EFFECTIVENESS AND SAFETY OF GABAPENTIN IN THE MANAGEMENT OF POST-OPERATIVE PAIN

Anwar Kamal Pasha[1], Kulsoom Farhat[2], Shabana Ali[3]

[1] Combined Military Hospital, Nowshera - Pakistan.
[2,3] Department of Pharmacology, Army Medical College / National University of Medical Sciences (NUMS) Rawalpindi - Pakistan.
Address for Correspondence:
Dr. Kulsoom Farhat
Assistant Professor, Department of Pharmacology, Army Medical College /National University of Medical Sciences (NUMS) Rawalpindi - Pakistan.
Email: kulsoompasha@yahoo.com
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ABSTRACT

Objective: To determine the effectiveness and safety of preoperative gabapentin administration on post-operative pain after laparoscopic cholecystectomy.

Methodology: Ninety patients undergoing laparoscopic cholecystectomy were divided into two groups. Group A received gabapentin in a dose of 300 mg two hours before surgery; and group B received placebo capsules in the same size and shape as gabapentin capsules. The pain scores, consumption of analgesics and adverse effects were compared between the two groups postoperatively at 2 hours, 6 hours, 12 hours and 24 hours after recovery.

Results: Group A had statistically less pain scores as compared to group B at 2, 6, 12 and 24 hours after recovery (p values were 0.0001, <0.0001, 0.0004, <0.0001 respectively). The requirement of analgesics was statistically lower in group A in comparison to group B at all the time intervals (p <0.0001). Both groups had no difference in the frequency of adverse effects except for vomiting which was significantly higher in group B (p =0.04).

Conclusion: Post-operative pain and the requirement for postoperative analgesics were significantly reduced in patients with administration of gabapentin before surgery and its use was found to be safe following laparoscopic cholecystectomy.

Key Words: Cholecystectomy, Gabapentin, Post-operative pain

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INTRODUCTION

The surgical procedures always come up with a handful of adverse effects. Among which the high incidence of post-operative pain is one of the nightmares both for the patients as well as for the surgeons[1]. It hinders the early mobilization of patients and adding up to the agony of the patients. The intensity of pain is dependent on multiple factors, among which the type and duration of anesthesia and surgery both play a pivotal role. In our operation settings most of the times opioids, anti-inflammatory agents and local anesthetics are used for alleviating pain. However, their adverse effects have limited their use. In an attempt to improve the quality of analgesia many a times these classes of drugs have contributed towards adverse effects on gastro-intestinal, renal and hematological system[2]. Most of the cholecystectomies are now a days performed via the laparoscopic approach. Though it has been a safe and valid alternative to open cholecystectomy[3] but associated with significant incidence of post-operative pain and necessitates the requirement of analgesics[4].

An anti-convulsant drug gabapentin is a structural analogue of gama amino butyric acid (GABA)[5]. It has been found to be effective in neuropathic pains, diabetic neuropathy and post herpetic neuralgia[6]. Its role in post-operative pain management is however a recent discovery and thus is not used for this purpose in routine practice so far. This drug when given as pre-treatment has been shown to decrease hyperalgesia and block the responses to noxious stimuli[7]. Gabapentin shares the same side effects with the drugs that are routinely used for this purpose as pre-medications and mostly include fatigue and somnolence. However the severity of its side effects is less as compared to the routinely used drugs in operative settings[8]. Moreover it does not interact with other commonly prescribed drugs.

The role of gabapentin in alleviating pain in post-operative settings has been evaluated in several studies which place gabapentin as a safe and efficacious drug for the treatment of postoperative pain[9]. However, it is not being used in postoperative settings routinely in our country. To validate its efficacy and recommend it for routine use in our clinical practice, more work is required to be carried out. We thus undertook this study to determine the effectiveness and safety of preoperative gabapentin administration on post-operative pain after laparoscopic cholecystectomy.

