

Cochrane for Clinicians

Putting Evidence into Practice

Probiotics for Persistent Diarrhea in Children

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The Cochrane Abstract on the next page is a summary of a review from the Cochrane Library. It is accompanied by an interpretation that will help clinicians put evidence into practice. Drs. Hitzeman and Romo present a clinical scenario and question based on the Cochrane Abstract, followed by an evidence-based answer and a critique of the review. The practice recommendations in this activity are available at <http://www.cochrane.org/reviews/en/ab007401.html>.



This clinical content conforms to AAFP criteria for evidence-based continuing medical education (EB CME). See CME Quiz on page 31.

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A collection of Cochrane for Clinicians published in *AFP* is available at <http://www.aafp.org/afp/cochrane>.

Clinical Scenario

A three-year-old boy who recently returned to the United States from India is admitted to the hospital for dehydration from diarrhea lasting more than two weeks.

Clinical Question

Are probiotics helpful for treating persistent diarrhea in children? If so, which probiotic works best?

Evidence-Based Answer

Limited data suggest that probiotic use decreases duration and frequency of loose stools, and reduces length of hospital stay in children with persistent diarrhea.¹ One high-quality study showed *Lactobacillus rhamnosus* GG to be effective. Probiotics are generally well tolerated. (Strength of Recommendation = B, based on inconsistent or limited-quality patient-oriented evidence)

Practice Pointers

Worldwide, 10.2 million children younger than five years die each year, and diarrhea causes approximately one-fifth of these deaths.² About one-half of deaths from diarrhea are caused by persistent diarrhea lasting longer than two weeks.¹ Adequate nutrition and hydration, good hygiene, clean water, rotavirus vaccination, and breastfeeding are important factors in preventing or mitigating diarrhea. Antibiotics are rarely helpful.³

Probiotics are microorganisms that have been proven to prevent and reduce the duration of illness in children with acute diarrhea.³ *L. rhamnosus* GG is the most-studied preparation. Fewer studies have examined the effects of probiotics on persistent diarrhea.

The authors of this Cochrane review analyzed four randomized controlled trials

comparing a specific probiotic agent with placebo in children with persistent diarrhea that was thought to be infectious. Patients with chronic diarrheal illness from other causes, such as malabsorption syndromes, were excluded. The four randomized controlled trials included 464 children in India, Mexico, Argentina, and Algeria. Only one of these studies was of high quality and considered at low risk of bias. In this study of 235 hospitalized children in India, one-half of whom were randomized to receive *L. rhamnosus* GG, the duration of diarrheal illness was reduced by four days in the probiotic group.⁴ The average hospital stay was reduced by eight days. There were no adverse effects reported.

A few studies have reported adverse effects from probiotics. A study of adults showed increased mortality in patients with acute pancreatitis who received probiotics.⁵ A German study of pregnant women who received *Lactobacillus* supplementation during the perinatal period to prevent atopic dermatitis in infants showed increased rates of wheezing bronchitis in infants of treated women.⁶ However, probiotics appear to have few adverse effects in otherwise healthy persons.^{1,3,7}

Evidence of varying quality shows that probiotics are also beneficial for antibiotic-associated diarrhea, traveler's diarrhea, irritable bowel syndrome, inflammatory bowel disease, and infantile colic.^{7,8}

Where There Is No Doctor: A Village Health Care Handbook can be used as a reference for physicians traveling to developing countries with high rates of diarrheal illnesses and other infectious diseases. A free online version is available at http://www.hesperian.info/assets/WTND/doctor_whole_book.pdf.

Cochrane Abstract

Background: Persistent diarrhea (diarrhea lasting more than 14 days) accounts for one-third of all diarrhea-related deaths in developing countries in some studies. Probiotics may help treatment.

Objectives: To evaluate probiotics for treating persistent diarrhea in children.

Search Strategy: In August 2010, the authors searched the Cochrane Infectious Diseases Group Specialized Register, CENTRAL, Medline, EMBASE, and LILACS. They also contacted authors of included trials and organizations working in the field, and checked reference lists.

Selection Criteria: Randomized controlled trials comparing a specified probiotic agent with placebo or no probiotic in children with persistent diarrhea.

Data Collection and Analysis: Two review authors assessed the eligibility and risk of bias, and extracted

and analyzed data. Differences were resolved by discussion. Statistical analysis was performed using the fixed-effect model, and the results were expressed as mean difference for continuous outcomes with 95% confidence intervals.

Main Results: Four trials were included, with a total of 464 participants; one trial had a low risk of bias. Meta-analysis showed that probiotics reduced the duration of persistent diarrhea (mean difference = 4.02 days; 95% confidence interval, 4.61 to 3.43 days; $n = 324$, two trials). Stool frequency was reduced with probiotics in two trials. One trial reported a shorter hospital stay, which was significant, but numbers were small. No adverse events were reported.

