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Original Research Article

The efficiency of Lower Abdominal Analgesia Using 600 Mg Gabapentin as Part of the Management of Post-Operative Pain

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Abstract

Introduction: Gabapentin is a medication approved as an anticonvulsant; however also used to treat neuropathic pain and hyperalgesia. It works by reducing the excitability of neurons in the posterior horn of the spinal cord, thereby reducing central sensitization. Gabapentin is effective in reducing postoperative pain, and its use can lead to a decrease in opioid consumption and related side effects.

Aims and objectives: To analyse the efficacy of gabapentin given at 600 mg to manage post-operative lower abdominal pain.

Methods: The study involved 50 randomly assigned participants receiving either gabapentin or a placebo before surgery. Standard monitoring and anaesthesia were used during the procedure, and postoperative pain was evaluated using the VAS score. Patients were given patient-controlled analgesia with morphine, and the primary outcome was the amount of morphine consumed in the first 24 hours. Secondary outcomes included VAS scores, the timing of analgesia rescue, and adverse events.

Results: This randomized experiment with 50 patients in each group indicated that gabapentin was related to significantly reduced pain scores at 0, 2, and 24 hours after surgery compared to a placebo. The trial was conducted on patients who had had surgery. After six and twelve hours following surgery, there was no discernible change in the levels of pain experienced by the patients. The placebo group reported significantly more instances of nausea, but the difference did not reach statistical significance.

Conclusion: Pre-emptive administration of gabapentin in the first 24 hours after surgery can effectively reduce postoperative opioid consumption and alleviate discomfort in patients undergoing non-obstetric lower abdominal surgery.

Keywords: Gabapentin, Post-Operative Analgesia, Analgesia, Opioid.

Introduction

Pain following surgery may include inflammatory, neurogenic, and visceral components and is not always strictly nociceptive. As a result, multimodal analgesic strategies that use various medications that work on several analgesic processes are becoming more and more common. Post-operative discomfort hinders surgical and anaesthetic recovery [1]. Although popular, due to their negative side effects and some types of pain are more severe, opioids cannot be used for patient-controlled analgesia. Do not react well to them. A combination of analgesics plan

using a mixture of analgesics, both opioid and non-opioid medicines, are frequently employed to improve the effectiveness of analgesics & decrease opioid needs and side effects. This is due to the diversity of mechanisms underlying postoperative pain [2].

Since 1993, gabapentin, a structural analogue like gamma-aminobutyric acid, has been approved as an anticonvulsant. It has also successfully treated reflex sympathetic dystrophy, neuropathic pain, post-herpetic neuralgia, and diabetic neuropathy. Gabapentin pre-treatment can stop the onset of hyperalgesia. Studies have shown a shared mechanism between experimental heat-induced secondary hyperalgesia and mechanical hyperalgesia around a wound in post-operative patients and how central neuronal sensitization affects postoperative pain [3,4]. The central sensitization-related nociceptive mechanism is specifically affected by gabapentin. Both in humans and in animals, gabapentin, as well as morphine, have complementary analgesic outcomes. The research aims to determine how pre-operative oral gabapentin administration affects post-operative pain in individuals having approximately two-hour abdominal operations [5].

To alleviate postoperative pain, primarily three groups of medications-anti-inflammatories, local anaesthetics, and opioids are used. Unfortunately, these drugs' negative effects prevent long-term clinical usage of them. Postoperative pain is managed with a brand-new drug called gabapentin. It differs from other commonly used drugs in its mode of action and possesses antihyperalgesic properties [6].

