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Original Research Paper

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TO STUDY THE ROLE OF PROBIOTICS IN PREVENTING NECROTIZING ENTEROCOLITIS IN PRETERM AND LOW BIRTH WEIGHT NEONATES

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ABSTRACT

Introduction: Necrotising Enterocolitis (NEC) is the most common gastrointestinal emergency in NICU, it is a life-threatening disease that occurs primarily in premature infants.1 Probiotics are the live microbial dietary supplements that when administered in adequate amount promotes health.2 In premature infants they are thought to improve the positive balance of colonizing bacteria that facilitate development of mucosal immunity and prevent the excessive inflammation associated with NEC.3 **Methods and Materials:** The present study is a Prospective Observational study conducted in the NICU at Prathima Institute Of Medical Sciences, Karimnagar,Telangana. During the period of 2 years between December 2020 and November 2022. Neonates of <37 weeks of gestation and with birth weight <1500 gms admitted into NICU are included in the study. The selected neonates would be administered probiotic 2 million spores of Bacillus clausii ampules per day along with expressed mother's own milk daily till they reach full feeds (150ml/kg/day). These neonates were observed clinically, investigated and studied during their period of admission in NICU for the development of Necrotising Enterocolitis and also the morbidity and mortality of such neonates was studied. **Results:** In the present study, out of 50 neonates, 11 (22%) preterms developed NEC while 39 (78%) of them did not. This was found to be statistically significant (p=0.01). Out of the 11 preterms, 1 (2%) belonged to ELBW while 10 (90%) belonged to VLBW. Out of the 11 preterms who developed developed NEC, 4 (8%) developed stage I NEC, 5 (10%) developed stage II NEC and 2 (4%) developed stage III NEC. This was statistically significant (p= 0.001) In our present study, 4 (8%) of the preterms developed with sepsis while 46 (92%) did not develop sepsis. This was statistically significant (p=0.001) **Conclusion:** Necrotizing Enterocolitis is a worldwide problem in Preterms Low Birth Weight neonates. The present study has found that Probiotic supplementation has reduced both the incidence and severity of NEC in such neonates.[4] Probiotic supplementation has also reduced the incidence of culture proven sepsis in preterm and Low Birth Weight neonates.[5]

KEYWORDS : Preterm, Low Birth Weight, Necrotising Enterocolitis, Probiotics

INTRODUCTION:

Necrotizing Enterocolitis (NEC) is one of the most common and devastating gastrointestinal emergencies in very-low birth weight (VLBW; <1500 g) preterm infants in the NICU. The greatest risk factor for NEC is prematurity, putting preterm infants less than 37 weeks gestation at the greatest risk. Risk factors associated with prematurity could account for this great risk, which include immunodeficiency, use of broad-spectrum antibiotics, delayed enteral feedings, and low availability of human milk. Other leading factors of NEC include hypoxia, formula feedings, abnormal colonization of the bowel, sepsis, and the release of inflammatory mediators that are stimulated by an ischemic-reperfusion injury in an immature gut.[6] Because of the association of feeding and bacterial infection with NEC, prevention strategies have focused on manipulating the feeding of premature infants as well as trying to manipulate the bacterial environment of the intestine. Probiotic bacteria, such as Lactobacillus GG, Bifidobacteria and Bacillus clausii, are live microbial supplements that help in maturation of intestines of preterms and provide benefit to them.

OBJECTIVES

(a) To study the role of probiotics in prevention of Necrotising Enterocolitis in preterm and low birth weight neonates (b) To study the safety profile, prevalence and prognosis of Necrotising Enterocolitis in preterm and low birth weight neonates on probiotics.

METHODS:

This study was conducted among Preterm and Low Birth Weight (<1500 gm) inborn neonates who were admitted into NICU at Prathima Institute Of Medical Sciences, Karimnagar, Telangana. This was done to study the role of oral probiotics in preventing NEC in preterm and low birth weight neonates.

Study Design- Prospective Observational study.

Study Setting-

In-born Preterm and Low Birth Weight neonates admitted into NICU

Study Duration: From December 2020 to November 2022 (24 months)

Study Population:

Preterm (<37 weeks of gestation) and Low Birth Weight (<1500gm) neonates were enrolled into the study.

