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TREATMENT STRATEGIES FOR GERD IN NEONATES AND INFANTS

In this Issue...

Gastroesophageal reflux (GER), the passage of gastric contents into the esophagus, is common in neonates and infants. Regurgitation with clinically significant sequelae constitutes a diagnosis of gastroesophageal reflux disease (GERD). Five current studies reviewed in this issue continue to support recommendations for nonpharmacologic treatment. Corvaglia, et al, Lasekan, et al, and Indrio, et al showed potential benefit from extensively hydrolyzed protein formula, low-lactose rice-thickened formula, and probiotic treatment, respectively. Davidson, et al and Hussain, et al continue to show no benefit to proton pump inhibitor (PPI) treatment of GERD with validated measures of GERD signs and symptoms. The sixth study, by Barnhart, et al, showed no benefit from prophylactic fundoplication to prevent GERD sequelae in high-risk neurologically impaired infants. This review will demonstrate the value of nonpharmacologic and nonsurgical treatment of GERD in neonates and infants.

LEARNING OBJECTIVES

After participating in this activity, the participant will demonstrate the ability to:

- Explain the impact of the distinction between gastroesophageal reflux and gastroesophageal reflux disease on interpretation of study end-points.
- Describe current evidence supporting nonpharmacologic vs pharmacologic treatment options for GERD in neonates and infants.
- Summarize the role of the natural history of GERD symptoms on symptomatic improvement in GERD treatment and GERD research.

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Program Directors' Disclosures

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LOW-LACTOSE, RICE STARCH-THICKENED FORMULA REDUCES REGURGITATION IN HEALTHY INFANTS

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COMMENTARY

Gastroesophageal reflux (GER), the passage of gastric contents into the esophagus, is common and normal in neonates and infants. Regurgitation with clinically significant sequelae constitutes a diagnosis of gastroesophageal reflux disease (GERD). Therefore, it is essential that trials of therapies for GERD assess GERD-defining symptoms, not only physiologic measures of GER. The North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition jointly recommend nonpharmacologic treatment approaches for GERD in neonates.[1] The six studies reviewed in this newsletter continue to support earlier literature recommending conservative nonpharmacologic interventions.

Three recent studies examine potential strategies for nonpharmacologic treatment in these infants. Corvaglia, et al. investigated the effect of extensively hydrolyzed protein formula to reduce GER in preterm infants. This pilot study in preterm infants used multichannel intraluminal impedance (MII) with pH probe to show a reduction in gastric pH and acid reflux episodes without a reduction in total reflux amount or frequency; symptoms were not assessed. Indrio, et al. conducted a randomized, double-blind, placebo-controlled trial of effectiveness of treatment with probiotic to establish a beneficial intestinal microbiota on functional gastrointestinal disorders in normal newborns. Less regurgitation was reported by parents in the treatment group at three months, although it is not clear how much of this represented GERD. Lasekan, et al., in a randomized, double-blind, placebo-controlled trial, assessed the efficacy of a low-lactose rice starch-thickened formula at reducing spitting frequency in healthy, full-term neonates and infants. Both groups had decreased spitting over time, with a benefit shown in the treatment group, along with high parental satisfaction with the thickened formula. This is an important benefit, as much of the treatment for physiologic GER is driven by parental distress and discomfort rather than harmful sequelae in the infant. While these studies all show promise, an important distinction must be made about all three: while they found a reduction in gastric acidity or regurgitation, none of them directly measured diagnosed GERD.

Recent studies of proton pump inhibitor (PPI) treatment in neonates support existing data on their ineffectiveness for treating GERD in infants.[2] Despite the current recommendations, PPIs continue to be prescribed off-label to neonates for nonspecific symptoms of GER and GERD.[3] Esomeprazole, a PPI, is currently recommended only as treatment for erosive esophagitis in infants. Davidson, et al. conducted a randomized, double-blind, placebo-controlled phase III efficacy study using esomeprazole in preterm and term neonates who had GERD. This study was novel in including preterm infants and using simultaneous video, cardiorespiratory monitoring, and MII with pH probe to correlate physiologic reflux episodes with signs and symptoms of GERD. No difference was shown in GERD-related signs and symptoms with esomeprazole treatment, while increased gastric pH was shown, consistent with the drug's mechanism of action. Hussain, et al. conducted a randomized, double-blind withdrawal, placebo-controlled phase III efficacy study of rabeprazole, a PPI, in infants 1-11 months with GERD. That study used validated parent questionnaires to assess GERD symptoms. Again, no benefit was found with treatment with rabeprazole, while improvement was shown in both groups over time. This study was novel in selecting only patients who first showed parent-reported improvement during an open-label treatment phase, selecting for patients who have perceived benefit of PPI. Both of these studies use validated measures to evaluate GERD and show no benefit to PPI treatment for preterm and term GERD in neonates and infants, further iterating the growing body of evidence against pharmacologic treatment in this group.

