

Effect of gabapentin in comparison with hydrocortisone on postlaparoscopic cholecystectomy pain control

Negin Ghadami¹, Arvin Barzanji², Karim Nasser^{1,3}, Farzad Sarshivi¹, Bijan Nouri³

¹Department of Anesthesiology, Faculty of Medicine, Kurdistan University of Medical Sciences, ²Department of Anesthesiology, Faculty of Paramedical, Kurdistan University of Medical Sciences, ³Social Determinants of Health Research Center, Kurdistan University of Medical Sciences, Sanandaj, Iran

ABSTRACT

Background and Aim: Although laparoscopic cholecystectomy causes less pain than open cholecystectomy, it is still not completely painless. Several methods have been used to relieve the pain of laparoscopic surgery. The aim of this research was to compare the effect of gabapentin and hydrocortisone on pain control after laparoscopic cholecystectomy. **Materials and Methods:** In this double-blind clinical trial, a total of 60 adult patients aged 18–70 years from both sexes American Society of Anesthesiologists Classification (ASA Classification 1 and 2) who were selected for laparoscopic cholecystectomy were divided into two groups of 30 subjects to be studied. 150 mg gabapentin and 100 mg hydrocortisone were administered to the first and second groups before the operation, respectively. Pain score and vital signs (systolic blood pressure and heart rate) were recorded. Data were fed into SPSS 23 software and analyzed using Fisher-test, independent *t*-test, and repeated measurement. $P < 0.05$ was considered as significance level. **Results:** Patients were similar in terms of age and sex. Mean score of visual analog scale (VAS) in the first 4 h after operation was 5.84 ± 2.33 and 5.20 ± 1.74 in the gabapentin group and was 7.03 ± 1.23 and 6.50 ± 1.30 in the hydrocortisone group ($P < 0.05$), respectively. Although mean VAS scores at 6, 12, and 18 h after operation showed no significant differences between gabapentin and hydrocortisone groups ($P > 0.05$), VAS score 24 hours after operation was 2.87 ± 1.57 and 3.92 ± 1.28 in gabapentin and hydrocortisone groups, respectively ($P < 0.05$), indicating a significant difference in VAS score between the two groups 2 and 24 h postoperation. **Conclusion:** The results of this study showed that gabapentin was more effective than hydrocortisone within the first 4 h of laparoscopic cholecystectomy. In addition, gabapentin was shown to be a better pain controller 24 h postoperation.

Keywords: Gabapentin, hydrocortisone, laparoscopic cholecystectomy, pain

Introduction

Pain is an unpleasant individual feeling and mental experience associated with active or potential tissue damage that can affect various systems in the body and lead to prolonged hospitalization.^[1] Acute pain is the pain caused by tissue damage and activation of sensory pain transducers in the site of lesion, which is developed after trauma, surgical procedures, and disease processes.^[2] Inappropriate pain treatment leads to continuation

and progression of pain to the chronic phase. Postoperative pain is the most common type of pain in nature, which is not adequately controlled in over 50% of surgical procedures. The incidence of pain immediately after laparoscopic cholecystectomy is a common side effect in this type of operation. Studies have indicated that postoperative pain in laparoscopic cholecystectomy can increase the chance of longer than one night stay in hospital up to 41%.^[3,4] Also, lack of proper acute pain control after laparoscopic cholecystectomy can lead to the development and progression of chronic pain (postlaparoscopic cholecystectomy syndrome).^[5]

Address for correspondence: Dr. Farzad Sarshivi, Department of Anesthesiology, Faculty of Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran.
E-mail: farzadsarshivimd@gmail.com

Access this article online

Quick Response Code:



Website:
www.jfmprc.com

DOI:
10.4103/jfmprc.jfmprc_407_18

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Ghadami N, Barzanji A, Nasser K, Sarshivi F, Nouri B. Effect of gabapentin in comparison with hydrocortisone on postlaparoscopic cholecystectomy pain control. J Family Med Prim Care 2019;8:652-6.

Gabapentin (Neurontin) is known as a seizure control spasmolytic drug as well as a structural analog of GAMA receptor^[6] with a proven effect in the treatment of chronic pain. Studies have indicated the usefulness of gabapentin in treatment of neuropathic pain as well as acute postoperative pain after breast and spinal surgeries. Gabapentin has also been effective in controlling acute pain after laparoscopic surgery.^[6-10]

Hydrocortisone is a member of nonsteroidal anti-inflammatory drug family. The benefits of this drug and its effectiveness in controlling postoperative pain have been demonstrated. Studies have shown that intraperitoneal hydrocortisone is useful to control postoperative laparoscopic cholecystectomy pain.^[11]

Laparoscopic cholecystectomy is a standard surgical procedure for the removal of gallbladder.^[12] Given that the damage caused by operation and the degree of incision in patients are similar, it can be concluded that the injury causing pain will be somewhat similar. Since the effect of gabapentin on controlling laparoscopic cholecystectomy postoperative pain has not been compared so far, this study was designed to compare the effect of gabapentin and hydrocortisone in postoperative pain management of laparoscopic cholecystectomy.