Gabapentin reduces the hyperexcitability of the posterior horn neurons brought on by lesions, which causes central sensitization. The postsynaptic binding of gabapentin to the dorsal horn neurons' voltage-dependent calcium channels may cause the antihyperalgesic activity, resulting in reduced entry of calcium into nerve terminals, which results in a decrease in neurotransmitter release [7,8]. The action effects of gabapentin, an antiepileptic drug (AED), upon the receptors for NMDA, sodium channels, monoaminergic pathways, and the opioid system are additional potential biological processes. In 1994, gabapentin was first made available as a drug used to treat epilepsy (AED), mostly partial seizures. After oral dosage with the maximum tolerated and well-absorbed side effects, it is an anticonvulsant. Over two to three hours, plasma concentration is observed. Gabapentin's most often reported side effects are drowsiness, somnolence, exhaustion, ataxia, and peripheral oedema [9,10].

A hysterectomy. To ascertain the adverse reactions of gabapentin (600 mg), Ajori et al. on nausea, vomiting, and meperidine intake before abdominal hysterectomy. A VAS, or visual analogue scale, measured pain at 1, 4, 6, 12, & 24 hours after surgery [11]. According to this study, the total amount of meperidine taken, Both the total amount ingested in the group receiving placebo and in the gabapentin treatment, were significantly less for the gabapentin group than the placebo group for every time. Interval. PONV and antiemetics are used in the gabapentin group. Medication usage was dramatically decreased [12].

Therefore, preventive administration of 600 mg gabapentin orally minimizes postoperative pain & PONV, as well as analgesic and antiemetic medication use in patients having abdominal hysterectomies [13].

There may be dose-restricting side effects with gabapentin, making it impossible for some individuals to reach therapeutic plasma levels. According to studies, there is no discernible difference between individuals receiving a larger dose of gabapentin and individuals receiving less of it regarding the frequency of side events

[14]. The negative effects of gabapentin that are most frequently mentioned include sleepiness and vertigo. Clinical withdrawal symptoms that neither resemble alcohol withdrawal nor benzodiazepine withdrawal can occur after the rapid stopping of strong-dose gabapentin used to avoid prolonged postsurgical pain. Within 1-2 days, irritation, agitation, nervousness, palpitations, and diaphoresis are among the signs and symptoms. A patient with persistent back pain experienced status epilepticus and generalized seizures due to gabapentin withdrawal [15].

Tapering should always be done, especially in patients receiving greater dosages; despite dose tapering, withdrawal symptoms can still occasionally be seen. It has been said that gabapentin is a safe and well-tolerated medication [15,18]. Studies on safety-related topics have documented negative side effects such as drowsiness, disorientation, headaches, nausea, ataxia, & weight gain. These adverse effects, however, often go away over time and may be uncomfortable for a postoperative patient in an acute environment, which was typically documented following long-term gabapentin use. Research documenting these side effects employed the medication for 8 weeks at levels adjusted to a daily maximum of 3600 mg or until serious negative effects appeared [19].

Methods

Study design

At our hospital's outpatient department, 50 patients participated in a randomised, double-blind trial. One day before the procedure, all Random assignment of eligible individuals to the medication group (600 mg oral) with the control group was done. Receiving placebo using a generated computer number. The research team unzipped the sealed envelope containing the random number two hours before the procedure. Following the opening of Each group received both 600 mg of gabapentin and a placebo pill from the research team. In the presence of the research team, the participants ingested the medications.

Standard noninvasive surveillance of the subjects was done in the operating theatre. Both 0.05 mg kg-1 of midazolam and 2 g kg-1 of fentanyl was given intravenously to all participants. Propofol intravenously dosed at 2 mg/kg was used to induce anaesthesia. Atracurium 0.5 mg kg-1 helped with endotracheal intubation. After surgery, all patients received Neostigmine, a muscular block antagonist, 0.04 mg kg-1. A simple mask for the face was used to administer 10 litres of oxygen per minute to the individual in the recovery area. The anaesthetist resident evaluated the initial postoperative pain score in the recovery area.

