International Journal of Research in Medical Sciences
Modak SD et al. Int J Res Med Sci. 2016 Sep;4(9):3755-3759
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20162607

Research Article

Pre-emptive gabapentin for postoperative pain relief in abdominal hysterectomy

Shailendra Deochandra Modak*, Jyoti Magar, Vinayak Kakad

Department of Anaesthesiology, Lokmanya Municipal Medical College and General Hospital, Sion, Mumbai, India

Received: 18 July 2016
Accepted: 22 July 2016

***Correspondence:**
Dr. Shailendra Deochandra Modak,
E-mail: shailendramodak@yahoo.com

ABSTRACT

Background: The relief of pain has always been a part of the anaesthesiologist's role in the most immediate postoperative period and the development of acute postoperative pain services has extended this interest beyond the post-anaesthesia care unit. The present study was carried out to evaluate the effects of preoperative oral gabapentin (600 mg) on postoperative pain relief, postoperative analgesic requirement and side effects in patients undergoing abdominal hysterectomy.
Methods: This prospective randomized placebo controlled study was conducted amongst sixty female patients of ASA grade I and II, age between 25-70 years, randomly allocated into two groups to receive either oral capsule gabapentin (600 mg) or placebo in the form of capsule multivitamin two hours prior to the surgery. Patients were observed 12 hours postoperatively for pain via visual analog scale (VAS), analgesic requirement and side effects.
Results: It was observed that patients in gabapentin group had statistically significant lower pain score during the entire observation period in comparison to placebo group. The mean number of rescue analgesic dose requirement in the gabapentin group (2.1±0.64) was substantially lower than that of the control group (4.3±0.88). The mean sedation scores were always higher in gabapentin group as compared to control group. Two patients in gabapentin group developed dizziness for a short duration and subsided by using ondensetron and required no further intervention.
Conclusions: Gabapentin significantly reduces post-operative pain and post-operative tramadol consumption with very few side effects.

Keywords: Gabapentin, Post-operative pain, Pre-emptive analgesia, Abdominal hysterectomy

INTRODUCTION

The relief of pain has always been a part of the anaesthesiologist's role in the most immediate postoperative period and the development of acute postoperative pain services has extended this interest beyond the post-anaesthesia care unit. The goal of postoperative pain relief is to achieve optimal analgesia, facilitating a quick return to normal physiological function.[1] The practice of treating pain only after it has been established is slowly being supplanted by a preventive approach. The idea behind pre-emptive analgesia is not simply that it reduces nociception and stress during surgery-although these are obviously worthwhile goals.

Primarily, three different classes of drugs are utilized for the treatment of postoperative pain (anti-inflammatories, local anesthetics, and opioids). Unfortunately long-term clinical use of these agents is limited by their side effects. Gabapentin is a novel drug used for the treatment of postoperative pain with antihyperalgesic properties and a unique mechanism of action, which differentiates it from other commonly used drugs. Various studies have shown that perioperative use of gabapentin reduces postoperative pain.

Gabapentin is an anticonvulsant drug that is widely and effectively used for the treatment of chronic neuropathic pain.[2,3] It has been found to decrease the pain scores and analgesic requirements following total abdominal hysterectomy laparoscopic cholecystectomy spinal surgery and ear, nose and throat (ENT) surgery.[4-8] Although the molecular mechanism of action of gabapentin is not clear, it is thought to alter the central neuronal sensitization (that amplifies postoperative pain) without affecting the pain transmission. Therefore, when used as a preemptive analgesic, gabapentin may reduce acute postoperative pain.[9] The use of gabapentin in acute postoperative pain management has been evaluated in recent studies. However, differences in the gabapentin dosages, the dosing regimen and types of surgery have yielded contrasting results. Thus we decided to study the effect of oral preemptive 600 mg gabapentin, given two hours before the surgery, for its opioid and anaesthetic sparing effects in patients undergoing spine surgeries.

