The effect of palonosetron on postoperative nausea and vomiting in supratentorial craniotomy patients

Halit MADENOĞLU, Cihan AKDEMİR, Recep AKSU, Cihangır BİÇER, Ayşe ÜLGEY, Adem BOYACI

Aim: Postoperative nausea and vomiting (PONV) is a condition that adversely affects postoperative patient comfort. Supratentorial craniotomy patients were therefore monitored to establish the therapeutic efficiency of 2 different doses of palonosetron.

Materials and methods: Patients scheduled for elective supratentorial craniotomy were randomly assigned to 3 groups: a control group (n = 30), a 0.05 mg palonosetron group (n = 30), and a 0.075 mg palonosetron group (n = 30). The drugs were given intravenously at the commencement of dura mater closure. Anesthesia maintenance was provided with 1 MAC sevoflurane in a 50% air and O2 mixture. After the extubation, the patients were monitored for 72 h with respect to postoperative nausea and vomiting.

Results: In the first 6 h, nausea was significantly lower in the 0.075 mg palonosetron group compared to the control group (P = 0.019). The incidences of nausea, retching, and vomiting at 0–72 h postoperatively were significantly lower in the 0.075 mg palonosetron group than in the 0.05 mg palonosetron or saline groups (P < 0.001).

Conclusion: In supratentorial craniotomy cases, PONV was reduced more effectively in the 0.075 mg palonosetron group than in the 0.05 mg palonosetron and control groups.

Key words: Supratentorial craniotomy, postoperative nausea and vomiting, palonosetron

Introduction

Postoperative nausea and vomiting (PONV) are frequent and distressing complications after neurosurgical procedures (1). The reported incidence of PONV after elective craniotomy has been found to be between 44% and 70% in different studies (2–5). Vomiting may increase intracranial and/or cerebral intravascular pressure, jeopardizing hemostasis and cerebral perfusion, and may cause an electrolyte imbalance like hyponatremia (5,6).

The area postrema of the brain stem, which is where the chemoreceptor trigger zone is located, is rich in dopamine, opioid, and serotonin (or 5-hydroxytryptamine; 5-HT3) receptors (7–9). These receptors may play an important role in the transmission of impulses to the emetic center (10).

The new generation of antiemetic agents, called 5-HT3 receptor antagonists (ondansetron, granisetron, ramosetron, and dolasetron), are superior to conventional antiemetics for the prevention and treatment of PONV (11). Palonosetron, a second-generation 5-HT3 receptor antagonist, has provided better PONV results, has higher receptor affinity, and has a much longer half-life (approximately 40 h) than other 5-HT3 receptor antagonists (12). However, there are no reports about the efficacy of different doses of palonosetron in elective craniotomy for supratentorial tumor resection. This prospective, randomized, double-blinded study was designed to evaluate the efficacy and safety of different doses of palonosetron for the prevention of postoperative nausea and vomiting in patients undergoing supratentorial craniotomy.
Materials and methods

After approval by the ethics committee, we obtained written informed consent from 90 American Society of Anesthesiologists (ASA) status I–III patients aged between 18 and 76 years old who were scheduled for elective supratentorial craniotomy for resection of mass lesions. The patients were randomly assigned into 3 groups to be administered 0.05 mg palonosetron (group P1), 0.075 mg palonosetron (group P2), or saline (group S) in a double-blinded fashion. The exclusion criteria were a history of vomiting such as motion sickness, antiemetic use preoperatively, allergy to palonosetron, pregnancy, breast-feeding, morbid obesity, cardiac dysrhythmia, clinical symptoms (hypertension, bradycardia, nausea–vomiting, confusion, and papilledema), radiological images due to increased intracranial pressure, mental retardation, or psychiatric illness. All patients in the 3 groups received corticosteroid therapy (dexamethasone: 4 mg/6 h) during the preoperative and postoperative periods. Patients were monitored with electrocardiography and for heart rate, noninvasive blood pressure, pulse oximetry, airway gas levels, and end-tidal CO2 concentration using a Datex–Engstrom AS/3 monitor (Datex–Engstrom, Helsinki, Finland). Saline was given to all patients at an hourly rate of 5 mL/kg during the study period. Anesthesia was induced with 2–2.5 mg/kg propofol (13) and 2 µg/kg fentanyl. Endotracheal intubation was facilitated by 0.1 mg/kg vecuronium. After orotracheal intubation with an armored tube resistant to kinking, general anesthesia was maintained with 1 MAC sevoflurane in a 50% air and oxygen mixture and intermittent bolus doses of 1 µg/kg fentanyl. At the end of the operation, residual neuromuscular blockade was antagonized with intravenous atropine (0.015 mg/kg) and neostigmine (0.04 mg/kg). The patient was extubated after adequate spontaneous ventilation and movement.

