**METOCLOPRAMIDE FOR THE PREVENTION OF POST-OPERATIVE ILEUS**

*in pediatric orthopaedic patients*

Evidence-Based Summary

**ASK THE QUESTION**

**Question 1:** In pediatric post-operative orthopaedic patients, does the use of metoclopramide (Reglan) reduce the likelihood of developing post-operative ileus?

**Question 2:** In pediatric post-operative orthopaedic patients, what are the side effects of using metoclopramide (Reglan)?

**CRITICALLY ANALYZE THE EVIDENCE**

**Question 1:** In pediatric post-operative orthopaedic patients, does the use of metoclopramide (Reglan) reduce the likelihood of developing post-operative ileus?

*Grade Criteria: Low Quality Evidence*

There were no studies found evaluating the role of metoclopramide (Reglan) in reducing the likelihood of developing post-operative ileus in pediatric patients. A number of trials conducted among adult patients, however, suggest that metoclopramide does not alter the length of ileus after surgery. Three RCTs (Cheape 1991, Davidson 1979, and Tolleson 1991), and one observational study (Seta 2001) found no significant difference in time to resolution of post-op ileus between patients receiving metoclopramide and controls (resolution of post-op ileus defined by either first flatus or bowel movement or commencement of fluid/solid intake). One RCT conducted in 1986 found that time to first flatus was significantly shorter in the control group than in patients receiving metoclopramide (Jepsen 1986). In a trial comparing metoclopramide to ceruletide, the study was stopped early because analysis demonstrated that ceruletide was significantly better than metoclopramide in resolving post-op ileus (defined by time to first flatus) (Lykkegaard-Nielsen 1984).

One observational study found that a protocol that included a regimen of metoclopramide used in patients undergoing colectomy, significantly reduced both length of stay and hospital charges (Hawalsi 1996). However, it is questionable whether the findings can be attributed to the early resolution of post-op ileus. A RCT conducted in 1971 found that patients administered metoclopramide experienced bowel sounds, and passed flatus sooner than individuals treated with placebo. The study combined both of these observations to produce a score for intestinal peristalsis. The score was significantly higher in the metoclopramide group, but the tool has not been validated (Breivik 1971).

There have not been any recent studies addressing the question, and most of the studies appraised had small sample sizes. The studies above were all conducted in adults, and in different patient populations (e.g. cholecystectomy, colorectal, laparotomy surgical patients). In addition, post-op ileus is difficult to define, and the outcome evaluated in the studies differed (e.g., first bowel movement, flatus, commencement of oral intake, LOS). Opioid use is an important consideration when assessing the impact of a medication on length of post-op ileus, and not all of the studies took this into account. These are important limitations, but there does not seem to be any compelling evidence to suggest that metoclopramide impacts the length of post-op ileus, or should be given routinely to pediatric post-op patients.
randomized to either ceruletide or metoclopramide IM given every 2 hrs until passage of flatus or placebo. Study evaluated time to first flatus and net oral intake.

Lykkegaard et al (1979): RCT of 60 women with uncomplicated cholecystectomies; patients randomized to either metoclopramide 10 mg given IM twice daily for 2 days or to placebo. Intestinal peristalsis was evaluated by auscultation for bowel sounds and questioning patients about flatus.

Cheape (1991): RCT of 93 adult and pediatric patients (mean age 59.5) who underwent elective abdominal colorectal surgery; patients randomized to either metoclopramide IV every 8 hrs from surgery until solid food diet tolerated or placebo. Study evaluated length of time before laparotomy and commencement of oral fluid.

Davidson (1979): RCT of 115 adult patients undergoing laparotomy; patients randomized to either 10 mg IM metoclopramide or placebo on the day of surgery, and then every day until solid food diet tolerated or placebo. Study assessed times until first flatus and net oral intake.

Jepsen (1986): RCT of 60 adult patients undergoing operation for arteriosclerotic stenosis; patients randomized to either metoclopramide 2 mg IV after the operation and then 4 x daily for 5 days, or to placebo. Study evaluated time to first flatus and net oral intake.

Hawalsi (1996): Prospective observational study of 24 adult patients undergoing colectomy. 30 patients from 7 months prior to study were used as control. Protocol for patients in study period consisted of outpatient bowel prep, IV metoclopramide started before the operation and continued every 6 hours.

