Al-Azhar University Journal
for Virus Research and Studies

The Role of Gabapentin as Multimodal for Postoperative Pain Control in a Patient Undergoing Elective Abdominal Surgeries

Manal Foad Abd ELmoniem [1*]

[1]Department of anesthesia, LCU and Pain management, Faculty of Medicine for Girls, Al-Azhar University, Cairo, Egypt.

***Email: d_taha66@yahoo.com**

Abstract

Gabapentin is widely used to manage chronic pain and has been shown to reduce postoperative opioid consumption. This study's objective was to assess the analgesic impact of gabapentinoids administered to adult patients before surgery. Research included randomization and control looking at the utilization of gabapentinoids in adult abdominal surgery 50 adult patients who were scheduled for voluntary abdominal surgery were randomly split into two equal groups. One hour prior to surgery, Group, I was given an oral placebo surgery, and Group II received oral gabapentin 600 mg. PONV prevalence, VAS, and the requirement for rescue analgesia were reported. There was a significant decrease in analgesia requirements. And a lower post-operative pain score in group II. The risk of nausea and vomiting following surgery was similarly decreased in group II. Gabapentin is effective as a Multimodal for postoperative pain control and VAS reduction of 24 hours.

Key words; Gabapentin, Postoperative, Pain control, VAS.

1. Introduction

A crucial component of surgical patient care is effective postoperative pain control. An early restoration of intestinal function, reduced risk of thrombosis, lower cardiopulmonary problems, earlier mobility, quicker recovery, and shorter hospital stays are all related to effective postoperative pain management. [1]. Morphine had been recommended as the first line to prevent postoperative pain; however, adverse effects like nausea and vomiting (PONV) have decreased the use of morphine. Gabapentin may be used as postoperative pain control and reduce the use of opioids [2]. In order to prevent the negative effects of an opioid like PONV, gabapentin has been increasingly proved in "fast-track" packages and better recovery following surgical procedures [3], Although gabapentin has a structural similarity with the neurotransmitter GABA (gamma-aminobutyric acid), it does not alter the radioligand binding of GABAA or GABAB, does not biologically transform into GABA or a GABA agonist, and does not impede the uptake or degradation of GABA [4]. In the central nervous system, gabapentin

also inhibits the production of the neurotransmitter glutamate [5] and binds to the alpha 2 delta subunits of calcium channels [6]. The European Society of Regional Anesthesia and Pain Management (Geneva, Switzerland) opposes the use of gabapentin during surgery, although the American Pain Society (Glenview, Illinois) favors it [7]. Modern multimodal anesthetic regimens for pain management include the use of a mixture of both opioid and nonopioid analgesic medications [8]. This study's objective is to assess gabapentin's effectiveness as a preventative analgesic for postoperative pain management in patients having abdominal surgery under general anesthesia.

2. Patients and Methods

AL-Zahra University Hospital in Cairo, Egypt, hosted this prospective, randomized, and double-blind control trial from August 2021 to August 2022. Fifty patients (ASA I and II) of all sexes, aged 21 to 60, having optional operation with general anesthesia provided their informed written permission. All patients had in-depth examinations. Routine tests for urea, creatinine, blood sugar, urine test, chest x-ray, and ECG were performed. *Exclusion* criteria: ASA grades III and IV, anemia, impaired renal function, heart illness, hypertension, COPD and asthma, diabetes, Patients who are pregnant, using oral medications that interfere with enteric absorption, taking sedatives, hypnotics, antidepressants, or other medicines that have an influence on the nervous system. According to the "chit in the box" approach, patients were divided into two groups of 25 each.

2.1 Control group or Group I- got an oral Placebo (VITAMINES).

2.2 Gabapentin group or Group II- got 600 mg of Gabapentin (UNIPHARMA) -Egypt.

One hour before the procedure, a separate anesthesiologist who was unrelated to the research administered the medication chosen for the study along with a drink of water.