The patients in group P1 (n = 30) received 0.05 mg of palonosetron (Aloxi, 250 µg/5 mL, Helsinn Birex Pharmaceuticals Ltd., Dublin, Ireland) diluted to 5 mL with 0.9% saline (1 mL palonosetron, 4 mL 0.9% saline), the patients in group P2 (n = 30) received 0.075 mg of palonosetron diluted to 5 mL with 0.9% saline (1.5 mL palonosetron, 3.5 mL 0.9% saline), and the patients in group S (n = 30) received 5 mL of 0.9% saline. The drugs were prepared and administered by anesthesia staff not involved in collecting the data. The drugs were given intravenously at the commencement of dural closure.

Postoperatively, the patients were transferred to the neurosurgical intensive care unit, and trained nursing staff recorded each episode of nausea and vomiting that occurred for 72 h. Although the nurses were aware of the nature of the study, they were blinded to the drug administered. Patient age, weight, and height; the duration of surgery; anesthesia; and intraoperative narcotic consumption were recorded. Episodes of nausea and vomiting and requests (plus time of request) for rescue antiemetic medication were recorded at 0 min and 6, 24, 48, and 72 h. Nausea was defined as a feeling of the urge to vomit as solicited by the investigators during assessments. Vomiting was defined as expulsion of stomach contents through the mouth. Retching was defined as an attempt to vomit that was not productive of stomach contents. An emetic episode was defined as a single vomit or retch or any number of continuous vomits or retches. Metoclopramide (10 mg) was given intravenously to the patients as a rescue antiemetic after more than 2 episodes of emesis within 30 min or persistent nausea lasting more than 10 min. All patients received 1 g of paracetamol (Perfalgan, Bristol-Myers Squibb Pharmaceuticals Ltd., New York, USA) intravenously every 8 h for postoperative pain management.

The primary outcome evaluated in this study was the efficacy (and safety) of using different doses of palonosetron to prevent postoperative nausea and vomiting in patients undergoing supratentorial surgery.

Statistical analyses were performed using SPSS (version 15.0, SPSS Inc., Chicago, IL, USA) software. The Kolmogorov–Smirnov test was used to assess the normal distribution of the data. One-way ANOVA was used to compare differences between the groups for parametric data with normal distribution. Statistical significance was determined by the Scheffe test, which is a post hoc multiple comparison test. Differences between measurements carried out before and after the drug administration or procedure were compared with paired t-tests. Pearson’s chi-square test was used to compare the differences between groups for categorical variables. A P-value less than 0.05 was accepted as statistically significant.
Results

There was no intergroup difference with regard to age, height, weight, sex, or ASA classification of the cases (P > 0.05) (Table 1).

The mean duration of surgery was 172.3 min in the control group, whereas it was 199 and 182 min in the 0.05 mg and 0.075 mg palonosetron groups, respectively. There was no statistically significant difference between the groups with regard to duration of surgery (P = 0.216) (Table 1).

The mean intraoperative fentanyl consumption was 246 µg in the control group, whereas it was 275 µg and 248 µg in the 0.05 mg and 0.075 mg palonosetron groups, respectively. There was no statistically significant difference between the groups with regard to mean intraoperative fentanyl consumption (P = 0.248) (Table 1).

