Effect of ondansetron on nausea and vomiting after middle ear surgery during general anaesthesia

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Summary

The efficacy of ondansetron 4 mg and 8 mg was compared with placebo in the reduction of postoperative nausea, retching and vomiting (PONV) after middle ear surgery during general anaesthesia, in 75 patients, in a double-blind and randomized study. Both doses of ondansetron were predictors for a decrease in PONV and the number of doses of rescue antiemetic needed per patient (droperidol: from 0.72 in the placebo group to 0.32 in both the 4-mg and 8-mg groups). No reduction in PONV was observed in patients with a history of motion sickness, whereas in patients without a history of motion sickness, ondansetron reduced both the proportion of patients suffering from PONV from 53 % to 20 % \((P < 0.05)\) and of those needing droperidol from 53 % to 17 % \((P < 0.05)\). (Br. J. Anaesth. 1996; 76: 316–318)

Key words


In two recent studies, 62 % and 80 % of patients in placebo groups developed postoperative nausea and vomiting (PONV) after middle ear operations [1, 2]. Ondansetron has been found to be effective in preventing and treating PONV after general anaesthesia, and its safety profile is good with the recommended doses of 4 and 8 mg. Ondansetron is said to have a significant antiemetic effect on patients suffering from opioid-induced emesis. Middle ear surgery may disturb the vestibular system, and opioids increase vestibular sensitivity. On the other hand, vestibular stimulation increases the incidence of nausea and vomiting caused by opioids. The site of inhibitory action of ondansetron on PONV after middle ear surgery might be the nucleus tractus solitarius which has a high concentration of 5-HT3 receptors.

The use of prophylactic ondansetron on PONV after middle ear operations has not been studied previously and the present study was designed to examine this area.

Methods and results

The Ethics Committee of the Otolaryngological Hospital approved the study, and informed consent was obtained from 75 patients undergoing middle ear surgery. All were ASA I–II, aged 15–62 yr. Exclusion criteria included: regular or temporary use of antiemetic drugs, and vomiting or retching within 24 h before operation. Twenty-five patients were allocated randomly to one of three groups; placebo, ondansetron 4 mg or ondansetron 8 mg. The design of the study was double-blind. On the preceding day, a history of motion sickness and PONV, and menstrual date were obtained.

A standard anaesthetic technique was used. Premedication comprised oxycodeone 0.1 mg kg\(^{-1}\) and atropine 0.01 mg kg\(^{-1}\). After insertion of an i.v. cannula, patients received the test drug in 5–7 min (ondansetron 4 mg or 8 mg (Zofran) or placebo diluted to 100 ml in 0.9 % NaCl) in a double-blind manner. Anaesthesia was induced with thiopentone 5 mg kg\(^{-1}\), preceded by fentanyl 2 μg kg\(^{-1}\), which was given thereafter during surgery as 50-μg doses. Alcuronium 2–2.5 mg was used for “precurarization” and tracheal intubation was facilitated with suxamethonium 1.5 mg kg\(^{-1}\). Anaesthesia was maintained with isoflurane (inspiratory concentration 0.5–1.5 vol %, mainly 0.75 vol %) and 66 % nitrous oxide (which was replaced by air before closing of the tympanic membrane) in oxygen. Arterial pressure and heart rate were maintained within 20 % of preanaesthetic values. End-tidal carbon dioxide concentration was kept at 5.0–5.5 %. Vecuronium was used for neuromuscular block and residual block was antagonized with neostigmine 2 mg and glycopyrronium 0.4 mg. Arterial pressure, capnogram, electrocardiogram, haemoglobin oxygen saturation \(\left(S_{O_2}\right)\) and neuromuscular block were monitored routinely.

Postoperative pain was treated with diclofenac 1 mg kg\(^{-1}\) twice daily or paracetamol 10 mg kg\(^{-1}\) four times daily in patients who did not tolerate diclofenac. In addition, oxycodone 50 μg kg\(^{-1}\) i.v. or 100 μg kg\(^{-1}\) i.m. was used if needed for additional analgesia.

A trained nurse, who was unaware of the nature of the study drug, assessed the incidence of nausea, retching and vomiting at the following times: 0–2, 2–6, 6–12, 12–18 and 18–24 h after the end of anaesthesia. Droperidol 10 μg kg\(^{-1}\) i.v. or i.m. was given for vomiting, retching or prolonged nausea, at a minimum interval of 30 min.