Patients' baseline vital signs, including pulse rate, SBP, DBP, and MAP O2 saturation, were taken one hour (h) prior to entering the operating room. Lactated ringer infusion was begun after the intravenous line was established using a 20G IV canula. Fentanyl 1 mcg kg-1 and Midazolam 0.05 mg kg-1 IV premedicated all patients in the same way. Propofol and atracurium were used to produce anesthesia after three minutes of preoxygenation with 100% oxygen. Patients were given an adequate size cuffed endotracheal tube for intubation, isoflurane to maintain anesthesia, and atracurium 0.1 mg/kg in a 1:1 combination of oxygen and air.

Patients' vital signs (HR and MAP) were monitored utilizing a monitor (Drager Vista XL; Drager Medical System, Inc. USA., Telford Germany) at 0, 5-, 10-, 15-, and 30-minutes following intubation. Neostigmine 0.05 mg kg-1 and atropine 0.01 mg kg-1 IV were administered after surgery to reverse any remaining neuromuscular inhibition. After a satisfactory reversal, patients were extubated. Ephedrine 4 mg IV was administered in progressive dosages to treat a mean arterial pressure reduction of more than 30% from the preanesthetic baseline value. Atropine 0.5 mg was administered in increasing dosages to patients whose heart rates fell below 50 beats per minute. IV After extubation (0 h), 1, 3, 5, 12, and 24 h post-operatively, postoperative pain was evaluated using the visual analog score (VAS)visual pain analog scale (VAS) from 0 to 10 cm (0 = no pain, 10 = greatest excruciating agony). Both groups received Pethdine 1 mg/kg slow intravenous every 12 hours for post-operative analgesia. It must be emphasized that the first

Rescue injection of Diclofenac 1.5 mg/kg was administered through intravenous in the Post anesthesia Care Unit.

2.3 Statistical Analysis

The Statistical Package for Social Science (SPSS), published in 2015 for Windows, version 23.0, was utilized to gather, review, code, and input the data. New York's Armonk: IBM Corporation. Both the qualitative and the quantitative variables were given as percentages and numbers including the mean, standard deviations, and ranges for the quantitative data. Chi-square was utilized to compare groups based on qualitative data, while independent t-test was used to compare two independent groups based on quantitative data and parametric distribution. The allowable margin of error was set at 5%, while the confidence interval was set at 95%. Consequently, the p-value was deemed substantial at <0.05.

3. Results

The tables below show main results.

Table 1: Demographic data

	Group I (no. = 25)	Group II (no. = 25)	Test value	P-value
	Mean ± SD	Mean ± SD		
Age(years)	44.25 ± 8.32	43.58 ± 6.34	0.320•	0.750
Sex			0.725*	0.394
Males	12 (48.0%)	15 (60.0%)		
Females	13 (52.0%)	10 (40.0%)		
ASA classification			2.381*	0.122
I	15 (60.0%)	20 (80.0%)		
II	10 (40.0%)	5 (20.0%)		
Duration of surgery (h)	1.32 ± 0.85	1.25 ± 0.72	0.314•	0.754

Demographic parameters like age, sex ratio, ASA, and Duration of surgery. P >0.05: Non-significant (NS).

Table 2: Heart rate (HR) (b\m).

Heart rate (beat/min)	Group I (no. = 25)	Group II (no. = 25)	Test value	P-value
	Mean ± SD	Mean ± SD		
Baseline	91.06 ± 7.32	90.54 ± 7.54	0.247	0.806
5 min	109.4 ± 5.62	106.2 ± 4.45	2.232	0.030
10 min	98.81 ± 7.23	89.7 ± 6.47	4.695	<0.001
15 min	93.74 ± 6.45	79.18 ± 6.75	7.798	<0.001
30 min	92.52 ± 7.08	78.21 ± 9.42	6.072	<0.001

There was a significant decrease in HR in group II at 5, and 10,15,30 min after intubation. P <0.05..

Table 3: Mean arterial blood pressure (MABP) (mmHg)

MABP (mmHg)	Group I (no. = 25)	Group II (no. = 25)	Test value	P-value
	Mean ± SD	Mean ± SD		
Baseline	91.81 ± 12.65	92.31 ± 9.65	0.157	0.876
5 min	91.35 ± 7.75	86.45 ± 8.14	2.180	0.034
10 min	89.41 ± 8.62	83.68 ± 8.65	2.346	0.023
15 min	90.50 ± 7.34	82.51 ± 7.65	3.768	<0.001
30 min	90.32 ± 10.47	80.77 ± 8.92	3.472	0.001

There was a significant decrease in HR in group II at 5, and 10,15,30 min after intubation. P <0.05..

