Comparison of droperidol and ondansetron prophylactic effect on subarachnoid morphine-induced pruritus

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KEYWORDS
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Morphine;
Ondansetron;
Pruritus;
Subarachnoid injection

Abstract
Background and objectives: The prophylactic effect of ondansetron on subarachnoid morphine-induced pruritus is controversial, while evidence suggests that droperidol prevents pruritus. The aim of this study is to compare the effects of droperidol and ondansetron on subarachnoid morphine-induced pruritus.

Methods: 180 ASA I or II patients scheduled to undergo cesarean sections under subarachnoid anesthesia combined with morphine 0.2 mg were randomized to receive, after the child’s birth, metoclopramide 10 mg (Group I = control), droperidol 2.5 mg (Group II) or ondansetron 8 mg (Group III). Postoperatively, the patients were assessed for pruritus (absent, mild, moderate or severe) or other side effects by blinded investigators. Patients were also blinded to their group allocation. The tendency to present more severe forms of pruritus was compared between groups. NNT was also determined.

Results: Patients assigned to receive droperidol [Proportional odds ratio: 0.45 (95% confidence interval 0.23–0.88)] reported less pruritus than those who received metoclopramide. Ondansetron effect was similar to metoclopramide [Proportional odds ratio: 0.95 (95% confidence interval 0.49–1.83)]. The NNT for droperidol and ondansetron was 4.0 and 14.7, respectively.

Conclusions: Ondansetron does not inhibit subarachnoid morphine-induced pruritus.

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Introduction

In a previous work, we compare the prophylactic effect of droperidol, alizapride, propofol, and promethazine on subarachnoid morphine-induced pruritus. Droperidol was the most effective agent; propofol and alizapride were less efficient; and promethazine, as other antihistamines, was ineffective. Kjebberg and Tramér, in a review study of pharmacological treatment of morphine-induced pruritus, concluded that droperidol was more effective than any other drug, other than morphine antagonists. But their review only included one study in which ondansetron was used to antagonize the alfentanil-induced pruritus in patients undergoing general surgery.

Evidences of ondansetron effectiveness are contradictory. Some studies have reported ondansetron effectiveness for treating or preventing pruritus. It has also been suggested that ondansetron reduces pruritus severity without reducing its incidence. On the other hand, other studies have reported the ineffectiveness of ondansetron or its lower efficacy compared to other drugs.

Given this contradiction and lack of comparison between droperidol and ondansetron, we decided to compare the prophylactic effect of the two drugs in patients undergoing cesarean section (C-section).

Methods

This study was approved by the Research Ethics Committee of the Universidade Católica de Pelotas (Ref: 2011/18), and written informed consent was obtained from all patients.
with fractionated doses of metaraminol. Shortly after birth, 
15–20 units of oxytocin were used to obtain good uterine 
contraction. In three cases, 0.2 mg of methylergometrine 
were used for the same purpose.

The distribution of 180 participants in three groups of 
60 patients was performed using a table of random 
numbers. According to this allocation table, immediately 
after birth, the patients in Group I received metoclo-
pramide (10 mg); patients in Group II received droperidol 
(2.5 mg); and patients in Group III received ondansetron 
(8 mg) (Fig. 1). In Group I, metoclopramide was used because 
it was shown that it has no effect on morphine-induced pru-
ritus, so it can be used to prevent nausea and vomiting 
and as a placebo for morphine-induced pruritus. Induction 
of anesthesia and administration of drugs in the operating 
room were performed by anesthesiologists (FFCB and MLH). 
In the postoperative period, patients were seen by anesthesi-
ologists unaware to their experimental allocation (APB, IS, 
MAN, RB, and RA). The patients were also blinded to the 
treatment received, characterizing the double-blind nature 
of this study. Patients were evaluated every six hours for 
a period of 24 h. After this period, they were evaluated twice 
daily until discharge from hospital. In addition to pruritus, 
any other adverse effects seen or reported by the patient, 
even if only in one of the visits, was recorded and considered 
positive.

Pruritus was classified as absent; mild (restricted to one 
area, such as face or arms, and not disturbing the patient, 
sometimes denied and only reported after insistence); 
moderate (affecting a larger area, such as face and arms or 
face and anterior surface of the chest, but not disturbing 
the patient and therefore not requiring treatment) or inten-

sive (extensive or generalized pruritus, often disturbing 
the patient to the point where treatment is indicated). It was 
registered according to the highest intensity seen or 
reported. If treatment was necessary, droperidol 1.25 mg 
was used intravenously.

Based on previous studies, we estimate that the inci-
dence of moderate or severe pruritus should be 30% in the 
control group, and that an effective intervention would 
reduce the incidence by 60%. The sample size calculation 
estimated 60 patients per group for a significance level of 
95% and a power of 80%.

For data analysis, we used logistic regression to estimate 
the trend of moderate or severe pruritus and the propor-
tional trend model to estimate the tendency to present a 
more severe pruritus. In ordinal regression, the proportional 
model was used to estimate the odds ratio and the presum-
on of proportional odds was assessed using Brant test. NNT 
evaluation was based on the incidence of moderate or severe 
pruritus.

**Results**

Table 1 shows that the distribution of some basic charac-
teristics (age, weight, height, BMI, fasting time, number 
of previous C-sections, and incidence of postoperative nau-
sea or vomiting) was similar between groups. There was no 
difference between groups in fluid replacement volume or 
proportion of patients who received treatment for hypoten-
sion.

