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Delivery type as a risk factor for infantile allergic proctocolitis

Tipo de parto como fator de risco para proctocolite alérgica no lactente

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ABSTRACT

Introduction: Allergic proctocolitis (AP) is a type of allergic reaction affecting the mucosa of the rectum and large intestine in infants within the first 6 months of life. It is characterized by the presence of mucus and bright red blood in the stools, with or without diarrhea. Low diversity in intestinal microbiota may be associated with allergic diseases. Infants born via cesarean section may have a higher likelihood of allergic issues.

Objective: To assess the incidences of cesarean and vaginal deliveries in infants suspected of having allergic proctocolitis and compare them with the rates in the general population.

Methods: Prospective cross-sectional study, in infants with suspected allergic proctocolitis, with analysis of the type of delivery and comparison with the incidences of cesarean and vaginal births in the general population of live births.

Results: Cesarean section was significantly more common in the group of 116 infants suspected of having allergic proctocolitis (87/116 - 75%) compared to births in 2020 and 2021 (63% of 57,694 deliveries). There is a substantial difference in the incidence of cesarean deliveries between the Unified Health System with 44.7% of deliveries, and the Supplementary Health System, with 81.7%. The incidence of cesarean deliveries remained significantly higher in infants suspected of having allergic proctocolitis even after adjusting for the difference in the utilization of health systems in this group compared to the general population.

Conclusion: This study's findings support the hypothesis that cesarean delivery may be one of the risk factors for allergic proctocolitis in infants.

KEYWORDS: Allergic proctocolitis. Cesarean section. Infants. Intestinal microbiota.

Central Message

Allergic proctocolitis is a type of allergic reaction of the mucosa of the rectum and large intestine of the infant in the first 6 months of life characterized by the presence of mucus and live blood in the stool, which may or may not be diarrhea. Low diversity of the gut microbiota may be associated with allergic diseases. It is possible that infants born by cesarean section are more likely to have allergic problems. Thus, it is pertinent to evaluate the incidences of cesarean section and vaginal delivery in infants with suspected allergic proctocolitis, and to compare them with the general population.

Prospect

Science has incessantly sought new knowledge about the effects of microbiota differences and, consequently, effects on the development of the immune system, in such a way that while the answers are not fully clarified, it is imperative that public managers and health professionals make efforts to curb the abusive performance of cesarean deliveries in developing countries. as is the explicit case of Brazil.

RESUMO

Introdução: A proctocolite alérgica é um tipo de reação alérgica da mucosa do reto e do intestino grosso do lactente nos primeiros 6 meses de vida caracterizada por presença de muco e sangue vivo nas fezes, podendo ou não haver diarreia. A baixa diversidade da microbiota intestinal pode estar associada a doenças alérgicas. É possível que lactentes nascidos por cesárea apresentem maior probabilidade de problemas alérgicos.

Objetivo: Avaliar as incidências de parto cesário e vaginal em lactentes com suspeita de proctocolite alérgica, e comparar com as incidências na população geral.

Métodos: Estudo transversal prospectivo em lactentes com suspeita da doença aferidos com análise do tipo de parto e comparação com as incidências de parto cesáreo e vaginal na população geral de nascidos vivos.

Resultados: Cesária foi significativamente mais realizada no grupo de 116 lactentes com suspeita de proctocolite alérgica (87/116 - 75%) do que naqueles nascidos nos anos 2020 e 2021 (63% dos 57.694 partos). A diferença na incidência de cesáreas é muito ampla entre o Sistema Único de Saúde com 44,7%, e o Sistema Suplementar de Saúde com 81,7% dos partos. A incidência de partos cesáreos permaneceu significativamente maior nos lactentes suspeitos de proctocolite alérgica mesmo após correção para a diferença de uso dos sistemas de saúde neste grupo em comparação com à população geral.

Conclusão: A presente pesquisa encontrou resultados que sustentam a hipótese de que o parto cesáreo pode ser um dos fatores de risco para a proctocolite alérgica no lactente.

PALAVRAS-CHAVE: Proctocolite alérgica. Cesárea. Lactentes. Microbiota intestinal.