Intergroup comparisons showed no difference with regard to mean blood pressure or heart rate (P > 0.05) (Tables 2 and 3).

Although group P2 demonstrated statistically significantly lower nausea rates at 0–6 h compared with group P1 and the control group (P < 0.043), no intergroup difference was observed at 6–24 or 24–72 h (P > 0.05) (Table 4). There was no statistically significant difference between the groups in terms of

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Table 1. Demographic and clinical data.

<table>
<thead>
<tr>
<th></th>
<th>Group S (n = 30) (mean ± SD)</th>
<th>Group P1 (n = 30) (mean ± SD)</th>
<th>Group P2 (n = 30) (mean ± SD)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49.8 ± 10.4</td>
<td>49.3 ± 14.1</td>
<td>47.8 ± 14.5</td>
<td>0.820</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>75.9 ± 11.6</td>
<td>72.7 ± 10.8</td>
<td>72.4 ± 13.3</td>
<td>0.450</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>164.8 ± 88</td>
<td>166.3 ± 7.8</td>
<td>166.8 ± 7.8</td>
<td>0.620</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>17/13</td>
<td>15/15</td>
<td>14/16</td>
<td>0.733</td>
</tr>
<tr>
<td>No. of patients with ASA physical status (I/II/III)</td>
<td>10/17/3</td>
<td>18/9/3</td>
<td>16/14/0</td>
<td>0.099</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>172.3 ± 47.6</td>
<td>199 ± 64.8</td>
<td>182 ± 63.5</td>
<td>0.216</td>
</tr>
<tr>
<td>Total intraoperative fentanyl (µg)</td>
<td>246 ± 64</td>
<td>275 ± 87</td>
<td>248 ± 64</td>
<td>0.248</td>
</tr>
</tbody>
</table>

P < 0.05 indicates statistical significance. S = control group, P1 = 0.05 mg palonosetron, P2 = 0.075 mg palonosetron.

Table 2. Mean blood pressure (mmHg).

<table>
<thead>
<tr>
<th></th>
<th>Group S (n = 30) (mean ± SD)</th>
<th>Group P1 (n = 30) (mean ± SD)</th>
<th>Group P2 (n = 30) (mean ± SD)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>MBP before induction</td>
<td>108.7 ± 17.3</td>
<td>101.1 ± 14.0</td>
<td>100.3 ± 13.8</td>
<td>0.067</td>
</tr>
<tr>
<td>MBP before intubation</td>
<td>85.0 ± 15.2</td>
<td>79.5 ± 12.2</td>
<td>82.7 ± 19.0</td>
<td>0.401</td>
</tr>
<tr>
<td>MBP after intubation</td>
<td>112.0 ± 20.9</td>
<td>104.1 ± 18.1</td>
<td>109.5 ± 19.3</td>
<td>0.283</td>
</tr>
<tr>
<td>MBP before medication</td>
<td>90.8 ± 12.5</td>
<td>92.3 ± 15.8</td>
<td>90.2 ± 10.7</td>
<td>0.815</td>
</tr>
<tr>
<td>MBP after medication</td>
<td>90.7 ± 14.6</td>
<td>90.7 ± 16.9</td>
<td>89.6 ± 12.4</td>
<td>0.947</td>
</tr>
<tr>
<td>MBP before extubation</td>
<td>110.8 ± 16.8</td>
<td>109.7 ± 19.4</td>
<td>110.5 ± 15.4</td>
<td>0.938</td>
</tr>
<tr>
<td>MBP 30 min after extubation</td>
<td>104.4 ± 23.5</td>
<td>98.9 ± 10.9</td>
<td>100.7 ± 16.6</td>
<td>0.335</td>
</tr>
</tbody>
</table>

MBP: Mean blood pressure. P < 0.05 indicates statistical significance. S = control group, P1 = 0.05 mg palonosetron, P2 = 0.075 mg palonosetron.
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Table 3. Heart rate (beats/min).

