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ANTIEMETIC EFFICACY OF PROPHYLACTIC ONDANSETRON IN LAPAROSCOPIC SURGERY: RANDOMIZED, DOUBLE-BLIND COMPARISON WITH METOCLOPRAMIDE

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SUMMARY

In a randomized, double-blind study, we have compared the prophylactic antiemetic efficacy of ondansetron with that of metoclopramide in 123 patients undergoing general anaesthesia for day-case gynaecological laparoscopic surgery. The patients received either i.v. ondansetron 4 mg or metoclopramide 10 mg immediately before a standard anaesthetic. The number of patients with no nausea or vomiting in the ondansteron group was 50 (82%) compared with 29 (47%) in the metoclopramide group ($P < 0.001$). In those patients with a previous history of postoperative nausea and vomiting, nausea was less severe in those receiving ondansetron compared with those receiving metoclopramide ($P < 0.05$). We conclude that preoperative prophylactic administration of i.v. ondansetron was superior to metoclopramide in preventing nausea and vomiting after general anaesthesia for day-case gynaecological laparoscopic surgery. (Br. J. Anaesth. 1993; **71**: 845–848)

KEY WORDS

Pharmacology: metoclopramide, ondansetron. Vomiting: nausea. Surgery: gynaecological.

The incidence of nausea and vomiting after gynaecological laparoscopic surgery is particularly great, with previous studies reporting rates of around 50% [1–7]. The antiemetics commonly used at present (metoclopramide, prochlorperazine, droperidol and hyoscine) have limited efficacy on postoperative nausea and vomiting (PONV) after laparoscopy [1, 6, 7] and are associated with side effects such as sedation and extrapyramidal signs which may be important in day-case surgery [8–13].

Less commonly used antiemetic drugs (perphenazine, cyclizine, atropine, ginger root, acupuncture) and avoidance of nitrous oxide have not been shown to have consistent antiemetic efficacy [3, 7, 14, 15].

Ondansetron is a relatively new antiemetic agent that appears to show promise in this surgical procedure in studies comparing it with placebo [16–18]. In this study, we have compared the prophylactic antiemetic efficacy of ondansetron with metoclopramide in day-case gynaecological laparoscopic surgery.

PATIENTS AND METHODS

We studied patients undergoing elective day-case gynaecological laparoscopic surgery, with Local District Ethics Committee approval and informed patient consent. Patients who were pregnant, breast feeding, taking any medication other than the oral contraceptive pill or currently being treated for nausea or vomiting were excluded. The study was conducted in a double-blind manner with coded ampoules and restricted and stratified randomization was used, with sealed envelopes, to ensure treatment groups of the same size and an equal number of patients with previous PONV in each group.

Immediately before anaesthesia, patients were given either i.v. ondansetron 4 mg or metoclopramide 10 mg. Anaesthesia was induced with thiopentone 3.5–5 mg kg^{-1} and the trachea intubated after administration of suxamethonium 100 mg. Anaesthesia was maintained with 66% nitrous oxide and 1% isoflurane in oxygen, fentanyl 1.5 μg kg^{-1}, atropine 0.6 mg and additional suxamethonium up to 80 mg. Each anaesthetic was administered by one of three anaesthetists (two consultants and a registrar) and the surgery performed by one of two consultant gynaecologists.

Nausea and vomiting were assessed in all patients by the same observer immediately before operation and upon awakening, at 2 h and 4–6 h after operation. In addition, nausea and vomiting were assessed after hospital discharge up to 24 h after surgery, using a patient questionnaire.

Nausea was assessed by asking patients if they felt nauseated or sick, and was classified as mild or severe.

Both vomiting and retching were considered as emetic events. The nursing staff noted such events in hospital and after discharge the patients recorded these events on the questionnaire.

At each patient assessment, the degree of sedation was classified as asleep, drowsy or awake. Patients were questioned specifically about the presence of headache and asked to volunteer any other complaints. They were observed on these occasions for any evidence of extrapyramidal signs.

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After operation, antiemesis was provided by i.m. prochlorperazine 12.5 mg and analgesia by i.m. morphine 10 mg at the discretion of the nursing staff.

Statistical analysis

Patient data were analysed by *t* test, Mann–Whitney *U* test and chi-square test; other results were analysed by chi-square test, Fisher's exact test and Kruskal–Wallis one-way analysis of variance. Significance was taken at $P < 0.05$.

RESULTS

Sixty-one patients received ondansetron and 62 received metoclopramide. One patient was excluded from the study after randomization because additional atropine was administered during operation to correct a bradycardia.

There were no significant differences between the groups in age, body weight, previous history of PONV, history of motion sickness, grade of anaesthetist, duration of anaesthesia or administration of postoperative opioid drugs. More patients in the metoclopramide group were in the luteal phase of the menstrual cycle and more patients in the ondansetron group were menstruating, but neither of these differences was significant (table I).

