SUBJECTS AND METHODS

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Accepted for publication October 25, 2006.

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Does Ondansetron or Granisetron Prevent Subarachnoid Morphine-Induced Pruritus After Cesarean Delivery?

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BACKGROUND: We compared the efficacy of granisetron and ondansetron for the prevention of subarachnoid morphine-induced pruritus after cesarean delivery.

METHODS: The incidence of pruritus was assessed in parturients who were randomly allocated into Group G (granisetron 3 mg IV, n = 45), Group O (ondansetron 8 mg IV, n = 42), and Group S (saline IV, n = 42).

RESULTS: The incidence of pruritus was not significantly different among the 3 groups (86.6% in Group S, 83.3% in Group O, and 88% in the Group G).

CONCLUSION: Neither prophylactic ondansetron nor granisetron reduced the incidence of subarachnoid morphine-induced pruritus when compared with the saline group.

(Anesth Analg 2007;104:421–4)
4, 6, 8, 12, and 24 h after placement of the spinal anesthetic. The location and degree of pruritus was classified as 1 = no pruritus, 2 = mild pruritus, 3 = moderate pruritus, 4 = severe pruritus. Nausea severity was graded according to a 4-point rating score with 1 = no nausea or vomiting, 2 = queasy, 3 = severe nausea, 4 = vomiting. Pain was assessed using visual analog scale with 0 = no pain, and 10 = worst pain imaginable. Cardiac dysrhythmia was evaluated with cardiac auscultation after any patient reported palpitations, and verified by electrocardiogram. Extrapyramidal signs were assessed by the anesthesiologist as the presence of twitching, dystonia, akathisia, or rigor.

The possible side effects were explained to the patients who were told that they could have treatment upon request. Pruritus was treated with diphenhydramine 12.5 mg IV every 4 h and, if the pruritus was not relieved, incremental doses of naloxone 0.04 mg IV were given. Nausea and/or vomiting were treated with metoclopramide 10 mg every 8 h. Diclofenac 100 mg suppository and/or paracetamol 1 g IV were used, if needed, for pain relief.

Continuous data are reported as means ± standard deviation and were analyzed using ANOVA. Categorical data are reported as numbers and percentages and were analyzed using χ² or Fisher’s exact test as appropriate. Nonparametric data such as scores are reported as medians and ranges and were analyzed using Mann–Whitney U test. The sample size was determined to be 44 patients per group to detect a decrease of pruritus from 80% to 55% at the 0.05 significance level with 80% power.

RESULTS
Six patients were excluded because of protocol violation (three from Group O and three from Group G), and 129 were analyzed.

Patients’ and operative characteristics were comparable among the three groups (Table 1). The sites of pruritus were mainly at the face, neck, trunk, and back. The overall incidence and highest score of pruritus, the number of patients requesting treatment for pruritus (Table 2), as well as the severity and incidence of pruritus at different time intervals (Fig. 1) were similar among the three groups.

There was no difference in the overall incidence and highest score of nausea and/or vomiting (Table 2), or in the severity and incidence of nausea and vomiting at different time intervals among the three groups (Fig. 2). However, the number of patients requesting treatment for nausea and/or vomiting was significantly less in Group O and group G when compared with Group S (Table 2).

Pain scores were not different among the three groups. The incidence of patients requiring supplemental analgesics postoperatively was 76% in Group S, 73% in Group O, and 80% in Group G (P > 0.05). The mean time for the first analgesic requirement in those patients was 11 ± 7 h, 11 ± 6.4 h, and 8.4 ± 6.7 h (P > 0.05). Mild headache was observed in two patients in Group O and two patients in group G. Cardiac dysrhythmia and extrapyramidal symptoms were not noted in any patient.

DISCUSSION
In the obstetric population, pruritus is very common after neuraxial opioids, possibly related to the interaction of estrogen with opioid receptors in the spinal cord and the increased cephalad spread of spinally administered drugs (12). In our parturients, the incidence of pruritus after SA morphine was more than 83% in all three groups, and peaked at 4–6 h after spinal injection. The incidence of pruritus in other obstetrical studies ranged between 70%–93% (4–7,13).

One of the mechanisms of SA morphine-induced pruritus seems to be related to direct stimulation of 5-HT₃ receptors by morphine in the dorsal horn of the spinal cord and medulla; thus, 5-HT₃ receptor antagonist may prevent this pruritus (14). However, our report showed that neither prophylactic ondansetron nor granisetron reduced the incidence or severity of pruritus when compared with the saline group. Similarly, two previous studies reported the failure of ondansetron and tropisetron to prevent pruritus after cesarean delivery (6,7). It seems that even with the use of higher doses of these 5-HT₃ receptor antagonists than are commonly used in the management of postoperative nausea and vomiting (15), neither ondansetron nor granisetron provided any benefit in the prevention of pruritus produced by SA morphine. However, Yeh et al. (4) and Charuluxananan et al. (5) demonstrated that prophylactic ondansetron reduced the frequency of SA morphine-related pruritus in patients undergoing cesarean delivery. These conflicting results may be attributed to the different doses of SA morphine administered, different scales and definitions used, as well as different time periods for assessment.

