

Thickened formula is only moderately effective in the treatment of gastroesophageal reflux in healthy infants

Horvath A, Dziechciarz P, Szajewska H. The effect of thickened-feed interventions on gastroesophageal reflux in infants: Systematic review and meta-analysis of randomized, controlled trials. *Pediatrics* 2008;122:e1268-77.

Question Among otherwise healthy infants with gastroesophageal reflux, do thickened feeds safely and effectively decrease episodes of reflux and vomiting compared with standard formula?

Design Systematic review and meta-analysis.

Data Sources Computerized databases, proceedings of the European and North American pediatric gastroenterology conferences (since 2000), additional references from reviewed articles.

Study Selection Fourteen randomized, controlled trials that evaluated thickened feeds used in infants for at least several days for the treatment of gastroesophageal reflux.

Intervention Administration of thickened feeds.

Outcomes Percentage of infants with regurgitation, number of vomiting episodes per day.

Main Results Use of thickened formulas compared with standard formula significantly increased the percentage of infants with no regurgitation, slightly reduced the number of episodes of regurgitation and vomiting per day (assessed jointly or separately), and increased weight gain per day. Thickened formula had no effect on the reflux index, number of acid gastroesophageal reflux episodes per hour, or number of reflux episodes lasting >5 minutes but significantly reduced the duration of the longest reflux episode of pH < 4. No definitive data showed that one particular thickening agent is more effective than another. No serious adverse effects were noted.

Conclusions Thickened food is only moderately effective in treating gastroesophageal reflux in healthy infants.

Commentary The age-old recommendation of thickening formula to treat infantile gastroesophageal reflux (GER) in otherwise healthy infants has not undergone rigorous scientific scrutiny. This is a meta-analysis that has limitations common to many meta-analyses: the inclusion criteria and definitions of GER were often vague and not consistent between studies. Nevertheless, the authors noted that though there were improvements in multiple measurements of reflux in the formula-thickened group, the clinical usefulness of these measurements is questionable. For example, there were a greater percentage of infants in the treatment group who had no regurgitation. But the specific measurement, such as a decrease of "0.6 episodes per day" of regurgitation is not likely to have clinical significance. This review also found an increased weight gain of 3.6 gm/d. However, the causal rela-

tionship for weight gain remains unclear. Increased weight gain may be due to increased formula retention (ie, improved GER) or to increased caloric content of thickened formula. This study largely supports the findings of previous reviews, which have found minimal to modest benefits to thickening of formulas for the treatment of GER in infants who are otherwise healthy.

Jeremy Adler, MD
Chris J. Dickinson, MD
University of Michigan
Ann Arbor, Michigan

Serious bacterial infections is uncommon in infants with bronchiolitis

Luginbuhl LM, Newman TB, Pantell RH, Finch SA, Wasserman RC. Office-based treatment and outcomes for febrile infants with clinically diagnosed bronchiolitis. *Pediatrics* 2008;122:947-54.

Questions Among infants with fever seen in the outpatient office setting, how common is serious bacterial illness? How are these patients managed?

Design Prospective cohort study.

Setting Pediatric Research in Office Settings network.

Participants A total of 3066 infants with fever (<3 months of age with temperatures $\geq 38^\circ\text{C}$).

Outcomes Frequency of sepsis evaluation, parenteral antibiotic treatment, and serious bacterial illness in infants with and without clinically diagnosed bronchiolitis. Predictors of sepsis evaluation and parenteral antibiotic treatment in infants with bronchiolitis were identified with logistic regression models.

Main Results Practitioners were less likely to perform a complete sepsis evaluation, urine testing, and cerebrospinal fluid culture and to administer parenteral antibiotic treatment for infants with bronchiolitis, compared with those without bronchiolitis. Significant predictors of sepsis evaluation in infants with bronchiolitis included younger age, higher maximal temperature, and respiratory syncytial virus testing. Predictors of parenteral antibiotic use included initial ill appearance, age of <30 days, higher maximal temperature, and general signs of infant distress. Among infants with bronchiolitis (n = 218), none had serious bacterial illness, and those with respiratory distress signs were less likely to receive parenteral antibiotic treatment. Diagnoses among 2848 infants with fever without bronchiolitis included bacterial meningitis (n = 14), bacteremia (n = 49), and urinary tract infection (n = 167).

Conclusions In office settings, serious bacterial illness in young infants with fever and clinically diagnosed bronchiolitis is uncommon. Limited testing for bacterial infections seems to be an appropriate management strategy.