The recovery room was equipped with PCA (patient-controlled analgesia) using morphine intravenously. Patients' pain levels are quantified on a scale resembling a straight, 100-mm-long straight line. The patient chooses a position on the contour line that best depicts the patient's level. of discomfort during the VAS evaluation. The VAS score is calculated using a ruler on the reverse of the sheet marked in mm. Scores of 0 indicate no pain, and 10 indicate intense, intolerable pain. If the VAS value was more than 3, The PCA device's operation was also demonstrated to the patients. The basic limits of the PCA pump were a minimum dose of 1 mg, a maximum dosage of 6 mg within an hour, and a time limit of 5 minutes.

The main result was the total morphine consumed in the first 24 hours following surgery. The score obtained from the VAS at rest and while moving, the timing of the initial postoperative rescuing analgesia, and the frequency of adverse events were secondary results.

Inclusion and exclusion criteria

We included Patients between the ages of 18 and 65 having an American Society of Anesthesiologists (ASA) health rating of I-II who were scheduled for elective

nonobstetric lower abdomen surgery during the general anaesthetic. If the participant's body weight was within 20% of their ideal weight range and their surgery was less than 4 hours, they were enrolled in the study.

(1) A prior history of using medication was one of the exclusion criteria for allergies; (2) analgesic and NSAID use within the first twelve hours of surgical procedures; (3) history of physical trauma within the first four days of surgical procedures; (4) the administration of psychiatric medications; (5) diabetes, kidney disease, or liver disease; (6) prior use of gabapentin before the perioperative period; and (7) contraindications to gabapentin, paracetamol, morphine; (8) breastfeeding and pregnant patients; (9) usage of the peripheral and neuraxial block prior or during the surgical procedure.

Statistical analysis

The study used SPSS 25 for effective statistical analysis. The continuous data has been written in mean ± standard deviation, while the discrete data has been presented as frequency and its respective percentage. As a statistical tool, ANOVA made proper percentage comparisons between the various groups. The level of significance was considered to be $p<0.05$.

Ethical approval

Each patient was explained the study process, and consent was obtained from each. The Ethical Committee of the concerned hospital has approved the study process.

Results

Two randomized treatment groups each received 50 patients, and the distribution of subjects was equal across both groups. The subjects' traits in the two categories were not significantly different. The percentage of females was 76% and 84% for gabapentin and placebo, respectively. The ASA II was 76% and 88% in gabapentin and placebo, respectively.

Table 1: Baseline characteristics of participants

Characteristics	Gabapentin (n=25)	Placebo (n=25)	P-value
Age (years)	42.67±10.31	44.65±10.56	0.422
Gender, n (%)			0.396
Male	6 (24)	4 (16)	
Female	19 (76)	21 (84)	
ASA physical status, n (%)			0.344
I	6 (24)	3 (12)	
II	19 (76)	22 (88)	
Body height (cm)	162.23±5.90	162.45±5.99	0.767
Body weight (kg)	61.12±8.09	60.23±8.19	0.319
Surgery duration (minutes)	137.12±41.78	130.08±34.5	0.397
The total amount of intraoperative fentanyl (µg)	177.89±59.7	186.56±60.7	0.485
the procedure, n (%)			0.157
herniotomy/hernioplasty	3 (12)	3 (12)	
Laparotomy myomectomy	3 (12)	2 (8)	
Laparotomy hysterectomy	7 (28)	6 (26)	
Appendectomy	2 (8)	2 (8)	
Laparotomy salpingo-oophorectomy	2 (8)	7 (28)	
Others	8 (32)	5 (20)	

When a patient activates PCA for the first time, postoperative rescue analgesia starts. When patients in the two groups used morphine PCA for the first time, there were noticeable timing disparities (Table 2).

Table 2: Time for first post-operative rescue analgesia

Morphine IV (PCA)	Gabapentin (n=30)	Placebo (n=30)	p-value
PCA requirement for the first time (minutes)	162.1 (27-992)	67.9 (11-372)	<0.001

The unfavourable effects of preventive analgesia were evaluated within the initial 24 hours following surgery; there were reports of heartburn, nausea, and vomiting disorientation. The placebo group experienced more nausea, but statistical analysis revealed no discernible difference (Table 3).

