Granisetron reduces the incidence of nausea and vomiting after middle ear surgery

Y. Fujii, H. Toyooka and H. Tanaka

Summary

We studied the efficacy of granisetron, a selective 5-hydroxytryptamine type-3 receptor antagonist, in preventing postoperative nausea and vomiting (PONV) after middle ear surgery. In a randomized, double-blind, placebo-controlled study, 60 ASA I patients received placebo (saline) or granisetron 40 μg kg⁻¹ i.v. immediately before induction of anaesthesia (n=30 in each group). A standard general anaesthetic technique was used. During the first 24 h after anaesthesia, the incidence of PONV in patients who had received granisetron was lower than in those who had received placebo (17% vs 63%; P<0.05). There were no clinically important adverse effects in either group. We conclude that granisetron, given before anaesthesia, reduced the incidence of PONV after middle ear surgery. (Br. J. Anaesth. 1997; 79: 539–540).

Key words

Methods and results

After obtaining approval from our institutional Ethics Committee and informed consent, we studied 60 ASA I patients (43 females), aged 20–65 yr, undergoing middle ear surgery (tymanoplasty or mastoidectomy). Patients who had gastrointestinal diseases, who were pregnant or menstruating, or who had taken antiemetics within 24 h before surgery were excluded.

Premedication was not used. Patients were given, in a randomized, double-blind manner, a single dose of placebo (saline) or granisetron 40 μg kg⁻¹ i.v., immediately before induction of anaesthesia. Anaesthesia was induced with thiopentone 5 mg kg⁻¹ i.v., and vecuronium 0.2 mg kg⁻¹ i.v. was used to facilitate tracheal intubation. After tracheal intubation, anaesthesia was maintained with 1.0–3.0% isoflurane (inspired concentration) and 66% nitrous oxide (which was replaced by air before closing of the tympanic membrane) in oxygen. Opioids were not given before or during maintenance of anaesthesia. Ventilation was controlled mechanically and was adjusted to maintain P_{E_CO2} at 4.6–5.2 kPa throughout surgery. Neuromuscular block was produced with vecuronium and antagonized by a combination of atropine 0.02 mg kg⁻¹ i.v. and neostigmine 0.04 mg kg⁻¹ i.v. at the end of surgery. The trachea was extubated when the patient was awake. If two or more episodes of vomiting occurred during the first 24 h after anaesthesia, standard antiemetic therapy (e.g. metoclopramide) was given. After operation, patients received indomethacin 50 mg orally when they complained of pain.

After operation, each episode of PONV (nausea, retching and vomiting) during the first 24 h after anaesthesia was recorded by nursing staff who had no knowledge of which treatment patients had received.

Honkavaara, Saarinyaara and Klemola and Reinhart, Klein and Schroff have demonstrated recently that the incidence of postoperative nausea and vomiting (PONV) after middle ear surgery is relatively high (62–80%) when no prophylactic antiemetic is given. Pharmacological methods to prevent PONV include antihistamines (e.g. hydroxyzine), butyrophenones (e.g. droperidol) and dopamine receptor antagonists (e.g. metoclopramide), but these drugs have undesirable side effects, such as sedation, hypotension, dry mouth, dysphoria, restlessness and extrapyramidal symptoms. Ondansetron, a selective antagonist of 5-hydroxytryptamine type-3 (5-HT_3) receptors, is effective in preventing PONV with little adverse effects. Another 5-HT_3 receptor antagonist, granisetron, is more potent and has longer acting activity against cisplatin-induced emesis than ondansetron. We conducted a prospective, randomized, double-blind, placebo-controlled study to examine the efficacy of granisetron in preventing PONV in patients undergoing middle ear surgery.
The treatment groups were comparable in characteristics and types of operation. During the first 24 h after anaesthesia, the incidence of PONV in patients who had received granisetron was lower than in those who had received placebo (17% vs 63%; \( P=0.001 \)) (table 1). Six patients who had received placebo required another rescue antiemetic (e.g. metoclopramide) for treatment of two more episodes of vomiting, compared with none who had received granisetron (\( P<0.05 \)). There were no adverse effects from the test drug in either group.

**Comment**

The aetiology of PONV after middle ear surgery (tympanoplasty or mastoidectomy) is not known precisely, but is probably associated with several factors. One of these factors is increased middle ear pressure caused by nitrous oxide.\(^6\) Others, including age, obesity, history of motion sickness, previous postoperative emesis, surgical procedure, anaesthetic technique and postoperative pain, are also considered to increase the incidence of PONV.\(^1\) In this study, however, no pressure was generated in the middle ear from diffusion of nitrous oxide which was replaced by air before closing of the tympanic membrane. The treatment groups were similar in characteristics, types of operation, anaesthetics administered and postoperative analgesics used. Therefore, the difference in the incidence of PONV between the groups can be attributed to differences in the drugs tested.

We found a relatively high incidence of PONV (63%) during the first 24 h after anaesthesia in patients who had received placebo. This incidence is in accordance with previous studies by Honkavaara, Saarinvaara and Klemola\(^1\) and Reinhart, Klein and Schroff \(^2\) who demonstrated an incidence of PONV of 62–80% in patients undergoing general anaesthesia for middle ear surgery.

It has been reported recently that granisetron is effective in the prevention of PONV after gynaecological surgery, and its safety profile is good with the recommended dose of 40 \( \mu \text{g} \) kg\(^{-1}\).\(^7\) The results of this study showed that the incidence of PONV after middle ear surgery in patients who had received granisetron was less than in those who had received placebo (\( P<0.05 \)). This suggests that granisetron is effective in preventing PONV after middle ear and gynaecological surgery. The exact mechanism of granisetron in the prevention of PONV is not known, but it has been suggested that it may act on sites containing 5-HT\(_3\) receptors with demonstrated antiemetic effects.\(^8\)

This study also showed that six patients who had received placebo required another rescue antiemetic (e.g. metoclopramide) for treatment of two or more episodes of vomiting, compared with none who had received granisetron (\( P<0.05 \)). Thus granisetron 40 \( \mu \text{g} \) kg\(^{-1}\) may reduce the severity of PONV after middle ear surgery.

**References**