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Comparison of Effects of Probiotics with Conventional Phototherapy versus Phototherapy Alone on Decreasing Hospitalization in Infants with Indirect Hyperbilirubinemia.

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ABSTRACT

Background: Objective: In recent years, the trend towards drug use in the treatment of neonatal jaundice has increased. Various medications are in practice since then, but the probiotics effect on serum bilirubin (SBL) is uncertain. This study was conducted to assess the probiotics effect on SBL and the length of phototherapy in infants with hyperbilirubinemia. Aim: The objective of this analysis was to determine the probiotics effect on neonatal jaundice in lessening hospitalization. Study Design: A Randomized clinical trial. Place and Duration: In the Department of Paediatrics, Sahiwal Medical College & DHQ Teaching Hospital Sahiwal for one year duration from March 01 2019 to February 29 2020. **Methods:** We examined 120 term neonate with jaundice who had been hospitalized for phototherapy. The affected children were divided into 2 groups; control group and probiotic group. Standard conventional phototherapy was used for both groups, but the intervention group received a 10 ml bag containing probiotics until the patient was discharged from the hospital. The result variables were SBL and phototherapy time. **Results:** The length of hospital stay in the first group was shorter significantly than in the second group. The first group showed 3.34 ± 0.70 days, the second group showed 3.7 ± 0.74 days. **Conclusion:** In neonates with jaundice, oral probiotics have a significant influence on serum bilirubin and the length of phototherapy. More researches are required with longer time follow-up.

Keywords: Jaundice, Bilirubin, phototherapy, newborn, probiotic.

INTRODUCTION

Jaundice is the yellow discoloration of the mucous membranes and skin. Jaundice is not a pathology but rather a sign of high bilirubin. Jaundice is a marker used to identify children at risk of severe hyperbilirubinemia. It may be noxious to the infant's central nervous system, which may cause brain tissue injuries.[1,2] One of the most common clinical conditions in hyperbilirubinemia is neonatal hyperbilirubinemia, which is a common clinical problem, particularly in the neonatal period during the first week of life. In childhood; the most communal cause of admission in hospitals is Hyperbilirubinemia. The most communal reason of hyperbilirubinemia in children is physiological jaundice identified by disregarding other main causes such as metabolic disorders, infections and hemolysis.[3,4] In hospitals; the usual cause of readmission in early childhood is hyperbilirubinemia.[5,6] In two percent of mature infants, bilirubin may exceed 20 mg / dL, which necessitates medical or phototherapy treatment and can cause impediments such as neurological damage and kernicterus.[7,8] The purpose of treating hyperbilirubinemia is to avert CNS damage. The most commonly used therapeutic method for an aging infantile jaundice and phototherapy is advised to avert its complications, which is considered as a beneficial technique for decades.

Probiotics are defined as non-pathogenic strains of the organisms that included in the diet to modify intestinal microbiological ecology and lead to beneficial functional and structural vagaries in the intestine.[7,8] Probiotics are microorganisms that can reduce the time it takes to transport materials in the intestine. Some studies evaluating the probiotics effect on bilirubin reduction have shown a reduction in the time required for phototherapy.[9,10] In addition, some may perform metabolic functions, such as storage of energy in the short chain fatty acids form and helping to ferment undigested fibers. Bifidobacteria and lactobacilli are considered to be two important bacteria that are beneficial to human health. The role of probiotics in the human body has been enlightened by various pharmacological mechanisms.[10-12] For example, it can quickly rise the quantity of anaerobic bacterial colonies, improve the balance of the microflora in the intestine, and in few cases is resistant to infection. The purpose of this

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study is to evaluate the probiotics effect on neonatal jaundice to shorten hospital stay.