Table 3: Adverse effects of anaesthesia in the first 24 hours after the surgical procedure

Side effects	Gabapentin (n=30)	Placebo (n=30)	p-value
dizziness, n (%)			1.000
Yes	2 (8)	2 (8)	
No	23 (92)	23 (92)	
Vomiting, n (%)			
Yes	1 (4)	1 (4)	1.000
No	24 (96)	24 (96)	
hyperacidity, n (%)			1.000
Yes	1 (4)	2 (8)	
No	24 (96)	23 (92)	
nausea, n (%)			0.261
Yes	2 (8)	4 (16)	
No	23 (92)	21 (84)	

At each time point, compared to the control group, the gabapentin group required considerably less morphine overall. (Table 4).

Table 4: Total requirement of morphine in first 24 hours in both gabapentin and placebo group

	Timing (hours)	Morphine (mg)
Gabapentin	2	0.5
	6	1.3
	12	2.0
	24	2.4
Placebo	2	1.4
	6	2.7
	12	4.0
	24	5.3

At 0, 2, and 24 hours after surgery, the gabapentin group's VAS scores were considerably lower than those of the placebo group both at rest and when moving. Both groups' VAS scores at six and twelve hours after surgery were comparable (Table 5).

Table 5: post-operative mean VAS in first 24 hours.

	Timing (hours)	Mean VAS score
Gabapentin	0	0.6
	2	1.4
	6	1.6
	12	1.5
	24	1.3
Placebo	0	1.6
	2	2.0
	6	1.8
	12	1.7
	24	2.3

Discussion

According to patients, one of the most typical side effects of lower abdominal surgery was postoperative pain. Pre-emptive analgesia with gabapentin, administered two hours before surgery, has been shown to lessen postoperative pain and the need for postoperative pain medication [16]. A study aimed to evaluate the effectiveness of oral gabapentin 600 mg as a preventive analgesic to lessen postoperative pain & morphine needs after nonobstetric low abdominal surgery. Two hours before the skin incision, eligible Patients were randomized into one of two groups: placebo or 600 mg of oral gabapentin. During the first 24 hours following surgery, the total amount of morphine needed, VAS result, and adverse effects including first-time analgesic demand and evaluation. Oral gabapentin 600 mg is used as an oral preventative analgesia after nonobstetric low abdominal surgery and lessens postoperative pain and morphine consumption [21].

According to preliminary clinical research, gabapentin may have analgesic effects and lessen the requirement of opioids for postoperative patients. Investigating the analgesic and opioid-sparing drug side consequences of gabapentin given within the initial day after an abdominal hysterectomy was the goal of the current investigation [17]. In a randomized, double-blind study, 80 patients received either a placebo or oral gabapentin dosages of 1200 mg one hour before surgery., followed by 600 mg or placebo doses eight, sixteen, and twenty-four hours later. Patients received 2.5 mg of morphine administered under patient control with a 10-minute lock-out period for the first 24 hours following surgery. Vomiting was graded as present or absent at 2, 4, 22, and 24 hours postoperatively, and the pain was measured using at rest and while moving using a visual analogue scale (VAS). Nausea, sleepiness, and light-headedness were evaluated verbally on a four-point scale. On the first day after an abdominal hysterectomy, gabapentin for the entirety dosage of 3000 mg resulted in a 32% reduction in morphine intake while having no discernible impact on pain scores. There were no discernible variations in side effects between trial groups [22].

Recently, the anticonvulsant gabapentin has been recommended as a successful "analgesic" after surgery. Evaluation regarding the analgesic strength, opioid-sparing effects, and negative outcomes of gabapentin administration following perioperative operations were the main objectives of the study. The outcome measures, which included the total quantity of opioids ingested in 24 hours, pain scores on the odds ratios, ratios for means, and mean weighting differences (as well as the adverse effects) for the visual analogue scale, were combined using either fixed or random effects models. However,

gabapentin increases the likelihood of sleepiness and opioid-related adverse effects, while decreasing analgesic consumption disorientation. Gabapentin also enhances the analgesic effects of opioids at both rest and with movement [23].