Materials and Methods

This prospective and double-blind clinical trial was designed to examine 60 adult patients aged 18–70 years from both sexes in ASA class 1 and 2 undergoing laparoscopic cholecystectomy. This study was approved by Ethics Committee of Kurdistan University of Medical Sciences, and informed consent was obtained after explaining the study process to patients.

The inclusion criteria were informed consent, ASA physical status 1 and 2, and 18–70 years of age. Recovery exclusion criteria were as follows: kidney and liver dysfunction, drug and alcohol abuse, history of chronic pain, associated diseases, such as blood pressure and diabetes, consumption of Non-steroidal anti-inflammatory drugs (NSAIDs) within 24 h before surgery, the need for additional sedative, and choice of open cholecystectomy.

After satisfaction of inclusion criteria, patients were divided into two groups of 30 subjects based on randomized blocking. Based on this randomization, patients received 150 mg of oral gabapentin or 100 mg of intravenous hydrocortisone 1 h before the operation. In the group receiving gabapentin, 150 mg of gabapentin was given in the form oral capsule 1.5 h before operation as well as 100 mL of normal saline. In the group receiving hydrocortisone, an empty capsule was orally given 1.5 h before the operation, and 100 mg of hydrocortisone solution in 100 mL of normal saline was injected to them.

The same anesthetization technique was used for both groups. Before induction of anesthesia in both groups, 500 mL of Ringer's serum was prescribed. Anesthesia was induced by administration of 2 µg/kg fentanyl, 2 mg/kg propofol, and

0.5 mg/kg atracurium per kilogram body weight. After intubation, maintenance of anesthesia was done with 1 MAC isoflurane and 4 L/min of oxygen. After the end of surgery, throat and mouth suction was performed. The effects of neuromuscular relaxant drug were reversed via administration of neostigmine (0.04 mg/kg body weight) and atropine (0.015 mg/kg body weight). The endotracheal tube was discharged when the patient was awake and the patient was transferred to recovery. 25 mg meperidine was used to relieve pain, and if necessary repeated.

The initial investigated outcome was the incidence and severity of pain among patients and the need for use of analgesics. The secondary outcome was the evaluation of sedation rate, vomiting, nausea, and respiratory problems. Pain assessment was performed using a 10 cm visual analog scale (VAS) ruler (0 indicating no pain and 10 most severe pain). Pain assessment was done 2, 4, 6, 12, 18, and 24 h after surgery by a trained nurse blinded to the used drugs. Moreover, the degree of nausea and vomiting, sedation level, and the need for analgesics were also recorded.

Data were fed into SPSS 23 software and analyzed using Fisher-test, independent *t*-test, and repeated measurement. $P < 0.05$ was considered as significance level.

Results

From February to November 2017, 60 subjects were evaluated from among the patients admitted to educational hospitals of Kurdistan University of Medical Sciences by satisfying inclusion criteria and attending up to the end of study. There was no significant difference in the number of subjects, sex, and ASA Classification between the two groups [Table 1].

In comparison of patients receiving gabapentin and hydrocortisone in the first 2 h and 24 h after operation, the former had a lower VAS score than the latter; however, no significant significance was observed in other hours. Furthermore, mean level of analgesic was significantly lower in the group receiving gabapentin than that of the group receiving hydrocortisone. Mean VAS score in the first 4 h after operation was 5.84 ± 2.33 and 5.20 ± 1.74 in the gabapentin group and was 7.03 ± 1.23 and 6.50 ± 1.30 in hydrocortisone group, respectively ($P < 0.05$). In addition, VAS score 24 h after operation in gabapentin and hydrocortisone groups was 2.87 ± 1.57 and 3.92 ± 1.28 , respectively ($P < 0.05$). The results showed that VAS scores were significantly different between

Table 1: Demographic data based on Fisher-test and independent *t*-test to determine the patients' age

Variable	Groups	
	Gabapentin (30)	Hydrocortisone (30)
Age (±SD)	43.33 (±11.82) yr.	47.70 (±12.73) yr.
Sex (Male:Female)	3:27	1:29
ASA Classification (I:II)	12: 18	9:21