METHODOLOGY

This double blinded placebo controlled randomized control study was carried out at Combined Military Hospital, Nowshera. After getting the approval from the ethical committee of the hospital, 90 patients with American Society of Anesthesiology (ASA) grade I and II, of either gender and between 18 to 65 years of age, who had elective laparoscopic cholecystectomy were included in the study. A sample size of 30 in each group assumed to be sufficient to detect a clinically important difference of (μ1−μ2) 20 points on the VAS scale of pain, assuming a standard deviation(σ) 20 with a power of 90% and a significance level of 1%10. To compensate for excluded patients and drop outs etc. 45 patients in each group were recruited between September 2016 and March 2017. A written informed consent was obtained from each patient who got enrolled in this study. Any patient having renal or hepatic disorder, any known allergy to drugs that were to be used, any history of prior use of gabapentin were all excluded from the study.

Once the patients were received in the operation theatre, the vitals were monitored. Patients were randomly allocated into 02 groups; group A and group B; each having 45 patients. Group A received 20 mg/kg gabapentin capsule 02 hours before the surgery. The group B received capsule in the same size and shape as gabapentin capsule. The randomization of each patient was carried out through sealed envelopes that were numbered and indicated the group. An anesthetic who was not part of patients' follow up did the assignment of each patient to the group and also confirmed the compliance of each patient.

Premedication was done with 10 μg/kg alfentanil (available in the market by the trade name of "alfenta") and 10 μg/kg atropine. Anesthesia was induced with 6 mg/kg thiopental and for endotracheal intubation atracurium in a dose of 0.5 mg/kg was given. Anesthesia was maintained with nitrous oxide and isoflurane. At the end of the surgery, anesthesia was reversed with neostigmine (70 μg/kg) and atropine (40 μg/kg). Once the patients were transferred from recovery to the wards the intensity of pain was measured by visual analog scale at 2, 6, 12 and 24 hours after the surgery by a person who was blind to the study. The pain was graded from 0 to 10 (0= no pain, 10= the worst possible pain).

Any episode of pain in the recovery room or in the ward was treated with 25 mg mepridine given intramuscularly (available by the trade name of "Demerol" given through I/M route as its preferred over I/V route). Patients were questioned about the occurrence of any adverse effects (including nausea, vomiting, dizziness, somnolence, diarrhea, constipation and allergic manifestations). These were recorded on a pre-designed proforma. Data were analyzed using SPSS version 21. Statistical analysis was done for significant difference in reduction of pain on VAS, adverse effects and analgesic consumption post operatively between the two groups. Pain score (observed on VAS) was analyzed using Man-Whitney test. Total analgesic consumption was calculated for significance by independent "t-test". Adverse effects being categorical variables were analyzed by Pearson chi-square test. P value <0.05 was considered significant.

RESULTS

The two groups were comparable with respect to demographic data including age, gender, ASA grade and duration of anesthesia (Table 1).

Pain score in group A was significantly less at 2 hours, 6 hours, 12 hours and 24 hours postoperatively than in group B (p values =0.0001, <0.0001, 0.0004, <0.0001, respectively, (Table 2).

Table 1: Comparison of group A and group B with respect to demographic data

Variables	Group A (n=45)	Group B (n=45)	P value
Gender (M/F)	29/16	30/15	0.825
ASA Grade I/ II	27/18	29/16	0.667
Age (Years)	42.13 ±10.24	43.02 ±10.21	0.6807
Duration of Anesthesia (min)	34.12 ±10.11	33.76 ±11.27	0.873

Table 2: Comparison of group A and group B with respect to pain scores at different time intervals

Time Intervals	Group A (Mean ± SD)	Group B (Mean ± SD)	P value
At 2 hours	55.13 ±12.24	78.45 ±11.21	<0.0001
At 6 hours	48.34 ±11.22	66.34 ±10.17	<0.0001
At 12 hours	32.22 ±13.31	45.27 ±14.21	<0.0001
At 24 hours	21.18 ±15.17	22.19 ±14.15	0.7447