The final study included in this review answers an important question about prophylactic surgical treatment of GERD in infants at high risk for GERD-related complications. Surgical treatment with fundoplication is considered an alternate treatment option for severe GERD and historically has been used prophylactically in patients considered to be at high risk for

complications related to GERD.[4] Fundoplication is a highly variable practice between centers and pediatric surgeons. Barnhart, et al. address the use of prophylactic gastric fundoplication at the time of gastrostomy tube (G-tube) placement for enteral feeding in neurologically impaired infants, who are at high risk for GERD because of disordered swallowing and abnormal muscle tone. This study was a retrospective observational cohort study aimed to determine whether a benefit of fundoplication exists. No difference was found in the first year after surgery in reflux-related hospitalization diagnoses, including pneumonia, aspiration pneumonia, esophagitis, GERD, and requirement for mechanical ventilation. No distinction was made between subjects on the basis of GERD diagnosis, so these results do not show whether the procedure is effective at treating GERD; rather, it shows that there is no clear benefit to performing this procedure prophylactically in this population.

Current research in neonatal and infant GERD continues to support the practice of non-pharmacologic treatment of GERD over medication. Corvaglia, et al. showed a possible benefit to extensively hydrolyzed protein formula, Lasekan, et al. demonstrated a reduction in physiologic GER with a low-lactose formula thickened with rice starch, and Indrio, et al. suggest benefit of probiotic treatment of healthy, term newborns. Davidson, et al. and Hussain, et al. continue to show no benefit to pharmacologic treatment of GERD in term and preterm neonates with validated measures of GERD signs and symptoms. Finally, prophylactic fundoplication to prevent GERD in infants at high risk was shown by Barnhart, et al. not to be beneficial. An important pattern, seen in many GERD treatment trials, was shown by Hussain, et al. and Lasekan, et al. of symptomatic improvement over time, regardless of treatment. The overwhelming trend of the literature continues to support the current recommendation of nonpharmacologic, nonsurgical treatment of physiologic GER and GERD in neonates and infants while awaiting physical maturation and the natural resolution of GER and GERD.

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PROPHYLACTIC SURGICAL TREATMENT FOR GERD IN NEUROLOGICALLY IMPAIRED INFANTS

Barnhart DC, Hall M, Mahant S, et al. Effectiveness of fundoplication at the time of gastrostomy in infants with neurological impairment. *JAMA Pediatr*. 2013;167(10):911-918.

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Infants with neurological impairment often have disordered feeding, swallowing and/or severe reflux, necessitating long-term tube feeding by gastrostomy tube (G-tube). To decrease the incidence of gastroesophageal reflux disease (GERD) and its comorbidities, some centers perform concomitant fundoplication at the time of G-tube placement to block retrograde passage of stomach contents to the esophagus.[1] In 2006 40% of all fundoplication surgeries were performed in neurologically impaired children.[2]

This study focused on prophylactic fundoplication at the time of G-tube placement in infants with neurological impairment. The hypothesis of the study was that infants with neurological impairment undergoing fundoplication at the time of G-tube placement would

experience fewer subsequent reflux-related hospitalizations. The study design was a retrospective observational cohort using a database of 42 freestanding, not-for-profit children's hospitals in the United States. Inclusion criteria were birth during the study period (2005-2010), admission to a neonatal intensive care unit within the first 90 days of life, diagnosis of neurological impairment, and G-tube placement during their initial hospitalization. No diagnosis of GERD was required. There were 2759 infants in the G-tube only group and 1404 in the G-tube and fundoplication group. The primary outcome was hospital readmission within one year after the procedure(s) with a diagnosis related to failure of fundoplication (esophagitis, GERD) or a pulmonary comorbidity of GERD (pneumonia, aspiration pneumonia, requirement for mechanical ventilation).