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INTRODUCTION

Allergic colitis, also called eosinophilic proctocolitis or allergic proctocolitis (APP), is a problem of high incidence, especially in the first 6 months of life and seems to be associated with several triggering factors. Many publications attribute its occurrence to an allergic immune response to food proteins, being recognized as a form of allergy not mediated by IgE in the mucosa of the rectum or large intestine. There are several possible triggering agents, and when it occurs due to an allergic response, cow's milk proteins are the most described, and the resolution occurs with the dietary elimination of these antigens. It usually begins in the first months of life, and in most cases disappears before 6 months. It is observed even in infants who are exclusively breastfed. The clinical manifestation is characterized by stools stained with live blood and mixed with mucus, with or without diarrhea. It is almost always a hematochezia of benign evolution, non-painful and that does not compromise the nutritional or hematological status.[1-4S]

The proctocolitis seen in these infants may be lymphoid nodular hyperplasia or erosive eosinophilic infiltrate in the colon, or both. It is possible that such inflammatory changes are the result of the association between the type of colonic microbiota and the immaturity of the immune system in the infant. After being born with an immature immune system, the colonization of the newborn's intestinal microbiota evolves rapidly, and will play a relevant role in building the immune tolerance of the intestinal mucosa. This colonization is critical for the maturation of CD4+, Th1, and T lymphocytes and for the production of immunoglobulin A and the development of lymphoid tissue.[2,5-7]

Based on the hypothesis that the diversity of the gut microbiota is associated with allergic diseases, it is possible that the type of delivery, vaginal or cesarean section, is an influencing factor. During the first week of the newborn's life, after vaginal delivery, the genus of microorganisms with the highest colonization rate is the Bifidobacterium, which protects against necrotizing enterocolitis and other diseases. After cesarean delivery, the genders Staphylococcus, Enterococcus among others inherent to the mother's skin flora are the most found. Bifidobacterium is scarce or even absent after cesarean section. Thus, the microbiota formed from vaginal delivery tends to be richer in better quality microorganisms, with the potential to prevent allergies or other diseases.

In order to evaluate the conjecture that the type of delivery may represent one of the risk factors for PDA in infants, this study compared the incidence of cesarean section and vaginal delivery in infants with suspected PDA and in the general population of live newborns.[6-8]

METHODS

This is a prospective cross-sectional study with information collection during anamnesis of infants referred with suspected PDA from September 2021 to March 2023, treated at the Nutritional Care Program for People with Special Food Needs – Curitiba (PAN-Curitiba) or at the Pediatric Gastroenterology Outpatient Clinic of the Mackenzie Evangelical University Hospital (HUEM) in Curitiba, PR, Brazil. The project was approved by the Human Research Ethics Committee of the Mackenzie Evangelical College of Paraná (FEMPAR), CAAE No. 61595122.1.0000.0103 and by the Research Ethics Committee of the Municipal Health Department of Curitiba, CAAE No. 61595122.1.3001.0101.

Suspicion of PDA was defined in infants under 6 months of age who were referred for having streaks of mucus and blood in the stool over a period of 3 days or more, with or without diarrhea. In all cases, the attending physicians referred the child already on an empirical diet for cow's milk protein allergy. It was decided to exclude infants referred with suspected PDA who were subsequently diagnosed with infectious colitis, inflammatory bowel disease, constipation, or only a history of fecal occult blood in laboratory testing. In the group of infants with suspected PDA, the type of delivery at birth was evaluated.

Data compiled by the Municipal Health Department of Curitiba were obtained regarding the number of live births in the municipality in the years 2020 and 2021, and type of delivery according to the care bond (SUS and Supplementary Health System).

The number and percentage of vaginal and cesarean deliveries in the group of infants with suspected PDA and in the total number of live births in the period were presented.

Statistical analysis

To compare the proportions of the 2 groups, the chi-square test was used, calculating the odds ratio (OR) and the 95% confidence interval (95%CI) of the proportion of cesarean sections in the group suspected of PDA compared to the percentage in the general population of births in the municipality. Logistical correction was performed for the appropriate proportions of linkage to the SUS and the Supplementary Health System in the group of infants with suspected PDA and in the general population. The differences were considered significant when $p < 0.05$ in two-tailed analysis.

RESULT

During the 19 months of the study, 116 infants with suspected PDA were included in the study, of which 87 (75.0% - 95%CI 67.1 to 82.9%) were born by cesarean section, while 29 (25.0%) were born vaginally. In 2020 and 2021, there were 57,694 live births in the city of Curitiba, of which 36,359 (63.0% - 95%CI 62.6 to 63.4%) were born by cesarean section. Of the total number of deliveries, 28,378 were performed by the SUS and 28,942 by the Supplementary Health System. Of the deliveries performed by the SUS, 12,685 (44.7%) were cesarean sections and of those performed by the Supplementary Health System, 23,659 (81.7%) were cesarean deliveries.