METHODS

This randomized, double-blind, prospective placebo controlled study was conducted after obtaining institutional review board approval and written informed consent from all patients. Sixty female patients of ASA grade I and II, age between 25 to 70 years, scheduled for abdominal hysterectomy under spinal anesthesia were selected for study. The patients with body weight within 20% of ideal body weight were included in the study. Patients with known history of hypersensitivity to the drug, history of ischemic heart disease, patient refusal to participate, patients with uncontrolled concomitant medical disorders, history of peptic ulcer or of bleeding diathesis or taking antacids, impaired kidney or liver functions, ingestion of analgesics within 24 hours before scheduled surgery, using antidepressant and calcium channel blocker were excluded from study. A detailed pre-anaesthetic evaluation including history, thorough clinical examination and all relevant investigations were done for all the patients. All patients were instructed preoperatively for the pain visual analog scale (VAS) for measurement of pain. The selected patients were randomly allocated into two groups using a computer-generated list of random numbers. On the day of the surgery, patient's starvation was confirmed. An anaesthesiologist, who had randomization chart, administered the drug gabapentin 600 mg in gabapentin group and placebo multivitamin capsule in control group orally with sips of water according to the number allocated to the patient approximately two hours prior to surgery.

All the patients were transferred to the operative theater; standard monitors like cardioscope, non-invasive blood pressure and pulse oximeter were applied and baseline parameters were noted before giving subarachnoid block. In both groups patients were premedicated with injection glycopyrolate 0.004 mg/kg, ranitidine 1 mg/kg and ondansetron 0.08mg/kg. Under all aseptic precautions, lumbar puncture was done in L3-L4 inter-space in sitting position with 25 G spinal needles. After clear and free flow of CSF and negative aspiration of blood the subarachnoid block was given with 3.75 ml plain bupivacaine (heavy) and spinal level achieved at around T5 level. Intraoperatively, patients' haemodynamics were maintained at ±20% of baseline value. After the end of the surgical procedure the degree of pain using VAS score was noted in each patient. When the visual analog scale score was more than 25, rescue analgesia in the form of injection tramadol 1mg/Kg was given. Patient had been withdrawn from the study if there is high spinal, patient required GA or patient having pain who received other analgesics supplementation.

Postoperatively patients were observed for visual analog scale score, total amount of rescue analgesic require and adverse effects in the post anaesthesia care unit for the next twelve hours by an anaesthesiologist who was blinded for the study.

Statistical analysis

Demographic parameters were analyzed by student's t-test. The binary data like sex and ASA grading were analyzed by chi-square test. Postoperative visual analog scale score and Ramsay's sedation score was analyzed. For finding statistical significance between the groups, t-test was applied to ascertain the pattern and magnitude of differences. A p-value of 0.05 was considered as significant and p-value of 0.01 was considered highly significant.

RESULTS

Sixty patients, thirty in each group were included in the study and analyzed. The groups were comparable with respect to demographic characteristics like age, weight, physical status and duration of surgery and difference was statistically not significant (Table 1).

Table 1: Demographic data and duration of surgery.

Variables	Control	Gabapentin	P value
Age (years)	43.2±11.8	39.5±13.3	0.26
Weight (kg)	56.9±8.8	55.2±7.7	0.44
ASA Grade (I/II)	30/0	27/3	0.69
Duration of surgery (hrs)	4.18±1.34	4.13±1.35	0.89

In present study, visual analog scale score was always found to be lower in the gabapentin group during the entire observation period as compared to control group in spite of more number of control patients receiving rescue analgesia. The difference in the mean scores were statistically found to be very highly significant $p < 0.001$ at first and twelfth post-operative hours, highly significant $p < 0.01$) during the second and sixth post-

operative hours and significant p <0.05) during fifth, seventh, eighth and tenth post-operative hours (Table 2).

Table 2: Comparison of mean VAS scores at various time periods.