MATERIALS AND METHODS

This Study was held in the Department of Paediatrics, Sahiwal Medical College & DHQ Teaching Hospital Sahiwal for one year duration from March 01 2019 to February 29 2020. We included 120 term neonates with jaundice in this randomized, controlled clinical trial who had been hospitalized for phototherapy. The affected neonates were divided into 2 groups; control group and probiotic group. Patients were randomly allocated to group 1 (probiotic group, n=60) and group 2 (control group, n=60) using a table of random numbers according to inclusion criteria. The probiotic group was treated with sachets containing probiotics (Lactobacillus acidophilus) and probiotics containing milk (Bifidobacteriumlactis, Bifidobacterium bifidum, Lactobacillus rhamnosus and Lactobacillus acidophilus). Bilirubin levels in patients were measured with serum samples before and after treatment. Phototherapy was used in all patients with high bilirubin. Neonates with bilirubin concentration between 14 mg / dl and 18 mg / dl were subjected to 8 lamp phototherapy. The phototherapy duration, blood group of infants, direct Coombs test results, bilirubin concentration before and after phototherapy, hemoglobin and reticulocyte concentration were recorded. The normal distribution variables were compared.

Inclusion Criteria:

Neonate with physiological jaundice, hemolytic jaundice and sepsis.

Exclusion criteria:

Other causes of jaundice:

Liver problems (hepatocellular disease)

Metabolic disorders

Exam:

- General examination: appearance, vital signs, measurements, gestational age assessment.
- Local examination: head, ear, nose, throat, neck, eyes, cardiopulmonary system, chest, skin, abdomen, gentalia, musculoskeletal system, neurological system.

Statistical analysis

- The data was coded, collected, corrected and included in the SPSS version 20. Data were presented as percentages and numbers for mean, standard deviations, qualitative data and ranges for quantitative data with parametric distribution, and median with inter quartile range (IQR) for the quantitative data with non-parametric distribution.
- The chi-square test was applied in two groups with qualitative data for comparison and when the estimated number in any cell was less than five, Fisher's exact test was applied.
- An independent t-test was used between two groups with parametric distribution and quantitative data, and the Mann-Whitney test was applied for comparison of two quantitative data with non-parametric distribution.
- The confidence interval is 95% and the margin of error is 5%. Therefore, the p-value is considered valid as follows:
  1. P value greater than 0.05 was taken insignificant (NS)
  2. P value less than 0.05: significant (S)
  3. P value less than 0.01: Highly significant (HS)

RESULTS

[Table 1] shows that there are no demographic differences between the study groups.

[Table 2] showed that there was no statistically significant difference between the study group in terms of blood group and relative culture.

Table 1: Comparison between 1st group & 2nd group as regards demographic data

		Probiotic group (No.=60)		Control group (No.=60)		Chi square test	
		No.	%	No.	%	X2/t*	P value
Sex	Male	38	63.33%	35	58.33%	0.396	0.544
	Female	22	36.67%	25	41.67%		
Age (days)	Mean ± SD	3.4 ± 1.3		4.1 ± 1.9		1.709*	0.102
	Range	2.6 - 4.9		2.3 - 5.25			
Gestational age (weeks)	Mean ± SD	37.7 ± 2.5		38.3 ± 3.8		-1.192*	0.34
	Range	32.8 – 40.8		32.4 - 40.3			
Weight (KM)	Mean ± SD	3.1 ± 0.91		3.2 ± 0.9		1.328*	0.29
	Range	2.6 - 4.2		2.6 - 3.7			

Table 2: Comparison between 1st group &2nd (control) group as regards blood group and consanguinity

		1st group (N0. = 60)		2nd group (N0. = 60)		Chi square test	
		No.	%	No.	%	X2	P value
Blood group	AB+	18	30.00%	15	25.00%	2.245	0.642
	B+	21	35.00%	16	26.67%		
	O+	14	23.33%	20	33.33%		
	A+	7	11.67%	9	15.00%		
Consanguinity	Positive	38	63.33%	43	71.67%	0.643	0.561
	Negative	22	36.67%	17	28.33%		

Table 3: Comparison between 1st group & 2nd group as regards HB and causes of jaundice

		1st group (N0. = 50)		2nd group (N0. = 50)		Chi square test	
		No.	%	No.	%	X2/t*	P value
HB level	Mean ± SD	14.1 ± 2.9		14.2 ± 2.8		0.700*	0.65
	Range	10.8 - 18.3		14.2 ± 2.8			
Jaundice	Septicemia	8	13.33%	6	10.00%		
	ABO	14	23.33%	17	28.33%	7.328	0.106
	RH	10	16.67%	8	13.33%		
	Unknown	28	46.67%	29	48.33%		

Table 4: Comparison between 1st group & 2nd group as Coomb's test and CRP.

