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Effectiveness of Oral Probiotics in Prevention of Necrotizing Enterocolitis in Preterm Infants

Naheem Ahmed [a*#], Tayyaba Siddique [bπ], Muhammad Aftab [cπ], Kiran Ashfaq Ahmed [a¥], Amna Mateen [d¥] and Rashada Bibi [e┤]

[a] Department of Pediatrics, AJ&K Medical College, Muzaffarabad, Pakistan.
[b] SKBZ/AK CMH Muzaffarabad, Pakistan.
[c] Craigavon Area Hospital, Southern Trust, Northern Ireland.
[d] Department of Neonatology, Children Hospital, PIMS, Islamabad, Pakistan.
[e] Department of Radiology, AJ&K Medical College, Muzaffarabad, Pakistan.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Objective: To determine the efficacy of probiotics in the prevention of necrotizing enterocolitis in preterm infants.
Materials And Methods: This randomized controlled trial was conducted at the paediatric department of CMH Muzaffarabad AJK. All preterm bottle and NG-fed neonates with an age of more than 24 hours and both genders were included. All the study subjects were divided into two groups randomly as group-A and group-B. Group-A was given probiotics (named Bifidobacterium prophylactically, hiflora, or gutcare, one sachet per day), while in Group-B probiotics were not given. All the cases were taken under observation. If they needed any critical or intensive care, they were excluded from the study and other treatments were given as per hospital protocol. Patients were followed for 7 days. Efficacy in both groups was measured in terms of no occurrence of NEC during one week. All related data was collected on a study proforma.

[#] Associate Professor
[π] Consultant Pediatrician
[¥] Senior Registrar
[┤] Assistant Professor
**Corresponding author: E-mail: drnaeem885@gmail.com;*

Results: The average age of the neonates in the probiotic group was 11.77 ± 6.52 days, and in the control group it was 13.41 ± 6.86 days. There were 42.1% boys and 57.9% girls were in the probiotic group, while 54% of males and 46% of females were in the control group. The frequency of NEC was statistically higher in control group 28 (11.9%) compared to the probiotic group 5 (2.1%), indicating the oral probiotic showed significant efficacy (p- 0.001).
Conclusion: Oral probiotics have been found to be efficacious, noninvasive, and beneficial in the prevention of NEC. Probiotics must be utilized to prevent necrotizing enterocolitis in preterm newborns in the future, in order to lessen the associated complications and infant mortality.

Keywords: Preterm infants; low birth weight; prevention; necrotizing enterocolitis; probiotics.

1. INTRODUCTION

Necrotizing enterocolitis (NEC) is a multifactorial illness caused by the combination of the loss of intestinal mucosa integrity and the host's responses to the damage or injury [1]. Mucosal injury, intestinal ischemia, ulceration, edema, and passage of bacteria or air through the wall, leading to mucosal and intestinal wall necrosis, are all factors [1]. This condition has become a global problem, specifically in preterm birth and very low birth weight neonates, with a highly variable incidence, i.e., reported as 2.6% to 28%, and causing 1% to 5% of admissions to the neonatal intensive care unit (NICU) [2]. Probiotics have been investigated the most in newborn medicine during the last several years [3]. In premature neonates around the world, optimizing enteral nutrition is a top priority. In premature infants, probiotics have been shown to increase gut maturation and function [4]. So far, different preventive interventions have been studied by different authors to prevent and minimize the risk of NEC in cases of preterm birth and low birth weight [5]. So, the use of probiotics in premature infants for the prevention of NEC includes numerous benefits, such as a decrease in the intestinal reservoir of the more pathogenic strains, improved enteral nutrition, and decreased reliance on intravenous nutrition, an enhanced gut mucosal barrier to the bacteria and products of the bacteria, increased expression of protective immunity, a decrease in the occurrence of sepsis, and antibacterial drug use [6]. A few studies have been done in order to see the reduction rate in NEC. As a study was done a decade ago, and they reported that the frequency of NEC was lower in cases who were given probiotics as compared to control groups with a significant difference [7,8]. A local study reported that NEC was developed in 4.7% of cases of the probiotic group, while in the control group, 24.7% developed NEC [9]. The current study was done to see the role of probiotics in pre-term neonates in terms of prevention of NEC incidence in our local population, as data on the local population is limited in that the NEC was reported higher (in probiotic and control groups) [9] when compared with other studies [7,8]. So, the higher frequency of published in the local population motivated us to do this study. The results of this study may be helpful to and be implemented in the future to decrease the risk of NEC. Moreover, in the probiotic treatment, the symbiotic organisms can stimulate the intestinal barrier function's maturity, inhibit the growth of potentially harmful organisms, increase the generation of anti-inflammatory cytokines, antioxidant activities enhancement, and apoptosis regularities, among other benefits to the host at the cellular level.

