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PROBIOTICS ROLE IN LOWERING BILIRUBIN LEVEL ON HYPERBILIRUBINEMIA NEONATES PERFORMED PHOTOTHERAPY AT NEONATOLOGY WARD OF ADAM MALIK GENERAL HOSPITAL

Drian Johan Khoman[*1], Supriatmo[2], Rita Evalina Rusli[3] & Emil Azlin[4]
[*1,2,3&4]Department of Child Health , Medical School North Sumatera University; Indonesia

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Abstract

Background : Hyperbilirubinemia is found in approximately 60% on full term infants hospitalized during their first week of life. The most widely used therapy in neonates with hyperbilirubinemia is phototherapy. Probiotics can accelerate the decrease in bilirubin levels by stimulating the peristaltics of the gastrointestinal tract, thus, increasing the amount of bilirubin being eliminated.

Objective : to proves whether probiotics has a role in helping to speed up the reduction of bilirubin levels in neonates with hyperbilirubinemia who are having phototherapy..

Method : A Cross-sectional study was conducted on full term neonates(38 - 42 weeks) in neonatology room at Adam Malik General Hospital, Medan, North Sumatera. The participants were grouped into 2 groups, one received probiotics and the other did not. Each group was evaluated on both total bilirubin serum and total direct bilirubin serum rates. The result data were analyzed using Anova and independent sample test.

Result : From 39 aterm neonates with hyperbilirubinemia. 3 samples were excluded. Out of these 36, 17 are boys (47.2 %)and 19 are girls (52.8%). The results showed a greater decrease in total bilirubin levels of prticipants in probiotic groups than those who are in non-probiotic groups. Anova test with P value = 0.0001
Anova test with P value = 0.0001

Conclusion : The mean decrease in total bilirubin levels was greater in the probiotic groups than non-probiotic groups among full-term neonates with hyperbilirubinemia.

Introduction

Neonatal hyperbilirubinemia is used to describe an increase in total serum bilirubin in neonates less than one month > 5 mg / dL (86 μmol / L). This physiological conditions can normal by itself. Hyperbilirubinemia pathology can interfere the nervous system.[1.,2] Hyperbilirubinemia is found approximately 60% of term neonates and 80% of premature neonates who are hospitalized, especially in the first week of life.[3] In the 2003, study in Indonesia show the prevalence of hyperbilirubinemia in RSCM was 58% in newborns with bilirubin levels above 5 mg / dL and 29.3% with bilirubin levels above 12 mg / dL.[4]

The therapy of physiological hyperbilirubinemia was phototherapy in 50 years.[5,6]. Probiotics can increase intestinal motility and prevent the occurrence of an enterohepatic cycle, so t bilirubin expenditure can occur more quickly. [7,8,9] Probiotics which are living microorganisms when given in sufficient quantities will provide benefits to the host as a supportive therapy in helping to accelerate the decrease in bilirubin levels in infants with hyperbilirubinemia who receive phototherapy.[10]

The aim of this study was to prove whether probiotics play a role in lowering bilirubin levels faster in neonates with unconjugated hyperbilirubinemia who received phototherapy

Materials And Methods

This study is an experimental clinial trial method to assess the decrease in bilirubin levels in neonates who received probiotics during phototherapy. The study was conducted on neonates who were treated in the

perinatology unit of Haji Adam Malik Hospital in Medan from October 2017 - April 2018 with a total of 39 neonates. The inclusion criteria included early neonates aged 0 to 7 days with physiological jaundice, and in 38-42 weeks gestational age. Exclusion criteria included gestational age <38 weeks, neonates with sepsis, blood tests showed high direct hyperbilirubinemia and phototherapy was performed before the examination. This study was approved by the University of North Sumatra Medical Faculty Research Ethics Committee and informed consent was obtained from parents.

The study sample was collected by consecutive sampling. The samples were examined for total serum bilirubin on day o, 3 and 5 using blood from the radial artery or femoral artery with ± 1cc sterile syringes. Patients with proven physiological jaundice were divided into 2 groups, a group was given Lactobacillus reuteri probiotics 1 time a day as much as 5 drops for 5 days while the control group was not given probiotics. All samples were given phototherapy with the same duration for 24 hours.

The collected data processing was done using computer software using SPSS version 19.0 with a significance level of P <0.05. Anova analytical design was used to analyze the effectiveness of probiotics on neonates with hyperbilirubinemia that received phototherapy.