The proportion of cesarean sections was significantly higher in the group suspected of PDA (75%) than in the general population (63%, p = 0.0076, OR = 1.76, 95%CI 1.16 to 2.68). Taking into account that 60% of the infants assisted by the PAN-Curitiba to receive high-cost infant formulas are users of the Supplementary Health System, the correction was made for this proportion due to the difference in the general population of live births in the city. Even so, the proportion of cesarean sections was significantly higher in infants with suspected PDA (OR = 1.55, 95%CI 1.02 to 2.35).

DISCUSSION

Although the incidence of cesarean sections in Brazil is unacceptably high,9 the present study detected an even higher incidence in the group of infants who developed conditions suggestive of PDA in the first months of life. In the comparison between the 2 health systems, cesarean deliveries are more prevalent in users of the Supplementary Health System than in the SUS in Brazil. Even after the correction that took into account the different distribution of users of the SUS and the Supplementary Health System in infants with suspected PDA and in the general population, the incidence of cesarean section continued to be significantly higher in the group with suspected PDA.

Some research has detected other risk factors for the occurrence of PDA in the first months of life, such as intake of cow's milk protein formula, prematurity, low birth weight, infections, antibiotic use, and hospitalization. Regarding the type of delivery, studies often associate cesarean section as a risk factor for the occurrence of allergic, atopic, and choatopic diseases, and this association takes into account the effects of delivery on the development of the intestinal microbiota. Researchers seem to converge that the intestinal colonization of the newborn by vaginal delivery has a predominance of beneficial genera, such as Lactobacillus and Bifidobacterium, among others, whose existence is associated with a decreased risk of atopy and a protective effect against necrotizing enterocolitis, respectively. On the other hand, intestinal colonization by cesarean delivery exhibits microbiota similar to that found in the mother's skin, such as bacteria of the genus Staphylococcus, Corynebacterium, Propionibacterium and Cocccidioides, being the first associated with the development of atopic dermatitis. Also, in the case of emergency cesarean delivery, the genders Klebsiella, Haeomophilus, Clostridium, Citrobacter, Enterococcus and the species Escherichia coli were the most frequently described. In addition, the protective genera were observed to be greatly diminished in newborns by cesarean section, so that there was less overall diversity of these organisms.[3,10-15]

In addition to the qualitative differences, quantitative differences were observed in the microbiota of infants according to the type of delivery, with greater microbiological diversity in infants born vaginally. This quantitative difference persists for many months, being demonstrated until preschool age. The poverty of the microbiota in cesarean delivery can be considered a form of dysbiosis, that is, a disadvantage in the composition of the microbiota in these infants, a possible risk factor for several allergic diseases, where PDA is inserted. The difference in the immune response to dysbiosis could even increase the likelihood of transient inflammation that promotes hematochezia occurring in these infants.[3,4,16]

Thus, it was possible to propose the conjecture of a relationship between cesarean section and the occurrence of PDA, based on a possible intersection between cesarean section and changes in the intestinal microbiota of the newborn, as inducers of an inflammatory process in the intestine of infants in the first months of life, a phase of marked immunological immaturity.[5,17,18]

Latin America is the geographic location with the highest number of cesarean sections in the world, and Brazil ranks second in the global number of these interventions. The repercussions for the mother-child binomial generated by cesarean section without correct indication and the costs of these practices, both for the SUS and for Supplementary Health, can be considered alarming. Furthermore, initiatives to address this problem stand out, such as the Adequate Birth Project, whose scope aims to reduce the number of cesarean sections without indication in Brazil, especially in the Supplementary Health System, with more than 80% of births.[9,19]

This study analyzed a single possible risk factor for the occurrence of PDA in infants, the type of delivery. The fact that this sample of 116 infants did not investigate the other known risk factors - cow's milk protein intake, neonatal ICU admission, prematurity, infections, use of antibiotics and application of vaccines - made it unfeasible to perform a multivariate analysis that could eventually assess whether cesarean delivery is in fact sustained as a variable independently associated with PDA in infants. Future research will be able to analyze the multiple risk factors and perform the appropriate advanced analysis to address this issue.[5]

Science has incessantly sought new knowledge about the effects of microbiota differences and, consequently, effects on the development of the immune system, in such a way that while the answers are not fully clarified, it is imperative that public managers and health professionals make efforts to curb the abusive performance of cesarean deliveries in developing countries. as is the explicit case of Brazil.

CONCLUSION

In conclusion, the present study found results that support the hypothesis that cesarean delivery may be, in fact, one of the risk factors for PDA in infants. Pathophysiology analysis studies need to be carried out, since the way the type of delivery influences the development of PDA may involve complex interactions between the gut microbiota and the newborn's immune system.

Authors' contributions

Conceptualization: Aristides Schier da Cruz
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Writing (original draft): All authors
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