Inclusion Criteria:

1)Heamodynamically stable2)Neonates less than 37 weeks of gestation3)Neonates less than 1500gm

Exclusion Criteria:

1)Heamodynamically unstable2)Neonates > 37 weeks of gestational age3)Neonates with birth weight of >1500 gm4)Neonates with congenital malformations

Sampling Method:

Convenience sampling technique until completing the number of required participants was used to enroll the neonates in the study.

Sample Size:

50 Preterm and Low Birth Weight neonates were admitted into NICU.

Materials Used:

The preterms enrolled into the study were administered a probiotic, "ENTEROGERMINA" vial. Each ampule of 5ml contains around 2 million spores of Bacillus clausii, manufactured by Sanofi Synthelabo(India) Pvt Ltd, Sanofi House C.T.S No: 117-B, L&T Business Park Vihar Road, Powai Mumbai - 400 072.

Study Procedure:

The Preterm and LBW neonates admitted into NICU at Prathima Institute of Medical Sciences were enrolled into the study as per the inclusion criteria after obtaining informed consent from parents or legal gaurdians.Clinical assessment was done with the help of the questionnaries and also general examination was done.Feeding was started when the neonate had stable vital signs, normal bowel sounds without abdominal distension and no bile or blood aspirate from nasogatric tube.A strict feeding protocol was followed of all the study neonates. Depending on the birth weight and gestational age of the neonate, expressed mother's own breast milk was started at 10-20ml/ kg/day . The neonates received their regular feeds plus daily probiotic supplement that is, 1 ampule(5ml) of Enterogermina given twice daily mixed with expressed mother's own milk from the onset of enteral feeding till the baby reaches full feeds.Feeding was stopped if there was any sign of feeding intolerance (defined as the presence of gastric aspirate more than half of previous feed or with abdominal distension) Standard practice guidelines were followed in the NICU for the care of the babies.On admission to NICU a septic work up was done which included, complete blood count, C- Reactive Protein, blood cultures. Whenever a study neonate was suspected to have NEC, clinical status and abdominal films were received and if the diagnosis of NEC was established, the newborn was assigned a score according to the Bell Staging criteria.The neonates were thus observed and treated during their duration of NICU stay.

RESULTS:

Gestational Age:

Out of 50 babies, 1 (2%) baby was < 28 weeks of gestational age, 20 (40%) babies between 28-30 weeks, 19 (38%) between 31-34 weeks and 10 (20%) between 34-37 weeks. The gestational age of the babies was statistically significant (p=0.001)

Birth Weight Distribution:

In the present study,1 (2%) of the neonate was less than 1000gm (ELBW) and 49 (98%) were VLBW. This is statistically significant (p=0.001)

Antenatal Risk Factors:

25 (50%) of the mothers had no associated risk factors,10 (20%) had PROM, 15 (30%) were associated with PIH or PE. The distributon of risk factors among the mothers was stastically significant (p=0.03)

Age Of Initiation Of Probiotics:

Among 50 babies, 24 (48%) were started with probiotics on 2nd day, while 15 (30%) were started on 3rd day, 2 (4%) on 4th day and 4 (8%) on 5th and 5 (10%) on 6th day. this was statistically significant (p=0.01)

Necrotizing Enterocolitis:

11 (22%) babies developed NEC while 39 (78%) of them did not. this was found to be statistically significant (p=0.01). Out of these 11, 1 (2%) belonged to ELBW and 10 (98%) belonged to VLBW.

Age Of Onset Of Nec:

In the study, out of the 11 neonates affected by NEC, the mean age of onset of NEC was 4 days.

NEC and BELL STAGING:

In our study, out of the 11 neonates who developed developed NEC,4 (8%) developed stage I NEC , 5 (10%) developed stage II NEC and 2 (4%) developed stage III NEC. This was statistically significant (p= 0.001)

MORTALITY ASSOCIATED WITH NEC In our study, 3 (27%)of the 11 neonates with NEC expired.

SEPSIS:

In our present study, 4 (8%) of the neonates were affected with sepsis while 46 (92%) did not develop sepsis. This was statistically significant (p=0.001) Here, out of the 4 preterms, 1 (25%) belonged to ELBW and 3 (75%) belong to VLBW.