General signs		1st group (N0. = 60)		2nd group (N0. = 60)		Chi square test	
		No.	%	No.	%	X2	P value
Coomb's test	Positive	20	33.33%	17	28.33%	1.561	0.326
	Negative	40	66.67%	43	71.67%		
CRP	Positive	10	16.67%	8	13.33%	0.643	0.561
	Negative	50	83.33%	52	86.67%		

Table 5: Comparison between 1st group & 2nd group as regards bilirubin level on admission (1st day)

	1st group (No. =60)	2nd group (No. = 60)	Independent t-test	
	Mean ± SD	Mean SD	T	P-value
1st day	18.63 ± 2.53	18.46 ± 3.33	3.108	0.003

Table 6: Comparison between 1st group & 2nd group as regards bilirubin level at 3rd day

	1st group (No. = 60)	2nd group (No. = 60)	Independent t-test	
	Mean ± SD	Mean SD	T	P-value
3rd day	11.41 ± 2.24	11.91 ± 2.88	1.67	0.129

Table 7: Comparison between 1st group & 2nd group as regards bilirubin level at 4th day

	1st group (No. = 60)	2nd group (No. = 60)	Independent t-test	
	Mean ± SD	Mean SD	T	P-value
4th day	10.25 ± 2.15	11.15 ± 2.49	3.481	0.001

Table 8: Comparison between 1st group & 2nd group as regards bilirubin level at 5th day

	1st group (No. = 60)	2nd group (No. = 60)	Independent t-test	
	Mean ± SD	Mean SD	T	P-value
5th day	9.49 ± 2.09	11.29 ± 2.41	7.242	0.001

Table 9: Duration of hospitalization

	1st group	2nd group	Independent t test	
	Mean ±SD	Mean ±SD	T	P value
Duration of hospitalization	3.54±0.90	3.9 ±0.94	2.599	0.015

[Table 3] showed that there was no statistically significant difference between study groups in terms of HB, absorption and jaundice.

[Table 4] shows a statistically insignificant difference when comparing the first group with the second group according to the Coomb's test and CRP on the first day.

[Table 5] showed that on the first day of entry it was not statistically significant when comparing the first group with the second group.

[Table 6] showed that there was no statistically significant variance in bilirubin level tendency between the probiotic group and the third day control group.

[Table 7] showed a statistically significant rise in bilirubin in comparison to the probiotic group on the fourth day in the control group.

[Table 8] showed a statistically significant rise in bilirubin in the control group compared to the probiotic group on day five.

The average length of hospital stay was 3.54 ± 0.90 days in the 1st group and 3.90 ± 0.94 days in the second group and average duration of stay was 3.35 ± 0.74 Table (9) showed that the duration of stay in the first group was significantly shorter than in the second group (P <0.00, [CI = 95%, - 1.31 to -0.64]).