<table>
<thead>
<tr>
<th></th>
<th>Group S (n = 30) (mean ± SD)</th>
<th>Group P1 (n = 30) (mean ± SD)</th>
<th>Group P2 (n = 30) (mean ± SD)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR before induction</td>
<td>83.2 ± 15.2</td>
<td>77.9 ± 12.5</td>
<td>83.0 ± 20.1</td>
<td>0.364</td>
</tr>
<tr>
<td>HR before intubation</td>
<td>79.1 ± 15.3</td>
<td>72.7 ± 10.5</td>
<td>74.1 ± 15.6</td>
<td>0.186</td>
</tr>
<tr>
<td>HR after intubation</td>
<td>86.7 ± 14.8</td>
<td>83.3 ± 13.8</td>
<td>84.6 ± 17.5</td>
<td>0.689</td>
</tr>
<tr>
<td>HR before medication</td>
<td>76.7 ± 10.5</td>
<td>71.8 ± 10.0</td>
<td>73.9 ± 12.6</td>
<td>0.234</td>
</tr>
<tr>
<td>HR after medication</td>
<td>76.0 ± 14.4</td>
<td>72.6 ± 12.3</td>
<td>75.1 ± 13.1</td>
<td>0.599</td>
</tr>
<tr>
<td>HR before extubation</td>
<td>95.0 ± 19.2</td>
<td>88.0 ± 14.5</td>
<td>91.1 ± 14.5</td>
<td>0.253</td>
</tr>
<tr>
<td>HR 30 min after extubation</td>
<td>87.4 ± 11.0</td>
<td>83.2 ± 12.4</td>
<td>84.3 ± 12.1</td>
<td>0.368</td>
</tr>
</tbody>
</table>

HR: Heart rate. P < 0.05 indicates statistical significance. S = control group, P1 = 0.05 mg palonosetron, P2 = 0.075 mg palonosetron.

Table 4. Postoperative retching, nausea, and vomiting.

<table>
<thead>
<tr>
<th></th>
<th>Group S (n = 30) n (%)</th>
<th>Group P1 (n = 30) n (%)</th>
<th>Group P2 (n = 30) n (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Retching</td>
<td>Nausea</td>
<td>Vomiting</td>
<td>Retching</td>
</tr>
<tr>
<td></td>
<td>9 (30)</td>
<td>14 (46.7)</td>
<td>9 (30)</td>
<td>5 (16.7)</td>
</tr>
<tr>
<td></td>
<td>Retching</td>
<td>Nausea</td>
<td>Vomiting</td>
<td>Retching</td>
</tr>
<tr>
<td></td>
<td>5 (16.7)</td>
<td>5 (16.7)</td>
<td>4 (13.3)</td>
<td>3 (10)</td>
</tr>
<tr>
<td></td>
<td>Retching</td>
<td>Nausea</td>
<td>Vomiting</td>
<td>Retching</td>
</tr>
<tr>
<td></td>
<td>4 (13.3)</td>
<td>5 (16.7)</td>
<td>2 (6.7)</td>
<td>3 (10)</td>
</tr>
<tr>
<td></td>
<td>Retching</td>
<td>Nausea</td>
<td>Vomiting</td>
<td>Retching</td>
</tr>
<tr>
<td></td>
<td>17 (56.7)</td>
<td>12 (40)</td>
<td>5 (16.7)*</td>
<td>0.006</td>
</tr>
</tbody>
</table>

P < 0.05 indicates statistical significance. S = control group, P1 = 0.05 mg palonosetron, P2 = 0.075 mg palonosetron. *Significantly reduced relative to control group (P < 0.05).

vomiting or retching at 0–6, 6–24, or 24–72 h (P > 0.05) (Tables 4). However, the incidence of retching, nausea, or vomiting was significantly lower in the 0.075 mg palonosetron group than in the control group (P = 0.003). There was no statistically significant difference between the 0.05 mg palonosetron and control group (P = 0.301) (Table 4).