Time (hours)	Control	Gabapentin	P-value
1	39.0±19.9	22.2±12.8	0.000†
2	28.0±12.9	18.7±09.7	0.002‡
3	27.5±12.8	25.8±14.4	0.637
4	25.5±13.5	21.5±11.7	0.225
5	25.0±13.9	18.0±08.5	0.021"
6	27.0±13.9	18.3±10.2	0.008*
7	26.8±16.3	19.3±11.4	0.044"
8	25.5±16.9	18.2±07.5	0.034"
9	26.2±15.7	21.5±10.4	0.181
10	25.8±13.6	19.8±0 9.7	0.044"
11	26.0±14.6	21.7±12.8	0.228
12	32.2±16.5	17.3±9.94	0.000†

†'p' < 0.001 = very highly significant, ‡'p' < 0.01 = highly significant, "'p' <0.05 = significant

Number of patients requiring rescue analgesia during the first postoperative hour was found to be of reduced magnitude in the gabapentin group (9) as compared to the control group (19). 26 patients of the control group required the first dose of rescue analgesic within the first two postoperative hours, as compared to a mere 11 patients from the gabapentin group. All 30 patients in the control group received their first dose of rescue analgesia within third postoperative hour, while in the gabapentin group this time duration was extended up to eighth postoperative hour. The mean number of rescue analgesic dose requirement in the gabapentin group (2.1±0.64) was substantially lower than that of the control group (4.3±0.88). During the entire twelve hour observation period, 129 rescue analgesic doses were required by the control group patients as compared to 62 by the gabapentin group patients (Table 3).

Postoperative sedation was assessed using Ramsay's sedation score. Mean sedation scores were always higher in the gabapentin group throughout the observation period, as compared to that of the control group. Though patients in gabapentin group showed significant levels of sedation, none of the patients had episodes of desaturation (SpO_2 <95%) and did not require any further intervention.

Very few side effects were observed in the study but two patients of the gabapentin group developed dizziness soon after administration of injection tramadol. Dizziness was for a short duration and subsided with administration of injection ondansetron and required no further intervention.

Table 3: Comparison of total number of patients requiring rescue analgesia.

Hours	Control	Gabapentin
1	19	9
2	13	2
3	10	10
4	10	8
5	9	3
6	9	3
7	8	3
8	9	2
9	7	8
10	12	5
11	10	7
12	13	2
Total no. of rescue analgesia	129	62
Mean±SD	10.75±3.2	5.17±3.0

DISCUSSION

Pain relief after surgery continues to be a major medical challenge. Improvement in perioperative analgesia is not only desirable for humanitarian reasons but is also essential for its potential reduction of postoperative morbidity and mortality. Unrelieved postoperative pain may delay discharge and recovery and result in an inability to participate in rehabilitation programs, leading to poor outcomes. Postoperative outcome improved by using multimodal analgesia technique which produces better pain relief. The pain-relieving effect of analgesics, become evident only in patients experiencing severe, but not mild or moderate pain. Postoperative pain in our model, i.e. spine surgery, was considered to be severe. This prompted us to hypothesize that our model was likely to be more reliable for the study.

Gabapentin was introduced in 1993 as an adjuvant anticonvulsant drug for the treatment of refractory partial seizures. Subsequently, it's antinociceptive and antihyperalgesic properties were identified and thus were shown to be effective in treating a variety of chronic pain conditions preemptive analgesia has been shown to be more effective in control of postoperative pain by protecting the central nervous system from deleterious effects of noxious stimuli and resulting allodynia, and increased pain. Several clinical studies have evaluated the use of a single dose of preemptive gabapentin, and have demonstrated convincing reductions in postoperative pain and in postoperative analgesic consumption.[10-12] These studies reflect many important areas of anaesthesia research and it is interesting that a single drug has multimodal effects. Thus gabapentin, with its myriad merits as an adjuvant analgesic agent providing preemptive analgesia and being a vital cog in the wheel of multimodal analgesic regimen, was chosen as our study drug. After oral administration, peak serum levels

of gabapentin are reached in 2-3 hours with an absolute bioavailability of 60%. Gabapentin bioavailability is not dose proportional; i.e. as dose is increased, bioavailability decreases. Absorption is linear up to 600 mg, after which the bioavailability decreases, reaching 35% at doses of 1600 mg. However, differences in the gabapentin dosages, the dosing regimen and types of surgery have yielded contrasting results. Thus we decided to study the effect of oral preemptive 600 mg gabapentin, given two hours before the surgery, for its opioid and anaesthetic sparing effects in patients undergoing spine surgeries.

