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The Effect Of Zinc Supplementation On Serum Bilirubin Levels In Term Neonates Undergoing Phototherapy

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Abstract
Background: *Zinc is a crucial micronutrient vital for several metabolic processes, including bilirubin metabolism. Neonatal jaundice, marked by elevated bilirubin levels in the blood, is commonly treated with phototherapy to prevent neurotoxicity if left untreated. This study aimed to assess the effect of zinc supplementation on serum bilirubin levels in term neonates undergoing phototherapy.*
Methods: *This randomized clinical control trial was conducted at the Department of Pediatrics, Chuadanga, Bangladesh from January 2022 to November 2022. A cohort of 60 full-term neonates with indirect hyperbilirubinemia was divided equally into two groups. The case group received oral zinc sulfate preparation at a dosage of 5 mg twice daily in conjunction with phototherapy. The control group received only phototherapy without oral zinc supplementation. Total serum bilirubin levels were assessed for both groups upon admission, at 12 hours, 24 hours, and at discharge. Statistical analysis was performed using the SPSS version 23.0 program.*
Results: *The duration of phototherapy was significantly shorter in cases (Zinc supplemented) compared to controls (38.3 ± 3.9 hours in cases vs. 57.7 ± 4.1 hours in controls, $p<0.001$). At 12 hours, 24 hours, and discharge, cases had significantly lower mean total serum bilirubin levels compared to controls ($p\leq0.001$ for all time points).*
Conclusion: *Administering oral zinc at a dose of 5 mg twice daily may significantly contribute to the management of neonatal jaundice by reducing total serum bilirubin levels, thereby potentially decreasing the duration of phototherapy required.*
Keywords: *Effect, Zinc supplementation, Serum bilirubin, Term neonates, Phototherapy*

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I. Introduction

Neonatal jaundice is a physiological phenomenon and the leading cause of hospitalization in neonates during the first months of life. [1] It affects approximately 60% of term and 80% of preterm infants [2]. The highest incidence of severe neonatal hyperbilirubinemia is reported in Asia, where jaundice is primarily physiological and diagnosed by excluding other causes of icterus, such as hemolysis, infections, or metabolic diseases. Severe jaundice necessitating intervention occurs in 5-10% of cases [3]. Bilirubin is the end product of heme catabolism, and its serum level is influenced by factors like bile production, hepatic conjugation, and enterohepatic circulation. While mild hyperbilirubinemia may have antioxidant properties and can be benign [4], elevated levels of indirect bilirubin are considered hazardous metabolic waste products that can pose a threat to the brain, necessitating timely detection and treatment [5]. The standard treatment for neonatal jaundice typically involves phototherapy and, in severe cases, blood transfusions based on bilirubin levels [1]. However, these interventions often require hospitalization, leading to issues like separation anxiety, disruption of the mother-infant relationship, high care costs, and increased risk of infection in infants [6]. Additionally, concerns have been raised regarding potential risks associated with phototherapy, including DNA changes [7]. Other reported complications of phototherapy include dehydration, patent ductus arteriosus, and reduced mother-infant interactions [8]. Oral zinc salts at normal body pH have demonstrated the ability to reduce total serum bilirubin levels by sequestering unconjugated bilirubin [9]. Research by Mendez-Sanchez et al. revealed that zinc salts at normal body pH can separate unconjugated bilirubin from unsaturated bile salts in mice intestines, binding to it and impeding reabsorption [10]. In another study [11], infants in the experimental group were administered zinc sulfate (5 mg) daily, while the control group received routine neonatal care. The results indicated a decrease in skin bilirubin levels in infants receiving zinc sulfate compared to the control group. In contrast, a study by Maamouri et al. found no significant difference in serum bilirubin levels of infants on the third and seventh day of zinc sulfate intervention compared to the placebo group. Moreover, the duration of phototherapy was notably longer in the control group [12]. The objective of this study was to assess the effect of zinc supplementation on serum bilirubin levels in term neonates undergoing phototherapy.

