Evaluating the effect of preoperative oral gabapentin on postoperative pain in patients receiving spinal anaesthesia for lower limb surgery

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Abstract

Background: Gabapentin has been used successfully as a non-opioid analgesic adjuvant for postoperative pain management. We hypothesised that gabapentin might be a useful adjuvant for postoperative analgesia in patients undergoing lower extremity surgery under subarachnoid block.

Method: Ninety male patients undergoing lower extremity surgery under subarachnoid block were randomly divided into three groups. Group I (n = 30) patients received oral gabapentin 1 200 mg one hour prior to surgery. Group II (n = 30) patients received oral gabapentin 600 mg one hour prior to surgery. Group III (n = 30) patients received an oral placebo one hour prior to surgery. Lumbar puncture was done with 23G Quincke's spinal needle and 2.5 mL of 0.5% heavy bupivacaine was administered intrathecally. Patients were monitored at 0, 1, 3, 5, 8, 12 and 24 hours for assessment of pain and side effects. Patients having pain scores ≥ 5 received rescue analgesia in the form of intravenous tramadol 0.5 $mg.kg^{-1}$. If the pain score persisted at ≥ 5 after ten minutes, 0.25 $mg.kg^{-1}$ tramadol was repeated.

Results: Pain scores at zero hour were statistically significantly lower in patients receiving 1 200 mg of gabapentin (group I) when compared with the other two groups. The total rescue analgesia (tramadol) requirement over the study period was also at the minimum in patients receiving 1 200 mg of gabapentin as compared to patients receiving 600 mg of gabapentin or placebo. However, sedation scores were significantly higher in patients receiving gabapentin 1 200 mg or 600 mg than placebo.

Conclusion: Preoperative gabapentin, when administered one hour prior to surgery in a dose of 1 200 mg, decreases postoperative pain scores at zero hour and the rescue analgesia requirement significantly over a period of 24 hours in patients undergoing lower limb surgery under spinal anaesthesia.

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Introduction

Pain is an unpleasant sensation that originates from ongoing and impending tissue damage. Acute pain accompanies almost all surgical procedures. In addition to immediate unpleasantness, painful experiences can imprint themselves indelibly on the nervous system, amplifying the response to subsequent noxious stimuli (hyperalgesia) and causing a typically painless sensation to be experienced as pain (allodynia). Moreover, even low levels of residual pain are associated with decreased physical and social function, as well as decreased overall health. The goal of postoperative pain relief is to achieve optimal analgesia, facilitating a quick return to normal physiological function.[1]

Postoperative pain management relies heavily on pharmacological interventions administered in response to a patient's demands. Traditionally, intramuscular, intravenous or epidural injection of opioids, local anaesthetics or nonsteroidal anti-inflammatory drugs (NSAIDS) are used. However, postoperative pain control is often unsatisfactory despite all these options.

Gabapentin was introduced for the treatment of epilepsy in the early 1990s. Later it was found to be effective in the treatment of neuropathic pain,[2] like post-herpetic neuralgia and diabetic neuropathy,[3] by its role in the prevention of sensitisation of neurons in the dorsal horn. The sensitisation of neurons in the dorsal horn has also been

demonstrated in acute postoperative pain models.[4] It has also been shown to reduce postoperative pain and opioid analgesic requirement in various studies involving general anaesthesia. As yet, not many patients undergoing surgery under regional anaesthesia have been exposed to gabapentin in the perioperative period. Hence we conducted a study to evaluate the pre-emptive effect of gabapentin in orthopaedic patients undergoing lower limb surgery under spinal anaesthesia.

Materials and methods

After approval by the Hospital Ethics Committee and obtaining written informed consent, ninety male patients in age group 22–40 years, classified as the American Society of Anesthesiologists (ASA) physical status I or II, and scheduled for single lower limb surgery under spinal anaesthesia, were included in the study. Patients with a history of central nervous system disorders, chronic pain conditions and taking analgesics, and impaired renal function were excluded from this study. Patients unfit for spinal anaesthesia were also excluded.

The patients were randomly divided into three groups (using sealed opaque envelopes). Group I (n = 30) patients received oral gabapentin 1 200 mg one hour prior to surgery. Group II (n = 30) patients received oral gabapentin 600 mg one hour prior to surgery. Group III (n = 30) patients received an oral placebo one hour prior to surgery.