In present study, it was observed that the mean visual analogue scale score was always found to be lower in the gabapentin group when compared with the control group, during the entire observation period. Sixty three percent of the control group patients required rescue analgesia soon after extubation, in the first postoperative hour as compared to thirty percent patients in the gabapentin group. This was found to be very highly significant ($p < 0.001$) in statistical terms. The total number of rescue analgesics required was also found to be significantly reduced in the gabapentin group as compared with the control group (2.1 vs. 4.3 with $p < 0.001$) confirming the opioid sparing effects of gabapentin along with providing good analgesia.

The mean sedation scores were always higher in the gabapentin group throughout the observation period, as compared to that of the control group. When comparing the mean sedation scores amongst the two groups, the difference was very highly significant $p < 0.001$) during the first seven post-operative hours. Though patients in gabapentin group showed significant levels of sedation, none of the patients had episodes of desaturation (SpO_2 <95% and did not require any further intervention. Our findings correlate with study of Pandey et al, Dirks et al and Durmus et al.[13-15]

Another important property of gabapentin is absence of major drug interactions and serious adverse effects. Various authors in their respective studies evaluating gabapentin on postoperative pain showed no significant side effects in gabapentin group as compared to control patients. In our study, two patients of the gabapentin group complained of symptom of dizziness.[13,16-19] Nausea/vomiting and dizziness are among the most common adverse effects seen after the administration of tramadol and these adverse effects treated by using ondansetron.[20-22] However dose titration schedule and slow initiation therapy have been proposed to reduce tramadol induced adverse effects.[21,22] Increased incidence of dizziness seen in patients receiving combination of gabapentin and tramadol could thus form an avenue for further research.

CONCLUSION

Result of the present study, suggested that preemptive oral gabapentin (600 mg) had significant effect on reducing postoperative pain and postoperative tramadol requirement in patients undergoing abdominal hysterectomy. Slightly increased incidence of sedation and dizziness was noted in gabapentin receiving patients, which did not require any further treatment.

ACKNOWLEDGEMENTS

The authors would like to thank the department of anaesthesiology, surgery, other staff of operation theatre and administration of LTMMC and LTMGH, Sion, Mumbai, (M.S.), for permission to study and providing facility to carry out the work.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Morgan GE, Mikhail MS, Murray MJ, eds. Pain management. In: Clinical Anesthesiology. New York: Lange Medical Books. 2002:309-358.
2. Backonja M, Beydoun A, Edwards KR, Schwartz SL, Fonseca V, Hes M, et al. Gabapentin for symptomatic treatment of painful neuropathy in patients with diabetes mellitus: A randomized controlled trial. J Am Med Asso. 1998;280:1831-6.
3. Rice AS, Maton S. Postherpetic neuralgia study group. gabapentin in postherpetic neuralgia: a randomized, double blind, placebo controlled study. Pain. 2001;94:215-24.
4. Dierking G, Duedahl TH, Rasmussen ML, Fomsgaard JS, Moiniche S, Romsing J, et al. Effects of gabapentin on postoperative morphine consumption and pain after abdominal hysterectomy: a randomized, double blind trial. Acta Anaesthesiol Scand. 2004;48:322-7.
5. Turan A, Karamanliolu B, Memi D, Usar P, Pamukcu Z, Ture M. The analgesic effects of gabapentin after total abdominal hysterectomy. Anesth Analg. 2004;98:1370-3.
6. Pandey CK, Priye S, Singh S, Singh U, Singh RB, Singh PK. Preemptive use of gabapentin significantly decreases postoperative pain and rescue analgesic requirements in laparoscopic cholecystectomy: a randomized, double-blind, placebo controlled study. Can J Anaesth. 2004;51:358-63.
7. Turan A, Karamanliolu B, Memi D, Hamamcioglu MK, Tukenmez B, Pamukcu Z, et al. The analgesic effects of gabapentin after spinal surgery: a randomized, double blind, placebo controlled trial. Anesthesiology. 2004;100:935-8.
8. Turan A, Memi D, Karamanliolu B, Yaiz R, Pamukcu Z, Yavuz E. The analgesic effects of gabapentin in monitored anesthesia care for ear-nose-throat surgery: a randomized controlled trial. Anesth Analg. 2004;99:375-8.