Subjects who underwent G-tube and fundoplication were significantly more likely to have been diagnosed during the index hospitalization with pneumonia or aspiration pneumonia, more likely to have had tracheostomy placement and mechanical ventilation, and more likely to carry a diagnosis of GERD at discharge (all $P < .001$) than those who underwent G-tube placement alone. Therefore, propensity-based matching was done between groups on the basis of presence of a gastrointestinal chronic condition, tracheostomy, and diagnosis of GERD, resulting in matched groups of $n = 1027$. Among propensity score-matched pairs there was no significant difference in reflux-related hospital readmissions between the two groups. Specifically, no difference was found between admission diagnoses of pneumonia, aspiration pneumonia, esophagitis, or GERD and requirement for mechanical ventilation.

The results of this study indicate there is no benefit to routine fundoplication at the time of G-tube placement in preventing reflux-related morbidity in infants with neurological impairment. This study does not distinguish between infants who had diagnoses of pneumonia or aspiration pneumonia prior to surgery, nor does it include patients who were readmitted for GERD-related pulmonary complications and subsequently received a fundoplication procedure. Thus, conclusions may not be drawn from the data about the effectiveness of the fundoplication procedure itself for treating GERD, rather for its use as a prophylactic measure among infants with neurological impairment. This suggests that in this population, routine fundoplication at the time of G-tube placement for long-term enteral feeding should not be performed, as there is no clear benefit in the first year after surgery.

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EXTENSIVELY HYDROLYZED PROTEIN FORMULA TO TREAT GER IN PRETERM INFANTS

Corvaglia L, Mariani E, Aceti A, et al. Extensively hydrolyzed protein formula reduces acid gastro-esophageal reflux in symptomatic preterm infants. *Early Hum Dev*. 2013;89:453-455.

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Formula-fed preterm infants have a higher prevalence of feeding intolerance during feed advancement than those fed fortified human milk.[1] Hydrolyzed protein formulas (HPF) have been shown in preterm infants to have faster gastrointestinal transit times and accelerated feeding advancement.[2,3] The question remains whether this faster transit time reduces GERD and represents a feasible nonpharmacologic treatment option.

This was a prospective pilot study of preterm infants for whom maternal breast milk was not available and who had established enteral feeds with preterm formula. Infants were started on standard protein formula (SPF), then transitioned to extensively HPF (eHPF) if they had "symptoms of feeding intolerance." The aim of the study was to assess the

impact of eHPF on GER symptoms in preterm infants with both feeding intolerance and GER. Inclusion criteria included gestational age ≤ 33 weeks with symptoms of feeding intolerance (defined as large gastric residuals, abdominal distension, and constipation) and GER (defined as frequent regurgitations or postprandial desaturations) as well as weight ≥ 1100 g and currently receiving at least 100 ml/kg/day of enteral feeds. Infants on drugs affecting gastric acidity and motility were excluded. Final study size was N = 18 infants.

Infants were fed eHPF for one week upon entrance to the study and according to unit protocol. They were then given alternating feeds of eHPF and SPF while pH and multichannel intraluminal impedance (MII) were measured to evaluate acid and nonacid GER at each feed for a 24 hour period. Caretakers and parents were not blinded to which formula was given at each feed. The investigator who interpreted pH-impedance results was blinded as to which type of formula was given at each feed.

Significant differences were found in the number of acidic GER events (P = .036), defined as single detection of pH < 4, and in the reflux index (P = .044), defined as percent of time the esophagus was exposed to pH < 4; both were lower with the eHPF feeds. No other differences were found in impedance or non-acid reflux episodes.

Interestingly, the results of this small study did not show a decrease in non-acid reflux, as expected from the previous finding of decreased gastrointestinal transit time; rather, there was a decrease only in pH when infants were fed eHPF. This makes it a possible substitute to acid-reducing medications, as this is also the desired effect of those medications. This study excluded infants who had not yet reached 100 ml/kg/day of enteral feeds (who may not have advanced due to intolerance of feeds), as well as those who were on acid-suppressing and promotility medications. There also is a potential problem with feeding eHPF made for term infants to preterm infants, as nutritional needs are different in this population and the nutritional implications were not assessed in this study. Notably, the study only evaluates presence of GER rather than symptomatic GERD. Future larger studies will be needed to assess clinically relevant outcomes and elucidate the mechanism of acid reduction.

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SAFETY AND EFFICACY OF ESOMEPRAZOLE FOR TREATMENT OF NEONATAL GERD

Davidson G, Wenzl TG, Thomson M, et al. Efficacy and safety of once-daily esomeprazole for the treatment of gastroesophageal reflux disease in neonatal patients. *J Pediatr*. 2013;163:692-698.