Patients were fasted for 6–8 hours prior to surgery. In the premedication room patients received either gabapentin or placebo, and no other premedication. In the operating theatre, the standard monitors were attached and intravenous cannulation was done. Either in lateral position or in sitting position, after asepsis, the L3-4 or L4-5 intervertebral space was infiltrated with 2 mL of 2% lignocaine. Lumbar puncture was done with a 23G Quincke spinal needle and 2.5 mL of 0.5% heavy bupivacaine was administered intrathecally. Patients were moved to the supine position and continuous monitoring was done intraoperatively. All patients received oxygen via face mask with a flow of 2–3 L/min. No sedative, analgesic or opioid was administered. Patients requiring general anaesthesia, either for incomplete subarachnoid block or for prolonged surgery, were excluded from this study. In the recovery room, the level of spinal anaesthesia was noted. The time at which patients complained of pain (VAS ≥ 5) was taken as zero hour. Patients were monitored at 0, 1, 3, 5, 8, 12 and 24 hours for assessment of the effect of drug or placebo for pain, sedation and any other side-effects. Pain was assessed on an 11-point visual analogue scale (VAS) for pain intensity. Patients having pain scores ≥ 5 received rescue analgesia in the form of intravenous tramadol 0.5 $mg.kg^{-1}$. If pain score remained ≥ 5 after 10 minutes, then 0.25 $mg.kg^{-1}$ tramadol was repeated. Sedation was recorded on a sedation scoring system at the above-mentioned time intervals. Scores were as follows: 1 = awake and alert; 2 = awake but drowsy, responding to verbal stimulus; 3 = drowsy but arousable, responding to physical stimulus, and 4 = unarousable, not responding to physical stimulus. Postoperative side-effects (e.g. nausea and vomiting, constipation, respiratory depression, dizziness, somnolence, peripheral oedema, diarrhoea, headache and pruritis) were recorded at 24, 48 and 72 hours after surgery.

Results

Demographic profiles and mean age, weight and height were comparable in all three groups (Table I).

Table I: Distribution of mean age, weight and height in the three groups

Group	Age (in years)	Weight (in kg)	Height (in m)
I	30.67 ± 6.88	60.17 ± 9.55	1.669 ± 0.049
II	30.9 ± 6.81	60.27 ± 8.63	1.673 ± 0.041
III	30.3 ± 6.22	57.57 ± 9.93	1.747 ± 0.050

Data is expressed as mean ± SD.

Pain score at 0 hour was statistically significantly lower in group I compared to the other two groups (Table II).

Table II: Pain (visual analogue score, VAS) at 0 hour

Group	VAS score
I	5.57 ± 0.86
II	6.23 ± 1.01
III	6.50 ± 1.10

Data is expressed as mean ± SD.

When compared statistically using a one-way ANOVA test, the difference in pain (VAS) at 0 hour in the three groups was statistically significant (F value = 7.518 and p value = 0.001). On statistical comparison, there was a significant difference between groups I and II (p = 0.008) and between groups I and III (p = 0.000). However, the difference in VAS score between groups II and III (p = 0.310) was comparable.

When compared statistically using a one-way ANOVA test, the difference in rescue analgesia (tramadol) requirement at 0 hour of patients in the three groups was statistically non-significant (F value = 1.905 and p value = 0.115). The rescue analgesia (tramadol) requirement at 0 hour was lowest in group I and greatest in group III, however this difference was not statistically significant (I vs II p = 0.081; I vs III p = 0.190; II vs III p = 0.623) (Table III).

Table III: Rescue analgesia (tramadol) requirement at 0 hour

Group	Rescue analgesia (tramadol in mg)
I	97.17 ± 26.80
II	107.50 ± 17.16
III	105.17 ± 19.36

Data is expressed as mean ± SD.

The total analgesic requirement was lowest in group I and greatest in group III. When compared statistically using a one-way ANOVA test, the difference in total rescue analgesia (tramadol) requirement by the patients in the three groups over the study period was statistically significant (F value 15.539 and p value 0.000). When compared statistically, significant differences between groups I and II and groups I and III were observed, but results were comparable between groups II and III (I vs II p = 0.0000; I vs III p = 0.000; II vs III p = 0.883) (Table IV).

Table IV: Total rescue analgesia (tramadol in mg) requirement

Group	Rescue analgesia (tramadol in mg)
I	132.66 ± 51.20
II	207.33 ± 67.21
III	209.83 ± 63.21

Data is expressed as mean ± SD.

When analysed using a one-way ANOVA test, the difference in sedation scores at 0 hour and at 1 hour was statistically significant (F value = 4.721, p value = 0.011 at 0 hour; and F value = 3.172, p value = 0.047 at 1 hour). The difference in sedation scores at 3 hours in the three different groups was statistically non-significant (F value = 2.071 and p value = 0.132).

The sedation scores were significantly higher in groups I and II than in group III, but were comparable between groups I and II (Table V). On analysing data statistically, groups I and II were comparable at all time intervals. However, a significant difference was seen between groups I and III, as well as between groups II and III at 0 and 1 hour.

