CRD summary
This review assessed the efficacy, effectiveness and toxicity of metoclopramide for the treatment of gastroesophageal reflux disease (GERD) in infants. Given the small number of studies found, the lack of similarity between the included studies in terms of population, metoclopramide doses and outcomes, and the small sample sizes and lack of consistency in the literature, the authors' conclusion that there is insufficient evidence to support or oppose the use of metoclopramide for GERD in infants seems appropriate.

Authors' objectives
To determine the efficacy, effectiveness and safety of metoclopramide for the treatment of gastroesophageal reflux disease (GERD) in infants.

Searching
PubMed was searched from 1980 to August 2005; the search terms were reported. The bibliographies of relevant reviews published between 1995 and 2005 with full-text, online access were also checked. Only full-text papers published in English were included in the review.

Study selection
Eligible study designs included cohort studies, case-control studies and controlled studies; case reports and case series were excluded. Controlled clinical trials, randomised controlled trials (RCTs) and one cohort study were included in the review.

Studies that assessed metoclopramide for reflux were eligible for inclusion in the review. In trials with more than one treatment arm, only analyses comparing metoclopramide with no intervention or placebo were considered for inclusion. Metoclopramide dosages varied between the studies, ranging from 0.1 to 1 mg/kg, given either in a single dose or up to 4 times daily.

Studies that assessed infants were eligible for inclusion in the review. The population ranged from pre-term infants (23 to 36 weeks) to infants aged 18 months old, and included neurologically impaired and post-operative infants.

Studies looking at efficacy, effectiveness and toxicity were eligible. The outcomes included clinical symptoms of GERD (e.g. reflux symptoms), pH-probe results, gastrointestinal motility, growth, tolerance to feeding and adverse events.

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
An agreed rating (two reviewers), based on the U.S. Preventive Services Task Force scale, was given for the overall strength of the evidence; criteria for level of evidence were based on the number of studies, sample sizes, quality of study design and consistency of the literature. The validity of the individual studies does not appear to have been systematically assessed, although blinding of controlled trials was reported.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
The studies were combined in a narrative, grouped by outcome. The RCTs were also grouped by blinding. Differences
Results of the review

Twelve studies (n=343) were included in the review: 6 RCTs, 5 non-randomised controlled trials and one retrospective cohort study. Study sizes ranged from 6 to 77.

The strength of the overall evidence was rated as ‘poor’. Five of the 6 RCTs were described as being blinded.

Eight studies found an improvement with metoclopramide on at least one outcome measure and one study found a worsening of symptoms with metoclopramide. Of the 5 blinded RCTs, two found no significant between-group differences on any of the reported outcomes (pH-probe parameters and weight), two found an improvement in gastric fractional emptying rate, and one found a significant improvement in the percentage of time that the oesophageal pH was less than 4 but no significant between-group differences in other pH parameters, symptom scores or scintigraphy. This trial also found an improvement in weight gain in favour of metoclopramide for a subgroup (>3 months). Four studies reported adverse events. The most commonly reported adverse event was irritability (9 events, 4 studies); other reported adverse events were drowsiness, oculogyric crisis, dystonic reaction, apnoea and emesis.

Authors' conclusions

There is insufficient evidence to support or oppose the use of metoclopramide for the treatment of GERD in infants.

CRD commentary

The review question was clearly supported in terms of the intervention, study design, outcome and population, though the definition of eligible population was somewhat broad ('infants') and is reflected in the study populations included in the review. Only one database was searched for studies and this was restricted to papers published in English; it is therefore possible that relevant studies were missed. The methods used for the study selection and data extraction processes were not reported, therefore the possibility of reviewer error or bias cannot be assessed at these stages. The validity of the individual studies does not appear to have been assessed. The studies differed in terms of patient populations, metoclopramide dosing and outcomes measured and, as such, a narrative synthesis was appropriate. The authors' statement that there is a lack of sufficient evidence to draw a robust conclusion seems appropriate.

Implications of the review for practice and research

Practice: The authors stated that, until further evidence becomes available, clinicians should continue to judiciously treat and monitor infants with GERD.

Research: The authors stated that further large blinded RCTs are required to determine the efficacy and safety of metoclopramide in infants. They also stated that work is needed to clarify the subpopulations most likely to benefit or be harmed by metoclopramide treatment, optimal dosing for these subgroups, and also the most valid and clinically significant outcome measures.

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