Commentary Serious bacterial infections among infants hospitalized with bronchiolitis are uncommon. This study, not surprisingly, shows that serious bacterial infections among infants treated for bronchiolitis in primary care settings is at least as unlikely. Notably, however, the infants with bronchiolitis were more ill-appearing than those without bronchiolitis; yet they were only half as likely to be evaluated for sepsis and receive parenteral antibiotics, suggesting that the clinical diagnosis of a viral infection primarily predicts the physician's management and comfort level. In contrast, infants hospitalized with bronchiolitis infection still frequently receive antibiotics and other therapies not recommended for bronchiolitis,^{1,2} despite laboratory confirmation of respiratory syncytial virus. This difference in the management of bronchiolitis in the hospital and office setting may have important implications clinically and economically. The practitioner's close relationship to the family and readily available follow-up may be major factors in diminishing unnecessary therapies and laboratory analyses. The economic importance of these potential cost savings in office-based care of bronchiolitis is emphasized by the significantly greater proportion of the bronchiolitis burden that results from office visits compared with hospitalization or emergency department visits, an estimated 24- to 8-fold, respectively.³ However, the infants with bronchiolitis in this study compared with those without bronchiolitis were significantly more likely to undergo chest radiography, oxygen saturation measurements, respiratory syncytial virus testing, to become hospitalized, and to require more follow-up visits. Thus do infants diagnosed with bronchiolitis in office settings actually have fewer total therapies, diagnostic procedures, and costs than infants with fever without bronchiolitis? That question remains to be answered.

Caroline Breese Hall, MD
University of Rochester
Rochester, New York

REFERENCES

1. American Academy of Pediatrics. Diagnosis and management of bronchiolitis. *Pediatrics* 2006;118:1774-93.
2. Behrendt C, Decker M, Burch D, Watson P. International variation in the management of infants hospitalized with respiratory syncytial virus. International RSV Study Group. *Eur J Pediatr* 1998;157:215-20.
3. Hall CB, Weinberg GA, Iwane MK, Blumkin AK, Edwards KM, Staat MA, et al. The burden of respiratory syncytial virus infection among healthy children. *N Engl J Med* 2009;360:588-98.

Combination of cognitive behavioral therapy and sertraline is more effective than monotherapy for pediatric anxiety disorders

Walkup JT, Albano AM, Piacentini J, Birmaher B, Compton SN, Sherrill JT, et al. Cognitive behavioral therapy, sertraline, or a combination in childhood anxiety. *N Engl J Med* 2008;359:2753-66.

Question Among children and adolescents with anxiety disorders, what is the relative and combined efficacy of cognitive behavioral therapy and selective serotonin-reuptake inhibitors?

Design Randomized, controlled trial.

Setting Six mental health treatment centers in the United States.

Participants A total of 488 children (age 7 to 17 years) who had a primary diagnosis of separation anxiety disorder, generalized anxiety disorder, or social phobia.

Intervention Fourteen sessions of cognitive behavioral therapy (CBT), sertraline (at a dose of up to 200 mg per day), a combination of sertraline and CBT, or a placebo drug for 12 weeks in a 2:2:2:1 ratio.

Outcomes Categorical and dimensional ratings of anxiety severity and impairment at baseline and at weeks 4, 8, and 12.

Main Results The percentages of children who were rated as very much or much improved on the Clinician Global Impression-Improvement scale were 80.7% for combination therapy ($P < .001$), 59.7% for CBT ($P < .001$), and 54.9% for sertraline ($P < .001$); all therapies were superior to placebo (23.7%). Combination therapy was superior to both monotherapies ($P < .001$, number needed to treat [NNT] = 5 for combination therapy over CBT; NNT = 4 for combination therapy over sertraline). Results on the Pediatric Anxiety Rating Scale documented a similar magnitude and pattern of response; combination therapy had a greater response than CBT, which was equivalent to sertraline, and all therapies were superior to placebo. Adverse events, including suicidal and homicidal ideation, were no more frequent in the sertraline group than in the placebo group. No child attempted suicide. There was less insomnia, fatigue, sedation, and restlessness associated with CBT than with sertraline.

Conclusions Both CBT and sertraline reduced the severity of anxiety in children with anxiety disorders; a combination of the 2 therapies had a superior response rate.

Commentary Anxiety disorders are relatively prevalent disorders (6% to 20%) in the pediatric age group. However, these disorders frequently go unrecognized by medical professionals, which is a critical concern because younger age of onset leads to increased rates of later anxiety disorders, depression, substance abuse, and educational underachievement. Once identified, treatment is essential to reduce both short- and long-term impairment. Earlier randomized controlled trials have demonstrated effectiveness of the individual treatments (antidepressant medications and CBT). This study is the first direct comparison of the 2 monotherapies, and the first to examine the combination of the 2 therapies. Both monotherapies (antidepressant treatment and CBT) demonstrated similar effectiveness, although CBT takes slightly longer (8 to 12 weeks), and the medications demonstrate quick improvements, with little continued improvement after 8 weeks. Combination treatment was very effective (80%) and was superior to both monotherapies. It appears unlikely that most children with severe and persistent anxiety disorders are receiving optimal evidence-based treatments in the community. The dissemination of clinical research to clinical practice