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Proton pump inhibitors (PPI) are recommended for moderate to severe GERD in children 1-17 years of age.[1] PPI treatment has generally been shown to be ineffective in reducing GERD symptoms in infants, suggesting symptoms likely result from relux volume rather than acidity of the contents.[2] However, most investigations have not focused on neonates or preterm infants. This study compares esomeprazole and placebo in the treatment of GERD symptoms documented by eight-hour video and cardiorespiratory monitoring in both preterm and term neonatal patients.

The study design was a randomized, double-blind, placebo-controlled phase III study conducted in Australia, Germany, and the United Kingdom, at one center in each country. Inclusion criteria were postconceptional age of < 44 weeks and suspicion of any two of the following: apnea, vomiting or gagging, or perceived irritability or pain with at least every other feed or twice in eight hours. Participants were randomized to receive enteral esomeprazole 0.5 mg/kg (n = 25) or placebo (n = 26) once daily for 14 days. Simultaneous cardiorespiratory and video monitoring was performed for eight hours, and pH/impedance was measured for 24 hours at baseline and again either at 14 days or on day of discontinuation if the study ended early. The primary outcome was change from baseline in number of GERD-related signs (from video) and symptoms (from respiratory monitoring). Secondary outcomes included mean change from baseline in signs and symptoms of GERD by category (gastrointestinal, cardiorespiratory, and neurobehavioral). Signs and symptoms were considered to correlate with reflux if the two occurred within two minutes of the start of an acidic reflux episode. Pharmacodynamic efficacy was measured by number of reflux episodes of varying acidity and consistency of reflux, as well as mean bolus and mean acid clearance time.

The study found no statistical difference in the number of GERD-related signs and symptoms between treatment and placebo groups. In both the treatment and placebo groups most symptoms improved over 14 days. No difference was found in total number of reflux episodes, but fewer acidic (pH < 4) reflux episodes were found in the treatment group versus placebo (P < .0001), consistent with the drug's mechanism of action. These data show no clinical benefit to esomeprazole. Many of the infants who had symptomatic GERD may not have been included because of illness and represent a large clinical population of neonates who routinely receive PPI treatment; conversely, well infants may have been excluded as not expected to be hospitalized for the duration of the study. Additionally, patients were included only if they had at least two signs or symptoms of GERD, while clinically patients may be treated for only one sign or symptom. Thus, as in many trials, the study population may have limited generalizability.

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SAFETY AND EFFICACY OF RABEPRAZOLE FOR TREATMENT OF INFANT GERD

Hussain S, Kierkus J, Hu P, et al. Safety and efficacy of delayed release rabeprazole in 1- to 11-month-old infants with symptomatic GERD. *J Pediatr Gastroenterol Nutr*. 2014;58:226-236.

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Esomeprazole is currently the only proton pump inhibitor (PPI) approved for use in infants 1-11 months and is approved only for erosive esophagitis. This approval was based on the agent's ability to raise gastric pH and pharmacokinetic analysis in patients aged 1-24 months,[1] not on symptom reduction. Previous studies have shown no efficacy of PPIs to reduce symptoms of GERD in 1-11 month olds.[2] The prevalent use of PPIs in the infant population[3] necessitates further investigation into whether a safe and effective PPI exists for this population.

The current study aimed to evaluate efficacy and safety of rabeprazole in infants 1-11 months with GERD who previously showed symptomatic benefit with open-label use. The

study design was a randomized, double-blind, placebo-controlled phase III trial. Inclusion criteria were age 1-11 months, a diagnosis of symptomatic GERD as made by a pediatric gastroenterologist, a score of ≥ 16 on the Infant Gastroesophageal Reflux Questionnaire-Revised (I-GERQ-R), and at least one of the following: failure to thrive, irritability/crying/disturbed sleep, or food refusal/back arching. Investigators were encouraged to choose patients who had failed nonpharmacologic management, and all other management was allowed to continue during the study period. Exclusion criteria were known history of ALTE (apparent life-threatening event) thought to be due to GERD or other non-GERD diagnosis known to cause reflux or vomiting. Acid suppressive medications were stopped three days prior to the first dose of study drug.