Table 1: Distribution of neonates according to gestational age

Gestational age (in weeks)	No. of cases	Percentage	P- value
<28	01	02	0.001*
28-30	20	40	
31-34	19	38	
35-37	10	20	
Total	50	100	

Table 2: Age of initiations of probiotics

Day	No. of cases	Percentage	P- value
Day 2	24	48	0.001*
Day 3	15	30	
Day 4	05	10	
Day 5	04	08	
Day 6	02	04	
Total	50	100	
Mean±SD	2.90±1.13		

Table 3: Affected with NEC

NEC	No. of cases	Percentage	P- value
Affected	11	22	0.001*
Not affected	39	78	
Total	50	100	

Table 4: Showing stages of NEC

Weight (Kg)	No. of cases	Percentage	P- value
No NEC	39	78	0.001*
Stage I	04	08	
Stage II	05	10	
Stage III	02	04	
Total	50	100	

Table 5: Showing Mortality associated with NEC

Status	No. of cases	Percentage	P- value
Mortality	03	27.3	0.132
Alive	08	72.7	
Total	11	100.0	

Table 6: Showing incidence of Sepsis

Sepsis	No. of cases	Percentage	P- value
Yes	04	08	0.001*
No	46	92	
Total	50	100	

DISCUSSION:

Necrotizing Enterocolitis (NEC) is the most commonly acquired neonatal intra- abdominal emergency and causes significant mortality and morbidity in preterm neonates with mortality approaching 30%.[7]

A proposed strategy for the prevention of NEC is the administration of oral probiotics. Emerging evidence suggests that probiotics may have a role in the control or prevention of NEC by reducing intestinal colonization with pathogenic organisms, reinforcing intestinal barrier and alleviating intestinal inflammation. Functions such as promotion of fermentation to produce organic acids and production of antimicrobial bacteriocins and fatty acids add further theoretical support to their role in the protection of NEC.[8]

Lastly, their colonization might reduce the pro- inflammatory mediators responsible for the intestinal tissue damage.[9] In our present study, out of 50 preterm neonates, 11 (22%) babies developed NEC while 39 (78%) of them did not. This was found

to be statistically significant (p=0.01). Out of these 11, 1 (2%) belonged to ELBW and 10 (98%) belonged to VLBW.

Similar observations were seen in study by Lin et al. They reported a lower incidence of NEC in the probiotic group (1.1% Vs 5.3%; p=0.04).[10]

In our study, out of the 11 neonates who developed developed NEC,4 (8%) developed stage I NEC , 5 (10%) developed stage II NEC and 2 (4%) developed stage III NEC. This was statistically significant (p= 0.001)

Similar observations were found in the study done by Lin et al. They reported 6 cases of severe NEC in the control group versus none in probiotic group(p=0.003).[11]

In our study, 3 (27%) of the 11 neonates with NEC expired. (p=0.132)

The study by Bin Nun et al. reported similar observations. They reported that three deaths in the control group were due to NEC, whereas there were no NEC- related deaths among the test neonates (p = 0.87).[12]

In our present study, 4 (8%) of the neonates were affected with sepsis while 46 (92%) did not develop sepsis. This was statistically significant (p=0.001)

Here, out of the 4 preterms, 1 (25%) belonged to ELBW and 3 (75%) belong to VLBW.

The study published by Hung–Chin Lin et al. in 2005 reported a lower incidence of sepsis in the probiotic group (22/180 Vs 36/183; p=0.03).[13]

CONCLUSION

Necrotizing Enterocolitis is a world wide problem in very low birth weight infants (VLBW), causing significant mortality and morbidity.

The present study found that probiotic supplementation has reduced both incidence and severity of NEC in preterm neonates < 37 weeks of gestation and in LBW neonates.

Probiotic supplementation has also reduced the incidence of culture proven sepsis in the preterm and LBW neonates

The appeal of probiotics in neonatology is threefold. First, its safety record renders it an attractive alternative to many of the more aggressive therapeutic options; second, it represents a simple, non-invasive attempt to recreate a natural or normal flora rather than a disruption of nature; and third, it appears to be effective in preventing a major source of morbidity in low birth weight infants.

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