



# REVISTA BRASILEIRA DE ANESTESIOLOGIA

Official Publication of the Brazilian Society of Anesthesiology  
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## SCIENTIFIC ARTICLE

### Comparison of droperidol and ondansetron prophylactic effect on subarachnoid morphine-induced pruritus<sup>☆</sup>



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Received 11 August 2013; accepted 20 November 2013

Available online 28 April 2015

#### KEYWORDS

Droperidol;  
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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**PALAVRAS-CHAVE**

Droperidol;  
Morfina;  
Ondansetron;  
Prurido;  
Injeção  
subaracnoidea

**Comparação dos efeitos profiláticos do droperidol e do ondansetron sobre o prurido provocado pela morfina subaracnoidea****Resumo**

**Justificativa e objetivos:** O efeito profilático do ondansetron sobre prurido provocado pela morfina subaracnoidea é controverso, enquanto evidências sugerem que o droperidol previne o prurido. O objetivo do presente trabalho é comparar o efeito do droperidol com o do ondansetron sobre o prurido provocado pela morfina subaracnoidea.

**Métodos:** 180 pacientes ASA I ou II programadas para serem submetidas a cesarianas sob anestesia subaracnoidea à qual foram acrescentados 0,2 mg de morfina foram divididas aleatoriamente para receber, logo após o nascimento da criança, 10 mg de metoclopramida (grupo I – controle), 2,5 mg de droperidol (grupo II), ou 8 mg de ondansetron (grupo III). No período pós-operatório as pacientes foram avaliadas quanto ao prurido (ausente, leve, moderado ou intenso) ou outros efeitos colaterais por observadores que não sabiam a alocação das pacientes. As pacientes também não sabiam da sua alocação. Os grupos foram comparados pela sua tendência a apresentar formas mais severas de prurido. Também determinamos o NNT.

**Resultados:** As pacientes alocadas para receber droperidol [Odds Ratio Proporcional: 0,45 (Intervalo de Confiança de 95% 0,23 – 0,88)] relataram menos prurido do que as que receberam metoclopramida. O efeito do ondansetron foi semelhante ao da metoclopramida [Odds Ratio Proporcional: 0,95 (Intervalo de Confiança de 95% 0,49 – 1,83)]. O NNT do droperidol foi 4,0 e o do ondansetron foi 14,7.

**Conclusões:** O ondansetron não inibiu o prurido provocado pela morfina subaracnoidea.

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**Introduction**

In a previous work,<sup>1</sup> 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,<sup>2</sup> was ineffective. Kjelberg and Tramér,<sup>3</sup> 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<sup>4</sup> or preventing pruritus.<sup>5,6</sup> It has also been suggested that ondansetron reduces pruritus severity without reducing its incidence.<sup>7</sup> On the other hand, other studies have reported the ineffectiveness of ondansetron or its lower efficacy compared to other drugs.<sup>8–10</sup>

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.

This randomized double-blind trial enrolled 180 patients ASA I or II scheduled for C-section, regardless of the cause of obstetric indication. In addition to the refusal to participate in this research, patients were excluded in the following cases: inadequate anesthesia, any itchy skin disease, recent use of opioids or any other drug that causes respiratory depression, hyperemesis, or inability to answer questions clearly.

Upon arrival at the operating room, patients received an infusion of Ringer's lactate and 50 mcg of fentanyl were intravenously (IV) administered. The total volume of fluid infused during surgery was recorded in three moments: at lumbar puncture; at the child's birth, and at the end of surgery. Standard monitoring (non-invasive blood pressure, SpO<sub>2</sub>, and ECG) was established.

Subarachnoid anesthesia was induced via the lateral approach<sup>11</sup> with Quincke needle at L2-L3 or L3-L4, using 2 mL of 5% lidocaine hyperbaric solution (100 mg) or 4 mL of 5% bupivacaine hyperbaric solution (20 mg). Two hundred micrograms of morphine was added to the injected anesthetic. The manual displacement of the uterus to the left was established prophylactically and, in case of hypotension (systolic blood pressure 70% of baseline values or below 90 mmHg), improvement in displacement was attempted and/or fractionated doses of metaraminol (0.5 mg each) were given. As the leading cause of hypotension before birth is cava compression, we made a distinction between its incidence before birth (initial hypotension), treated with metaraminol only if persisting after improving the manual displacement, and hypotension after child birth (final hypotension), which has the same pathophysiology of hypotension from any spinal anesthesia and was treated



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

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

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

Drugs	Pruritus			
	Absent	Mild	Moderate	Severe
Metoclopramide	9 (15%)	19 (31.7%)	25 (41.7%)	7 (11.7%)
Droperidol	14 (23.3%)	29 (48.3%)	12 (20%)	5 (8.3%)
Ondansetron	9 (15%)	23 (38.3%)	17 (28.3%)	11 (18.3%)

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.<sup>12</sup> 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.<sup>5</sup>

Regarding the safety of the use of droperidol, there are reports of arrhythmias,<sup>13</sup> 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 3** Ordinal and logistic regression of groups 2 and 3 (droperidol and ondansetron, respectively), having group 1 (metoclopramide) as a reference.

	Group 1	Group 2	Group 3
Ordinal regression – odds ratio (95% confidence interval)	Reference	0.45 (0.24–0.88)	0.95 (0.49–1.83)
Logistic regression – odds ratio of persisting moderate to severe pruritus (95% confidence interval)	Reference	0.35 (0.16–0.74)	0.77 (0.37–1.57)

## Conflicts of interest

The authors declare no conflicts of interest.

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