Hawalsi et al (2001): RCT of 93 adult and pediatric patients (mean age 59.5) who underwent elective abdominal colorectal surgery; patients randomized to either metoclopramide IV every 8 hrs from surgery until solid food diet tolerated or placebo. Study evaluated length of time before laparotomy and commencement of oral fluid.

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<td>Case Reports</td>
<td>Publication Bias Evident</td>
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### Design Limitations

- None
- Lack of blindness (Hawalsi 1996, Seta 2001)
- Lack of allocation concealment (Hawalsi 1996, Seta 2001)
- Large losses to F/U
- Incorrect analysis of ITT
- Stopped early for benefit (Lykkegaard-Nielsen 1984)
- Selective reporting of measured outcomes (e.g., no effect outcome)

### Summary of Consistency

- No inconsistencies
- Wide variation of treatment effect across studies
- Populations varied (e.g., sicker, older)
- Interventions varied (e.g., doses)
- Outcomes varied (e.g., diminishing effect over time)

### Indirectness of Comparison

- Head-to-head comparison in correct population
- Indirect comparisons (e.g., interventions to placebo but not each other)
- Different interventions (Lykkegaard-Nielsen 1984)
- Different outcomes measured (Cheape 1991, Hawalsi 1996)
- Comparisons not applicable to question/outcome

### Dichotomous outcomes

- Sample size lower than calculated
- Optimal information size
- Total # of events is < 300 based on simulations & dependent on baseline risk & effect sizes
- 95% CI includes negligible effect and appreciable benefit or harm

### Continuous outcomes

- 95% CI includes no effect and the upper or lower limit crosses the minimal important difference (MID), either for benefit or harm (Cheape 1991, Davidson 1979, Hawalsi 1996, Seta 2001)
- Upper or lower limit crosses an effect size of 0.5 in either direction (if MID is not known or differences in outcomes require the calculation of an effect size)

### Sample

Breivik (1971): RCT of 60 women with uncomplicated cholecystectomies; patients randomized to either metoclopramide 10 mg given IM twice daily for 2 days or to placebo. Intestinal peristalsis was evaluated by auscultation for bowel sounds and questioning patients about flatus.

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Lykkegaard-Nielsen (1984): RCT of 26 adult patients undergoing abdominal surgery; patients randomized to either ceruletide or metoclopramide IM given every 2 hrs until passage of flatus or...
There are a number of adverse effects associated with the use of metoclopramide (Reglan). In pediatric patients, these effects may include diarrhea, drowsiness, restlessness, gynecomastia, and galactorrhea. The FDA issued a black box warning regarding long-term or high-dose use of metoclopramide due to the risk of developing tardive dyskinesia, particularly in children. The primary side effect of the drug is extrapyramidal reactions, which can include parkinsonian symptoms, dystonic reactions, oculogyric crises, and acute dystonic reactions. The manufacturer reports that 1 in 500 patients treated with metoclopramide may experience an extrapyramidal reaction, but the incidence of these reactions appears to be as high as 25% in children.

There were no studies found that assessed the side effects of metoclopramide in pediatric post-op orthopaedic patients. One systematic review of infants treated with metoclopramide for gastroesophageal reflux disease noted that adverse effects of metoclopramide were reported in 4 out of the 12 studies included in the review. The events reported included dystonic reactions, oculargic crisis, irritability, drowsiness, emesis, and apnea. In another systematic review of adult patients treated with metoclopramide for the prevention of postoperative nausea and vomiting, the review found that minor drug-related adverse effects (sedation, dizziness, drowsiness) were not significantly associated with metoclopramide, and found that only 1 adult of the 3260 subjects in the review experienced extrapyramidal symptoms.

Table 1: \[\text{Reference:}\]

Question 2: In pediatric post-operative orthopaedic patients, what are the side effects of using metoclopramide (Reglan)?

There were a number of adverse effects associated with the use of metoclopramide in children including diarrhea, drowsiness, restlessness, gynecomastia, and galactorrhea. The primary side effect of the drug is extrapyramidal reactions. The manufacturer reports that 1 in 500 patients experience an extrapyramidal reaction, but the incidence of these reactions appears to be as high as 25% in children.
Reference: