Cochrane for Clinicians

Putting Evidence into Practice

Feed Thickener for Newborn Infants with Gastroesophageal Reflux

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Clinical Question

Are feed thickeners an effective treatment for the symptoms of gastroesophageal reflux (GER) in formula-fed infants?

Evidence-Based Answer

Feed thickeners decrease the number of reflux episodes in full-term formula-fed infants (mean difference [MD] = –1.97; 95% confidence interval [CI], –2.32 to –1.61). Additionally, full-term formula-fed infants with GER who are given thickeners are more than twice as likely to be asymptomatic compared with infants not receiving thickeners at one to eight weeks of follow-up (number needed to treat [NNT] = 5).[1] (Strength of Recommendation: A, based on consistent, good-quality patient-oriented evidence.)

Practice Pointers

GER is characterized as reflux of gastric contents into the esophagus caused by lower esophageal sphincter dysfunction. It affects at least 40% of infants.[2] Although GER is a normal physiologic process in healthy infants, symptoms of GER—including regurgitation, vomiting, posseting (i.e., milk or formula being regurgitated immediately after feeding), irritability, and disordered sleep—can be distressing to parents and account for frequent office visits, medication use, and subspecialist referral. Thickened infant feeds are thought to prevent symptoms of GER by increasing the "stickiness" of formula in the stomach and preventing retrograde movement of stomach contents into the esophagus. The authors of this review sought to evaluate the effectiveness of feed thickeners in formula-fed infants up to six months of age with GER.[1]

This Cochrane review included eight randomized controlled trials and 637 participants up to six months of age. Most participants were healthy, formula-fed infants. However, breastfed infants were included, as were preterm infants until their corrected age was six months. Trials including participants with congenital, gastrointestinal tract, or neurologic abnormalities were excluded. Carob bean gum, rice cereal, cornstarch, and alginate feed thickeners were compared with standard formula in most of the trials. One study used 25% thickened formula as the control, whereas another used a matching placebo. One study included two intervention groups that used carob bean gum–thickened formula and cornstarch-thickened formula. Primary outcomes included symptoms or signs of GER and measurement of gastric and esophageal acidity using pH probe studies. Assessment of symptoms or signs of GER and adverse effects were based on parental report.[1]

A meta-analysis of six studies including 442 participants showed that use of thickened feeds was associated with fewer episodes of regurgitation, posseting, or vomiting per day (MD = –1.97; 95% CI, –2.32 to –1.61). Data combined from two separate trials including 186 participants demonstrated that infants with GER receiving thickened feeds were more likely to be without regurgitation or vomiting after one to eight weeks compared with the control group (relative risk = 2.50; 95% CI, 1.38 to 4.51; NNT = 5). No type of feed thickener was statistically superior to another.[1]

The authors of this Cochrane review note that parents were likely to notice the viscosity of thickened formula, thus complicating attempts at blinding. One study reported diarrhea as an adverse effect, but most of the studies showed no significant differences in adverse effects between the control and treatment groups. Despite the inclusion of preterm infants in this review, the

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authors caution against applying these results to this patient population due to potentially different clinical presentations and nutritional requirements. Furthermore, because most of the participating infants were formula-fed, these results may not be generalizable to breastfed infants.[1] Initiation of complementary solid foods before four months of age is associated with childhood obesity.[3-5] Although feed thickeners increase the caloric density of infant feeds, larger trials with longer follow-up periods are necessary to adequately assess the long-term risk of weight gain.[1]

Guidance from the American Academy of Pediatrics recommends against introducing solid foods before six months of age.[6] Current guidelines by the National Institute for Health and Care Excellence (NICE) recommend reassurance and parental education for initial treatment of GER, and suggest the modification of feeds—to include decreasing feed volumes; using smaller, more frequent feeds; and using thickened formula—only for infants exhibiting signs and symptoms of distress or frequent episodes of regurgitation.[2] Pharmacologic management is indicated for infants who do not respond to conservative management or who meet criteria for gastroesophageal reflux disease. The findings in this Cochrane review[1] support the NICE guidelines.[2]

The practice recommendations in this activity are available at http://www.cochrane.org/CD003211.