Recently, the anticonvulsant gabapentin has been recommended as a successful "analgesic" after surgery. The research aimed to investigate the analgesic efficacy and opioid-sparing effects of using gabapentin as preventative analgesia in a single dosage. In brief, preventive gabapentin administration reduces scores for pain and the first day's use of painkillers following inguinal hernia repair [24].

A key aspect influencing anaesthesia and surgery is postoperative pain. In the present research, the ramifications of 1200 mg of the anticonvulsant gabapentin works by blocking Ca2+-dependent voltage-dependent channels were evaluated for their ability to reduce patients' postoperative discomfort having belly hysterectomy surgery [20]. The current study included 50 patients with hysterectomies. 2 hours before surgery; subjects were given either a placebo or 1200 mg of gabapentin. Two hours, six hours, twelve hours, and twenty-four hours following surgery, the quantity of morphine used and the intensity of the postoperative pain were assessed. Age, length of operation, Body mass index, and anaesthesia did not significantly differ between the two groups [25].

In comparison to the placebo group, the gabapentin group's mean pain intensity was considerably reduced. The average amount of morphine given to the placebo group was significantly larger than the gabapentin drug class. Within the control group, nausea and vomiting were more frequent than in the gabapentin category. Following surgery, the group taking gabapentin needed considerably less ambulation time than the placebo group. The patient could ambulate sooner because of the 1200 mg of gabapentin, which also decreased postoperative pain & the requirement for opioids. No negative side effects of note were found [25].

Conclusion

The study has concluded that gabapentin is effective in reducing post-operative pain at a dosage of 600 mg and may reduce the necessity of opioid infusion post-operatively. In the first 24 hours following surgery, pre-emptive gabapentin reduces postoperative opioid consumption. As it prevents neurotransmitter excitation, gabapentin significantly lessens the 2 current-dependent calcium channel subunit that experiences severe postoperative discomfort. Following non-obstetric lower abdominal surgery, pre-emptive analgesic medication successfully reduced morphine requirements and postoperative discomfort with 600 mg oral gabapentin. Overall, this study has highlighted clinically important management of postoperative analgesia, which would benefit by avoiding opioid consumption.

References

1. Block BM, Liu SS, Rowlingson AJ, Cowan AR, Cowan JA, Block CL. Efficacy of postoperative epidural analgesia: A meta-analysis. JAMA. 2003; 290:2455–63
2. Dickenson A. Neurophysiology of opioid poorly responsive pain. Cancer Surv. 1994;21:5–16.
3. Fishman S, Borsook D. Opioids in pain management. In: Benzon H, Raja S, Molloy RE, Strichartz G, editors. Essentials of pain medicine and regional anesthesia. New York: Churchill Livingstone; 1999; 51–4.
4. Rosner H, Rubin L, Kestenbaum A. Gabapentin adjunctive therapy in neuropathic pain states. Clin J Pain. 1996;12:56–8.
5. Backonja M, Beydoun A, Edwards KR, Schwartz SL, Fonseca V, Hes M, et al. Gabapentin for the symptomatic