II. Methodology

This was a randomized clinical control trial that was conducted at the Department of Pediatrics, Chuadanga, Bangladesh from January 2022 to November 2022. A cohort of 60 full-term neonates with indirect hyperbilirubinemia was evenly divided into two groups after obtaining written consent from all participants. The case group received oral zinc sulfate preparation at a dosage of 5 mg twice daily alongside phototherapy, while the control group underwent phototherapy alone without oral zinc supplementation. Neonates with pathological jaundice, underlying gastrointestinal conditions hindering oral intake, sepsis, chromosomal abnormalities, congenital anomalies, and prior surgical interventions or anticipated surgical requirements were excluded from the study. Both groups underwent a thorough history-taking process, including demographic information, complete maternal and perinatal histories, family history of jaundice in siblings, medication history, feeding practices, signs of zinc deficiency, and potential toxicity manifestations. Furthermore, all participants underwent a thorough general examination, including respiratory and abdominal examinations, neurological assessments, and evaluations for signs of zinc deficiency. Both groups underwent additional laboratory tests, including complete blood count (CBC), Coombs test, and reticulocyte count for both mothers and neonates upon admission. Serum zinc levels were measured before and after phototherapy in both groups. Total serum bilirubin levels were assessed at admission, 12 hours, 24 hours, and discharge for both groups. In statistical comparison, either the student's t-test or regression analysis was performed. Statistical analysis was conducted using the SPSS version 23.0 software, with a significance level set at a p-value of <0.05.

III. Result

Baseline characteristics were compared between cases (n=30) and controls (n=30). The mean birth weight was similar between cases (3107.4 ± 430.7 g) and controls (3133.2 ± 412.2 g). Hemoglobin levels were also comparable between cases (16.44 ± 2.1 gm/dL) and controls (16.25 ± 2.2 gm/dL). The mean gestational age was slightly higher in cases (38.2 ± 1.2 weeks) compared to controls (37.8 ± 1.3 weeks). In terms of gender distribution, there were 17 female babies (56.7%) and 13 male babies (43.3%) in the case group, while the control group had 16 female babies (53.3%) and 14 male babies (46.7%). The mean age at the onset of phototherapy did not significantly differ between the groups (86.5 ± 19.8 in cases vs. 87.2 ± 20.1 in controls, p=0.892). However, the duration of phototherapy was significantly shorter in cases compared to controls (38.3 ± 3.9 hours in cases vs. 57.7 ± 4.1 hours in controls, p<0.001). Regarding side effects, there was no significant difference in the incidence of rash between cases (3.3%) and controls (6.7%, p=0.561). Similarly, there were no differences in the incidence of vomiting or diarrhea between the two groups (both p=1). At admission, there was no significant difference in mean total serum bilirubin levels between cases (16.7 ± 1.1) and controls (16.6 ± 1.2, p=0.738). However, at 12 hours, 24 hours, and discharge, cases had significantly lower mean total serum bilirubin levels compared to controls (p≤0.001 for all time points).

Table 1: Baseline characteristics

Variable	Case		Control	
	(n=30)		(n=30)	
	Mean ±SD/n(%)		Mean ±SD/n(%)	
BW (g)	3107.4 ±430.7		3133.2 ±412.2	
Hb (gm/dL)	16.44 ±2.1		16.25 ±2.2	
GA (week)	38.2 ±1.2		37.8 ±1.3	
Female baby	17	56.7%	16	53.3%
Male baby	13	43.3%	14	46.7%

BW: Birth weight, Hb: Hemoglobin, GA: Gestational age

Table 2: Phototherapy parameters

Variable	Case		Control		p-value
	(n=30)		(n=30)		
	Mean/n (%)		Mean/n (%)		
Age at onset of phototherapy & duration (Hour)					
Age	86.5 ±19.8		87.2 ±20.1		0.892
Duration	38.3 ±3.9		57.7 ±4.1		<0.001
Side effects of phototherapy					
Rash	1	3.3%	2	6.7%	0.561
Side effects of zinc therapy					

Vomiting	2	6.7%	2	6.7%	1
Diarrhea	1	3.3%	1	3.3%	1

Table 3: Total serum bilirubin statuses

Variable	Case (n=30) Mean ±SD	Control (n=30) Mean ±SD	p-value
At admission	16.7 ±1.1	16.6 ±1.2	0.738
At 12 hours	13.9 ±0.9	14.9 ±1.3	0.001
At 24 hours	11.9 ±1.1	13.5 ±1.4	<1.001
At discharge	8.8 ±0.4	9.2 ±0.5	0.001