2. MATERIALS AND METHODS

This randomized controlled trial was conducted at pediatric Department of CMH Muzaffarabad AJK during a study period of six months from April 2018 to October 2018. All preterm bottle and NG-fed neonates with necrotizing enterocolitis with an age of more than 24 hours and both genders were included. All the neonates on mechanical ventilator support, IUGR, birth asphyxia, neonates having need of oxygen inhalation, congenital cyanotic heart diseases, and persistent cyanosis were excluded. The study was conducted after receiving approval from the hospital's ethical committee. After taking informed consent from parents or attendants, 470 cases meeting inclusion criteria were taken. All data was taken from inpatient department of pediatric medicine of CMH Muzaffarabad AJK. The basic information like age, sex and contact details was taken than their gestational and birth history was noted from their available medical record or from their parents. All the study subjects were divided into two groups randomly as group-A and group-B. Group-A was given probiotics (named Bifidobacterium prophylactically, hiflora, or gutcare, one sachet per day), but in Group-B

probiotics were not given. All the cases were under observation. If they needed any critical or intensive care, they were excluded from the study and other treatments were given as per hospital protocol. Patients were followed for 7 days. Efficacy in both groups was measured in terms of no occurrence of NEC during one week. All related data was collected on a given proforma by the researcher himself. Using SPSS version 22, all data was entered and analyzed using the same software.

3. RESULTS

The average age of the neonates in the probiotic group was 11.77 ± 6.52 days, and in the control group it was 13.41 ± 6.86 days. The mean gestational age in the probiotic group was 32.07 ± 2.50 weeks and in the control group the mean gestational age was 32.06 ± 2.61 weeks. The mean weight of babies was 2002.88 g in the probiotic group and in the control group it was 2042.47 ± 305.74 g. There were 226 (48.1%) boys and 244 (51.9%) were girls, while in the probiotic group there were 99 (42.1%) male and 136 (579%) female cases, whereas in the control group there were 127 (54%) male and 108 (46%) female cases Table 1.

In the probiotic group, only 5 (2.1%) cases developed NEC, while in the control group, 28 (11.9%) cases developed NEC. The frequency of NEC was statistically higher in the control group (p-0.001) Table 2.

The frequency of NEC was statistically significant according to gestational age, gender and weight (p-0.001) as shown in Table 3.

Table 1. Mean comparison of Age (days) in both study groups n=224

Variables		Mean	S. D	Minimum	Maximum
Age (years)	Probiotic	11.77	6.52	1.00	24.00
	Control	13.41	6.86	1.00	24.00
Gestational age	Probiotic	32.07	2.50	28.00	36.00
(weeks)	Control	32.06	2.61	28.00	36.00
Weight (g)	Probiotic	2002.88	292.43	1501.00	2498.00
	Control	2042.47	305.74	1501.00	2496.00
Gender	**Frequency (%)**				
	Probiotic	**Control**	**Total**		
	Male	99(42.1%)	127(54.0%)	226(48.1%)	
	Female	136(57.9%)	108(46.0%)	244(51.9%)	

Table 2. Comparison of NEC in both study groups n=224

Variables		Study group		Total	p-value
		Probiotic	Control		
NEC	Yes	5(2.1%)	28(11.9%)	33(7.0%)	0.0001
	No	230(97.9%)	207(88.1%)	437(93.0%)	
Total		235(100.0%)	235(100.0%)	470(100.0%)	

Table 3. Comparison of NEC in both study groups with respect to gestational age, gender and weight n=224