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Patients in the placebo and ondansetron groups did not differ significantly in age, weight, sex, phases of the menstrual cycle, details of anaesthesia, duration of anaesthesia or operation, mean concentration of inspired isoflurane, total dose of fentanyl given, dose of lignocaine given topically during surgery or vomiting, respectively. The corresponding values in the ondansetron 4 mg group were 16%, 4% and 8%, and in the 8 mg group, 4%, 16% and 16%.

In the search for factors associated with PONV, logistic regression analysis revealed that ondansetron, both 4 mg ($P < 0.05$) and 8 mg ($P < 0.05$), a history of motion sickness ($P < 0.05$) and female sex ($P < 0.01$) were predictors of PONV and the need for rescue antiemetic, but the amount of oxycodone was not a predictor of these effects.

Twelve patients in the placebo group needed droperidol, but only six and seven patients in the ondansetron 4 and 8 mg groups, respectively. The need for rescue antiemetic, in mean doses per patient, was 0.72 (0.89) in the placebo group, 0.32 (0.63) in the ondansetron 4 mg and 0.32 (0.56) in the ondansetron 8 mg group.

In the 49 patients without a history of motion sickness, prophylaxis with ondansetron 4 mg and 8 mg decreased both the proportion of patients suffering from PONV and the need for droperidol (table 1).

### Table 1

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Ondansetron</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>19</td>
<td>30</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>11/8</td>
<td>18/12</td>
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<tr>
<td>Ondansetron 0/4 mg/8 mg</td>
<td>19/0/0</td>
<td>0/16/14</td>
</tr>
<tr>
<td>Patients free of PONV (%)</td>
<td>47</td>
<td>80*</td>
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<tr>
<td>Patients suffering from</td>
<td></td>
<td></td>
</tr>
<tr>
<td>or vomiting (%)</td>
<td>37</td>
<td>10*</td>
</tr>
<tr>
<td>Patients needing droperidol(%)</td>
<td>53</td>
<td>17*</td>
</tr>
<tr>
<td>Doses of droperidol needed per patient (median (range))</td>
<td>1 (0–3)</td>
<td>0 (0–2)**</td>
</tr>
</tbody>
</table>

### Comment

The main finding in this study was that prophylaxis with ondansetron reduced PONV and the need for droperidol. There was a marked reduction in the number of patients suffering from PONV and also the need for droperidol in those without a history of motion sickness.

The overall percentage of placebo-treated patients reporting emetic symptoms in this study was in agreement with two recent studies on PONV after middle ear surgery under general anaesthesia [1, 2].

The mechanism of PONV after ear operation is still obscure. Increased middle ear pressure caused by nitrous oxide has been postulated as one of the mechanisms. This was unlikely in the present study as nitrous oxide was replaced by air well before closing of the tympanic membrane and thus no pressure was generated in the middle ear from diffusion of nitrous oxide.

One of the causes of PONV after middle ear surgery could be the physical stimulus caused by the otologist drilling and irrigating the bone adjacent to the inner ear. High levels of noise caused by drilling and suctioning have been reported in ear surgery, and noise exceeding 107 dB(A) has been measured in the mastoid cavity [3]. The otologist also causes low frequency vibrations, especially when using a slowly rotating cutting burr. These vibrations may act in the same way as infrasound on the vestibular system. It has been shown that low-frequency sound stimulation provokes postural instability in patients undergoing surgery for chronic otitis media [4].

This action of noise is termed the Tullio phenomenon, and is caused by loud sound waves activating the vestibular part of the inner ear [4]. The postulate that physical stimulation is one of the causes of a high incidence of PONV after middle ear surgery is supported by the fact that transdermal hyoscine, a drug used in motion sickness, is more potent in reducing PONV [1, 2] than ondansetron, which lacks an anti-motion sickness effect [5].

Zacopride, another 5-HT3 antagonist, overcomes the cognitive impairment which occurs with hyoscine [6]. Thus the combination therapy of transdermal hyoscine and a 5-HT3-antagonist should cover patients with and without motion sickness and may lead to less PONV with lesser side effects, but this hypothesis requires evaluation before it can be recommended.

We conclude that the use of prophylactic ondansetron reduced PONV and the need for antiemetics after surgery of the middle ear under general anaesthesia. Patients without a history of motion sickness benefited more from this prophylaxis. We recommend a dose of 4 mg, as increasing the dose to 8 mg did not decrease PONV or the need for rescue antiemetic.

### References