IV. Discussion

In this study, baseline characteristics were compared between the cases and controls. The mean birth weight showed no significant difference between the two groups. Hemoglobin levels were also found to be comparable between the groups. However, the mean gestational age was slightly higher in the cases (38.2 ± 1.2 weeks) compared to the controls (37.8 ± 1.3 weeks). These results were consistent with those reported in a previous study [1]. In our study, the mean age at the onset of phototherapy did not show a significant difference between the groups. However, the duration of phototherapy was notably shorter in the cases compared to the controls ($p<0.001$). Nevertheless, concerning side effects, there was no significant difference observed between the groups. These results were consistent with those reported in another recent study [13]. The current study revealed a notable reduction in the duration of phototherapy in the intervention group compared to the control group ($p < 0.001$). This observation is consistent with prior research conducted by Hashemian et al. [14], where zinc administration was found to decrease the duration of phototherapy needed to treat neonatal hyperbilirubinemia. Likewise, Maamouri et al. [15] reported significant disparities in admission and phototherapy durations between the intervention and control groups. In contrast, Agrawal et al. [16] found that there was no significant reduction in the proportion of neonates requiring phototherapy or in the duration of phototherapy compared to the control group. In our study, there was no significant difference in the mean total serum bilirubin (TSB) levels between cases and controls at admission ($p=0.738$). However, at 12 hours, 24 hours, and discharge, cases exhibited significantly lower mean total serum bilirubin levels compared to controls ($p\leq0.001$). Sharma et al. [17], in line with the findings of our study, reported significant differences in total serum bilirubin (TSB) levels at 12 hours and 24 hours between the intervention and control groups. Additionally, Hashemian et al. [14] found that oral zinc sulfate administration led to a reduction in TSB levels in neonatal jaundice. Similarly, Agrawal et al. [16] demonstrated that oral zinc supplementation, administered at a dosage of 10 mg/day in two divided doses, significantly decreased the incidence of hyperbilirubinemia within the first seven days of life and resulted in a reduction in the mean TSB level on day 7 in healthy near-term and full-term at-risk neonates. On the contrary, Patton et al. [18] observed no effect of zinc on the incidence and median duration of hyperbilirubinemia. These diverse findings contribute valuable insights to the body of literature and may guide future research in this area.

Limitation of the study:

The limitations of this study include its single-centered nature and small sample size. Additionally, the study was conducted over a relatively short period. As a result, the findings may not fully represent the broader population or provide a comprehensive understanding of the topic at a national or global level. Assessment of the pre-and post-treatment zinc levels of the patients was not performed. Further research with larger sample sizes and longer study durations is warranted to validate and generalize the findings of this study.

V. Conclusion

Administering oral zinc at a dose of 5 mg twice daily holds promise as a potential intervention for the management of neonatal jaundice. Research suggests that zinc supplementation may contribute to reducing total serum bilirubin levels, which could consequently decrease the duration of phototherapy required for affected infants. By facilitating the metabolism and excretion of bilirubin, zinc supplementation may offer a safe and effective adjunctive therapy for neonatal jaundice, particularly in cases where phototherapy alone may not suffice. Assessment of the pre- and post-treatment zinc levels of the patients may help get more authentic results. However, further clinical studies are needed to confirm the efficacy and safety of oral zinc supplementation in this context before widespread adoption into clinical practice.

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References

[1] Beiranvand Sh, Hosseinabadi R, Firouzi M, Almasian M, Anbari Kh. Impact Of Combined Oral Zinc Sulfate And Phototherapy On Serum Bilirubin Levels In The Term Neonates With Jaundice. Iranian Journal Of Neonatology. 2018 Sep: 9(3). Doi: 10.22038/Ijn.2018.27173.1361.

[2] Mohammadzadeh A, Shahfarhat A, Alizadeh-Kaseb A, Khorakian F, Ramezani M. Prophylactic Effect Of Zinc Sulfate On Hyperbilirubinemia In Premature Very Low Birth Weight Neonates: A Randomized Clinical Trial. Iran J Neonatol. 2014; 5(4):6-10.

[3] Hashemian S, Mohammadzadeh A, Ataee Nakhaei A. Efficacy Of Zinc Sulfate In Reducing Unconjugated Hyperbilirubinemia In Neonates. Rev Clin Med. 2014; 1(4):229-32.