Results

From 39 moderately term neonates with physiological hyperbilirubinemia, 3 samples were excluded because 1 sample with direct biliruybin increase and 2 samples had been previously phototherapy. Most respondents were female gender, 19 people (52.8%). The average body weight and body length in this study were 2867.5 grams and 46.7 cm. The mean initial bilirubin value for total bilirubin is 18.5 mg / dl while for direct bilirubin is 0.55 mg / dl. The mean bilirubin value on day 3 after administration of probiotics for total bilirubin was 14.04 mg / dl while for direct bilirubin was 0.53 mg / dl. The mean bilirubin value on the fifth day after the administration of probiotics for total bilirubin was 9.99 mg / dl while direct bilirubin was 0.5 mg / dl.

Table 1 Respondents research characteristics neonates with hyperbilirubinemia

Characteristics	Hyperbilirubinemia
1. Sex, n (%)	
a. Male	17 (47.2)
b. Female	19 (52.8)
2. Mean of ages, days (SD)	4 (1.43)
3. Mean of body weights, gram (SD)	2867.5 (204.9)
4. Mean of body lenghts, cm (SD)	46.7 (1.27)
5. Initial bilirubin valuel, mg/dl (SD)	
a. Total bilirubin	18.5 (1.5)
b. Direct bilirubin	0.55 (0.16)
6. Value of bilirubin after treatment on day 3, mg/dl (SD)	
a. Total bilirubin	14.04 (1.37)
b. Direct bilirubin	0.53 (0.15)
7. Value of bilirubin after treatment day 5, mg/dl (SD)	
a. Total bilirubin	9.99 (5.55)
b. Direct bilirubin	0.5 (0.15)

Table 2 Mean BST days 0, 3, 5 after phototherapy in both groups

Groups	Time			P-value*
	Day 0	Day 3	Day 5	
Probiotic	18.49 ± 1.63	13.18 ± 1.18	8.74 ± 7.73	<0.0001
No probiotic	18.31 ± 1.44	14.89 ± 0.96	11.24 ± 0.69	<0.0001
P-value**	0.731	0.0001	0.181	

* : ANOVA Test; ** : Independent Samples Test

Through the Anova test, it was found that the decrease in the mean total bilirubin was higher in the group with probiotics compared to the no probiotic group. (P <0.05)

Discussion

Physiological hyperbilirubinemia is caused by several factors, including the less optimal work of the enzyme uridine diphosphoglucoronate glucoronosyltransferase (UGT1A1) in conjugating unconjugated bilirubin, increased bilirubin formation due to shorter erythocyte life cycle, prematurity, polycythemia, disruption of meconum expenditure, and breastfeeding. Bilirubin usually reaches its peak on the third to fifth day of life and then decreases afterwards. In term infants will be normal on the seventh day, while in preterm will be normal for the longest until the 14th day. [2,3] From this study, 36 neonates were found with physiological hyperbilirubinemia with phototherapy with the most female gender respondents.

Phototherapy plays an important role in the reduction of serum bilirubin with an important mechanism by weakening the double bonds on bilirubin at positions 4 and 15, causing rotation in the isomer configuration so the fat soluble bilirubin becomes water-soluble so it is more easily excreted.[11] The efficacy of phototherapy depends on the distance to the baby's body and the wavelength of the light. The distance from the baby's body is recommended at a distance of 30-50 cm with a wavelength of 420-500nm. Phototherapy is given for 24 hours.[12]

In the last decade, probiotics are considered as an alternative theraphy to reduce the duration of phototherapy in neonates with hyperbilirubinemia. Probiotics can reduce food transit time in the channel of digestion, regulate the contraction of the gastrointestinal smooth muscle and increase enterocyte production. [13] The role of probiotics in neonates with hyperbilirubinemia is explained by different mechanisms : increasing the number of anaerobic bacteria that improve the balance of the intestinal microflora, increasing the oxidation of conjugated bilirubin, increasing gastrointestinal peristalsis, and suppressing glucoronidase enzyme activity. Probiotics can improve the neonatal immune system by affecting the activation and proliferation of immunoglobulin A and T lymphocytes which are part of the active immune system. [14,15] Probiotics facilitate the growth of bacterial colonies in the neonatal gastrointestinal tract to produce metabolites that are effective against an alkaline environment which can weaken beta glucoronidase activity, prevent bilirubin from binding and do hydrolysis process. This results in increased activity in the liver and increases the excretion of conjugated bilirubin.[16]

Probiotics can increase gastrointestinal motility so the transit time of bilirubin reduced and inhibit reabsorption in the enterohepatic circulation. This process can reduce bilirubin levels quickly. In recent years, studies have shown that probiotics improve the gastrointestinal barrier and modulate the immune system.[17,18] Research conducted by Demirel et al on the effect of Saccharomyces boulardii probiotics on 179 low birth weight infants with hyperbilirubinemia and found a lower duration of phototherapy in neonates who received probiotics compared to controls.[7] From the results of this study found a mean decrease in total bilirubin value was higher in the group given probiotics than the group not given probiotics.

