A systematic review of the efficacy of domperidone for the treatment of diabetic gastroparesis

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CRD summary
This review concluded that there was insufficient evidence to support the use of domperidone in gastroparesis and recommended further research. The conclusions were appropriately cautious, but search limitations reduced the likelihood of all relevant evidence being identified and made the included studies unlikely to be representative. It was not possible to determine the reliability of the conclusions.

Authors' objectives
To evaluate the efficacy of domperidone in patients with diabetic gastroparesis.

Searching
PUBMED was searched for English language papers from 1979 to July 2007. Reference lists of retrieved articles were searched for additional trials. Search terms were reported. Both published articles and abstracts were eligible for inclusion.

Study selection
Studies of domperidone in patients with gastroparesis were eligible for inclusion. RCTs (randomised controlled trials), open label trials and a retrospective study were included. Duration ranged from one week to 48 months. Dose ranged from 10 to 20 mg four times a day. Of the 1,016 patients included, 928 had diabetic gastroparesis, 26 had idiopathic gastroparesis, five had other causes of gastroparesis and 57 were healthy controls. Studies reported a change in symptoms or gastric emptying. Prolactinemia and other adverse events were assessed.

The authors stated neither how the papers were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
Full text published articles were appraised for quality using a set of criteria based on a modified form of the methods described by Schofield and Jadad. The criteria were modified to include the most frequently endorsed criteria for quality measurement. Eleven criteria were used to give a maximum score of 15. Two reviewers independently appraised each full-text article for quality. The final scores were decided by consensus.

Data extraction
Data were extracted into standard templates. The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
The studies were combined using a narrative synthesis. Data were displayed in detailed tables.

Results of the review
Twenty-eight studies (n=1,016) were included: 18 RCTs; nine open trials; and one compassionate use programme. Eleven of the 28 studies were full text articles and 17 were conference abstracts (including five unpublished pharmaceutical company trials). Quality scores for the 11 full-text articles ranged from 5 to 13 (mean score of 8.3) out of 15. Study numbers ranged from five to 287 (mean number 37).

Symptom improvement
Twenty-seven studies assessed symptoms: Eighteen showed a statistically significant improvement either from baseline...
or compared to control; eight studies showed no statistical difference in improvement; and one study showed no improvement. Eleven studies provided quantifiable data with symptom scores improved by an average of 59.4 per cent (±14.5%). Six of nine uncontrolled studies that showed improvement in symptoms compared with baseline exhibited a statistically significant difference; mean improvement was 63.2 per cent (±10.5%).

Thirteen studies compared domperidone with placebo: Four studies used an enrichment process by which only those who responded to domperidone were included in a second phase in which domperidone was compared with placebo; all four showed a statistically significant improvement in the domperidone group. Of the remaining nine studies comparing domperidone with placebo (without enrichment) one study showed significant improvement in the domperidone group.

Four studies compared cisapride with domperidone: One study showed a statistically significant improvement in the domperidone group; two showed no significant difference; and the remaining study showed a significant improvement with a combination of cisapride and domperidone compared with results from either drug alone.

Two studies compared metoclopramide with domperidone: One showed significant improvement in the domperidone group; the other showed no significant differences.

Gastric emptying

Fifteen studies assessed gastric emptying before and after domperidone. Nine studies showed a statistically significant improvement in emptying compared with baseline; three studies compared domperidone with placebo and showed improvement in gastric emptying in the domperidone group. Four studies compared cisapride with domperidone; one study showed domperidone to be more effective. One study comparing metoclopramide to domperidone favoured domperidone.

Other outcomes

All four studies that assessed the impact of domperidone on quality of life for gastroparesis patients showed improvement, but only one study was statistically significant. Four of six studies that investigated the impact of domperidone on hospital admissions showed a statistically significant reduction in admissions, with the frequency of admissions decreased by an average of 73 per cent. Three studies showed non-significant weight gain. Some studies reported prolactin-related adverse events.

Authors' conclusions

There was insufficient evidence to confidently support the use of domperidone in gastroparesis. Additional, well-designed studies were required.

CRD commentary

The review addressed a reasonably clear research question. The review implied that patients with diabetic gastroparesis were included, however, the discussion section reveals that non-diabetic patients were also included. It was unclear whether study design was pre-specified, which may have led to subjective decisions regarding inclusion. The inclusion of only one database coupled with the number of unpublished studies (17 conference abstracts) identified from the reference lists of included studies alone, suggested that the search was not comprehensive enough to identify all relevant trials. There did not appear to be any systematic efforts to identify unpublished studies. Publication bias was not assessed in the report. It was unclear whether steps were taken to minimise the risk of error and bias in the processes of study selection and data extraction. The decision to use a narrative analysis was appropriate given the heterogeneity of the included studies.

The authors recognised the poor quality and heterogeneity among the primary studies. They graded the evidence as level 3 and reported a c-grade recommendation: poor evidence either in support of or against the use of domperidone in the treatment of diabetic gastroparesis. The authors made an appropriately cautious conclusion. The search was limited to one database, unpublished material was not sought and publication bias was not assessed. Thus, it was unlikely that all the relevant evidence was identified and there was a strong probability that the included studies were not representative. It was not possible, therefore, to determine the reliability of the conclusions.
Implications of the review for practice and research
Practice: The authors reported a grade-c recommendation of poor evidence either in support of or against the use of domperidone in patients with gastroparesis.

Research: The authors stated that additional large well-designed studies were needed to provide more conclusive evidence for domperidone in gastroparesis patients.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.