SA morphine induces not only pruritus, but also nausea and vomiting, by acting on 5-HT₃ receptors in

Table 1. Patients’ and Operative Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Group S (n = 45)</th>
<th>Group O (n = 42)</th>
<th>Group G (n = 42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>32.7 ± 4.8</td>
<td>32.9 ± 4.2</td>
<td>30.9 ± 6.7</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>162 ± 5.2</td>
<td>160.1 ± 15.1</td>
<td>163.1 ± 7.2</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>76.8 ± 9</td>
<td>79.4 ± 10.9</td>
<td>80.1 ± 11.5</td>
</tr>
<tr>
<td>Gestational age (wk)</td>
<td>37.8 ± 1.7</td>
<td>37.7 ± 1.2</td>
<td>37.9 ± 1.7</td>
</tr>
<tr>
<td>Primigravida</td>
<td>18 (40%)</td>
<td>12 (28.5%)</td>
<td>17 (40.4%)</td>
</tr>
<tr>
<td>Urgent cesarean delivery</td>
<td>9 (20%)</td>
<td>8 (19%)</td>
<td>9 (21.4%)</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>62.2 ± 15.8</td>
<td>61.2 ± 12.9</td>
<td>58.7 ± 10.5</td>
</tr>
</tbody>
</table>

Values are means ± SD. No statistical significance was found among the three groups.

Group S – saline group, Group O – ondansetron group, Group G – granisetron group.
the chemoreceptor trigger zone (16). Serotonin recepto-
tor antagonists might be effective in the prevention of
SA morphine-induced nausea and vomiting. Al-
though our report showed that the incidence of nausea
and vomiting was not significantly different among
the three groups, fewer patients requested rescue
antiemetics in the ondansetron group and granisetron
group when compared with those in the saline group.
This lack of significant difference in the incidence of
nausea and vomiting among the three groups may
have been related to the possibility that other mecha-
nisms, independent of serotonin receptors, are involved
in the pathogenesis of SA morphine-induced nausea and
vomiting, or to insufficient statistical power of the study
to investigate this secondary outcome.

In conclusion, the prophylactic administration of
ondansetron or granisetron did not reduce the inci-
dence of pruritus. However, both drugs resulted in a
significant decrease in the number of patients request-
ing rescue antiemetics.

Table 2. Evaluation Results of the Study Patients

<table>
<thead>
<tr>
<th></th>
<th>Group S (n = 45)</th>
<th>Group O (n = 42)</th>
<th>Group G (n = 42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of pruritus</td>
<td>39 (86.6%)</td>
<td>35 (83.3%)</td>
<td>37 (88%)</td>
</tr>
<tr>
<td>Highest pruritus score recorded</td>
<td>2 (1–4)</td>
<td>2 (1–4)</td>
<td>2 (1–4)</td>
</tr>
<tr>
<td>Number of patients treated for pruritus</td>
<td>18 (40%)</td>
<td>16 (38%)</td>
<td>12 (28.5%)</td>
</tr>
<tr>
<td>Number of times antipruritic treatment needed</td>
<td>1 (1–5)</td>
<td>1 (1–4)</td>
<td>1 (1–3)</td>
</tr>
<tr>
<td>Incidence of nausea</td>
<td>9 (20%)</td>
<td>5 (11.9%)</td>
<td>9 (21.4%)</td>
</tr>
<tr>
<td>Incidence of vomiting</td>
<td>7 (15.5%)</td>
<td>5 (11.9%)</td>
<td>4 (9.5%)</td>
</tr>
<tr>
<td>Incidence of nausea and/or vomiting</td>
<td>14 (31.1%)</td>
<td>10 (23.8%)</td>
<td>12 (28.5%)</td>
</tr>
<tr>
<td>Highest nausea score recorded</td>
<td>1 (1–4)</td>
<td>1 (1–4)</td>
<td>1 (1–4)</td>
</tr>
<tr>
<td>Number of patients treated for nausea and/or vomiting</td>
<td>13 (28.8%)</td>
<td>4 (9.5%)*</td>
<td>5 (11.9%)†</td>
</tr>
<tr>
<td>Number of times antiemetic treatment needed</td>
<td>1 (1–3)</td>
<td>1 (1–1)</td>
<td>1 (1–1)</td>
</tr>
</tbody>
</table>

Values are numbers or medians and ranges. No statistical significance was found among the three groups unless otherwise specified.

Group S = saline group, Group O = ondansetron group, Group G = granisetron group.

* P = 0.03 between Group S and Group O; † P = 0.05 between Group S and Group G.

Figure 1. Pruritus. (A) Severity of pruritus. (B) Incidence of pruritus at different time intervals.

Figure 2. Nausea and vomiting. (A) Severity of nausea. (B) Incidence of nausea and/or vomiting at different time intervals.

REFERENCES