The study began with an open-label phase during which all participants (N = 344) received 10 mg/day of rabeprazole and were monitored with weekly I-GERQ-R scores, I-GERQ-DD (Daily Diary), and primary caregiver Clinical Global Impression of Improvement (CGI-I) for up to three weeks, to assess tolerance as well as to enrich the study population with those who have shown a previous response. When participants received a CGI-I score of good or excellent (n = 268) they were then randomized to receive either 10 mg/day or 5 mg/day of rabeprazole, or placebo for five weeks. Weekly assessments were done in person or by phone by the investigator. The primary outcome was change from baseline at the time of randomization in frequency of regurgitation, weight-for-age z score, weekly I-GERQ-R, and daily I-GERQ-DD. Secondary efficacy endpoints were volume of regurgitation and specific parameters on the I-GERQ-DD. Safety was assessed with recording of treatment-emergent adverse events (TEAEs), lab tests and physical exam.

No difference was found between groups from baseline to study completion in any of the primary or secondary efficacy measures. Improvement was seen in almost every parameter in all three groups, with no difference between treatments. Post hoc analysis separated subjects by age and still no difference was found. Of the infants in the open-label phase, 34.6% experienced at least one TEAE, of which 4.1% were considered treatment related. In the blinded phase, 47% of all infants had at least one TEAE reported, one of which was thought to be possibly related to study drug in the placebo group, while eight were thought to be related in the drug treatment groups.

The caregiver-reported improvement during the run-in open-label phase of the trial can be explained by placebo effect of entering a trial of an "experimental drug," as well as the natural history of GERD in infants. In the randomization phase, all groups continued to improve equally. This finding reinforces previous efficacy studies of PPIs in infant GERD and also demonstrates the role of physical maturation in improving symptoms. This study supports the body of evidence indicating no effectiveness of PPI to improve GERD symptoms in infants less than 12 months old, with potential adverse effects.

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EFFICACY OF PROBIOTIC TREATMENT TO REDUCE FUNCTIONAL GASTROINTESTINAL DISORDERS IN INFANTS

Indrio F, Di Mauro A, Riezzo G, et al. Prophylactic use of a probiotic in the prevention of colic, regurgitation, and functional constipation. *JAMA Pediatr*. 2014;168(3):228-233.

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Common functional gastrointestinal disorders (FGIDs) in infancy include infant colic, gastroesophageal reflux disease (GERD), and functional constipation.[1] Recent studies have suggested the importance of early colonization of the gastrointestinal tract and the significance of the composition of the intestinal microbiota on FGIDs.[2] This study suggests a possible role for probiotic treatment in infants to establish colonization with a healthy microbiota to help prevent FGIDs.

This study was a prospective, multicenter, double-blind, placebo-controlled, randomized clinical trial evaluating efficacy of newborn supplementation with Lactobacillus reuteri DSM 17938 (probiotic) on development of FGIDs and on reducing the socioeconomic impact of these disorders. Eligibility criteria included gestational age between 37-41 weeks, age < 1 week at initiation, appropriate-for-gestational-age birth weight, and 10 minute Apgar score > 8. Infants with congenital disorders were excluded. Infants were randomized to receive either probiotic (n = 276) or placebo (n = 278) for 90 days. The dose of probiotic was 1 x 108 colony-forming units daily. Caregivers recorded daily number of regurgitations, daily inconsolable crying time (to represent colic), and number of evacuations for the entire three-month period. The primary outcome was change in parent-reported symptoms after one month and three months of treatment; secondary outcomes included a cost-benefit evaluation of the supplementation, and included lost work days, medical care sought, feeding changes, hospitalizations and use of medications for gastrointestinal symptoms. No adverse events were reported that were related to the trial.

At one month of treatment crying time was significantly decreased ($P < .01$) and evacuations were more frequent ($P < .01$) in the probiotic group versus placebo, while no difference was found in number of regurgitations. At three months the significant improvement in crying time and evacuations continued (both $P < .01$); significantly fewer regurgitation episodes were also noted ($P < .01$). An assessment of the secondary outcomes showed a significant reduction in emergency room visits, pediatrician visits, parental lost work days, and use of medications and natural or herbal products (all $P < .05$), with no difference in feeding changes. Cost analysis (based on costs in Italy) estimated a mean savings of $118.71 per participant for their family and a mean savings of $140.30 per participant for the community.

This study elegantly shows a benefit to immediate establishment of favorable gut microbiota through supplementation with probiotic in healthy, term newborns without any apparent risk of harm. This is difficult to translate practically to use in the United States, however, because of the difficulty in obtaining a probiotic with guaranteed composition. Additionally, no specific GERD-defining outcomes were studied, representing a future direction for this research to delineate whether the decreased regurgitation and crying indicates any decrease in GERD.