9. Woolf CJ, Chong MS. Preemptive analgesia-treating postoperative pain by preventing the establishment of central sensitization. Anesth Analg. 1993;77:362-79.
10. Timothy JB, Peter KZ, Esther M. Pogatzki Z. Mechanisms of incisional pain. Anesthesiology Clin N Am. 2005;23:1-20.
11. Charles P. Taylor, Timothy Angelotti, Eric Faumanc Pharmacology and mechanism of action of pregabalin: The calcium channel subunit as a target for antiepileptic drug discovery. Epilepsy Research 2007;73:137-50.
12. Fassoulaki A, Triga A, Meleemeni A, Sarantopolous C. Multimodal analgesia with gabapentin and local anesthesia prevents acute and chronic pain after breast surgery for cancer. Anaesth Analg. 2005;101:427-32.
13. Pandey CK, Priya S, Singh S, Singh U, Singh RB, Singh PK. Preemptive use of gabapentin significantly decreases postoperative pain and rescue analgesic requirements in laparoscopic cholecystectomy. Can J Anesth. 2004;51:358-63.
14. Dirks J, Fredensborg BB, Christensen D, Fomsgaard JS, Flyger H, Dahl JB. A randomized study of the effects of single-dose gabapentin versus placebo on postoperative pain and morphine consumption after mastectomy. Anesthesiology. 2002;97:560-4.
15. Durmus M, Kadir A, Saricicek V. The postoperative analgesic effects of a combination of gabapentin and paracetamol in patients undergoing abdominal hysterectomy: a randomised clinical trial. Acta Anaesthesia Scand. 2007;51(3);299-304.
16. Turan A, Karamanlioglu B, Memis D, Usar P, Pamukcu Z, Ture M. The analgesic effects of gabapentin after total abdominal hysterectomy. Anesth Analg. 2004;98:1370-3.
17. Menigaux, Adam F, Guignard B, Sessler DI, Chauvin M. Preoperative gabapentin decreases anxiety and improves early functional recovery from knee surgery. Anesth Analg. 2005;100:1394-9.
18. Mujadi, Refai, Katzarov MG, Dehrab NA,Batra YK, Qattan. Preemptive gabapentin reduces postoperative pain and opioid demand following thyroid surgery. Can J Anesth. 2006;53;268-73.
19. Bartholdy J, Hilsted KL, Hjortsoe NC, Engbaek J Dahl J. Effect of gabapentin on morphine demand and pain after laparoscopic sterilization using filshie clips. a double blind randomized clinical trial. British Med Anaesthesiology. 2006;12:1471-4.
20. Lenzhofer R, Moser K. Analgesic effect of tramadol in patients with malignant diseases. Wiener Medizinische Wochenschrift. 1984;134(8):199-202.
21. Ruoff GE. Slowing the initial titration rate of tramadol improves tolerability. Pharmacotherapy. 1999;19(1):88-93.
22. Tagarro, I, Herrera J, Barutell C, Diez MC, Marin M, Samper D, et al. Effect of a simple dose-escalation schedule on tramadol tolerability: assessment in the clinical setting. Clinical Drug Investigation. 2005;25(1):23-33.

Cite this article as: Modak SD, Magar J, Kakad V. Pre-emptive gabapentin for postoperative pain relief in abdominal hysterectomy. Int J Res Med Sci 2016;4:3755-9.