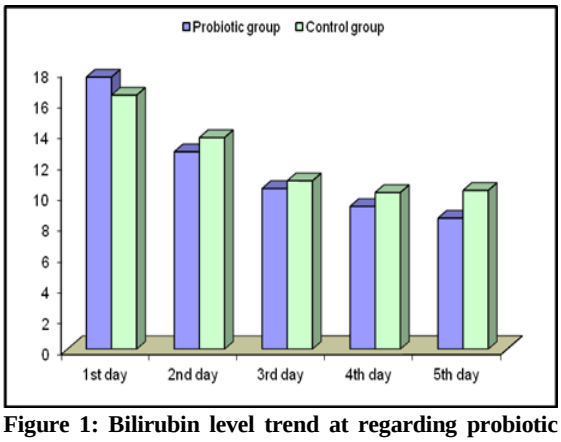

Figure 1: Bilirubin level trend at regarding probiotic group and control group

DISCUSSION

In this study there were 63.3% males and 36.66% females in the probiotic group, while in control group there were 58.33% males and 41.23% females which has no significant or need other studies to confirm that hyperbilirubinemia is more in male than in females. In the probiotic group, the average age was 3.5 ± 1.2 days, and initially jaundice was 4 ± 1.7 days. Gestational age is 37.7 ± 2.5 weeks in the probiotic group and 38.8 ± 3.8 weeks in the control group, further studies are needed to establish the relationship between gestational age and jaundice. 3.1 ± 0.91 kg in the probiotic group and 3.2 ± 0.9 kg in the control group. According to blood groups, AB+ was 30%, B + and 36%, O + and 24%, and A + and 10%. These results are incompatible with other studies in terms of number of cases and distribution in blood groups.[13,14] Relative culture is 10% negative in the probiotic group and 6% in the control group, and due to our traditions it is not compatible with other studies, which is a very low relative compared to the highest relative in our country.[15] Hemoglobin levels were 13.5 ± 2.6 gm / dl in the probiotic group and 13.8 ± 2.4 gm / dl in the control group, which may require further testing to establish a relationship between Hb levels and jaundice with a probiotic effect. Regarding the causes of jaundice in the study, 13% were caused by sepsis, 23% by ABO incompatibility, 17% by Rh incompatibility, and 47% by unknown cause in the probiotic group.[16,17] As for general symptoms, 26% in the probiotic group were pale, 18% had edema, 33% Coomb's positive and 17% CRP positive. These results are consistent with other studies.[16,17] General signs are not important when comparing two groups, but this allows us to consider each case individually.

On the first day, bilirubin levels in the first group were 17.63 ± 1.53 in the second group and 17.44 ± 2.33 in the second group. In the 3rd day, it was 10.41 ± 1.24 1st group and 10.91 ± 1.88 in 2nd group. On the fourth day, bilirubin concentration was found as 9.25 ± 1.15 in the first group and 10.15 ± 1.49 in the second group. On the fifth day, bilirubin was found in the first and second groups of 8.49 ± 1.09 and 10.29 ± 1.41, respectively. These results are same as of Torkaman et al. 92 patients data with an average age of 5.30 ± 2.40 days were analyzed. Most children (52.2%) had 3000 to 3500 grams.[18,19] There were no momentous variances in birth weight distribution among the two groups (p = 0.18). Most children in the control (79%) and probiotic (74%) groups were born with normal vaginal delivery.[20] 85 (92.4%) children were breastfed, and from 5 in the control group and 2 in the probiotic group were breastfed and modified milk.[18,19] There was no substantial variance in the type of diet between the two groups (p = 0.43).

The goal of hyperbilirubinemia treatment was to prevent bilirubin from reaching an intermediate point at which neurotoxicity could occur.[20] The hyperbilirubinemia possible complications are kernicterus and deafness. Phototherapy is preferred for hyperbilirubinemia treatment in children and has been used equally in infants in both groups in this study. To shorten hospital stay, it was proposed to prescribe various medications such as clofibrate and phenobarbital. The role of probiotics is to rise the amount of beneficial bacteria in the intestines.[21,22] There were no side effects of probiotics were noted in this study. Probiotics have recently been shown to help treat gastroenteritis by reducing bacterial growth. They can reduce the transport time of materials in the intestine.

CONCLUSION

We concluded that these 120 cases of randomized controlled trials evaluated the clinical value of probiotic supplement therapy for neonatal jaundice treatment. Evidence has been provided that the combination of routine supplement therapy with probiotic supplement therapy, including S. boulardii, Bifidobacterium, probiotic oligosaccharides, C. butyricum, and B. subtilis has a marked increase in efficacy in neonatal jaundice. Furthermore, administration of probiotics not only improves neonatal jaundice significantly by decreasing time of jaundice fading and total bilirubin but also shortened the length of hospitalization and phototherapy.

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