Table 4: Visual analogue scale (VAS)

VAS	Group I (no. = 25)	Group II (no. = 25)	Test value	P-value
	Mean ± SD	Mean ± SD		
0 hr	2.51 ± 0.68	1.82 ± 0.54	3.973	<0.001
1 hr	2.95 ± 0.51	2.21 ± 0.67	4.394	<0.001
3 hrs	3.32 ± 0.46	2.32 ± 0.75	5.683	<0.001
5 hrs	3.60 ± 0.35	3.18 ± 0.81	2.380	0.021
12 hrs	4.52 ± 1.36	3.64 ± 0.92	2.680	0.010
24 hrs	4.57 ± 1.41	3.87 ± 0.82	2.146	0.037

There was a significant decrease in VAS in group II at (0 h), 1, 3, 5, 12, and 24 h post-operatively P <0.05.

Table 5: Time of first rescue of analgesic requirement

Group I (no. = 25)	Group II (no. = 25)	Test value	P-value
Mean ± SD	Mean ± SD		
180.0 ± 63.0(min)	360.0 ± 40.0(min)	12.060	<0.001

There was a significant increase in Time to first rescue of analgesic requirement in group II P <0.05.

Table 6: Analgesia requirement and Total requirement of analgesia. (mg)**.**

	Group I (no. = 25)	Group II (no. = 25)	Test value	P-value
	No. (%)	No. (%)		
Analgesia requirement				
No	**15 (60.0%)**	**23 (92.0%)**	**7.018**	**0.008**
Yes	**10 (40.0%)**	**2 (8.0%)**		
Total requirement of analgesia(mg)				
Mean±SD	**300.0 ± 50.0**	**75.0 ± 25.0**	**20.125**	**<0.001**

There was a significant decrease in analgesia requirement and total requirement of analgesia.in group II post-operatively. P <0.05.

4. Discussion

Commonly recommended for controlling seizures is gabapentin. In animal models, gabapentin has been shown to lessen hypersensitivity related to nerve damage (hyperalgesia), postsurgical pain, and inflammation. Gabapentin operates on the nociceptive mechanisms involved in central sensitization [9]. Interestingly, trials involving breast tumor patients showed a considerable decrease in chemotherapy-induced nausea with the use of gabapentin, which led to the initial recognition of gabapentin's antiemetic benefits. The benefits of gabapentin on nausea and vomiting are most likely due to decreased tachykinin neurotransmission and a reduction in the need for postoperative opioids [10] regards hemodynamics. At 5, 10, 15, and 30 minutes after intubation, group II's HR and MAP substantially decreased. Neither group's ECGs showed any signs of hypotension, bradycardia, arrhythmias, or other abnormalities during the trial period. Memis and colleagues 2006 [11] stated that Patients who took gabapentin 800 mg one hour prior to surgery saw substantially lower MAP and HR in the first 10 minutes after endotracheal intubation than those who took 400 mg of the medication or a placebo ($p<0.05$). Fassoulaki and colleagues 2002 [12] revealed that the hemodynamic effects of laryngoscopy and intubation are considerably lowered when oral gabapentin is administered as a premedication. when they compared gabapentin as a premedication divided doses (400mg/6h) with a placebo. Serhat and colleagues 2007 [13], also observed the same response when they gave to patients 1000 mg of oral1000 mg gabapentin given I h before the operation. On the other hand, Jain et al. 2021 [14] found that There was no substantial difference in HR between the two groups (>0.05), however median BP, systolic BP, and diastolic BP changes from prepneumoperitoneum values were considerably reduced in group GB during pneumoperitoneum.

