Effects of gabapentin on pain and opioid consumption after abdominal hysterectomy

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BACKGROUND: Postoperative pain is an important factor affecting anesthesia and surgery. Opioids are commonly used for pain control, but are associated with complications that limit their use. Combination regimens of opioid and nonopioid drugs are used to increase the effects and decrease complications of opioids (2). Gabapentin is an anticonvulsant drug that acts through voltage-dependent calcium channels (3). This drug causes the release of amino acids in the dorsal horn of the spinal cord and decreases response to neural inputs, thus reducing or stabilizing the activity of the damaged nerves (4). Gabapentin can, therefore, be used to control chronic pain, as in diabetic neuropathy (5), herpetic neuralgia (6) and other neuropathic disorders (7). Recent studies examined the effectiveness and usefulness of gabapentin for postoperative pain and the inhibition of brain excitability (8). To date, no conclusive information is available (9-11). In the present study, we assessed the effect of 1200 mg gabapentin on postoperative pain in patients undergoing abdominal hysterectomy.

METHODS: Fifty patients undergoing hysterectomy were enrolled in the present study. Subjects received either 1200 mg gabapentin or placebo 2 h before surgery. The amount of morphine consumption and level of postoperative pain at 2 h, 6 h, 12 h and 24 h after surgery were measured.

RESULTS: There were no significant differences in age, duration of surgery and anesthesia, or body mass index between the two groups. The mean intensity of pain in the gabapentin group was significantly lower than in the placebo group. The mean amount of morphine used in the placebo group (5.2±2.8 mg) was significantly higher than in gabapentin group (1.2±0.29 mg; P=0.001). Nausea and vomiting in the placebo group was more common than in the gabapentin group (P=0.001). The time interval for initial ambulation after surgery was significantly shorter in the gabapentin group (12.2±2.18 h) compared with the placebo group (15±3.61 h; P=0.002).

CONCLUSION: 1200 mg gabapentin reduced postoperative pain and the need for opioids, and enabled earlier ambulation of the patient. Significant side effects were not observed.

Key Words: Gabapentin; Hysterectomy; Opioid; Pain; Placebo

Les effets de la Gabapentine sur la douleur et la consommation d’opioïdes après une hystérectomie abdominale

HISTORIQUE: La douleur postopératoire est un facteur important qui influence sur l’anesthésie et la chirurgie. Les opioïdes sont couramment utilisés pour le contrôle de la douleur, mais sont associés à des complications qui limitent leur utilisation. Les combinaisons d’opioïdes et de nonopioïdes sont utilisées pour augmenter les effets et réduire les complications des opioïdes (2). Le Gabapentin est un anticonvulsivant qui agit par l’intermédiaire des canaux calciques voltage-dépendants pour contrôler la douleur postopératoire chez des patients subissant une hystérectomie abdominale.

OBJECTIFS: La présente étude visait à évaluer les effets de 1 200 mg de Gabapentin, un anticonvulsivant qui agit par les canaux calciques voltage-dépendants pour contrôler la douleur postopératoire chez des patients subissant une hystérectomie abdominale.

MÉTHODOLOGIE: Cinquante patientes qui avaient subi une hystérectomie ont participé à la présente étude. Elles ont reçu soit 1 200 mg de Gabapentin, soit un placebo deux heures avant l’opération. La quantité de morphine consommée et le taux de douleur postopératoire ressentie ont été mesurés deux heures, six heures, 12 heures et 24 heures après la chirurgie.

