A prospective, randomized, double blinded, placebo controlled trial of cisapride after colorectal surgery

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The use of cisapride, a prokinetic drug in the banzamine class of agents, aimed at increasing acetylcholine release in the intramural plexuses of the bowel wall, was examined. The dosing regimen was 20 mg by mouth, four times a day.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients undergoing elective or emergent colorectal surgery for, at the minimum, the resection of a proportion of the large bowel. Patients undergoing extraintestinal surgery delaying hospitalisation beyond return of bowel function were excluded. Those presenting with intestinal motility disorder and gastropathy were also excluded.

Setting
The setting of the study was a hospital. The economic study was carried out at the General Surgery Service, Madigan Army Medical Center, Tacoma (WA) USA.

Dates to which data relate
The dates during which the effectiveness and resource data were collected were not reported. The price year was not reported.

Source of effectiveness data
The effectiveness evidence were derived from a single study.

Link between effectiveness and cost data
The costing was undertaken prospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations were performed in the planning phase to define the total number of patients required to detect a statistically significant difference between the study groups. These were based on a decrease in the median hospital stay of 1 day, using 5 (+/- 2) days as the mean. Thirty-five patients presenting at the authors' institution over a 2-year period were enrolled. There were 17 patients in the cisapride group, of which 13 were men, and 18 patients in the control
group, of which 12 were men. The mean age of the patients was 65 years in the cisapride group and 67 years in the control group.

**Study design**
This was a randomised, double-blinded, clinical trial carried out in a single centre. The patients were randomised using a sealed envelope assignment. The nursing and physician staff were blinded to the patient allocation. The patients were not followed after discharge.

**Analysis of effectiveness**
All patients included in the study were accounted for in the analysis. The primary health outcomes assessed in the analysis were:

- length of hospital stay;
- adjusted length of hospital stay, defined as the period of time at which the patient is tolerating a regular diet, having bowel movements, and would otherwise be discharged if not for a separate cause unrelated to bowel motility;
- post-operative days to first bowel movement and regular diet intake; and
- peri-operative complications.

The study groups were comparable in terms of their demographics and medical characteristics.

**Effectiveness results**
The mean length of hospital stay was 5.5 (+/- 1.4) days in the study group and 6.7 (+/- 2.1) days in the control group, (p=0.06).

The mean adjusted length of hospital stay was 5.1 (+/- 1.0) days in the study group and 6.3 (+/- 1.5) days in the control group, (p=0.006).

The mean post-operative days to first bowel movement were 3.7 (+/- 0.7) days in the study group and 4.8 (+/- 1.2) days in the control group, (p<0.05).

The mean post-operative days to regular diet intake were 4.1 (+/- 0.8) days in the study group and 4.9 (+/- 1.1) days in the control group, (p<0.05).

A median one-day difference was found in all of these outcome measures.

There were 4 complications in the study group and 3 complications in the control group.

**Clinical conclusions**
The analysis of the effectiveness showed that cisapride significantly improved bowel motility, compared with placebo.

**Measure of benefits used in the economic analysis**
The health outcomes were left disaggregated and no summary benefit measure was used. A cost-consequences analysis was therefore carried out.

**Direct costs**
No discounting was carried out due to the short timeframe of the study. The unit costs and the quantities of resources were only reported separately for hospital stay. The cost/quantity boundary adopted was not clearly stated, but appears
to have been that of the patients paying for the intervention. The costs included in the analysis were for hospital stay and the drug (cisapride). The costs were estimated from the patients’ bills. The source of the cost data was not stated. The period during which the quantities of resources were collected was not reported. The price year was not reported.

**Statistical analysis of costs**

Statistical analyses of the costs were not conducted.

**Indirect Costs**

The indirect costs were not included.

**Currency**

US dollars ($).

**Sensitivity analysis**

No sensitivity analyses were carried out.

**Estimated benefits used in the economic analysis**

See the 'Effectiveness Results' section.

**Cost results**

The cost of a 7-day course of cisapride was $130 and the cost per hospitalisation day was $600. Since hospital stay was one-day shorter in the study group than in the control group, the cisapride-based treatment was associated with cost-savings ranging from $400 to $500.

**Synthesis of costs and benefits**

Not relevant.

**Authors’ conclusions**

Cisapride proved to be safe and effective when used as adjunct treatment for patients who underwent colorectal surgery, and was associated with cost-savings in comparison with placebo.

**CRD COMMENTARY - Selection of comparators**

The rationale for the choice of the comparator was clear. Placebo was selected since the objective of the analysis was to assess the active value of cisapride. You should assess whether it represents a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**

The analysis of the effectiveness used a randomised, double-blind clinical trial. Although the sample size was small, appropriate power calculations were performed in the planning phase. In addition, the study groups were comparable at baseline. These factors enhanced the internal validity of the analysis.

**Validity of estimate of measure of benefit**

No summary benefit measure was used in the economic analysis. A cost-consequences analysis was therefore carried out.
Validity of estimate of costs
The cost estimates appear to have been quite specific to the study setting. No sensitivity analyses were carried out and the costs were treated deterministically. The period during which the resource data were collected was not reported. The price year was also not reported. These issues tend to limit the internal and external validity of the analysis.

Other issues
The authors made some comparisons of their findings with those from other studies. However, the issue of the generalisability of the study findings to other settings was not addressed and sensitivity analyses were not carried out. Therefore, the generalisability of the study was quite low.

Implications of the study
The authors suggest that cisapride should be used as adjunct treatment to post-operative care after colorectal surgery.

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