Discussion

In this study, 0.075 mg of palonosetron was observed to reduce the incidence of nausea within the first 6 h postoperatively. Kathirvel et al. (14) found the incidence of nausea–vomiting among elective craniotomy cases at 24 h postoperatively to be 44%, whereas it was 24% in patients treated with 4 mg of
ondansetron. The need for an antiemetic was reported
to decrease from 15% to 5%. Fabling et al. (3) conducted
a retrospective study of 199 adult cases with a history
of elective craniotomy, among which the incidence of
nausea at 48 h was 50% and the incidence of vomiting
at 48 h was 39%. Postoperatively, 61% of the cases
required an antiemetic (used intraoperatively in
7%). However, infratentorial craniotomy, female sex,
and young age have been reported to be important
risk factors for this complication. Madenoglu et
al. (15) maintained anesthesia with isoflurane and
nitrous oxide in oxygen in their earlier supratentorial
cranio-tomy procedures, and they reported the
incidence of nausea and vomiting as 46.7% and 56.7%,
respectively, while noting a drop in these values down
to 30% and 26.7%, respectively, due to delivery of 2
mg of tropisetron.

In the present study, anesthesia was maintained
with sevoflurane and an oxygen–air mixture. Known
emetic potentials of opioids probably did not affect
the rate of nausea and vomiting between the 3
groups because there was no statistically significant
difference between the groups with regard to mean
intraoperative fentanyl consumption.

In the current study, only nausea presented a
statistically significant decline at 0–6 h in the 0.075
mg palonosetron group. The incidences of retching,
nausea, or vomiting were 56% in the control group,
40% in the 0.05 mg palonosetron group, and 16.7%
in the 0.075 mg palonosetron group at 0–72 h
postoperatively. These incidences were lower in
the 0.075 mg palonosetron group than in the other
groups, which suggests that palonosetron is more
effective at reducing PONV when used at 0.075 mg
compared to 0.05 mg.

White et al. (16) compared the effect on PONV
of 0.1–30 µg/kg palonosetron versus a placebo in
381 patients who underwent major gynecological
surgery, and they found that palonosetron at doses
of ≥1 µg/kg successfully decreased the incidence of
nausea 0–24 h postoperatively.

Kovac et al. (17) conducted a study on 544
patients with a history of gynecological or breast
surgery. They delivered 0.025, 0.050, and 0.075 mg
doses of palonosetron for PONV prophylaxis, and
0.075 mg palonosetron was found to be significantly
more effective than a placebo at preventing nausea
and vomiting at both early (0–24 h) and late (24–72
h) postoperative periods.

Candiotti et al. (18) assessed the prophylactic effect
of palonosetron at doses of 0.025, 0.050, and 0.075
mg in 574 patients who underwent laparoscopic day
surgery, and the total incidence at 0–72 h of retching,
nausea, and vomiting and early vomiting and the
severity of nausea were found to be lower in the 0.075
mg palonosetron group than in the placebo group.

In our study, similarly to the above-mentioned
studies, 0.075 mg of palonosetron reduced nausea
episodes at 0–6 h and decreased the incidence of
nausea and vomiting at other times. We
observed no significant change in hemodynamics
following delivery of the drug. None of the patients
demonstrated postoperative side effects (such as
constipation or bradycardia) due to palonosetron.
Based on this study, we can recommend palonosetron
as a safe agent with regard to hemodynamics and
postoperative side effects at the aforementioned
doses. In the present study, 51.1% of the patients were
female and 48.9% were male. There was no statistically
significant difference between the groups in terms
of sex or age. Similarly, analgesic consumption and
duration of surgery were almost the same in the
groups in our study.

Due to the increasing cost of treatment for PONV,
cost-effectiveness continues to be a major concern
when choosing therapeutic agents. However, there
is a large cost difference between palonosetron and
other 5-HT3 receptor antagonists. With respect to
palonosetron, it is difficult to decide how much
extra cost the added benefit is worth. A limitation
of this study is that sample size calculation was not
performed.

In conclusion, we suggest that intraoperative
palonosetron is more effective at 0.075 mg than at
0.05 mg; therefore, it would be more appropriate to
use palonosetron at 0.075 mg for the prevention of
PONV in supratentorial craniotomy cases.

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