati M, Falahi V, Rezaee M. The effect of oral zinc sulfate on the amount of bilirubin measured through the skin in healthy term neonates. Journal of Kermanshah University of Medical Sciences. 2013; 17(11):680-6.

17. Badfar G, Shohani M, Nasirkandy MP, Mansouri A, Abangah G, Rahmati S, et al. Epidemiology of hepatitis B in pregnant Iranian women: A systematic review and meta-analysis. Archives of Virology. 2018; 163(2):319-30. [DOI:10.1007/s00705-017-3551-6] [PMID]

18. Badfar G, Shohani M, Mansouri A, Soleymani A, Azami M. Vitamin D status in Iranian pregnant women and newborns: A systematic review and meta-analysis study. Expert Review of Endocrinology & Metabolism. 2017; 12(5):379-89. [DOI:10.1080/17446651.2017.1365596] [PMID]

19. Mafinezhad S, Bayani G, Bozorgnia Y, Khodaparast M, Jodat S. Effect of oral zinc sulfate on reducing hyperbilirubinemia among newborns under 1800 gram. Journal of North Khorasan University of Medical Sciences. 2016; 7(4):897-904 [DOI:10.29252/jnkums.7.4.897]

20. Nabavizadeh S, Keshavarz K, Sadati S, Abidi H, Poursamad A, Zoladl M. Impact of oral zinc sulfate on uncomplicated neonatal jaundice. Armaghanedanesh. 2015; 20(6):460-71.

21. Mohammadzadeh A, Farhat A, Ghasemian A, Ramezani M, Esmaily H, Musavi B. Effects of oral zinc sulfate on hyperbilirubinemia in low-birth-weight neonates. Iranian Journal of Neonatology. 2016; 7(2):11-5. [DOI:10.22038/ijn.2016.7107]

22. Hashemian S, Mohammadzadeh A, Farhat A, Ramezani M, Seyedi S. The therapeutic effect of zinc sulfate on neonatal hyperbilirubinemia. Iranian Journal of Neonatology, 2017; 8(2):13-17. [DOI:10.22038/ijn.2016.7777]

23. Beiranvand S, Hosseinabadi R, Firouzi M, Almasian M, Anbari K. Impact of Combined Oral Zinc Sulfate and Phototherapy on Serum Bilirubin Levels in the Term Neonates

with Jaundice. Iranian Journal of Neonatology. 2018; 9(3):20-5. [DOI:10.22038/ijn.2018.27173.1361]

24. Mohammadzadeh A, Farhat A, Alizadeh Kaseb A, Khorakian F, Ramezani M. Prophylactic effect of zinc sulphate on hyperbilirubinemia in premature very low birth weight neonates: A randomized clinical trial. Iranian Journal of Neonatology. 2015; 5(4):6-10. [DOI:10.22038/ijn.2015.3139]

25. Boskabad H, Khakshor A, khorashadizadeh F. [Prenatal complications causing neonatal jaundiceinGhaem Hospital, Mashhad- Iran (Persian)]. Journal of North Khorasan University of Medical Sciences. 2011; 3(2):7-12. [DOI:10.29252/jnkums.3.2.7]

26. Oladokun A, Otegbayo JA, Adeniyi AA. Maternal and fetal outcomes of jaundice in pregnancy at the University College Hospital, Ibadan. Nigerian Journal of Clinical Practice. 2009; 12(3):277-80.

27. Hermansen MC. Nucleated red blood cells in the fetus and newborn. Archives of Disease in Childhood - Fetal and Neonatal Edition. 2001; 84:211-5. [DOI:10.1136/fn.84.3.F211] [PMID] [PMCID]

28. Christenson J. Reference ranges for blood concentration of NRBC in neonate. Neonatology. 2011; 99:289-94 [DOI:10.1159/000320148] [PMID]

29. Samiee Rad F, EyzadianMehr N , karimfar M , habibi M. A Study on the correlation between bilirubin, NRBC and reticulocyte levels of cord blood with neonatal hyperbillirubinemia. Journal of Zabol University of Medical Sciences and Health Services. 2013; 4(2):23-31.

30. Esteghamati A, Khalilzadeh O, Mohammad K, Meysamie A, Rashidi A, Kamgar M, et al. Secular trends of obesity in Iran between 1999 and 2007: National surveys of risk factors of noncommunicable diseases. Metabolic Syndrome And Related Disorders. 2010; 8:209-13. [DOI:10.1089/met.2009.0064] [PMID]

31. Karbonel S. Prediction of hyperbilirubinemia in term newborns by umbilical cord Blood Bilirubin. Vajira Medical Journal. 2010; 54:147-57.

32. Mendez-Sanchez N, Roldan-Valadez E, Flores MA. Zinc salts precipitate unconjugated bilirubin in vitro and inhibit enterohepatic cycling of bilirubin in hamsters. European Journal of Clinical Investigation. 2001; 31:773-80. [DOI:10.1046/j.1365-2362.2001.00879.x].