Antiemetic prophylaxis in cardiac surgery: comparison of metoclopramide and ondansetron

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We have compared the effectiveness of ondansetron (115 patients) and metoclopramide (101 patients) for prevention of postoperative nausea and vomiting in patients undergoing cardiac surgery involving cardiopulmonary bypass. In a prospective, randomized, controlled, double-blind study, patients received oral ondansetron 16 mg or oral metoclopramide 10 mg, 1–2 h before surgery. Anaesthesia was not standardized. Assessments of the severity of nausea and occurrence of vomiting were made at intervals after extubation and until discharge from the intensive care, or for a total of 24 h. Compared with the metoclopramide group, the ondansetron group had a higher incidence of nausea (49.6% vs 33.7%; P<0.05) and vomiting (42.6% vs 24.8%; P<0.01). There was no difference between groups in the number of patients who accepted postoperative antiemetics (ondansetron 43.4% vs metoclopramide 32.6%) and there was no difference in the incidence of symptoms of moderate or severe nausea.

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In recent years, postoperative nausea and vomiting have been recognized as a major cause of postoperative morbidity. Many studies have demonstrated the superiority of ondansetron over metoclopramide in the prophylaxis of postoperative nausea and vomiting in some patient groups, although not all.1 Information on the incidence of postoperative nausea and vomiting in patients undergoing cardiac surgery is limited, but Grebenik and Allman2 suggest it may be as high as 45%.

A pilot survey in our unit indicated an incidence of postoperative nausea and vomiting of almost 50% of patients undergoing cardiac surgery, with more than 40% of patients requiring postoperative antiemetic treatment. These patients had all received metoclopramide or prochlorperazine with their premedication.

In this study, we have compared the effectiveness of ondansetron and metoclopramide in the prevention of postoperative nausea and vomiting in patients undergoing cardiac surgery involving a period of cardiopulmonary bypass.

Methods and results

This was a prospective, randomized, controlled, double-blind study performed within the cardiac intensive care unit (CICU) of the Northern General Hospital, Sheffield, over a 12-month period. The study received local Ethics Committee approval and written, informed consent was obtained from each patient.

We studied male and female patients, ASA II or III, aged 18–80 yr, who were undergoing first time elective cardiac surgery involving cardiopulmonary bypass. Patients who had experienced nausea or vomiting or had received antiemetic medication in the 24 h before surgery and those who weighed more than 100 kg were excluded. A history of previous postoperative nausea and vomiting was noted. The method of scoring of nausea and vomiting was explained to all patients by one of the investigators (D. K. W.).

A total of 115 patients received ondansetron 16 mg orally,3 1–2 h before operation and 4 mg i.v. after operation, if indicated, and 101 patients received metoclopramide 10 mg orally, 1–2 h before operation and 10 mg i.v. after operation, if indicated. The randomization process and preparation of all study drugs were controlled by the hospital pharmacy department clinical trials unit. All medical and nursing staff were blinded.

Patients received lorazepam 1–2 mg orally at 22:00 on
the night before surgery. Temazepam 10–20 mg orally at 08:00 on the day of surgery was allowed as an anxiolytic for patients who were scheduled for surgery after 11:00. Morphine 10–15 mg i.m. and the study drug were given 1–2 h before operation, then oxygen 4 litre min\(^{-1}\) was given by face mask until anaesthesia. All patients received fentanyl 10–20 μg kg\(^{-1}\) for analgesia and pancuronium 0.1–0.15 mg kg\(^{-1}\) for neuromuscular block. Induction and maintenance of hypnosis varied according to the individual anaesthetist and the drugs used are summarized in Table 1. On completion of surgery, patients were transferred to the cardiac intensive care unit. Weaning to spontaneous ventilation and tracheal extubation were performed in accordance with existing unit protocols. Sedation with i.v. midazolam or propofol infusion was allowed before extubation. Patients in whom the trachea was not extubated within 12 h of surgery were withdrawn. Analgesia was provided by morphine 2 mg i.v. as required.

The timing of assessments was started at extubation and performed hourly for 4 h and then every 4 h until the patient was discharged from the CICU, or for a maximum of 24 h. The nursing staff who were trained in the assessments recorded the scores. Assessment of the severity of nausea was scored as none (0), mild (1), moderate (2) or severe (3). The patient’s assessment of their worst sensation of nausea in the preceding time period was recorded. Episodes of vomiting or retching were recorded as vomiting. Patients were offered antiemetic treatment with the study drug if they suffered any nausea or vomiting. The medical and nursing staff were blind to the study drug used and therefore cyclazine 50 mg i.v. was used as rescue treatment for further episodes of postoperative nausea and vomiting.