treatment of painful neuropathy in patients with diabetes mellitus: a randomized controlled trial. JAMA. 1998; 280:1831–6.
6. Rowbotham M, Harden N, Stacey B, Bernstein P, Magnus-Miller L. Gabapentin for the treatment of postherpetic neuralgia: A randomized controlled trial. JAMA. 1998;280:183 7–42.
7. Mellick GA, Mellick LB. Reflex sympathetic dystrophy treated with gabapentin. Arch Phys Med Rehabil. 1997;78:98–105.
8. Mao J, Chen LL. gabapentin in pain management. Anesth Analg. 2000; 91: 680–7.
9. Dirks J, Moiniche S, Hilsted KL, Dahl JB. Mechanisms of postoperative pain: Clinical indications for a contribution of central neuronal sensitization. Anesthesiology. 2002;97:1591–6.
10. Shimoyama M, Shimoyama N, Inturrisi CE, Elliott KJ. gabapentin enhances the antinociceptive effects of spinal morphine in the rat tail-flick test. Pain. 1997;72:375–82.
11. Eckhardt K, Ammon S, Hofmann U, Riebe A, Gugeler N, Mikus G. Gabapentin enhances the analgesic effect of morphine in healthy volunteers. Anesth Analg. 2000; 91: 185–91.
12. Caraceni A, Zecca E, Martini C, De Conno F. Gabapentin as an adjuvant to opioid analgesia for neuropathic cancer pain. J Pain Symptom Manage. 1999; 17:441–5.
13. Y. P. Maneuf, M. I. Gonzalez, K. S. Sutton, F. Z. Chung, R. D. Pinnock, and K. Lee, Cellular and molecular action of the putative GABA-mimetic, gabapentin, Cellular and Molecular Life Sciences, BioMed Research International. 2003; 60(4):742–750.
14. B. Gidal and R. Billington, New and emerging treatment options for neuropathic pain, The American Journal of Managed Care, 2006; 12: S269–S278.
15. J. B. Dahl, O. Mathiesen, and S. Møiniche, Protective premedication': an option with gabapentin and related drugs? A review of gabapentin and pregabalin in the treatment of post-operative pain, Acta Anaesthesiologica Scandinavica, 2004; 48(9): 1130–1136, 2004.
16. G. J. Sills, Not another gabapentin mechanism!, Epilepsy Currents, 2005; 5(2):75–77.
17. R. D. C. Elwes and C. D. Binnie, Clinical pharmacokinetics of newer antiepileptic drugs. Lamotrigine, vigabatrin, gabapentin and oxcarba zepine, Clinical Pharmacokinetics, 1996; 30(6):403–415.
18. J. D. Markman and R. H. Dworkin, Ion channel targets and treatment efficacy in neuropathic pain, Journal of Pain, 2006; 7:S38–S47.
19. A. Z. Segal and G. Rordorf, Gabapentin as a novel treatment for postherpetic neuralgia, Neurology, 1996; 46(4): 1175–1176.
20. H. Rosner, L. Rubin, and A. Kestenbaum, Gabapentin adjunctive therapy in neuropathic pain states, Clinical Journal of Pain, 1996; 12(1): 56–58.
21. C. P. Taylor, N. S. Gee, T. Z. Su et al., A summary of mechanistic hypotheses of gabapentin pharmacology, Epilepsy Research, 1998; 29(3):233–249.
22. Sukmono R, Ramlan A, Andy A, Satoto D, Septica R. Pre-emptive 600 mg oral gabapentin reduces morphine requirements and postoperative pain following non-obstetric lower abdominal surgery. Anaesthesiol Intensive Ther. 2022;54(1):42-47.
23. Dierking G, Duedahl TH, Rasmussen ML, Fomsgaard JS, Møiniche S, Rømsing J, Dahl JB. Effects of gabapentin on postoperative morphine consumption and pain after abdominal hysterectomy: a randomized, double-blind trial. Acta Anaesthesiol Scand. 2004 Mar;48(3):322-7.

24. Peng PW, Wijeysundera DN, Li CC. Use of gabapentin for perioperative pain control - a meta-analysis. Pain Res Manag. 2007 Summer;12(2):85-92.
25. Mahoori A, Noroozinia H, Hasani E, Hosainzadeh S. The effect of pre-operative administration of gabapentin on post-operative pain relief after herniorrhaphy. Saudi J Anaesth. 2014 Apr;8(2):220-3.
26. Frouzanfard F, Fazel MR, Abolhasani A, Fakharian E, Mousavi G, Moravveji A. Effects of gabapentin on pain and opioid consumption after abdominal hysterectomy. Pain Res Manag. 2013 Mar-Apr;18(2):94-6.