RÉSULTATS: Il n’y avait pas de différence significative d’âge, de durée d’opération et d’anesthésie ou d’indice de masse corporelle entre les deux groupes. L’intensité moyenne de la douleur dans le groupe prenant de la Gabapentine était considérablement plus faible que dans celui prenant un placebo. La quantité moyenne de morphine utilisée dans le groupe prenant un placebo (5,2 mg±2,8 mg) était considérablement plus élevée que dans celui prenant de la Gabapentine (1,2 mg±0,29 mg) (P=0,001). Les nausées et les vomissements étaient plus courants dans le groupe prenant un placebo que dans celui prenant de la Gabapentine (P=0,001). Après la chirurgie, l’intervalle avant l’ambulation initiale était considérablement plus faible dans le groupe prenant de la Gabapentine (12,24 heures±2,18 heures) que dans celui prenant un placebo (15 h±3,61 h; P=0,002).

CONCLUSION: Une dose de 1 200 mg de Gabapentin réduit la douleur postopératoire et les besoins en opioïdes et favorise une ambulation plus rapide du patient. On n’a pas observé d’effets secondaires significatifs.
TABLE 1
Mean age, duration of surgery and anesthesia, and body mass index of the gabapentin and placebo groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Gabapentin</th>
<th>Placebo</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>43.8±5</td>
<td>44.6±5.07</td>
<td>0.57</td>
</tr>
<tr>
<td>Duration of surgery, min</td>
<td>90.4±18.47</td>
<td>94.6±17.49</td>
<td>0.41</td>
</tr>
<tr>
<td>Duration of anesthesia, min</td>
<td>119±16.16</td>
<td>126±17.61</td>
<td>0.2</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>24.14±3.97</td>
<td>25.36±3.85</td>
<td>0.52</td>
</tr>
</tbody>
</table>

Data presented as mean ± SD unless otherwise indicated.

TABLE 2
Mean pain intensity, measured using a visual analogue scale, experienced by the gabapentin and placebo groups at 2 h, 6 h, 12 h and 24 h after surgery

<table>
<thead>
<tr>
<th>Time after surgery, h</th>
<th>Gabapentin</th>
<th>Placebo</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>6.4±1.78</td>
<td>8.4±1.44</td>
<td>0.001</td>
</tr>
<tr>
<td>6</td>
<td>3.5±1.5</td>
<td>6.5±1.8</td>
<td>0.001</td>
</tr>
<tr>
<td>12</td>
<td>2.4±1.85</td>
<td>4.6±1.29</td>
<td>0.001</td>
</tr>
<tr>
<td>24</td>
<td>0.5±0.58</td>
<td>1.7±2.27</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Data presented as mean ± SD unless otherwise indicated.

RESULTS
The two groups showed no significant difference in age, duration of surgery and anesthesia, or body mass index (Table 1).

The mean pain intensity at 2 h, 6 h, 12 h and 24 h in the gabapentin group was significantly lower than in the placebo group (Table 2).

A sample size of 25 patients in each group was calculated to detect a significant difference of 15% in morphine consumption (as derived from pilot data), with a power of 85% and a significance level of 5%. Statistical tests, such as Student’s t test, the Mann-Whitney U test and the χ² test, were used to assess significant differences between the two groups.

DISCUSSION
The present study showed that 1200 mg gabapentin administered 2 h before surgery reduced pain and opioid consumption and helped the patients to recover more quickly (gain motion) after surgery. Pain after surgery is due to both surgical stimulation and neurogenic factors such as visceral tissue edema. Current pain treatment methods include gabapentin and gabapentin with acetaminophen. In addition, nausea and vomiting were significantly more common in the placebo group compared with the gabapentin group.

Finally, the results showed that patients in the gabapentin group recovered earlier, indicated by the time until first ambulation (12.2±2.18 h versus 15±3.61 h in the placebo group; P=0.002).

hysterectomy patients. Pain intensity and morphine requirement decreased in both groups compared with the placebo group, but differences between the gabapentin group and the gabapentin with acetaminophen group were observed only shortly after surgery. Other studies on mastectomy (16) and thyroidectomy (14) revealed similar results.

