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ROLE OF SACCHAROMYCES BOULARDII IN PREVENTION OF NECROTIZING ENTEROCOLITIS (NEC) IN PRETERM VERY LOW BIRTH WEIGHT INFANTS IN A TERTIARY CARE HOSPITAL IN NORTHERN INDIA.

Paediatrics

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ABSTRACT

Background : Saccharomyces boulardii is a yeast which acts both as a probiotic and a polyamine producer and it has strain specific effects. The role of probiotic bacteria has been studied extensively but the effects of fungi in preventing diseases in preterm infants have been investigated poorly. **Aims and objective:** The main aim of the study is to determine the efficacy of Saccharomyces boulardii in prevention of necrotizing enterocolitis in preterm VLBW babies. **Methods:** A prospective-retrospective type of study was done over a period of one year in NICU of post graduate department of pediatrics, GB Pant hospital, GMC Srinagar. **Results:** Out of 120 patients who received probiotic, NEC stage > 2 was seen in 7.5 % (9/120) of patients whereas mortality was 5% (6/120). In control group 9.1 % (11/120) patients developed NEC stage > 2 with mortality of 5.8 % (7/120). There was no significant difference in incidence of NEC stage > 2 and mortality between these two groups. (P value 0.64) **Conclusion:** Single strain probiotic in the form of Saccharomyces boulardii failed to reduce the incidence or mortality in patients of NEC significantly.

KEYWORDS

Saccharomyces boulardii, probiotics, necrotizing enterocolitis, mortality, outcome.

INTRODUCTION

Necrotizing enterocolitis is one of the most common gastrointestinal emergencies in newborn infants.1 It is a multifactorial disease in which the functional immaturity of the intestine plays an important role in its pathogenesis.2,3 Its pathogenesis is frequently accompanied by intestinal ischemia, colonization of the intestine by pathogenic bacteria, or excess protein substrate in the intestinal lumen4. Bacterial colonization of the intestine in preterm infants may differ from that in healthy, breastfed term infants. In particular, exposure to postnatal antibiotic therapies, total parenteral nutrition (TPN), delayed enteral feeding and especially a delay in breastfeeding may impair the intestinal colonization of preterm infants in the neonatal intensive care unit (NICU) 5. This may favor the overgrowth of pathologic microorganisms, which can lead to NEC and sepsis.[6-8]

It occurs in approximately 2-5% of infants admitted to the neonatal intensive care unit. Although incidence varies among centers, recent studies report up to 9000 cases of NEC in the United States every year, with a case fatality rate of 15% to 30%.

The mortality of necrotizing enterocolitis is probably about 20-40 %. Probiotics supplementation has been proposed as a promising new intervention for the prevention of NEC.

Although some studies showed that probiotics such as Bifidobacterium and lactobacillus reduce the incidence of NEC in VLBW infants2, others showed no effect. The outcomes of meta-analysis of clinical trials suggested that further trials are necessary to accurately determine suitable probiotic preparations, the optimal dose, the best timing of administration and duration of the treatment.

Researchers have generally selected strains belonging to bacterial species naturally present in the intestinal flora. Saccharomyces boulardii [probiotic] is yeast which acts both as a probiotic and a polyamine producer. Polyamines which are essential for cell growth and differentiation enhance intestinal maturation. S.boulardii is used for the treatment of a number of gastrointestinal disorders related to abnormal bacterial growth.

Therefore the Saccharomyces boulardii (due to ability to produce amines), can be a better option for the prevention of NEC, which is characterized by bacterial colonization causing mucosal injury, and sepsis by overwhelming bacterial translocation with effects on intestinal maturation .

MATERIALS AND METHODS

DESIGN: This is a hospital based, prospective-retrospective study. The study was conducted in neonatal intensive care unit of post-graduate department of pediatrics, G. B. Pant hospital, an associated hospital of government medical college Srinagar. Prospective study was done from April 2014 to April 2015. Retrospective case analysis was done for patients admitted from April 2013 to April 2014.

The study was approved by ethical committee of GMC Srinagar.

INCLUSION CRITERIA: All neonates ≤1500g admitted in neonatal intensive care unit (NICU) of G. B. Pant hospital, Srinagar, were included in the study.

EXCLUSION CRITERIA: Babies with birth asphyxia (stage 3), Cyanotic congenital heart disease, Major congenital anomalies, Life threatening chromosomal alterations and/or congenital infections diagnosed at birth.

APPROACH: A written informed consent was taken from parents. In all neonates fulfilling the inclusion criteria detailed history and clinical examination was recorded on a predesigned proforma. Gestational age of the neonates by using the expected date of delivery (EDD) and New Ballard scoring was determined.

The study group received 5 billion CFU or 250 mg of Saccharomyces boulardii admixed with 3 ml of mother's milk, starting with the first feed.

The amount of feeding was advanced slowly if tolerated, with no more than 20 ml/kg per day increment.