Regarding VAS measurements for postoperative pain the study's most recent findings revealed a substantial drop in VAS in the gabapentin group at 0 h, 1, 3, 5, 12, and 24 h post-operatively, which may indicate a synergistic interaction between gabapentin and fentanyl. The gabapentin group's reduced need for rescue analgesics further supports the synergistic effects of gabapentin pethidine. In abdominal procedures, gabapentin used beforehand greatly reduces postoperative discomfort and the need for rescue analgesics. These are consistent with our investigation; other studies have shown that preemptive gabapentin in dosages ranging from 300 mg to 1200 mg for the treatment of acute pain was associated with reduced VAS ratings for pain and decreased postoperative analgesic needs [15-21]. Soltanzadeh et al. 2011 [22] revealed that Patients who administered gabapentin had substantially reduced pain levels throughout the first postoperative day, both at rest and after coughing at 2 hours, 6 hours, and 12 hours following extubation. Ucak et al. 2011 [23] revealed a reduced pain score with the administration of gabapentin at 6 hours, 12 hours, 18 hours, 24 hours, 48 hours, and 72 hours during rest and cough). The VAS score was considerably lower, and the analgesia duration was longer in the gabapentin group. The synergistic impact of gabapentin and pethidine may also be responsible for the considerable rise in Time to First Rescue of Analgesic Requirement in Group II, according to recent research. Because of its affinity for the alpha-2 delta subunits of voltage-gated Ca++channels, gabapentin inhibits calcium influx, which in turn prevents the release of glutamate (excitatory neurotransmitter) [24]. As regards

postoperative nausea and vomiting or respiratory depression the current study found there were patients in the gabapentin group suffering from nausea or respiratory depression while there were two patients in the control group suffering from it.
Jain et al. 2021 found that no PONV- with significantly higher in the gabapentin group ($P < 0.01$), when he used Oral gabapentin as premedication in patients undergoing laparoscopic cholecystectomy [14]. Also. Kiani 2019 [25] stated that Gabapentin is a good drug for reducing PONV. Algharabawy and Abdelrahman 2021, [26] found that prior to laparoscopic abdominal surgery, gabapentin dosages of 600 mg or 900 mg were helpful in preventing PONV and reducing VAS in the 24-hour post-operative period without causing any negative side effects.

5. Conclusion

According to our study, gabapentin 600 mg administered one hour prior to abdominal surgery is useful for controlling PONV and lowering VAS over the 24-hour postoperative period. Additionally, gabapentin 600 mg has fewer negative effects.

References

1. Joshi GP, Ogunnaike BO. Consequences of inadequate postoperative pain relief and chronic persistent postoperative pain. Anesthesiol Clin North America. 2005;23(1):21–36.

2. Federico CA, Wang T, Doussau A, Mogil JS, Fergusson D, Kimmelman J: Assessment of pregabalin postapproval trials and the suggestion of efficacy for new indications: A systematic review. JAMA Intern Med 2019; 179:90–7.

3. Page AJ, Ejaz A, Spolverato G, et al. Enhanced recovery after surgery protocols for open hepatectomy – phy sociology, immunomodulation, and implementation. J Gastrointest Surg. 2015; 19:387–399.

4. Su Transport of gabapentin a amino acid drug by system L-amino acid transporter; a comparative study in astrocytes synaptosomes and CHO cells. Neurochem. 1995; 64:2125–2131. [PubMed] [Google Scholar].

5. Patel Placebo controlled study of gabapentin treatment of panic disorder. Pain. 2001; 90:217–226. [PubMed] [Google Scholar].

6. Gee NS, Brown JP, Dissanayake VU. The novel anticon-vulsant drug,gabapentin, binds to alpha 2 delta subunit of calcium channel. J Biol Chem. 1996; 271:5768–76. [PubMed] [Google Scholar].

7. The European Society of Regional Anaesthesia and Pain Therapy: Prospect. Available at: https://esraeurope.org/prospect/. Accessed June 14, 2020.
8. Meng FY, Zhang LC, Liu Y, et al. Efficacy and safety of gabapentin forthe treatment of postherpetic neuralgia: a meta-analysis of randomizedcontrolled trials. Minerva Anestesiol 2014; 80:556–67.

9. Mao J, Chen LL. Gabapentin in pain management. Anesth Analg. 2000;91(3):680–687.

10. Guttuso T Jr, Roscoe J, Griggs J. Effect of gabapentin on nausea induced by chemotherapy in patients with breast cancer. Lancet. 2003;361(9370):1703–1705.