Conclusion

From the results of this study found a mean decrease in total bilirubin value was higher in the group given probiotics than the group not given probiotics.

References

[1] Sukadi A. Hiperbilirubinemia. Dalam: Kosim MS, Yunanto A, Dewi R, Sarosa GI, Usman A, penyunting. Cetakan ke-3. Buku ajar Neonatologi. Jakarta: Ikatan Dokter Anak Indonesia;2012. h.147-69.
[2] Martiza I. Ikterus. Dalam: Juffrie M, Soenarto SSY, Oswari H, Arief S, Rosalina I, dkk, penyunting. Cetakan ke-3. Buku ajar Gastroenterohepatologi. Jakarta: Ikatan Dokter Anak Indonesia;2012.h.263-84.
[3] Suganthi V, Das AG. Role of Saccharomyces boulardii in reduction of neonatal hyperbilirubinemia. J of Clin Diag R. 2014;10:SC11-15.
[4] Sastroasmoro S et al. 2004. Tatalaksana ikterus neonatorum. Jakarta : HTA – Indonesia.
[5] Amlavanan N, Carlo WA. Jaundice and hyperbilirubinemia on the newborn. Nelson Textbook of Pediatrics 20th ed. Dalam: Kliegman RM, Stanton BF, Geme JWS, Schor NF, Behrman RE(Eds). Philadelphia: Elsevier; 2016. h.871-4.
[6] JNPK-KR. Hiperbilirubinemia pada neonatus. Paket pelatihan pelayanan obstetri dan neonatal emergensi komprehensif (PONEK). Jakarta: Bakti Husada; 2008. h.183-94.
[7] Liu W, Liu H, Wang T, Tang X. Therapeutic effects of probiotics on neonatal jaundice. Pak J Med Sci. 2015;31:1175-2.
[8] Demirel G, Celik IH, Erdeve O, Dilmen O. Impact of probiotics on the course of indirect hyperbilirubinemia and phototherapy duration in very low birth weight infants. The journal of maternal-fetal and neonatal medicine. 2013;26:215-18.
[9] Serce O, Gursoy T, Ovali F, Karatekin G. Effects of Saccharomyces boulardii on neonatal hyperbilirubinemia : A randomized controlled trial. American J of Perinatology. 2015;32:137-41.
[10] Hansen TWR. Recent advances in the pharmacotherapy for hyperbilirubinaemia in the neonate. Expert Opin. Pharmacother. 2003;11:1939-48.
[11] Bhutani VK, Lamola AA. Mechanistic aspects of phototherapy for neonatal hyperbilirubinemia. Dalam : Polin RA, Abman S, Rowitch DH, Benitz WE, Fox WW, penyunting. Cetakan ke-5. Neonatal physiology. Philadelphia : Elsevier. 2017. h.942-52.
[12] Sastroasmoro S et al. 2004. Tatalaksana ikterus neonatorum. Jakarta : HTA – Indonesia.
[13] Jape GA, Deshpande G, Rao S, Patole S. Benefits of probiotics on enteral nutrition in preterm neonates: a systematic review. Am J Clin Nutr. 2014;100:1508–19.
[14] Vandenplas Y, Wauters GV, Greef ED, Peeters S, Casteels A, dkk. Probiotics and prebiotics in prevention and treatment of diseases in infants and children. J Pediatr (Rio J). 2011;87:292-300.
[15] Nieuwboer MVD, Claassen E. Morelli L, Guarner E, Brummer RJ. Probiotic and synbiotic safety in infants under two years of age. Wageningen Academic Publishers. 2014;4:1-16
[16] Makhoul G, Mardini J, Ojaimi MA, Hanna P, Alameddine A, dkk. Effect of probiotic L. Reuteri association on the reduction of serum bilirubin in neonatal jaundice. European scientific journal. 2018;14:384-91.
[17] Midvedt T. Establishment of intestinal microbial function at birth : bilirubin and bacteria. Acta Pediatr. 2001;90:7-8.
[18] Cardona ME, Vanay VV, Midvedt T, Norin E. Effect of probiotics on five biochemical microflora-associated characteristics, in vitro and in vivo. Scandinavian journal of nutrition. 2002;46:73-9.