Infants were evaluated twice a week or earlier if indicated, for the purpose of study using Modified Bell's staging for Necrotizing enterocolitis. Subjects were followed till their discharge or a minimum of 4 weeks, at which time the final outcome was recorded at the predesigned proforma.

RESULTS AND OBSERVATIONS The patients were stratified into two groups VLBW (1000g- 1500g) and ELBW (<1000 g). (Table 1) A total of 240 infants were enrolled in study, those who met the inclusion criteria, 120 each in study and control group.

Table 1: WEIGHT DISTRIBUTION IN BOTH GROUPS

	1 -1.5 kg, n (%) (VLBW)	< 1 kg, n (%) (ELBW)	Total
Probiotic group	84 (70 %)	36 (30%)	120
Control group	81 (67.5 %)	39 (32.5 %)	120
Total	165 (68.75 %)	75 (31.25 %)	240

P value = 0.175, statistically insignificant

There was no significant difference in weight distribution in both groups. (Table 1)

Table 2: Gestational age of patients in both groups

Group	GA (weeks)			Total
	31-32	29-30	<28	
Probiotic	21	69	30	120
Control	21	72	27	120
Total	42	141	57	240

Mean GA of patients in study population was 29.2± 2.3 weeks as compared to 29.2 ± 2.5 weeks in control group, which was comparable and difference was not significant statistically. (P value = 0.45) (Table 2)

Table 3: Comparison Of Demographic Features Of The Patients In Both The Groups:

	Study group (n = 120)	Control group (n = 120)	P value (< 0.05)
Mother age, year, median (min – max)	28 (17-45)	27 (18-40)	0.77
Gravida, median (min – max)	2 (1-8)	2 (1-8)	0.89
Parity, median (min –max)	2 (1-6)	2 (1-5)	0.83
Gestational age, week, mean ±SD	29.2± 2.3	29.2 ± 2.5	0.45
Birth weight, g, mean ± SD	1163 ± 260	1130±274	0.56
Female, n (%)	51 (42.5 %)	48 (40%)	0.45
Caesarean section, n (%)	12 (10 %)	13 (10.8 %)	0.69
Apgar, 5 min, median (min – max)	6 (1-7)	6 (1-7)	0.63
PROM, n (%)	16 (13.3%)	15(12.5%)	0.94
PROM, prolonged rupture of membranes			

Table 4: Comparison Of Primary Outcome Features Of Study

	cases (120), n %	Controls (120), n %	P value (< 0.05=significant)
NEC stage II	5(4.16%)	7 (5.8%)	0.55
NEC stage III	4 (3.33%)	4 (3.33%)	1
Death	6 (5%)	7 (5.8%)	0.77
Total	9 (7.5%)	11 (9.16%)	0.64

DISCUSSION

The purpose of the study was to find the efficacy of S. boulardii in prevention of NEC in PTVLBW neonates admitted in NICU of our hospital.

In the present study neonates ≤ 1500 grams were taken as subjects. The mean gestational age of patients in our study was 29.2± 2.3 weeks in study group as compared to 29.2 ± 2.5 weeks in control group, which was comparable with insignificant p value of 0.45. In a study done by Ozge Serce et al., the mean GA of patients was 28.8 ± 2.2 weeks in study group vs 28.7 ±2.1 weeks in control group which was almost consistent with our study.

Outcome:

The primary subject of interest in present study was to compare occurrence of NEC ≥2 and mortality between probiotic and control groups. In the present study, the overall occurrence of NEC ≥2 was 8.3% (20/240) and the overall mortality was 5.4% (13/240) in study population.

NEC stage ≥2: In the present study the overall occurrence of NEC ≥2 was 7.5% (9/120) in probiotic group as compared to 9.1% (11/120) in control group. In our study we did not detect any significant differences in the incidence of NEC between the probiotic and control groups. (P value = 0.64) This was in accordance with the results shown by Ozge Cerce et al.15 in which no significant reduction in NEC ≥2 was observed , with 6.7% in study group vs. 6.7% in control group; p value = 1.

Mortality in study population:

In our study the overall mortality was 5.4% (13/240). In probiotic group 5% (6/120) patients died whereas in control group 5.8% (7/120) had died. There was no significant difference in mortality between the two groups. Similar results were also found by Ozge Cerce et al.15 (4.8% [5/104] in study group vs. 3.8% [4/104] in control group; p value=0.74).

CONCLUSION

In our study, S. boulardii supplementation at a dose of 5 billion CFU reduced the incidence of NEC ≥2 from 9.16% in control group to 7.5% in study group. However it was not statistically significant. There was no significant effect of S.boulardii on overall mortality in probiotic group. These findings can be attributed to the type of strain used, which warrant further studies using mixed probiotics which contain both yeast and bacteria with different mechanisms and synergistic effect. There are many other advantages of S. boulardii over other probiotic strains.

In a developing country like India which is still having alarmingly high incidence of LBW and neonatal mortality rates, these probiotic strains needs to be studied extensively as a hopeful preventive strategy.

Limitations Of Study: A randomized controlled trial was not approved by ethical committee which could have allowed simultaneous observation of both cases and controls.

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