Statistical analysis of data was performed using SPSS for Windows version 6.0, on a Gateway 2000 PC. Student’s t test was used to compare age, height and weight, and duration of surgery, cardiopulmonary bypass and aortic cross clamp times between groups. The chi-square test was used to compare the type of operation, anaesthesia and the incidence of nausea and vomiting between groups. Forward stepwise logistic regression analysis was used to test the association of the study drug group, anaesthetic induction drugs and sex of the patient with the incidence of both nausea and vomiting.

Of 294 patients recruited, 78 were withdrawn because of study violations. The reasons for withdrawal were: tracheal intubation beyond 12 h (n=40); required antiemetic before tracheal extubation (n=16); and breached other inclusion criteria (e.g. administrative error, cardiopulmonary bypass not used, etc.) (n=22).

The groups were comparable in patient characteristics, operations performed and maintenance of anaesthesia (Table 1). The induction agents used were different between groups (P=0.035) and more patients in the ondansetron group received etomidate. In the cardiac intensive care unit, 8% of patients received propofol and 5% received midazolam for sedation; mean morphine requirement was 32 mg (SD 16.5; range 2.5–125.5 mg). There was no difference between groups in sedation or morphine requirements.

The overall incidence of nausea (i.e. nausea scoring >0 at any time) was significantly higher in the ondansetron group than in the metoclopramide group (49.6% vs 33.7%; P<0.05) (Table 2). The incidence of vomiting was significantly higher in the ondansetron group than that in the metoclopramide group (42.6% vs 24.8%; P<0.01). Only 3.7% of all patients complained of severe nausea. There was no difference between groups in the incidence of moderate or severe symptoms. Despite the different incidences of both nausea and vomiting between groups, the number of patients who accepted postoperative antiemetics (ondansetron group 43.4% vs metoclopramide group 32.6%) was not significantly different. The use of rescue medication, interval between premedication and postoperative antiemetic and duration of postoperative tracheal intubation were similar between groups.
Using logistic regression, the study drug group had an impact on the likelihood of vomiting ($P=0.005$) and patients in the ondansetron group were more likely to experience postoperative nausea and vomiting. The sex of the patient did not affect the likelihood of nausea ($P=0.26$) but affected the likelihood of vomiting ($P=0.022$). The induction agent used did not affect the likelihood of nausea ($P=0.591$) or vomiting ($P=0.155$).

**Comment**

Interest in the subject of postoperative nausea and vomiting has increased in recent years, but there are few data in relation to cardiac anaesthesia.

There were problems with the methodology of this study. Twenty six percent of patients were withdrawn for study violations and, in view of this large number, we performed the chi-square test to assess if they had an impact. Of the 40 patients withdrawn for tracheal intubation beyond 12 h, a greater number (27) were in the metoclopramide group. It seems unlikely that the use of metoclopramide is causally related to prolonged postoperative ventilation. Another 16 patients were withdrawn because they required antiemetic medication before tracheal extubation, but they were distributed equally between groups and had no effect on the results.

The groups were well matched for patient and surgical characteristics. A history of postoperative nausea and vomiting was recorded but motion sickness (a weak risk factor for postoperative nausea and vomiting) was not. A history of postoperative nausea and vomiting was not used in the analysis as it was reported in only 10% of cases and was dependent on whether there was previous surgery and what type. Anaesthesia was not standardized. It was difficult to gain consensus between anaesthetists and we considered that the impact of individual anaesthetic drugs in the context of major surgery involving cardiopulmonary bypass and postoperative ventilation was likely to be small. We were surprised that there was a difference between groups in the use of anaesthetic induction drugs. In particular, etomidate was used more frequently in the ondansetron group, but the dose of etomidate was small, typically 4–10 mg, and analysis suggests that it had no impact. Maintenance was designated ‘propofol’ if an infusion was used at any time during maintenance of anaesthesia or ‘volatile agent’ if isoflurane or enflurane, with or without midazolam but without propofol, was used. This distinction was made in case a protective effect of propofol on postoperative nausea and vomiting was detected. On analysis, the anaesthetic maintenance drugs had no impact on postoperative nausea and vomiting. A standardized anaesthetic would have been the ideal, but difficult to implement in the clinical setting.

In our study population of 216 patients, we demonstrated an overall incidence of postoperative nausea of 42% and vomiting, 34%. The incidences of nausea and vomiting were less in the group who received oral metoclopramide before operation.

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**References**