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Is the Use of Probiotics in Premature Newborns Preventive for the Development of Necrotizing Enterocolitis?
Study Carried Out in the Neonatal Units of Epic Latino, 2015 – 2020 Period

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ABSTRACT: This retrospective cross-sectional study investigated the relationship between probiotic use and necrotizing enterocolitis (NEC) prevention in premature newborns at the Neonatal Units of Epic Latino between 2015 and 2020. The study included 8,632 premature newborns, 309 of whom developed enterocolitis. Results showed that gestational age was the primary risk factor for NEC development, with incidence inversely proportional to gestational age. Probiotic administration was not found to be a significant protective factor against NEC. The study suggests that further research on probiotic type, dosage, and administration is required to determine their effectiveness in preventing NEC in premature infants

INTRODUCTION

Necrotizing enterocolitis is defined as ischemic or toxic damage to the intestinal wall, which can lead to necrosis and gangrene, because of bacterial overgrowth from enteral feeding and is possibly associated with the host's immune system (1). It is a frequent pathology in preterm newborns, especially in those with low or very low weight, which, associated with their biological immaturity, represents high neonatal mortality and morbidity, since they are highly likely to present complications by intestinal perforation. It can also be present in some term neonates, especially those with perinatal stress such as asphyxia, but its probability decreases due to greater gestational age.

Probiotics are defined as live microorganisms, which if administered in adequate amounts can help protect and prevent the development of enterocolitis and its complications through different mechanisms of action: stimulus of a pH of less than 4, inhibition of pathogenic bacteria growth, production of lactic acid, decreased intestinal permeability, among others (2) in addition to reducing hospital stay. They are an important and affordable proposal. Among the best-known are *Lactobacillus rhamnosus* and *Bifidobacterium lactis*.

GOALS

To determine the relationship between the use of probiotics in necrotizing enterocolitis in premature newborns of the Neonatal Units of EPIC Latino and a reduction in the incidence of necrotizing enterocolitis.

MATERIALS AND METHODS

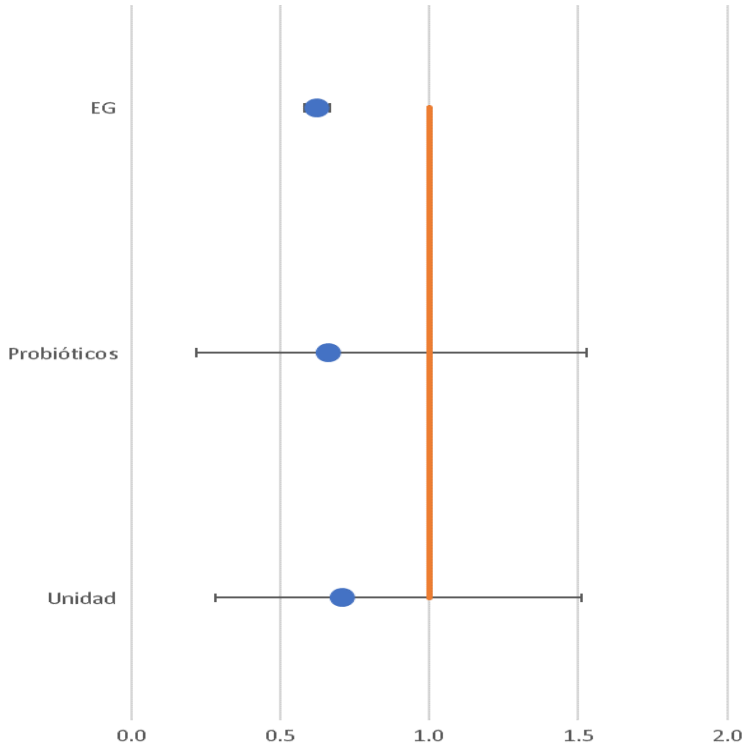
Our study is a retrospective cross-sectional analysis, which takes into account all preterm newborns with a diagnosis of enterocolitis registered in the Epic Latino software in the various Neonatology units. As selection criteria, all premature newborns with diagnosed enterocolitis from Epic Latino units from the 2015 to 2020 period were considered, and from this group, it was determined who received probiotics and who did not. Records with incomplete data in the Epic Latino software, term patients, and those who did not develop enterocolitis were excluded.

RESULTS

Table 1. Probiotics use based on the Gestational Age of the Newborn Probiotics use and Gestational Age

GA	Probiotic Use		Total
<25	5	5%	91
25-26	30	9%	334
27-28	68	10%	681
29-30	89	10%	853
31-32	156	12%	1,333
33-34	384	15%	2,520
35-36	514	18%	2,820
Total	1,246		8,632

Graph 1. Use of probiotics, Gestational Age (EG), and Units as factors that affect the development of Enterocolitis.



As observed, the only factor that influences the development of Necrotizing Enterocolitis is gestational age. Probiotics are not evidenced as a protective factor.

Table 2. Gestational Age and Stages of Necrotizing Enterocolitis.

NEC Stages							
GA Groups	II		III		Unknown		Total
<25	1	20%	4	80%	0	0%	5
25-26	18	36%	29	58%	3	6%	50
27-28	38	52%	34	47%	1	1%	73
29-30	23	42%	28	51%	4	7%	55
31-32	29	63%	15	33%	2	4%	46
33-34	31	58%	12	23%	10	19%	53
35-36	18	67%	7	26%	2	7%	27
Total	158		129		22		309

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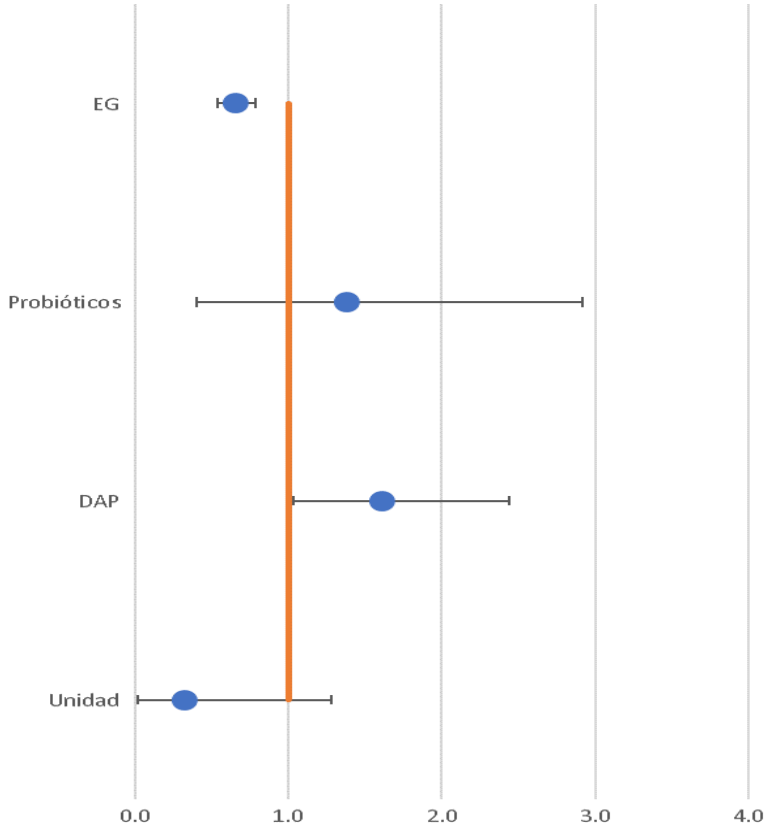
Enterocolitis Stage III (all prematures ≤ 32 weeks)

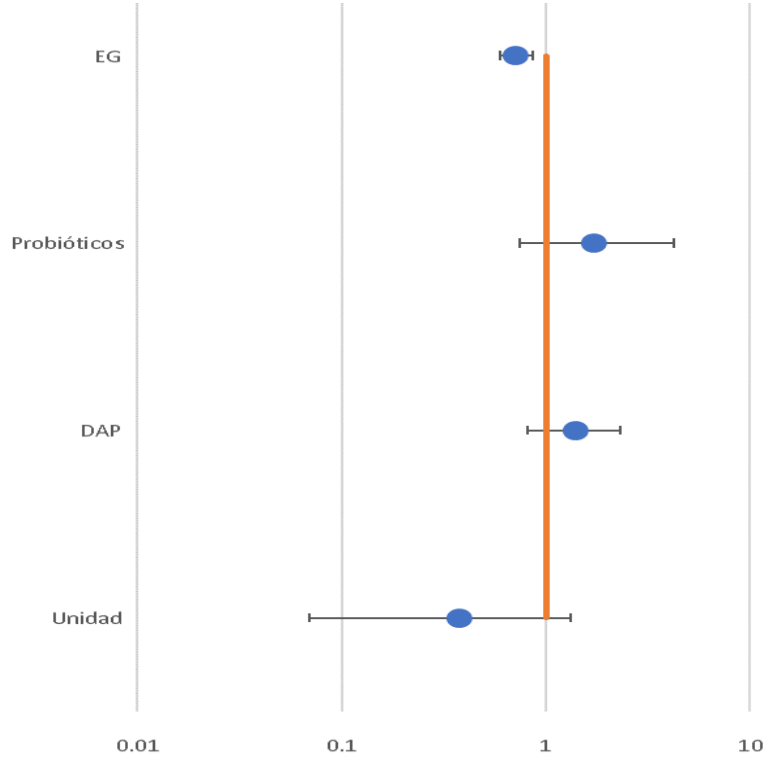


In this graph, persistent Ductus Arteriosus is added and, as in the previous graphs, it can be observed that probiotics are not a determining as protective factor for enterocolitis, regardless of its stage.

Table 3. Number of patients receiving different treatments for enterocolitis, according to their gestational age.

Gestational Age	Surgical Treatment*		Drainage*		Medical Treatment		# of Enterocolitis Patients
<25	1	20%	2	40%	3	60%	5
25-26	21	42%	20	40%	17	34%	50
27-28	30	41%	18	25%	35	48%	73
29-30	23	42%	17	31%	24	44%	55
31-32	10	22%	7	15%	31	67%	46
33-34	8	15%	11	21%	35	66%	53
35-36	4	15%	6	22%	19	70%	27
Total	97		81		164		309
*May have received more than one treatment							

Surgical Treatment for Enterocolitis (all prematures ≤ 32 weeks)



Once again, no statistically significant relationship between probiotics and enterocolitis can be observed among patients who received Surgical Treatment.

DISCUSSION

Necrotizing enterocolitis (NEC) is a studied pathology since the 1940s. It continues to be considered a devastating gastrointestinal emergency in premature and preterm newborns. Associated mortality falls between 20 and 40% and up to 50% when the patient requires surgical intervention (1), especially in premature newborns with very low birth weight (2) (3).

Throughout the study of NEC prevention practices, different factors have been assessed, such as the type of diet and its rate of onset, enteral nutrition coinciding with blood transfusions, umbilical catheters, or the use of drugs. Currently, the prevention of NEC is based on three basic pillars: the use of breastfeeding, the appropriate and justified administration of antibiotics, and the use of pre and probiotics.

In our study, a sample of 8,632 premature newborns admitted to the Epic Latino system was collected, of which 309 patients developed enterocolitis and 1,246 received probiotics.

Regarding sex distribution, the sample comprised 4,627 males and 3,989 females, of which 163 males developed enterocolitis, as opposed to 144 females, in line with studies that have established an important difference in terms of mortality distribution based on sex, with a predominance of male mortality.

Its incidence increases inversely proportional to gestational age and birth weight. Up to 90% of those affected are under 34 weeks of gestation (4). In our study, it was observed that 73 premature infants, corresponding to weeks 27 to 28 of gestation, developed enterocolitis, while at a higher gestational age, that is, between weeks 35 to 36, there is a lower risk of developing enterocolitis.

The risk of developing secondary enterocolitis at the altitude of the Unit (Hospital or Clinic) where the newborns were treated was assessed. The results showed that the risk did not vary significantly.

Regarding the use of probiotics, systematic studies and quality reviews that support the correct use of probiotics for the prevention of NEC have not yet been published. However, our study revealed that in patients who were administered probiotics, this was not as protective a factor as expected. Related to the PIPS study, we agreed that perhaps the dose administered was below the required threshold, so it is necessary to consider that a multicenter study may be needed to determine the dose, type, and probiotic activation, as well as economic studies to determine its cost-effectiveness in health systems.

CONCLUSION

Gestational age is the most important risk factor for the development of enterocolitis, besides finding a higher incidence in males. Based on the results of our study, it is concluded that probiotics are not significantly protective for the reduction of enterocolitis,

however, it can be speculated that the type of probiotic and the dose are not the appropriate ones, in addition to considering that probiotics are not administered to the entire premature population, so the sample may be insufficient.

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