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LOW-LACTOSE, RICE STARCH-THICKENED FORMULA REDUCES REGURGITATION IN HEALTHY INFANTS

Lasekan JB, Linke HK, Oliver JS, et al. Milk protein-based infant formula containing rice starch and low lactose reduces common regurgitation in healthy term infants: a randomized, blinded, and prospective trial. *J Am Coll Nutr*. 2014;33(2):136-46.

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Physiologic reflux can be a source of discomfort to infants and distress to parents even without harmful sequelae. Nonpharmacologic treatment of physiologic infant reflux is recommended before pharmacologic treatment and includes positioning and other feeding strategies, as well as thickening feeds, often with a form of rice starch.[1]

This study was a controlled, double-blind, randomized, multicenter trial comparing a premixed low-lactose, milk protein-based formula containing rice starch for thickened consistency (thickened) to a standard milk protein-based formula with lactose as the source of carbohydrate and no rice starch (standard). The two formulas were compared for growth and regurgitation frequency in normal, healthy, term infants (ie, no diagnosis of GERD) conducted at six study centers in the United States. Inclusion criteria were infants who were healthy, singleton, gestational age of 37-42 weeks, appropriate for gestational age, birth weight of ≥ 2500g, and age of 14 ± 3 days at study initiation. Patients could not be on acid suppression, as gastric acidity (pH < 4) is required to fully thicken the formula. Participants were randomized to receive thickened formula (n = 132) or standard formula (n = 132) and no other feeds during the study period. Primary outcome measures were parental records of volume and frequency of intake, regurgitation frequency, and stool frequency, color, and consistency daily until 28 days of age. Parameters were also recorded by parents for three days prior to study visits at 2, 3, and 4 months of age. Secondary outcome measures were parent-reported stool pattern and color, formula satisfaction questionnaires, and growth parameters at baseline and study visits.

There was no difference in weight gain between formula groups. Regurgitation frequency was reduced in the thickened group as compared to the standard group. There was a 53% reduction at one month ($P < .0005$), 54% at two months ($P < .001$), 48% at three months ($P < .003$), and 32% at four months ($P < .046$).

This study shows an improvement in spitting frequency with rice-thickened, low-lactose formula. Importantly, parental satisfaction was increased, which often is the driving factor in formula changes and medication initiation for reflux. This study did not assess infants with known GERD, which is an important next step to this investigation. It is also unclear whether the improvement in the treatment group is due to thickening with rice starch or low lactose content. Decreased spitting has previously been shown with a thickened commercial formula1 - this study does not clarify whether low lactose adds any benefit. It is important to note that this study was funded by a formula manufacturer comparing one of its products to a standard formula, presenting a potential conflict of interest. Finally, an important trend was shown in this data with a decrease in the improvement in spitting with the thickened formula over the four-month period, presumably because of physical maturation and physiologic reduction in reflux, showing that physiologic reflux decreases over time, regardless of treatment.

Reference

1. Orenstein SR, McGowan JD. Efficacy of conservative therapy as taught in the primary care setting for symptoms suggesting infant gastroesophageal reflux. *J Pediatr*. 2008;152:310-314.

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IMPORTANT CME/CE INFORMATION

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LAUNCH DATE

May 28, 2015; activities expire 2 years from the date of each publication.

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STATEMENT OF NEED

NUTRITION

- Physicians may not be aware of recent evidence-based recommendations on recognizing and treating GERD in neonates.
- Physicians may not be aware of recent evidence-based recommendations on recognizing and treating GERD in neonates.
- Current neonatal nutritional management practices may be enhanced to optimize and meet the specific needs of low birth weight preterm infants.
- Current neonatal nutritional management practices may be enhanced to optimize and meet the specific needs of low birth weight preterm infants.
- Clinicians who treat neonates are uncertain of optimal strategies for prevention and early recognition and treatment of necrotizing enterocolitis.

RESPIRATORY-RELATED ISSUES

- Clinicians may be unfamiliar with some of the newest evidence-based approaches for treating neonatal persistent pulmonary hypertension.
- Clinicians treating preterm infants may not be fully aware of the most recent developments in optimal management of bronchopulmonary dysplasia and respiratory distress syndrome.

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• An HTML5 compliant web browser or Internet Explorer 8 (and higher)

This activity was developed in collaboration with DKBmed.

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Click on link to download instructions for the post-test and evaluation

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