In contrast to the studies showing a positive effect of gabapentin on pain and opioid consumption, some studies have reported no or low effects. This may be due to confounding factors in experimental design. Dierking et al (17) found no difference in pain after hysterectomy between patients treated with 3000 mg gabapentin and placebo, although they showed that gabapentin decreased morphine consumption by 32%. These results are likely due to either differences in the time of morphine administration, or the fact that each patient in the test group was administered 25 mg/h of morphine regardless of reported pain level. The placebo group had a mean morphine consumption of 63 mg. In our study, morphine was only administered when the patient’s pain score rose above 4. Similarly, in a study by Radhakrishnan et al (2), pain level and opioid consumption were examined after lumbar laminectomy and discectomy in patients receiving either 800 mg gabapentin or a placebo. No difference was observed between groups in terms of pain score or narcotic consumption. However, the investigators used a relatively low dose of gabapentin compared with other studies, which may have been insufficient to prevent sensitization to painful stimuli. Local anesthetic infiltration at the surgical site may also be an important factor. Neural sensitization and hyperalgesia induced by surgical stimulation are blocked using a local anesthetic, which blunts the antihyperalgesic effects of gabapentin.

In a study examining patients undergoing laparoscopic tubal ligation surgery, no significant difference was observed between gabapentin and placebo groups in terms of pain or morphine consumption (18). This lack of effect may have been due to either the administration of 80 mg of lornoxicam, which may have confounded the results, or the time frame in which the gabapentin effect was expected to have occurred. Previous research has shown that gabapentin requires 1 h to 2 h to take
effect; however, the patients examined by Bartholdy et al (18) received gabapentin only 30 min before surgery. Because the duration of surgery was also quite short (30 min), there may have been insufficient time for the drug to take effect. Similarly, in a study by Adam et al (19), administering 800 mg of gabapentin to patients undergoing arthroscopic shoulder surgery had no effect on pain or opioid consumption after surgery. However, patients received gabapentin as well as bupivacaine, a drug used for intercostal block (localized nerve blocking), and surgery was performed under general anesthesia. Thus, the use of multiple methods of pain control may have confounded the study results; indeed, synergistic effects between specific drugs have been shown in humans and animals (20). In addition, gabapentin is known to have an anxiolytic effect (21,22). This can reduce preoperative anxiety and result in reduced postoperative pain (23).

Based on these studies, we hypothesize that the effectiveness of gabapentin in postoperative pain management is determined by the following specific factors:

1. Drug dosage according to type of surgery: In various studies, the dose of gabapentin has ranged between 300 mg and 3000 mg. The optimal dose may vary according to the type of surgery, the severity of inflammation and tissue damage and the type of pain generated (ie, somatic versus visceral). During surgical dissection, for example, the optimal dose that reduces pain and opioid usage was reported to be 600 mg before surgery (24). On the other hand, increasing the dose to 1200 mg can lead to complications (2). According to various studies, a dose of 1200 mg before surgery, regardless of the type of action, is acceptable. Further studies are required to determine the optimal dose of gabapentin in specific surgeries.

2. Timing of administration: Gabapentin crosses the blood-brain barrier and has a therapeutic effect after 2 h to 3 h of administration (25). Consequently, it should be administered 1 h to 2 h before anesthesia and may not produce the desired result if administered later. Postoperative nausea and vomiting are common complications of surgery. Gabapentin affects postoperative nausea and vomiting through two mechanisms. The central antiemetic effects are due to reduced consumption of opioids (26). In a study conducted by Al-Mujadi et al (14), only 21% of patients in the gabapentin group required treatment for vomiting after thyroidectomy surgery, compared with 31% of patients in the placebo group. Similarly, in a study by Durmus et al (8), the incidence of nausea and vomiting was lower in the gabapentin group. The results of the present study are consistent with these studies in that nausea and vomiting were less common in the gabapentin group compared with the placebo group.

CONCLUSIONS

The present study shows that 1200 mg of gabapentin reduces postoperative pain and the need for opioids, and enables patients to move more quickly after surgery. Significant side effects were not observed.

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REFERENCES


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