11. Memis D, Turan A, Karamanlioglu B, Seker S, Ture M. Gabapentin reduces cardiovascular responses to laryngoscopy and tracheal intubation. Eur J Anaesthesiol. 2006;23(8):686–90. [PubMed] [Google Scholar].

12. Fassoulaki A, Patris K, Sarantopoulos C, et al. The analgesic effect of gabapentin and mexiletine after breast surgery for cancer. Anesth Analg. 2002;95 (4):985–991.

13. Serhat KOC, Dilek Memis, Necdet Sut. The preoperative use of gabapentin, dexamethasone and their combination in vericocele surgery: A randomised controlled trial. Anesth Analg. 2007; 105:1137–1142. [PubMed] [Google Scholar].

14. Jain R, Kumar M, Singh T, Rautela RS, Kumar S. Effect of oral gabapentinpremedicationon hemodynamic parameters and postoperative pain in patients of laparoscopic cholecystectomy: A randomized double-blind controlled study.J Anaesthesiol ClinPharmacol. 2021 Jan-Mar;37(1):67-72. DOI: 10.4103/joacp.JOACP_439_19. Epub 2021 Apr 10. PMID: 34103826 Free PMC article.

15. Pandey CK, Priye S, Singh S, et al. Preemptive use of gabapentin significantly decreases postoperative pain and rescue analgesic requirements in laparoscopic cholecystectomy. Can J Anaesth. 2004; 51:358–363.

16. Rorarius MG, Mennander S, Suominen P, et al. Gabapentin for the prevention of postoperative pain after vaginal hysterectomy. Pain. 2004; 110:175–181.

17. Dierking G, Duedahl TH, Rasmussen ML, et al. Effect of gabapentin on postoperative morphine consumption and pain after abdominal hysterectomy: a randomized, double-blind trial. Acta Anaesthesiol Scand. 2004; 48:322–327.

18. Turan A, Memis D, Karamanhoglu B, et al. The analge sic effects of gabapentin in monitored anesthesia care for ear–nose–throat surgery. Anesth Analg. 2004; 99:375–378. https://pubmed.ncbi.nlm.nih.gov/ 15271709.

19. Turan A, Karamanhoglu B, Memis D, et al. The analge sic effects of gabapentin after total abdominal hysterectomy. Anesth Analg. 2004; 98:1370–1373.

20. Turan A, Karamanhoglu B, Memis D, et al. Analgesic effects of gabapentin after spinal surgery. Anesthesiology. 2004; 100:935–938.

21. Eckhardt K, Ammon S, Hofmann U, et al. Gabapentin enhances the analgesic effect of morphine in healthy volunteers. Anesth Analg. 2000; 91:185–191.

22. Soltanzadeh M, Ebad A, Pipelzadeh M, et al. Gabapentin may relieve post-coronary artery bypass graft pain: a double-blind randomized clinical trial. Iran Cardiovasc Res J. 2011;5: 79---82.

23. Ucak A, Onan B, Sen H, et al. The effects of gabapentin on acuteand chronic postoperative pain after coronary artery bypassgraft surgery. J Cardiothorac Vasc Anesth. 2011; 25:824---9.

24. Stahl SM. Mechanism of action of alpha2delta ligands: voltage sensitive calcium channel (VSCC) modulators. J Clin Psychiatry. 2004; 65:1033–1034.

25. Kiani MH, Shayesteh AA, Ahmadzadeh A.An investigation into the effect of gabapentin capsules on the reduction of nausea and vomiting after chemotherapy in cancerous patients under platinum-based treatment J Family Med Prim Care. 2019 Jun;8(6):2003-2007. DOI: 10.4103/jfmpc.jfmpc_212_18.PMID: 31334170 Free PMC article.

26. Algharabawy WS and AbdElrahman TN. Optimal dosing of preoperative gabapentin for prevention of postoperative nausea and vomiting after abdominal laparoscopic surgery: A randomized prospective comparative study. EGYPTIAN JOURNAL OF ANAESTHESIA .2021, VOL. 37, NO. 1, 174–181.

27. Cavalcante AN, Sprung J, Schroeder DR,Weingarten TN. Multimodal analgesic therapy with gabapentin and its association with postoperativerespiratory depression. Anesth Analg. 2017;125(1):141-146.