Table 3: Consumption of analgesic at different time intervals in two groups

Time Intervals	Group A (Mean ± SD)	Group B (Mean ± SD)	P value
At 2 hours	1.00 ± 0.11	1.22 ± 0.21	<0.0001
At 6 hours	1.15 ± 0.44	2.34 ± 0.17	<0.0001
At 12 hours	1.51 ± 0.31	3.27 ± 0.21	<0.0001
At 24 hours	2.18 ± 0.17	4.19 ± 0.15	<0.0001

Table 4: Frequency of adverse effects in group A and B

Adverse Effects	Group A (n=45)	Group B (n=45)	P value
Nausea	3	6	0.293
Vomiting	2	8	0.04*
Dizziness	12	10	0.624
Somnolence	7	5	0.535
Diarrhea	4	3	0.696
Constipation	4	6	0.502
Allergic Manifestations	3	3	1

The total consumption of analgesic in group A was significantly less as compared to group B at 2 hours, 6 hours, 12 hours and 24 hours (Table 3). We observed that both the groups had no significant differences in the incidence of adverse effects except for vomiting which was significantly higher in group B (Table 4).

DISCUSSION

Though gabapentin has not been routinely used in the operative settings, however, the recent year's research is focusing on its effectiveness in the same. Moreover, this drug has an advantage of less drug interactions that are routinely observed with the other drugs used in pre-emptive analgesia. Surprisingly the amount of experience with gabapentin being limited, has made its use in routine a little difficult. So this study was designed to validate the effectiveness of this drug in post-operative pain management. In any surgical intervention there is injury to peripheral tissues. This surgical insult in turn modifies the response of nervous system in multiple ways. It produces peripheral sensitization in which there is increased sensitivity to afferent nerve stimuli and thus the threshold of nociceptive nerve endings is decreased. Central sensitization also occurs in which excitability of spinal neurons increases and a pain response is triggered. Both these peripheral and central effects produce a hypersensitivity state. Gabapentin has been found to be effective in decreasing central sensitization[11].

Both the groups were comparable regarding the duration of surgery. The study drug was administered 2 hours before surgery as the peak plasma concentration of gabapentin is achieved in 2 to 3 hours. In this way the time to peak plasma concentration would coincide with the time to surgical insult. The data from other studies also support the efficacy of gabapentin when administered 2 hours before surgery[12].

Measurement of pain by VAS is a widely used dependable method hence it was used in the present study. We found that the intensity of pain was significantly decreased in the study group that was pre-medicated with gabapentin. The similar findings have been reported by Vasigh and colleagues[13], Mishra and colleagues[14] and Elnakera and colleagues[15]. Moreover the requirement of analgesics was also decreased in the same group which was in accordance with the findings of Ajori et al[16] and Khaki et al[17]. The untoward effects in the form of dizziness, somnolence, nausea and gait disturbance with gabapentin are usually seen when this drug is given over a prolonged period of time[18]. Similar findings were observed by Mogadam et al[19] in their study on patients undergoing tonsillectomy. Since we gave a single dose of the drug thus the adverse effects were observed minimally. Therefore gabapentin in a single dose can be a good choice for alleviating pain in postoperative settings as it has decreased pain scores, postoperative opioid consumption with minimal side effects. Our pretreated gabapentin group had significantly less vomiting as compared to the placebo group. The same were observed by Sourosh et al[20], Panday et al[21]and Khademi et al while observing the efficacy of gabapentin in controlling nausea and vomiting in a setting of laparoscopic cholecystectomy[22].

CONCLUSION

Post-operative pain and the requirement for postoperative analgesics were significantly reduced in patients with administration of gabapentin before surgery and

its use was found to be safe following laparoscopic cholecystectomy.

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CONTRIBUTORS

AKP conceived the idea, planned the study and drafted the manuscript. KF and SA helped acquisition of data, did statistical analysis, editing and final approval of the manuscript. All authors contributed significantly to the submitted manuscript.