

Review: thickened feeds or metoclopramide may reduce symptoms of gastro-oesophageal reflux in healthy infants

Craig WR, Hanlon-Dearman A, Sinclair C, *et al.* Metoclopramide, thickened feedings, and positioning for gastro-oesophageal reflux in children under two years. *Cochrane Database Syst Rev* 2004;(4):CD003502.

Q What is the effectiveness of thickened feeds, positioning, and metoclopramide for treatment of gastro-oesophageal reflux (GER) in developmentally normal infants 1–24 months of age?

METHODS



Data sources: Cochrane Central Register of Controlled Trials (*Cochrane Library*, Issue 1, 2003), Medline (1966 to January 2003), EMBASE/Excerpta Medica (1985 to January 2003), and reference lists of retrieved reviews.



Study selection and assessment: randomised controlled trials that compared thickened feeds with unthickened feeds; metoclopramide with no intervention or placebo; or various positions in developmentally normal children 1–24 months of age with GER (diagnosed by signs or symptoms or pH monitoring). 3 independent reviewers assessed the methodological quality of individual studies using the Jadad scale.



Outcomes: signs and symptoms of GER (regurgitation, respiratory symptoms, and weight gain), reflux index (percentage of total time oesophageal pH <4), number of reflux episodes, number of reflux episodes lasting >5 minutes per unit time, adverse effects such as coughing (thickened feeds) and fussiness, drowsiness, and extrapyramidal reactions (metoclopramide).

MAIN RESULTS

20 trials met the selection criteria. 8 trials (median sample size 26; 3 had Jadad scores $\geq 3/5$) assessed the effectiveness of *thickened feeds* using a cows' milk based formula thickened with rice cereal/starch or carob flour (bean gum or St John's Bread). Pooled analyses showed that thickened feeds reduced regurgitation severity scores (2 trials, $n = 48$, standardised mean difference [SMD] -0.94 , 95% CI -1.35 to -0.52) and frequency of emesis (3 trials, $n = 88$, SMD -0.91 , CI -1.22 to -0.61), but not reflux index (2 trials, $n = 61$, weighted mean difference [WMD] 0.48 , CI -3.27 to 4.23) or volume of emesis (2 trials, $n = 60$, SMD -0.92 , CI -3.13 to 1.28). Thickened feeds were also associated with more coughs/hour (2 trials, $n = 90$, SMD 0.38 , CI 0.16 to 0.59).

5 crossover trials (median sample size 15; 2 had Jadad scores $\geq 3/5$) assessed *variations in positioning*. The findings of 4 trials (1983–97) that assessed various prone positions are not summarised here because of more recent findings that such positioning is associated with an increased risk of sudden infant death syndrome, and subsequent recommendations that infants should be placed in a supine position. 1 trial ($n = 10$) found no difference between horizontal and elevated supine positioning.

7 trials (median sample size 30; 4 had Jadad scores $\geq 3/5$) compared *metoclopramide* with placebo, with doses ranging from 0.1 mg/kg 4 times daily to 0.3 mg/kg 3 times daily. Meta-analysis showed that >1 week of metoclopramide reduced daily symptoms after 1 week (2 trials, $n = 101$, SMD -0.72 , CI -0.98 to -0.45) and the reflux index (2 trials, $n = 99$, SMD -0.43 , CI -0.72 to -0.14), but did not differ from placebo for number of refluxes >5 minutes (2 trials, $n = 99$, SMD 0.57 , CI -1.16 to 2.30), number of reflux episodes with pH <4.0 during monitoring (2 trials, $n = 99$, SMD 0.59 , CI -0.04 to 1.23), proportion of patients with perceived improvement (2 trials, $n = 71$, odds ratio 2.81 , CI 0.03 to 276), or adverse effects (4 trials, $n = 120$, risk difference 0.26 , CI -0.02 to 0.53).

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CONCLUSIONS

In healthy infants 1–24 months of age with gastro-oesophageal reflux, thickened feeds may reduce symptoms, but are also associated with increased coughing. Some evidence suggests that metoclopramide may reduce symptoms. Evidence from 1 small trial suggests that supine positioning with head elevation does not differ from horizontal positioning.

Commentary

GER, the back flow of gastric contents into the oesophagus, afflicts 50% of infants aged 0–3 months; this drops to 5% once infants are 10–12 months of age.¹ 3% of parents of 10–12 month old infants view this as a problem.¹

The systematic review by Craig *et al* included a comprehensive search for all published randomised controlled trials and used 3 reviewers to independently assess the quality of each study and to extract data. The review could have been strengthened with the inclusion of unpublished studies and consideration of the influence of method of infant feeding (ie, bottle or breast feeding) on study results, and ultimately, conclusions. Breastfed babies are known to have shorter episodes of GER than formula fed infants.²

Information gleaned from this review may be useful for nurses who advise pregnant parents, as well as nurses who provide guidance to parents of infants with GER. Thickened feeds may be somewhat helpful in reducing the symptoms of GER, although the American Academy of Paediatrics recommends exclusive breast feeding for the first 6 months of life and discourages the introduction of solid foods before the recommended age.³ Although prone and left sided positioning decrease the reflux index compared with supine positioning, these positions are associated with a higher risk of sudden infant death syndrome⁴ and therefore are not recommended. Prokinetic agents such as metoclopramide may have only some benefit in treating symptomatic GER but also put the child at risk of adverse drug effects.

Explaining to parents that GER will subside on its own over time without treatment and that interventions may have only limited effects may give them the encouragement they need to weather the GER storm with their infants. Indeed, the safest treatment for infants with GER may be reassurance from a knowledgeable professional. However, poor infant weight gain or growth retardation signals the need for more aggressive intervention.

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- 2 Heacock HJ, Jeffery HE, Baker JL, *et al.* Influence of breast versus formula milk on physiological gastroesophageal reflux in healthy, newborn infants. *J Pediatr Gastroenterol Nutr* 1992;**14**:41–6.
- 3 Gartner LM, Morton J, Lawrence RA, *et al.* for the American Academy of Pediatrics Section on Breastfeeding. Breastfeeding and the use of human milk. *Pediatrics* 2005;**115**:496–506.
- 4 Oyen N, Markestad T, Skjaerven R, *et al.* Combined effects of sleeping position and prenatal risk factors in sudden infant death syndrome: the Nordic epidemiological SIDS study. *Pediatrics* 1997;**100**:613–21.