[4] Cuperus Fj, Hafkamp Am, Hulzebos Cv, Verkade Hj. Pharmacological Therapies For Unconjugated Hyperbilirubinemia. Curr Pharm Des. 2009; 15(25):2927-38.

[5] Uhrikova Z, Zibolen M, Javorka K, Chladekova L, Javorka M. Hyperbilirubinemia And Phototherapy In Newborns: Effects On Cardiac Autonomic Control. Early Hum Dev. 2015; 91(6):351-6.

[6] Kumar A, Bagri Nk, Basu S, Asthana Rk. Zinc Supplementation For Neonatal Hyperbiliru- Binemia: A Randomized Controlled Trial. Indian Pediatr. 2014; 51(15):375-8.

[7] Ramy N, Ghany Ea, Alsharany W, Nada A, Darwish Rk, Rabie Wa, Et Al. Jaundice, Phototherapy And Dna Damage In Full-Term Neonates. J Perinatol. 2016; 36(2):132-6.

[8] Iranpour R, Mohammadizadeh M, Nazem-Sadati Ss. Comparison Of Two Phototherapy Methods (Prophylactic Vs Therapeutic) For Management Of Hyperbilirubinemia In Very Low Birth Weight Newborns. Iran J Pediatr. 2011; 21(4):425-30.

[9] 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 J Pediatr. 2011; 78(9):1073-8.

[10] Méndez-Sánchez N, Roldán-Valadez E, Flores Ma, Cárdenas-Vázquez R, Uribe M. Zincsalts Precipitate Unconjugated Bilirubin In Vitro And Inhibit Enterohepatic Cycling Of Bilirubin In Hamsters. Eur J Clin Invest. 2001; 31(9):773-80.

[11] Babaei H, Hemmati M, Fallahi V, Rezaei M. Effect Of Oral Zinc Sulfate In Prevention Of Jaundice In Healthy Term Newborns. J Kermanshah Univ Med Sci. 2014; 17(11):680-6. (Persian)

[12] Maamouri G, Boskabadi H, Mafinejad S, Bozorgnia Y, Khakshur A. Efficacy Of Oral Zinc Sulfate Intake In The Prevention Of Neonatal Jaundice. Iran J Neonatol. 2013; 4(4):11-6.

[13] Eldesoky Mei, El-Samannody Mi, El-Ghannam Mz, El-Mazahy Mm. Effect Of Zinc Supplementation On Serum Bilirubin Level In Term Neonates Undergoing Phototherapy. Ijma 2020; 2[4]: 736-740. Doi: 10.21608/Ijma.2020.31551.1131.

[14] Hashemian S, Mohammad Zadeh A, Ataee Nakhaei A. Efficacy Of Zinc Sulfate In Reducing Unconjugated Hyperbilirubinemia In Neonates. Reviews In Clinical Medicine. 2014;1(4): 229-32. Doi: 10.17463/Rcm. 2014. 04.011.

[15] Maamouri G, Boskabadi H, Mafinejad S, Bozorgnia Y, Khakshur A. Efficacy Of Oral Zinc Sulfate Intake In The Prevention Of Neonatal Jaundice. Iranian Journal Of Neonatology Ijn 2014; 4(4): 11-16. Doi:10. 22038/Ijn. 2013.2006.

[16] Agrawal K, Kumar S, Sethi R. Efficacy Of Oral Zinc Acetate In Reducing Hyperbilirubinemia In Full-Term And Near-Term High-Risk Neonates. Iosr J Dental Med Sci. 2018; 17 (1): 14-18. Doi: 10.9790/0853- 17020927 31.

[17] Sharma D, Farahbakhsh N, Sharma P, Shastri S. Role Of Oral Zinc Supplementation For Reduction Of Neonatal Hyperbilirubinemia: A Systematic Review Of Current Evidence. J Matern Fetal Neonatal Med. 2017; 30 (16): 1953-1962. Doi: 10.1080/ 14767058. 2016. 1234600.

[18] Patton P, Rachmadi D, Sukadi A. Effect Of Oral Zinc On Hyperbilirubinemia In Full Term Neonates. Paediatrica Indonesiana. 2011; 51(2): 107-110. Doi: 10.14238/ Pi51.2.2011.107-10.