Authors' Conclusions: There is limited evidence suggesting probiotics may be effective in treating persistent diarrhea in children.



These summaries have been derived from Cochrane reviews published in the Cochrane Database of Systematic Reviews in the Cochrane Library. Their content has, as far as possible, been checked with the authors of the original reviews, but the summaries should not be regarded as an official product of the Cochrane Collaboration; minor editing changes have been made to the text (<http://www.cochrane.org>).

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REFERENCES

- Bernaola Aponte G, Bada Mancilla CA, Carreazo Pariasca NY, Rojas Galarza RA. Probiotics for treating persistent diarrhoea in children. *Cochrane Database Syst Rev*. 2010;(11):CD007401.
- Bryce J, Boschi-Pinto C, Shibuya K, Black RE; WHO Child Health Epidemiology Reference Group. WHO estimates of the causes of death in children. *Lancet*. 2005; 365(9465):1147-1152.
- McFarland LV, Elmer GW, McFarland M. Meta-analysis of probiotics for the prevention and treatment of acute pediatric diarrhea. *Int J Probiotics Prebiotics*. 2006;1(1):63-76.
- Basu S, Chatterjee M, Ganguly S, Chandra PK. Effect of *Lactobacillus rhamnosus* GG in persistent diarrhea in Indian children: a randomized controlled trial. *J Clin Gastroenterol*. 2007;41(8):756-760.
- Besselink MG, van Santvoort HC, Buskens E, et al.; Dutch Acute Pancreatitis Study Group. Probiotic prophylaxis in predicted severe acute pancreatitis: a randomised, double-blind, placebo-controlled trial [published correction appears in *Lancet*. 2008;371(9620):1246]. *Lancet*. 2008;371(9613):651-659.
- Kopp MV, et al. Randomized, double-blind, placebo-controlled trial of probiotics for primary prevention: no clinical effects of *Lactobacillus* GG supplementation. *Pediatrics*. 2008;121(4):e850-e856.
- Probiotics. *Med Lett Drugs Ther*. 2007;49(1267):66-68.
- Savino F, Cordisco L, Tarasco V, et al. *Lactobacillus reuteri* DSM 17938 in infantile colic: a randomized, double-blind, placebo-controlled trial. *Pediatrics*. 2010;126(3):e526-e533.

Cochrane Briefs

Instruments for Assisted Vaginal Delivery

Clinical Question

For assisted vaginal delivery, does the use of forceps or vacuum devices result in lower morbidity for the mother and newborn?

Evidence-Based Answer

Use of forceps is more likely to result in a vaginal delivery than use of vacuum devices (relative risk [RR] = 1.5; 95% confidence interval [CI], 1.1 to 2.2), but has a higher rate of perineal trauma, tears, pain, and incontinence, and a trend toward more cesarean deliveries. Use of metal-cup vacuum devices is more likely to result in a vaginal delivery than use of soft-cup devices, but is more likely to cause neonatal scalp injury and cephalohematoma. (Strength of Recommendation = A, based on consistent, good-quality patient-oriented evidence)

Practice Pointers

Assisted vaginal deliveries are recommended for fetal distress, failure to deliver after a prolonged second stage of labor, or maternal

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factors that would make pushing dangerous, such as exhaustion or medical problems. The choice of instrument depends on factors such as the training of the physician, fetal position, and the degree of anesthesia. Vacuum extraction does not require as much anesthesia for the mother as forceps.¹

To determine the safest delivery method for the mother and newborn, the authors of this Cochrane review searched for randomized controlled trials comparing methods of assisted vaginal delivery at term. The authors found 32 studies including 6,597 women. Seventeen of the studies compared types of vacuum devices, and 13 studies compared forceps with vacuum devices. Although the failure rate was lower with forceps than with vacuum devices, third- and fourth-degree perineal tears were more common with forceps (RR = 1.9; 95% CI, 1.6 to 3.9). Facial injuries in newborns were also more common with forceps (RR = 5.1; 95% CI, 1.1 to 23). There were no differences between forceps and vacuum devices in Apgar score, shoulder dystocia, need for intubation, severe morbidity, death, or use of maternal analgesia. Compared with soft-cup vacuum devices, use of metal cups was more likely to result in a vaginal delivery but had higher rates of neonatal bruising, cephalohematoma, and scalp injury.

There are risks and benefits with different assisted vaginal delivery methods, with no clear superiority of one device over another. However, this review supports the use of vacuum extraction with a soft cup as the first-line method because of its lower risk of harming the newborn.

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REFERENCE

1. Operative vaginal delivery. ACOG Technical Bulletin Number 196—August 1994 (replaces No. 152, February 1991). *Int J Gynaecol Obstet.* 1994;47(2):179-185. ■