Table 2: Scoring based on visual analog scale at different times (mean±SD) based on independent *t*-test and repeated measurement

	Time						Mean (±SD) meperidine received (mg)
	At 2 h	At 4 h	At 6 h	At 12 h	At 18 h	At 24 h	
Gabapentin	5.77±2.23	5.20±1.74	5.03±1.02	4.17±1.62	3.70±1.64	2.87±1.57	30.12±7.21
Hydrocortisone	7.03±1.67	6.50±1.30	5.47±1.57	4.73±1.41	4.47±1.47	3.93±1.28	41.83±8.34
<i>P</i>	0.016	0.04	0.329	0.154	0.063	0.006	0.004

the two groups 2, 4, and 24 h after surgery and that the mean analgesic received by gabapentin group was significantly lower than the hydrocortisone group [Table 2].

Restlessness rate in recovery was higher in the hydrocortisone recipient group (60%) relative to gabapentin recipient group (43%). Moreover, the incidence of nausea and vomiting in the group receiving hydrocortisone (26%) was lower than the group receiving gabapentin (40%) [Table 3].

In addition, the level of changes in vital signs (systolic blood pressure and heart rate) in both groups was measured in baseline and in different times. Heart rate was not significantly different between the two groups at predetermined times. Systolic blood pressures in the first 2 h after operation (gabapentin group 125.33 ± 20.36, hydrocortisone group 135.97 ± 15.34), 2–4 h after operation (gabapentin group 123.23 ± 13.78, hydrocortisone group 130.67 ± 13.45), 6–12 h after operation (gabapentin group 114.43 ± 12.38, hydrocortisone group 121.40 ± 14.13), and 12–18 h (gabapentin group 110.30 ± 22.60, hydrocortisone group 120.63 ± 11.85) were lower in gabapentin group following operation, and the difference with hydrocortisone group was different ($P < 0.05$) [Table 4].

Discussion

Postoperative pain is inevitable following laparoscopic surgery. The pain involves different parts of the body including membranous and visceral organs as well as shoulder, which is affected by various factors such as the nature of disease, factors related to operation, the amount of remaining gas, and its type.^[11,13] For this reason, treatment of pain is one of the most important concerns of therapeutic staff for the comfort and convenience of patients. The aim of the present research was to compare the administration effect of 150 mg oral gabapentin and 100 mg intravenous hydrocortisone prior to operation on postoperative pain control after laparoscopic cholecystectomy.

Gabapentin is a gamma aminobutyric acid (GABA) analog initially produced for the treatment of epilepsy,^[14] however, it is currently administered for pain relief, in particular pains with a neurological origin (such as headache and back pain), among other applications.^[15] Gabapentin is structurally similar to gamma butyric acid, does not have the ability to bind to plasma proteins, and does not convert to gamma aminobutyric acid or its agonists in the body. Gabapentin does not inhibit or eliminate gamma butyric acid resorption. Also, the mechanism through which

Table 3: Postoperative complications of the study groups in recovery unit (based on the number) according to Fisher-test

	PONV*	Agitation
Gabapentin	<i>n</i> =12 (40%)	<i>n</i> =11 (37%)
Hydrocortisone	<i>n</i> =8 (26%)	<i>n</i> =18 (60%)

*PONV: Postoperative nausea and vomiting

gabapentin exerts its analgesic or antiseizure effect in humans has not yet been determined. Gabapentin is excreted by kidneys with an excretion half-life of 5–7 h following administration of 200–400 mg oral gabapentin dose. The bioavailability of this drug is also about 60% with this same dose.^[6] Hydrocortisone is a member of glucocorticoid family, which has been shown to play an essential role in the regulation of inflammatory responses and reduction of pain. The mechanism of analgesic effect of corticosteroids is not well known. However, suppression of tissue bradykinin levels, release of neuropeptides from nerve terminals, reduced production of prostaglandins, and the inhibition of other anti-inflammatory mediators (e.g., Interleukin 6 (IL-6) and Tumor Necrosis Factor (TNF α)) are the proposed mechanisms for analgesic effects of steroids.^[16-19]

As shown in our study's results, within the first 4 h after operation, the pain score based on VAS was lower in the Gabapentin group. Accordingly, it was found that the amount of received analgesic was lower in the gabapentin group, which could confirm that gabapentin is more effective in controlling postoperative pain. In the study of Karaca *et al.*, it was also shown that VAS score decreased in patients receiving gabapentin at postrecovery hours.^[20] Although the VAS score in this study was measured at the rest (passive movement) as well as during active movement and while the average VAS scores during rest were significantly lower than our study at the same time, but our results were in line with this research at during active movement since the patients of our study were active at the time of pain assessment (i.e. they moved their lower extremity).