One hundred and six patients (86%) completed the questionnaire: 50 in the ondansetron group and 56 in the metoclopramide group. Of the patients who failed to complete the questionnaire, the proportion in each group with no nausea and vomiting in the first 6 h was similar to that found in those who did complete the questionnaire. None of the patients with a previous history of PONV failed to complete the questionnaire (table II).

Nausea and vomiting

The administration of postoperative antiemesis was considered as treatment failure and these patients were deemed to have experienced emesis.

The number of patients with no postoperative nausea and vomiting in the first 6 h after operation was 53 (87%) in the ondansetron group and 37 (60%) in the metoclopramide group ($P < 0.001$) (table III). Combining the data collected in hospital with those revealed by the questionnaire (tables II and III) revealed the number of patients with no PONV in the first 24 h after operation to be 50 (82%) in the ondansetron group and 29 (47%) in the metoclopramide group ($P < 0.001$). Of those who were nauseated during the first 6 h after operation, the worst degree of nausea was less in the ondansetron group, although this did not reach statistical significance ($P < 0.1$) (fig. 1). The incidence of PONV was smaller in the ondansetron group at all times; this difference was significant except for data at 2 h after operation (fig. 2).

In those patients with previous PONV, the severity of nausea was less in those given ondansetron than in those given metoclopramide ($P < 0.05$) (fig. 3).

Side effects

There was no significant difference between the groups in the time to awakening (table I) or sedation at 2 h and 4–6 h.

TABLE I. *Patient characteristics and anaesthetic data (median (range), mean (SD) or No. patients)*

	Ondansetron ($n = 61$)	Metoclopramide ($n = 62$)
Age (yr)	35 (16–44)	33 (23–57)
Weight (kg)	68.0 (12.1)	67.3 (9.3)
Previous PONV	14	14
Motion sickness	9	10
Junior anaesthetist	28	25
Menstruating	16	8
Luteal phase	10	18
Anaesthetic duration (min)	14.0 (3.8)	13.6 (3.4)
Postop. morphine	10	8
Recovery time (min)	8.2 (1.8)	8.6 (2.0)

TABLE II. *Results from the questionnaire on emesis (nausea and vomiting) after hospital discharge between 6 and 24 h after operation*

	Ondansetron ($n = 61$)	Metoclopramide ($n = 62$)
Number of replies	50	56
Emesis after discharge	6	22
Emesis after discharge; no emesis in hospital	3	8

TABLE III. *Comparison of the incidence of emesis (nausea and vomiting) in both treatment groups and in the subgroups with a previous history of PONV, in the first 6 h after operation. **P < 0.001 compared with metoclopramide*

	Emesis	No emesis
Ondansetron group ($n = 61$)	8	53**
Metoclopramide group ($n = 62$)	25	37
Ondansetron group with previous PONV ($n = 14$)	5	9
Metoclopramide group with previous PONV ($n = 14$)	10	4

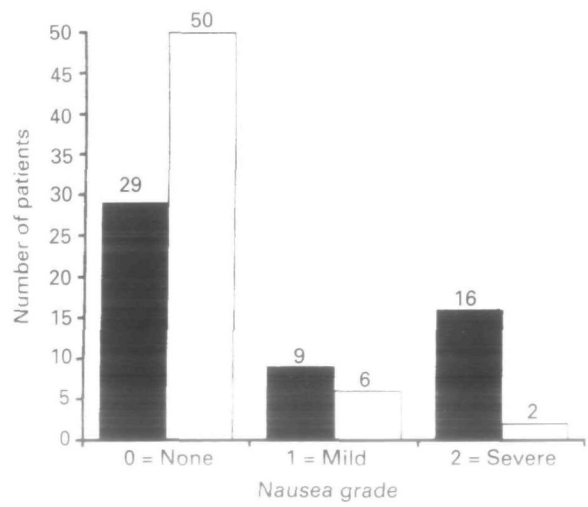

FIG. 1. Number of patients given metoclopramide (■) or ondansetron (□) who experienced nausea in the 6 h after operation.

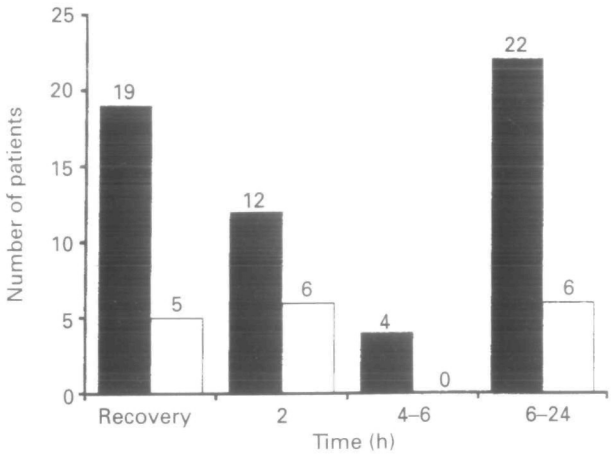

FIG. 2. Number of patients given metoclopramide (■) or ondansetron (□) who experienced emetic events within the defined time bands. Significance of differences between groups: recovery, $P < 0.01$; 2 h, $P > 0.1$; 4–6 h, $P < 0.05$; 6–24 h, $P < 0.001$.

