

Systematic review and meta-analysis

No consistent evidence to date that prenatal or postnatal probiotic supplementation prevents childhood asthma and wheeze

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Michael D Cabana

Division of Pediatrics, University of California, San Francisco, San Francisco, California, USA

Correspondence to: Professor Michael D Cabana, Division of General Pediatrics, University of California, San Francisco, 3333 California Street, Suite #245, San Francisco, CA 94118, USA; michael.cabana@ucsf.edu

Commentary on: Azad MB, Coneys JG, Kozryskyj AL, *et al.* Probiotic supplementation during pregnancy or infancy for the prevention of asthma and wheeze: systematic review and meta-analysis. *BMJ* 2013;347:f6471.

Context

Probiotics are 'live microorganisms, that when administered in adequate amounts, confer a health benefit on the host'.¹ Based on the hygiene hypothesis and the potential effects of probiotics on the developing microbiota of the infant, it is thought that early probiotic supplementation might help decrease the likelihood of wheeze or asthma in children.²⁻³ Results from several clinical trials have been mixed. This systematic review and meta-analysis examines the effectiveness of prenatal and postnatal probiotic supplements for the primary prevention of asthma or childhood wheeze.

Methods

This study reviewed randomised controlled trials (RCTs) of probiotic supplements administered to mothers prenatally or to newborns in the first year of life. The primary outcome was physician-diagnosed asthma; wheezing was a secondary outcome. There was a clear research question, as well as a description of the search strategy, study selection, assessment of study quality, data extraction and synthesis, which was consistent with guidelines for meta-analyses from the Cochrane Collaboration and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Subgroup analyses, based on aggregated data from each study, were included. The results are reported as relative risk (RR) estimates and CI.

Findings

The RCTs reviewed in the study assessed a wide variety of interventions featuring different probiotic strains, doses and regimens. Only 5 of the 20 trials included data on children beyond 6 years of age. Overall asthma and wheezing rates were 10.7% and 33.3%, respectively. When data from different interventions were combined, 3257 infants (enrolled in nine trials) contributed asthma data, while 1949 infants (also enrolled in nine trials) contributed wheezing data. The data from the combined studies

using varied probiotic strains suggest that probiotic interventions were not effective in decreasing the risk of asthma (RR=0.99, 95% CI 0.81 to 1.21) or wheezing (RR=0.97, 95% CI 0.87 to 1.09).

Commentary

One of the issues in interpreting data from clinical trials of probiotic interventions is the heterogeneity of the literature. Each study in this well-executed meta-analysis used a unique combination of probiotic strain, dosage, matrix and/or duration of therapy. The interpretation of pooled results of different interventions can be helpful but should be viewed with some caution when the treatments fall into different therapeutic classes. Although the term 'probiotic' suggests a similar therapeutic class, probiotic interventions are not homogenous. Different, individual probiotic strains may be effective due to different mechanisms of action, or may have vastly different levels of effectiveness in immune modulation.⁴ The authors recognise this issue and note that subgroup analysis was not possible due to the large variety of strains used.

Many factors are thought to be associated with the later development of asthma, such as mode of delivery, antibiotic exposure and diet.⁵⁻⁷ It is possible that certain subgroups of patients may be more likely to benefit from probiotic interventions. Subgroup analysis was not possible for those infants who were exclusively formula fed, due to a lack of studies that included this population, while analysis based on early antibiotic exposure was not possible due to the lack of studies reporting this variable. Subgroup analyses based on each study's caesarean section rate failed to show differences; however, this approach used aggregated data across each study, which may not be sensitive enough to detect a potential effect. An individual participant data meta-analytic approach, that relates the data recorded for individual participant, might be more sensitive in detecting an effect in this subgroup.⁸

At this time, there is insufficient evidence to recommend the use of probiotic supplements for the prevention of asthma and wheezing—for the general population, or for specific subgroups of patients. Further research with adequately powered long-term clinical trials needs to be conducted to assess the effectiveness of specific strains of probiotics for asthma and wheezing.

Competing interests None.

References

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