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Blood Pressure Targets for Patients with Hypertension and Cardiovascular Disease

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Clinical Question

Are lower blood pressure (BP) targets for patients with hypertension and a history of cardiovascular disease associated with decreased morbidity and mortality?

Evidence-Based Answer

Achieving a target BP of 135/85 mm Hg or less does not decrease the risk of total cardiovascular events vs. treating to a target of 140 to 160/90 to 100 mm Hg. Further, treating to the lower BP target does not improve total mortality, cardiovascular mortality, or serious adverse effects. More patients discontinue treatment because of adverse effects when treated to the lower BP target.[1] (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

From 2007 to 2014, the age-adjusted prevalence of hypertension was 29.6% in the United States. Of those patients with hypertension, only 75% were receiving treatment and only 51.8% had their hypertension under control.[2] Between 2003 and 2013, the death rate attributable to hypertension increased by 8.2%.[3] During this time, the goal of hypertension treatment was a BP of 140/90 mm Hg or less, but this Cochrane review looked at lower BP targets for patients with a history of cardiovascular disease to determine if there is added benefit with more aggressive treatment.[1]

This Cochrane review included six randomized controlled trials and 9,484 patients. Participants were being treated for hypertension and had a documented cardiovascular history of myocardial infarction, stroke, ischemic heart disease, peripheral vascular disease, or angina. The intervention was a lower BP target (135/85 mm Hg or less) vs. standard BP targets (140 to 160/90 to 100 mm Hg or less). Primary outcomes included total and cardiovascular mortality, serious adverse effects, and total cardiovascular events, defined

SUMMARY TABLE: STANDARD VS. LOWER BP TARGETS IN PATIENTS WITH HYPERTENSION AND CARDIOVASCULAR DISEASE

Outcomes (average of 4 years)	Risk with standard BP target (≤ 140 to 160/90 to 100 mm Hg)	Risk with lower BP target (≤ 135/85 mm Hg)	NNT or NNH (95% CI)	Number of participants (number of studies)	Quality of evidence
Total mortality	68 per 1,000	72 per 1,000	NA*	9,484 (6)	Moderate
Serious adverse effects	252 per 1,000	255 per 1,000	NA*	9,484 (6)	Low
Total CV events	127 per 1,000	113 per 1,000	NA*	9,484 (6)	Low
CV mortality	31 per 1,000	32 per 1,000	NA*	9,484 (6)	Moderate
Withdrawals because of adverse effects	7 per 1,000	60 per 1,000	19 (4 to 111)	690 (2)	Very low

BP = blood pressure; CI = confidence interval; CV = cardiovascular; NA = not applicable; NNH = number needed to harm; NNT = number needed to treat.

*—No statistical difference in outcomes.

as the number of participants with at least one of the following: myocardial infarction, stroke, sudden death, and hospitalization or death from congestive heart failure.[1]

Lower BP targets revealed no apparent difference in total mortality or cardiovascular mortality compared with standard BP targets. No differences in serious adverse effects were noted. Lower BP targets did not reduce total cardiovascular events over five years.[1]

Notably, more participants in the lower BP target group withdrew from the study because of adverse effects (two studies; n = 690; relative risk = 8.16; 95% confidence interval, 2.06 to 32.28), required more drugs to lower BP (2.4 vs. 1.9 drugs, on average), and achieved BP goals less often (64% vs. 75% of the time) compared with those in the standard BP target group.[1]

The 2017 American College of Cardiology/American Heart Association Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults recently adopted a stringent BP target (less than 130/80 mm Hg) for secondary prevention of cardiovascular events in patients with clinical cardiovascular disease.[4] This Cochrane review reveals that lower BP targets in the treatment of hypertension appear to have no effect on total cardiovascular events and no change in overall and cardiovascular mortality.[1] Physicians should discuss the new BP goals with patients before pursuing these targets to reduce the risk of cardiovascular events.

The practice recommendations in this activity are available at http://www.cochrane.org/CD010315.

Editor's Note: The numbers needed to treat/numbers needed to harm reported in this Cochrane for Clinicians were calculated by the authors based on raw data provided in the original Cochrane review.

The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Department of Defense, the U.S. Army, the U.S. Air Force, or the Uniformed Services University of the Health Sciences.

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