Should domperidone be used for the treatment of gastro-oesophageal reflux in children: systematic review of randomized controlled trials in children aged 1 month to 11 years old

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CRD summary
This review assessed the efficacy of domperidone for symptoms of gastro-oesophageal reflux and gastro-oesophageal reflux disease in children. The authors concluded that there is no strong evidence to support the use of domperidone. Despite limitations to the review, the authors’ conclusion regarding the limitations of the evidence appear reliable.

Authors’ objectives
To assess the efficacy of domperidone for the treatment of symptoms of gastro-oesophageal reflux (GOR) and GOR disease in children.

Searching
The Cochrane Library (2004), MEDLINE (1966 to present) and EMBASE (1974 to present) were searched using the reported search terms. The reference lists of identified RCTs were screened.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies that compared oral domperidone given for at least one week with either placebo or a nonsurgical treatment (other drugs, dietary measures or positioning) were eligible for inclusion. The included studies compared domperidone alone (0.3 or 0.6 mg/kg three times daily or before meals) versus placebo or metoclopramide (0.3 mg/kg). The studies were between 2 and 8 weeks in duration.

Participants included in the review
Studies in children (aged younger than 18 years) with a probable diagnosis of GOR (using any definition) were eligible for inclusion. In the included studies, the children were aged from 3 weeks to 11 years. GOR was diagnosed clinically, radiologically and by pH-meter; two studies made the diagnosis using clinical assessment alone.

Outcomes assessed in the review
Studies were eligible if they assessed any of the following primary outcomes: symptoms or change in symptoms of GOR (regurgitation, crying, irritability, vomiting or gagging), adverse effects, clinical complications of GOR, or weight change. GOR symptoms or changes in symptoms were assessed subjectively by the child's parent and/or the treating physician or other investigator. The secondary outcomes reported in the review were: episodes of reflux measured by extended oesophageal pH monitoring; lower oesophageal sphincter pressure measured by oesophageal manometry; and histological evidence of oesophagitis on biopsy.

How were decisions on the relevance of primary studies made?
At least two reviewers selected studies independently. The methods used to resolve any disagreements were not reported.

Assessment of study quality
A formal assessment of validity does not appear to have been conducted, although elements of methodological quality were noted in the data extraction tables and the discussion. At least two reviewers assessed methodological quality independently. The methods used to resolve any disagreements were not reported.
Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Results data were extracted. Data from two treatment arms in one study, in which domperidone was combined with other agents, were not included in the review.

Methods of synthesis
How were the studies combined?
The studies were combined in a narrative, with accompanying tables.

How were differences between studies investigated?
Some differences between the studies were discussed in the text. Additional differences were apparent from inspection of the tables.

Results of the review
Four RCTs (n=176) were included. The sample size ranged from 17 to 80.

Methodological limitations of the studies included small sample sizes, short duration of treatment, treatment groups not comparable at baseline, and the potential for selective reporting of the results.

Two of the four studies reported improvements in symptoms with domperidone. One of these studies (n=32) reported that domperidone statistically significantly increased the proportion of children with a good or excellent result compared with placebo (93% versus 33%; P<0.05). The second study (n=47) reported that domperidone increased the proportion of children with no vomiting after 2 weeks in comparison with metoclopramide and placebo (75% with domperidone versus 43% with metoclopramide versus 7% with placebo). The third RCT (n=80) reported no significant difference in improvement (not defined in study) between domperidone alone and placebo. The fourth RCT (n=17) was poorly reported; the authors stated that it was difficult to interpret and concluded that it did not show evidence of any benefits of domperidone. All four studies noted no adverse effects.

Authors' conclusions
There was no robust evidence supporting the use of domperidone for the treatment of GOR in children.

CRD commentary
The review question was clear in terms of the study design, participants, intervention and outcomes. Several relevant sources were searched and some attempts were made to locate unpublished studies. It was unclear whether any language limitations had been applied, thus the potential for language bias could not be assessed. Methods were used to minimise reviewer errors and bias in the study selection and quality assessment processes, but it was unclear whether similar steps were taken in the extraction of data. Only RCTs were included, but since study validity was not adequately assessed then the results from these studies and any synthesis may not be reliable.

A narrative synthesis was appropriate given the differences between the studies. The text only reported results from two studies reporting positive outcomes, while aspects of study quality were only reported in the discussion. However, the authors' conclusion about the limitations of the evidence appears to be supported by the data presented in the review, and their conclusions appear reliable.

Implications of the review for practice and research
Practice: The authors stated that the widespread use of unlicensed medicines for GOR is not warranted.

Research: The authors stated that there is a need for studies to assess the efficacy, safety and optimal dose of domperidone in proven, severe cases of GOR and GOR disease that require medical management and where there are few nonsurgical alternative treatments. They also stated that there is a need for further pharmacokinetic studies.
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