Table 2 shows that the proportion of subjects who 
reported the occurrence of pruritus or the occurrence of 
mild pruritus was higher among patients in droperidol group.
Moreover, the incidence of severe pruritus was lower in women assigned to receive droperidol. Table 3 shows that the tendency to present with a stronger form of pruritus was lower among patients assigned to receive droperidol. The tendency to present with a stronger form of pruritus was 0.45 (95% CI: 0.23–0.88) for patients receiving droperidol compared with those in the metoclopramide group. However, ondansetron group was similar to metoclopramide group. In another approach, we also evaluated the tendency to present with moderate or severe pruritus, using logistic regression. The results of this analysis were similar to those observed in ordinal regression, with patients assigned to receive droperidol presenting less tendency to have moderate or severe pruritus [odds ratio 0.35 (95% CI, 0.16–0.74)].

The NNT for droperidol was 4.0, while that for ondansetron was 14.7.

**Discussion**

Our results show that droperidol was more effective than metoclopramide and ondansetron both when we approached the trend toward moderate or severe pruritus or when the severity of pruritus was the approach point.

There are some possible explanations for the differences in our results and those reported in the literature. First, opioids are different in their pharmacokinetics, and morphine has a very long action when administered by the subarachnoid route. Therefore, it is very difficult to compare fentanyl or sufentanil with morphine. Another difference is that the incidence of pruritus in C-section is higher than in other surgeries.

Regarding the safety of the use of droperidol, there are reports of arrhythmias, but it was not seen in our previous investigation, when we use 1.25 mg of droperidol in 60 patients, neither in this study with the dose of 2.5 mg. In any case, it seems interesting to use lower doses of droperidol in order to study its effectiveness.

In summary, our study shows that ondansetron does not inhibit subarachnoid morphine-induced pruritus in patients undergoing C-section. These results, combined with our previous results, allow us to say that droperidol is a satisfactory drug to antagonize the subarachnoid morphine-induced pruritus.

**Table 1** Distribution of the basic characteristics of the three groups.

<table>
<thead>
<tr>
<th></th>
<th>Metoclopramide</th>
<th>Droperidol</th>
<th>Ondansetron</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>27.1</td>
<td>27.6</td>
<td>26.8</td>
<td>0.82</td>
</tr>
<tr>
<td>ASA I patients (%)</td>
<td>55.0</td>
<td>58.3</td>
<td>63.3</td>
<td>0.65</td>
</tr>
<tr>
<td>Weight</td>
<td>81.5</td>
<td>84.7</td>
<td>78.7</td>
<td>0.20</td>
</tr>
<tr>
<td>Height</td>
<td>162.1</td>
<td>163.1</td>
<td>162.0</td>
<td>0.78</td>
</tr>
<tr>
<td>Body mass index</td>
<td>30.8</td>
<td>31.8</td>
<td>29.4</td>
<td>0.18</td>
</tr>
<tr>
<td>Fasting time</td>
<td>8.12</td>
<td>8.84</td>
<td>8.18</td>
<td>0.41</td>
</tr>
<tr>
<td>Previous cesarean</td>
<td>26.7</td>
<td>35.6</td>
<td>45.0</td>
<td>0.11</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>3.3</td>
<td>5.0</td>
<td>6.6</td>
<td>0.7</td>
</tr>
<tr>
<td>Volume up to anesthesia</td>
<td>146.8</td>
<td>143.1</td>
<td>163.0</td>
<td>0.74</td>
</tr>
<tr>
<td>Volume up to birth</td>
<td>245.7</td>
<td>254.6</td>
<td>308.7</td>
<td>0.23</td>
</tr>
<tr>
<td>Final volume</td>
<td>504.2</td>
<td>538.8</td>
<td>369.1</td>
<td>0.67</td>
</tr>
<tr>
<td>Hypotension (%)</td>
<td>40.0</td>
<td>35.0</td>
<td>48.3</td>
<td>0.16</td>
</tr>
</tbody>
</table>

**Table 2** Incidence and severity of pruritus in the three groups.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Absent</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metoclopramide</td>
<td>9 (15%)</td>
<td>19 (31.7%)</td>
<td>25 (41.7%)</td>
<td>7 (11.7%)</td>
</tr>
<tr>
<td>Droperidol</td>
<td>14 (23.3%)</td>
<td>29 (48.3%)</td>
<td>12 (20%)</td>
<td>5 (8.3%)</td>
</tr>
<tr>
<td>Ondansetron</td>
<td>9 (15%)</td>
<td>23 (38.3%)</td>
<td>17 (28.3%)</td>
<td>11 (18.3%)</td>
</tr>
</tbody>
</table>

**Table 3** Ordinal and logistic regression of groups 2 and 3 (droperidol and ondansetron, respectively), having group 1 (metoclopramide) as a reference.

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ordinal regression – odds ratio (95% confidence interval)</td>
<td>Reference</td>
<td>0.45 (0.24–0.88)</td>
<td>0.95 (0.49–1.83)</td>
</tr>
<tr>
<td>Logistic regression – odds ratio of persisting moderate to severe pruritus (95% confidence interval)</td>
<td>Reference</td>
<td>0.35 (0.16–0.74)</td>
<td>0.77 (0.37–1.57)</td>
</tr>
</tbody>
</table>
Conflicts of interest

The authors declare no conflicts of interest.

References