Editorial

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Probiotics for the Prevention of Respiratory Infections in Children: Between Immunomodulatory Promise and Clinical Evidence

Probióticos para prevenção de infecções respiratórias na infância: entre a promessa imunomoduladora e a evidência clínica

Probióticos para la prevención de infecciones respiratorias en la infancia: entre la promesa inmunomoduladora y la evidencia clínica

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Since ancient times, fermented products such as yogurt have been associated with digestive benefits and overall health, although without a microbiological basis. In the late 19th and early 20th centuries, Henry Tissier isolated bifidobacteria from infants, and Alfred Nissle described a non-pathogenic strain of *E. coli* with therapeutic potential, expanding the concept of "beneficial" microorganisms.[1] Since then, a vast number of publications have addressed the topic, both before and after the definitions of probiotics, prebiotics, and synbiotics were established by Hill et al. (2014)[2], Gibson et al. (2017)[3], and Swanson et al. (2020)[4], respectively.

Acute respiratory infections (ARIs) remain among the leading reasons for pediatric consultations worldwide and, in their severe form, among the leading causes of childhood morbidity and mortality.[5] In the context of high prevalence and impact, low-cost interventions that are easily accepted and have a favorable safety profile attract the interest of physicians and society. This appeal is reinforced by a biological narrative: the modulation of the immune response mediated by the microbiota, with effects described in dendritic cells, regulatory and effector T lymphocytes, *natural killer* cells, and in the production of secretory IgA.[2]

From the perspective of the clinical immunologist, it is important to note that the body of findings points to a disconnect: the robustness of the effects observed in vitro and ex vivo—modulation of dendritic cells, expansion of regulatory T cells, activation of NK cells, induction of secretory IgA—does not translate, in most clinical trials, into a consistent reduction in clinically relevant outcomes.[6]

The question that remains, with direct implications for healthcare practice, particularly in the pediatric population, is: do probiotics ultimately prevent respiratory infections in children?

The systematic review by Rodrigues et al., published in this issue, addresses this question with formal rigor. Structured according to the PRISMA guidelines, with an assessment of risk of bias using the Cochrane RoB 2 tool and an independent, double-blind review, the study screened 1,157 articles across five relevant databases (PubMed, Embase, Scopus, Scielo, and ClinicalTrials.gov), of which 33 were included in the final analysis. The authors stratified the analysis by upper respiratory tract infections (URTI) and lower respiratory tract infections (LRTI) and by specific clinical conditions—otitis, pharyngitis, laryngitis, tracheitis, rhinitis, sinusitis, bronchitis, pneumonia, and the common cold—which constitutes a more informative approach than the generic composite outcome typically used in the literature. Adherence to a well-established methodological framework, inclusion of trials in different geographical contexts, attempt to stratify the outcome by clinical condition, and explicit recognition of heterogeneity in strain, dose, vehicle, duration of use, and population profile are qualities that distinguish this review from previous syntheses that treat "probiotics" as a monolithic intervention. The inclusion of atopy variables among the discussed confounding factors is particularly important.

The central, lucid, and uncomfortable finding is that most evidence does not support the routine use of probiotics to prevent ARI in children, and heterogeneity of results is the rule, not the exception.

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The findings of Rodrigues et al. are consistent with recent major international guidelines. The approach outlined by the authors warrants further emphasis: strain- and disease-specific randomized clinical trials with homogeneous populations stratified by age, presence of atopy, recurrent infections, and daycare exposure; prior protocol registration in PROSPERO and ClinicalTrials.gov; standardized outcomes (rate of episodes per person-time, days with symptoms, antibiotic use, hospitalization); minimum duration covering at least one full respiratory season; and pre-specified analysis of effect modifiers, including mode of delivery, breastfeeding, and prior antibiotic therapy.

For pediatricians, the message is clear: the routine recommendation of probiotics as a preventive strategy for ARI in children is not supported by the best available evidence. Interventions with established efficacy in preventing ARIs include maintaining an up-to-date vaccination schedule, breastfeeding, hand hygiene, adequate ventilation and air quality in environments, control of secondhand smoke, and careful consideration of early exposure to daycare centers.

May this work serve, above all, as an invitation to apply scientific rigor in both research and clinical practice.

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