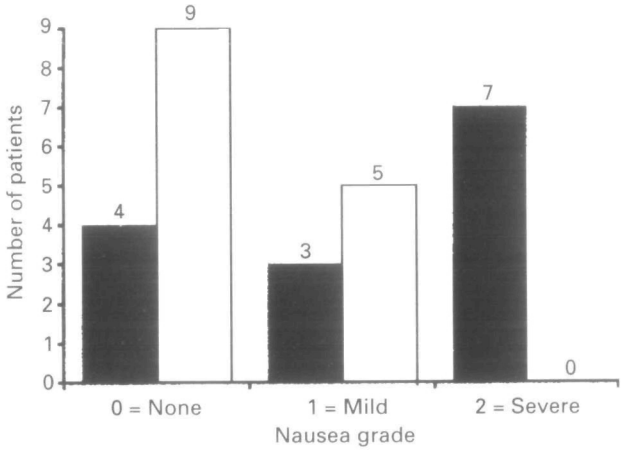

FIG. 3. Number of patients with previous PONV given metoclopramide (■) or ondansetron (□) who experienced nausea.

In the ondansetron group, headache occurred in two patients, urticaria at the injection site in one and a short-lived flush phenomenon in another. No other adverse effects were observed in this group. In the metoclopramide group, four patients reported headache, two complained of dizziness and two were noted to be restless.

DISCUSSION

The incidence of nausea and vomiting in the group that received metoclopramide (53%) was similar to that reported by others. In studies of patients having laparoscopic surgery alone or major gynaecological surgery that included laparoscopy, the incidence of nausea and vomiting after receiving metoclopramide is 30–60% [1, 6, 7].

There was less nausea and vomiting in the group receiving ondansetron. This difference was significant after awakening from anaesthesia and between 4 and 24 h after operation, but did not reach statistical significance at 2 h after operation.

In patients with previous PONV, there was a significant reduction in the degree of nausea in the group given ondansetron; however, the power of the study was insufficient to demonstrate any significant difference in the incidence of nausea and vomiting.

There was no significant difference between the two groups in time to awakening and sedation and there were no serious side effects recorded in each group.

The anaesthetic technique used in this study may differ from others. The anaesthetists involved in this study use thiopentone rather than propofol because patients remain in hospital for 6 h after laparoscopic surgery; there have been no problems with delayed hospital discharge. Various studies have demonstrated a smaller incidence of emesis associated with a propofol infusion technique compared with thiopentone and inhalation agents [19].

Intermittent suxamethonium was used to allow controlled ventilation because the median time of operation was short (14 min in this study). Although this technique is uncommon in day-case surgery, it may result in less emesis than is associated with the use of non-depolarizing neuromuscular blocking drugs, by avoiding the requirement for the antagonism of neuromuscular block with neostigmine [20].

Postoperative pain is associated with nausea and vomiting, but the relief of pain by appropriate doses of opioids results in less nausea [21]. We did not use non-steroidal anti-inflammatory agents in addition to opioids as the incidence and severity of postoperative pain appeared acceptable with an intraoperative opioid alone.

Nausea and vomiting are common unpleasant experiences associated with surgery which, on occasions, may lead to delayed discharge and even unexpected hospital admission for day-cases. The incidence of nausea and vomiting is particularly great with laparoscopic surgery [1–7]. The antiemetics used commonly at present (droperidol, prochlorperazine and metoclopramide) have limited efficacy and are associated with a variety of side effects. Droperidol appears to be the most effective, but is associated with a relatively large incidence of extrapyramidal symptoms [8, 9]. There is only limited information on the efficacy of prochlorperazine in day-case surgery and there are data to suggest that there may be a greater incidence of extrapyramidal effects with prochlorperazine than with metoclopramide [22]. Although i.v. metoclopramide appears to have little effect in preventing PONV after gynaecological surgery, we elected to compare it with i.v. ondansetron because the former is administered commonly by this route in day-case anaesthetic practice.

We have demonstrated that i.v. ondansteron was superior to i.v. metoclopramide as a prophylactic antiemetic in gynaecological laparoscopy. Those patients with previous PONV are important to consider because of their greater susceptibility to emesis [23]. They are both clinically and economically an important group to target, as the widespread prophylactic use of an expensive antiemetic may be difficult to justify. Although this study showed a reduction in the degree of nausea suffered by patients with previous PONV given

ondansetron, it was of insufficient power to determine if ondansetron significantly attenuated nausea and vomiting in this subgroup of patients.

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