Systemic metoclopramide to prevent postoperative nausea and vomiting: a meta-analysis without Fujii’s studies
De Oliveira GS, Castro-Alves LJ, Chang R, Yaghmour E, McCarthy RJ

CRD summary
The authors concluded that one dose of metoclopramide significantly reduced postoperative nausea and vomiting for patients having surgery under general anaesthesia. Publication bias was possible, the included trials were of variable quality, and the generalisability of the findings was uncertain, making the reliability of the authors’ conclusions unclear.

Authors’ objectives
To evaluate the effectiveness of systemic metoclopramide, as a single agent or in combination with other drugs, for the prevention of postoperative nausea and vomiting.

Searching
PubMed, EMBASE, Cochrane Database of Systematic Reviews and the Internet, using Google Scholar, were searched for studies published in any language, up to March 2012. Search terms were reported. The bibliographies of identified studies were handsearched.

Study selection
Published randomised controlled trials (RCTs) comparing one perioperative 10mg intravenous dose of metoclopramide, with placebo or no treatment, for patients aged 18 years or older, were eligible for inclusion. Trials had to report the incidence of early (one- to six-hour) or 24-hour postoperative nausea and vomiting. They were excluded if they investigated emergency medicine, non-surgical patients, or multiple perioperative metoclopramide doses, or if metoclopramide was used as a treatment rather than for prevention. Trials, in which another antiemetic was used, were included if a direct comparison of metoclopramide and placebo could be made. Trials published by Yoshitaka Fujii were excluded, as their reliability had been questioned.

Most of the included trials investigated patients undergoing minor or major gynaecological surgery. Some were of patients undergoing laparoscopic cholecystectomy, abdominal surgery, cataract extraction, or other surgical procedures. The anaesthetics were thiopental, isoflurane, nitrous oxide, fentanyl, propofol, sevoflurane, etomidate, halothane, desflurane, sufentanil, atracurium, enflurane or methohexital. The primary outcomes were 24-hour nausea and vomiting, combined and separate, and early nausea and vomiting, combined and separate. Secondary outcomes were the need for rescue antiemetic therapy and adverse events.

Two authors independently selected the trials for the review, with disagreements resolved by discussion. Where agreement could not be reached another investigator was consulted.

Assessment of study quality
The quality of the included trials was assessed using a modified Jadad scale. This covered randomisation, validity of randomisation, double-blinding, allocation concealment, and completeness of follow-up, with a maximum score of five.

Two authors independently assessed the quality of the included trials, and disagreements were resolved by discussion. Where agreement could not be reached another reviewer was consulted.

Data extraction
The number of events in each group was extracted and used to calculate odds ratios, with 95% confidence intervals. For adverse events, their presence or absence was extracted and converted to incidence.

Two reviewers independently extracted data into a predefined form. Discrepancies were resolved through discussion, or another reviewer was consulted.

Methods of synthesis
Pooled odds ratios, with 95% confidence intervals, were calculated, using a random-effects model. For adverse events, the Peto odds ratio was used to adjust for zero counts in some cells. Statistical heterogeneity was assessed using $I^2$. Publication bias was assessed using Egger's test. Where bias was found, Rosenthal's file-drawer analysis was performed.

A subgroup analysis was performed to investigate the effects of single versus combination therapy. The number needed to treat was calculated, and a post-hoc analysis of the trials by Yoshitaka Fujii was carried out.

**Results of the review**

Thirty RCTs (3,327 patients) were included. Three trials scored 5 on the Jadad scale, thirteen scored 4, nine scored 3 and five scored 2.

**Nausea and vomiting:** Metoclopramide significantly reduced the incidence of 24-hour nausea and vomiting (OR 0.58, 95% CI 0.43 to 0.78; NNT 7.8; 13 RCTs; 836 patients), and early nausea and vomiting (OR 0.52, 95% CI 0.36 to 0.75; NNT 7.6; 11 RCTs; 869 patients), compared with placebo. Statistical heterogeneity was low ($I^2=0$ for 24-hour, and 24% for early incidence). There was no evidence of publication bias. One trial assessed metoclopramide combination therapy, and did not find a significant benefit for either early or 24-hour nausea and vomiting.

**Nausea:** Metoclopramide significantly reduced the incidence of 24-hour nausea (OR 0.51, 95% CI 0.38 to 0.68; NNT 7.1; 10 RCTs; 1,810 patients), and early nausea (OR 0.49, 95% CI 0.35 to 0.68; NNT 5.9; 13 RCTs; 1,125 patients), compared with placebo. Statistical heterogeneity was low ($I^2=8\%$ for 24-hour, and 7% for early nausea). There was evidence of publication bias (p=0.03 for 24-hour, and p=0.001 for early nausea).

**Vomiting:** Metoclopramide significantly reduced the incidence of 24-hour vomiting (OR 0.51, 95% CI 0.40 to 0.66; NNT 8.3; 10 RCTs; 2,810 patients), and early vomiting (OR 0.44, 95% CI 0.29 to 0.65; NNT 10.5; 12 RCTs; 1,088 patients), compared with placebo. Statistical heterogeneity was low ($I^2=0$ for 24-hour, and 5% for early vomiting). There was evidence of publication bias for early vomiting (p=0.03), but not for 24-hour vomiting (p=0.07).

**Other outcomes:** Metoclopramide significantly reduced the need for rescue antiemetics, compared with placebo (OR 0.41, 95% CI 0.19 to 0.92; NNT 6.0; three RCTs). Metoclopramide was not associated with an increased risk of extrapyramidal symptoms, dizziness, headache or sedation, compared with placebo. There was no evidence of significant statistical heterogeneity for these outcomes.

**Authors' conclusions**

One dose of metoclopramide significantly reduced postoperative nausea and vomiting for patients having surgery under general anaesthesia.

**CRD commentary**

The review addressed a clear question with well-defined inclusion criteria. Several relevant databases were searched. No language restrictions were applied, minimising the risk of language bias. There was evidence of publication bias for some outcomes. Appropriate steps were taken throughout the review to minimise the risks of reviewer error and bias. The methodological quality of the included trials was assessed using a suitable tool, and the quality was variable. Subgroup analyses by quality were not carried out, so the reliability of the findings is unclear.

The range of surgical interventions was relatively limited. The authors did not report the proportion of male and female participants, but most trials were of gynaecological surgery, so there were more female than male participants, making it unclear if the findings can be generalised to men or to other surgical procedures. Suitable methods were used to combine the data. Statistical heterogeneity was assessed and was found to be low for all outcomes.

Given the presence of publication bias, the variable quality of the included trials, and uncertainty about the generalisability of the findings, the reliability of the authors' conclusions is unclear.

**Implications of the review for practice and research**

**Practice:** The authors stated that metoclopramide was a reasonable alternative to other antiemetic treatments.

**Research:** The authors stated that further research was needed into the impact of metoclopramide on the time to hospital discharge.
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