Infant Colic and Microbiota

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In 1906, the word "genetics" was coined. Shortly after, genetics began to be blamed for all human ills until Freud (1856-1939) included the parents. More recently, gut microbiota joined the list of culprits. Like the Gods of Olympus, the microbiota, at a very early stage in our lives, begins to direct our destiny. To keep it happy, we must have been born vaginally, the mother must not have received antibiotics in the last months of pregnancy, nor the newborn in the first months of life, and the newborn must have been fed exclusively on human milk for several months.

And sometimes, despite all these conditions, the microbiota rebels and causes short-term functional disorders in the baby, infantile colic (IC), or, in the long term, inflammatory diseases. The article by Vinderola et al.[1] in this issue of the Revista del Hospital Italiano details the role of the intestinal microbiota in modulating the immune system and how its alterations can lead to the development of certain disorders. IC is one of the disorders in which an alteration of the microbiota appears. While the first infant cry is very welcome by parents, persistent or excessive crying is one of the most distressing problems of infancy for the baby, the parents, and the physician[2]. IC is a benign, self-limiting entity that resolves with time. However, just as one knows that turbulence in an airplane does not have severe consequences and resolves with time, the passenger does not stop worrying and wishing it would end as soon as possible. In a systematic review and meta-analysis of 28 studies involving 8690 infants, colic (defined as crying/restlessness ≥ 3 hours per day on ≥ 3 days in any week) was documented in 17 to 25% of infants younger than six weeks, 11% of those aged 8 to 9 weeks, and 0.6% of those aged 10 to 12 weeks[3]. Treatment of a healthy infant with IC should be tailored to the medical history, physical examination, and family characteristics, considering that some families tolerate crying less well than others. The goals are to help parents cope with the crying, identify potential risks to the infant's health and well-being, anticipate long-term consequences in parent-child bonding, and, where necessary, prescribe an appropriate approved treatment[4]. There is an unfortunate correlation between early crying and abuse, reaching, in exceptional cases, the shaken baby[5]. It is also relevant to identify possible maternal depression6. Interestingly, in addition to alterations in the intestinal microbiota, an elevation in fecal calprotectin, a marker of intestinal inflammation[7], has also been described in infants with IC. Infants who develop allergic proctitis (to cow's milk protein) also have microbiota alterations and elevated calprotectin. Approximately 25% of infants with moderate or severe IC symptoms are allergic to cow's milk protein[8]. The combination of altered microbiota and cow's milk protein allergy may explain some incidence data but not others. A prospective study (89 breastfed and formula-fed infants) found that, at two weeks of age, the prevalence of crying for more than 3 hours per day was 43% among formula-fed infants and 16% among breastfed infants[9]. However, at six weeks of age, the prevalence was 12% among formula-fed infants and 31% among breastfed infants.

That would give the impression that breastfeeding only delays the onset of IC. And for what reasons would the microbiota be altered in exclusively breastfed infants? Among the proposed treatments for IC are the reduction of lactose in the formula feed, the elimination of cow's milk protein in the mother's diet, or the use of formulas with partially and extensively hydrolyzed protein (we recommend the latter). In 2018, a Cochrane review concluded that the evidence about the efficacy of dietary modifications for the treatment of IC was sparse and with a significant risk of bias[10]. The few studies available were of small sample sizes, and most had severe limitations. There were insufficient studies, which made the use of meta-analysis unfeasible. The benefits reported for hydrolyzed formulas were inconsistent. Regarding pain management in IC, another

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Cochrane review found no evidence to support the use of simethicone, herbal agents, sugar, or dicyclomine[11]. Other treatments studied include spinal manipulation, chiropractic, and acupuncture. Finally, probiotics appeared, mainly Limosilactobacillus reuteri. The best studies demonstrating their efficacy for IC treatment have been in breastfed infants. A systematic review and meta-analysis concluded that the effects of the intervention were dramatic in breastfed infants but negligible in formula-fed infants. The number needed to treat for improvement at day 21 of treatment is 2.6 [95% CI 2.0 to 3.6]. Another Cochrane review concluded that there is no clear evidence that probiotics are more effective than placebo in preventing IU; however, daily crying time appeared reduced by using probiotics compared to placebo[12]. There are still many questions and issues to investigate: 1) Is it necessary for the microbiota to "normalize" for babies to improve? No studies have investigated whether there is a change in microbiota in babies who improved their IQ with or without probiotic treatment; 2) What factors lead to altered microbiota in vaginally delivered, breastfed babies who did not receive antibiotics? 3) Why do cow's milk protein allergy and IC improve spontaneously, and does this coincide with a "normalization" of the microbiota? 4) Why are some treatments, including probiotics, effective in some babies and not in others? As a curiosity, much of the IC studies come from Europe, particularly Italy. In conclusion, it may be that IC is an umbrella with diverse etiologies and that the cause is not only altered microbiota. Or is it?

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