Variables		*NEC*	Study group		p-value
			Probiotic	Control	
	28-32	Yes	3(2.4%)	14(10.9%)	0.007
Gestational age		No	123(97.6%)	115(89.1%)	
(weeks)	32.1-36	Yes	2(1.8%)	14(13.2%)	0.001
		No	107(98.2%)	92(86.8%)	
	Male	Yes	1(1.0%)	15(11.8%)	0.002
Gender		No	98(99.0%)	112(88.2%)	
	Female	Yes	4(2.9%)	13(12.0%)	0.006
		No	132(97.1%)	95(88.0%)	
Weight (grams)	1501-2000	Yes	2(1.7%)	16(15.0%)	0.001
		No	115(98.3%)	91(85.0%)	
	2001-2499	Yes	3(2.5%)	12(9.4%)	0.025
		No	115(97.5%)	116(90.6%)	

4. DISCUSSION

In premature newborns, necrotizing enterocolitis (NEC) is among the most surprising and deadly infections. Till now, no one cause for NEC has been identified; nevertheless, most studies agree that the pathophysiology is multifaceted and has been linked to enteral feedings, intestinal ischemia, and viral reasons [10]. The ischemia or toxic event that causes damage to the juvenile gastrointestinal mucosa and loss of mucosal integrity is regarded to be the precursor to NEC. [10,11]. It is a significant and costly issue, particularly for newborn babies with a low birth weight (VLBW). It's critical to pay attention to respiratory conditions, electrolyte balances, acid-base, and coagulation profile [12]. Depending on the severity of the condition, in NEC, the death rate of newborns is 10– >50% among those having births of less than 1500 g, compared to a mortality rate of 0–20% for neonates having birth weights of more than 2500 g. In the current study, in the probiotic group, only 5 (2.1%) cases developed NEC, while in the control group, 28 (11.9%) cases developed NEC. The frequency of NEC was statistically higher in the control group, p-value < 0.001. A few studies have been done in order to see the reduction rate in NEC. As a study was done a decade ago, and they reported that the frequency of NEC was lesser in cases who were given probiotics (in 1.84%) as compared to the control group (6.45% infants) with a significant difference (p-0.02) [7]. In the current study, we also found the NEC was less in the treatment group as compared to placebo. Another study was done also reported significantly lesser NEC in the probiotics group (1.1%) when compared to the control group (5.3%), (p- 0.04) [8]. A local study reported that NEC was developed in 4.7% of cases of the probiotic group, while in the control group, 24.7% developed NEC [9]. These statistics are in agreement to our findings too. Consistently, a prospective randomized controlled trial study reported that the probiotic group had a reduced risk of NEC only 2.7% compared to the control group as 9.3%, and the death rate was also significantly lower than the controls. Hence, in premature infants, probiotic therapy has decreased the rate of necrotizing enterocolitis and its severity [13]. Another a systematic review was carried out to analyze the effectiveness of the probiotics in the prevention of NEC among preterm infants babies, and they observed that the probiotics significantly prevented the NEC in the very low birth weight preterm infants (p 0.00001); although, there is inadequate event till now regarding specific probiotic strain that should be used, as well as the effectiveness of the probiotics in high-risk populations like extremely low-birthweight newborns, before widespread use.[14] Similarly, a meta-analysis found that the risk of NEC was much lower in the probiotic group, and that probiotic supplementation could dramatically reduce the risk of NEC in preterm newborns independent of gestational age or NEC stage [15]. Another meta-analysis was conducted in 2009 to evaluate the safety and effectiveness of prophylactic enteral probiotics against placebo or no therapy in preventing severe NEC and other morbidities among preterm newborns. Nine trials with a total of 1,425 infants were involved in the study. Enteral probiotic treatment dramatically reduced the frequency of the NEC severity and rate of the death, according to the findings of the study. The probiotics supplementary organism caused no systemic infection in the experiments. As a result of the study's findings, enteral probiotic supplementation reduces the incidence of severe NEC and mortality in preterm newborns [16]. There were some problems with the study, like the small sample size and the fact that it was only done in one place. The patients were also only followed for one week, and those who were in the NICU for ventilation support were not followed. large-scale studies should be done on this subject.

5. CONCLUSION

Oral probiotics have been found to be efficacious, noninvasive, and beneficial in the prevention of NEC. Probiotics must be utilized to prevent necrotizing enterocolitis in preterm newborns in the future, in order to lessen the associated complications and infant mortality.

CONSENT

As per international standard, parental written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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