In a study by Agarwal *et al.*, gabapentin (150 mg oral 1 h before surgery) was compared with placebo to control the pain of patients after laparoscopic cholecystectomy, which showed that single dose of gabapentin reduced postoperative pain relative to placebo.^[3] In the research conducted by Paech *et al.*, a 100 mg single dose of gabapentin was not effective in controlling the pain of patients after a minor surgery.^[21] In this study, a 100 mg dose was used, while the recommended dose is 150 mg, which was used in our study. However, limitations of the present study

Table 4: Vital signs of patients in the two groups in different times (mean±SD)

	Base time		At 2 h		At 4 h		At 6 h		At 12 h		At 18 h		At 24 h	
	HR*	SBP**	HR	SBP	HR	SBP	HR	SBP	HR	SBP	HR	SBP	HR	SBP
Gabapentin	80.90±11.91	131.67±14.51	80.83±10.16	125.33±20.06	79.90±9.65	123.24±13.78	79.50±7.00	118.37±13.64	78.27±6.99	114.43±12.38	76.57±5.55	110.30±22.60	74.83±6.11	112.77±12.23
Hydrocortisone	82.73±9.73	138.47±19.50	83.53±11.48	135.97±15.34	79.50±6.50	130.67±13.45	79.27±7.84	118.37±12.95	77.27±5.84	121.40±14.13	76.00±5.05	120.63±11.85	75.20±5.32	119.30±10.76
<i>P</i>	0.513	0.131	0.332	0.061	0.853	0.033	0.901	0.053	0.554	0.047	0.688	0.031	0.803	0.051

*Heart rate (beats per minute), **Systolic blood pressure (mmHg)

are that we did not evaluate the dose–response or the effect of continuation of therapy.

In Agarwal study's, the incidence of nausea and vomiting was not significantly different between the two groups,^[3] but in our study, nausea and vomiting in the group receiving hydrocortisone (26%) were lower than that of the gabapentin group (40%), which could have been caused by antinausea and vomiting properties of steroids.

In an investigation by Sarvestani *et al.*, the effect of 100 mg intraperitoneal hydrocortisone together with 250 mL normal saline was assessed to control the pain of patients after laparoscopic cholecystectomy in comparison with 250 mL of normal saline (placebo group).^[22] In this study, postoperative pain was lower in the hydrocortisone group than in the placebo group. In this research, the average VAS scores in both the hydrocortisone and placebo groups were lower than mean VAS values in the hydrocortisone group of our study. Nevertheless, it could be argued that 250 mL normal saline was used in both patient groups of Sarvestani *et al.* study, which could have managed reduce pain after laparoscopic surgery.^[19] Similarly, the administration method of hydrocortisone was different between the two studies.

Moreover, based on our findings, while the incidence of nausea and vomiting in gabapentin recipients was higher than hydrocortisone recipients, the prevalence of restlessness and agitation was lower in gabapentin group in which almost one third of patients experienced restlessness. Furthermore, hemodynamic changes recorded in this study showed that there was no significant difference in heart rate between the two groups of patients. Blood pressure changes, which were measured as systolic blood pressure, indicated that in the patients receiving gabapentin, the systolic blood pressure in most hours of the study was lower than that of the hydrocortisone recipient group, which could reveal a lower pain level and higher hemodynamic stability of patients.

Conclusion

The results of this study showed that gabapentin was more effective than hydrocortisone in the first 2 h after laparoscopic cholecystectomy. In addition, gabapentin was shown to be better in controlling pain 24 h after surgery. It seems that more studies are needed to further investigate the analgesic effects of gabapentin in the postoperative phase.

Study limitations

It appears that a larger population is necessary to acquire more accurate results. In order to achieve better results, it seems necessary to have a control group as well as other groups with different doses of drug. Likewise, in subsequent studies, it is better to check other items, including the time patients leave their beds and depart the hospital, the period of starting oral feeding, and so on.

Financial support and sponsorship

The Research and Technology Deputy of Kurdistan University of Medical Sciences, Sanandaj, Iran is greatly appreciated for the financial supports they provide for the present study.

Conflicts of interest

There are no conflicts of interest.

References

- Alavi SM, Kish RF, Farsad F, Imani F, Sheikhvatan M. Intravenous sufentanil and morphine for post-cardiac surgery pain relief using patient-controlled analgesia (pca) device: A randomized double-blind clinical trial. *Pakistan J Med Sci* 2010;26:137-41.
- Kamali A, Fateme Seidi F, Shokrpour M, Jamilian M. Comparing the effects of adding fentanyl vs ketamine to 1/5% lidocaine in para-cervical block in order to reduce of post-operative pain among the patients applying for curettage. *Biomed Pharmacol J* 2016;9:949-55.
- Agarwal A, Gautam S, Gupta D, Agarwal S, Singh P, Singh U. Evaluation of a single preoperative dose of pregabalin for attenuation of postoperative pain after laparoscopic cholecystectomy. *Br J Anaesth* 2008;101:700-4.
- Dubois F, Icard P, Berthelot Ga, Levard H. Coelioscopic cholecystectomy. Preliminary report of 36 cases. *Ann Surg* 1990;211:60-2.
- Bisgaard T, Rosenberg J, Kehlet H. From acute to chronic pain after laparoscopic cholecystectomy: A prospective follow-up analysis. *Scand J Gastroenterol* 2005;40:1358-64.
- 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. *Can J Anesth* 2004;51:358-63.
- Bryans JS, Wustrow DJ. 3-Substituted GABA analogs with central nervous system activity: A review. *Med Res* 1999;19:149-77.
- Fassoulaki A, Patris K, Sarantopoulos C, Hogan Q. The analgesic effect of gabapentin and mexiletine after breast surgery for cancer. *Anesth Analg* 2002;95:985-91.
- Kong V, Irwin M. Gabapentin: A multimodal perioperative drug? *Br J Anaesth* 2007;99:775-86.
- Turan A, Karamanlioğlu B, Memiş D, Hamamcıoğlu MK, Tükenmez B, Pamukçu Z, *et al.* Analgesic effects of gabapentin after spinal surgery. *Anesthesiology* 2004;100:935-8.
- Sharma M, Kharbuja K, Sharma NR. Intraperitoneal hydrocortisone plus bupivacaine versus bupivacaine alone for pain relief after laparoscopic cholecystectomy: A randomized controlled trial. *J Lumbini Med College* 2016;3:41-4.
- Kama NA, Kologlu M, Doganay M, Reis E, Atli M, Dolapci M. A risk score for conversion from laparoscopic to open cholecystectomy. *Am J Surg* 2001;181:520-5.
- Mansori M, Bagheri SM. sonographic evaluation of clinically occult inguinal hernias in patients with scrotal pain and normal scrotal color doppler sonography. *Biotech Res Asia* 2016;13:1611-6.
- Goa KL, Sorkin EM. Gabapentin. *Drugs* 1993;46:409-27.
- Dahl JB, Mathiesen O, Møiniche S. 'Protective premedication': An option with gabapentin and related drugs? *Acta Anaesthesiol Scand* 2004;48:1130-6.
- Callery MP. Preoperative steroids for laparoscopic surgery. *Ann Surg* 2003;238:661.
- Fukami Y, Terasaki M, Okamoto Y, Sakaguchi K, Murata T, Ohkubo M, *et al.* Efficacy of preoperative dexamethasone in patients with laparoscopic cholecystectomy: A prospective randomized double-blind study. *J Hepatobiliary Pancreat Surg* 2009;16:367-71.
- Sapolsky RM, Romero LM, Munck AU. How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions. *Endocr Rev* 2000;21:55-89.
- Sarvestani AS, Amini S, Kalhor M, Roshanravan R, Mohammadi M, Lebaschi AH. Intraperitoneal hydrocortisone for pain relief after laparoscopic cholecystectomy. *Saudi J Anaesth* 2013;7:14-7.
- Karaca O, Pinar HU, Turk E, Dogan R, Ahiskalioglu A, Solak SK. Effects of Single-Dose Preemptive Pregabalin and Intravenous Ibuprofen on Postoperative Opioid Consumption and Acute Pain after Laparoscopic Cholecystectomy. *Journal of Investigative Surgery* 2017:1-7.
- Paech MJ, Goy R, Chua S, Scott K, Christmas T, Doherty DA. A randomized, placebo-controlled trial of preoperative oral pregabalin for postoperative pain relief after minor gynecological surgery. *Anesth Analg* 2007;105:1449-53.
- Tsimoyiannis EC, Glantzounis G, Lekkas ET, Siakas P, Jabarin M, Tzourou H. Intraperitoneal normal saline and bupivacaine infusion for reduction of postoperative pain after laparoscopic cholecystectomy. *Surg Laparosc Endosc* 1998;8:416-20.