Table V: Sedation scores at different time intervals

Group	0 hour	1 hour	3 hours
I	1.27 ± 0.45	1.20 ± 0.41	1.07 ± 0.25
II	1.17 ± 0.38	1.13 ± 0.35	1
III	1	1	1
P values:			
I vs II	0.356	0.497	0.155
I vs III	0.002	0.009	0.155
II vs III	0.019	0.039	–

Data is expressed as mean ± SD.

Nausea and vomiting scores and bowel and bladder functions were comparable in the three groups over the entire study period.

Discussion

In this study we observe that preoperative gabapentin, when administered 1 hour prior to surgery in a dose of 1 200 mg, decreases postoperative pain scores at zero hour and the rescue analgesia requirement significantly over a period of 24 hours in patients undergoing lower limb surgery under spinal anaesthesia. The decreased need for rescue analgesia with gabapentin 1 200 mg could be explained by the prevention or reduction of the development of central neuronal hypersensitivity induced by surgical procedure when gabapentin was given in a dose of 1 200 mg.[5,6] Results of various other studies that have been carried out to investigate the effect of gabapentin on postoperative pain have also revealed a significant reduction in postoperative pain and analgesic requirement.[7–11] There is considerable evidence in support of the role of gabapentin in preemptive analgesia, in patients undergoing surgery under general anaesthesia. However, no study has as yet been carried out to determine the role of gabapentin in patients undergoing surgery under spinal anaesthesia.

The focus of the present study was therefore to determine the effect of gabapentin on postoperative pain in orthopaedic patients undergoing lower limb surgery under spinal anaesthesia. Ninety ASA physical status I and II male patients, aged 22–40 years, were selected to eliminate age-related and gender-related bias in pain perception. In the present study the demographic profile of patients, e.g. age, weight and height, are comparable.

Dirks et al[7] and Turan et al[12] used a 1 200 mg preoperative oral dose of gabapentin. However, a recent dose-response study by Pandey et al[13] defined 600 mg as the optimum pre-emptive dose for postoperative pain relief, beyond which increasing the dose did not improve analgesia but increased the risk of side-effects. However, Adam et al[14] did not find a dose of 800 mg to be effective in decreasing postoperative pain in patients undergoing arthroscopic shoulder surgery under general anaesthesia with interscalene brachial plexus block, and concluded that perhaps higher doses are required. Hence we elected to use two different doses of oral gabapentin, 600 mg and 1 200 mg, to be administered preoperatively, to determine the analgesic effects and side effects in the postoperative period of 24 hours.

Postoperative pain scores at 0 hour were 5.57 ± 0.86, 6.23 ± 1.01 and 6.50 ± 1.10 in groups I, II and III, respectively, implying that the pain scores were lowest in group I (gabapentin 1 200 mg) and highest in group III (placebo group). We did not compare pain scores at subsequent intervals, as rescue analgesia was given at 0 hour and, subsequently, whenever the pain score was ≥ 5, so that the pain score remained < 5. Using this rescue analgesia approach allowed the patients to avoid escalating pain and the pain score to remain similar in all the groups. The rescue analgesia requirement at 0 hour was lowest with gabapentin 1 200 mg (97.17 mg) and greatest in the placebo group (107.5 mg). We found that the total rescue analgesia requirement over a 24-hour period (132.67 ± 51.20 mg) was significantly lower with gabapentin 1 200 mg (group I) than in the other two cases (207.33 ± 67.21mg in group II and 209.83 ± 63.21 mg in group III). The total rescue analgesia requirements of groups II and III were similar. The decreased need for rescue analgesia with gabapentin 1 200 mg could be explained by the prevention or reduction of the development of central neuronal hypersensitivity, induced by surgical procedure, when gabapentin was given in a dose of 1 200 mg.[4,15] Gabapentin blocks the excitatory amino acid and neuropeptide transmitters that induce central sensitisation, enabling more direct treatment of injury-induced sensory hypersensitivity. Gabapentin, l-aminomethylcyclohexanoic acid, is a novel amino acid prepared by the addition of a cyclohexyl group to the chemical backbone of γ-amino butyric acid (GABA). It also has structural similarities to L-leucine, and interacts with the auxiliary protein subunits of voltage-gated calcium channels, N-methyl-d-aspartate (NMDA) receptors, and sodium channels.[15]

One important limitation of our study is that we did not evaluate rest pain and movement-evoked pain separately. An improvement in study design could have been to evaluate the degree of pain relief in the immediate postoperative period by assessing the patient satisfaction score with postoperative pain management.

Conclusion

To conclude, preoperative gabapentin, when administered an hour before surgery in a dose of 1 200 mg, decreased postoperative pain scores at zero hour and reduced analgesia requirements significantly over a period of 24 hours in patients undergoing lower limb surgery under spinal anaesthesia. However, gabapentin in doses of 600 mg did not demonstrate efficacy in decreasing rescue analgesia requirement over the study period. No significant side-effects apart from mild sedation were observed with either of the doses.

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