A COMPARISON OF PREEMPTIVE GABAPENTIN WITH PREGABALIN FOR RELIEF OF POSTOPERATIVE PAIN IN PATIENTS UNDERGOING CHOLECYSTECTOMY

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ABSTRACT

Objective: To compare the mean time duration of patient's first request for analgesic for pain relief after open cholecystectomy with preoperative use of pregabalin or gabapentin.
Study Design: Randomized controlled trial.
Place and Duration of Study: Department of anesthesia, Combined Military Hospital (CMH) Peshawar during a period of six months, from May 2014 to Nov 2014.
Material and Methods: This study included a total of 126 patients with clinical and ultrasound diagnosis of acute cholecystitis. Patients were distributed randomly into two groups equally (63 patients in each group). Group A was given 300mg pregabalin and group B was given 900mg gabapentin one hour before surgery by mouth.
Results: Mean age was 46.68 ± 8.074 years for group A and 46.33 ± 8.046 years for group B. In group A, there were 49.2% males and 50.8% females while in group B, there were 42.9% males and 57.1% females. Weight of patients was 68.54 ± 6.283 kg in group A and 69.75 ± 5.778 kg in group B respectively. Mean time duration score was 37.48 ± 7.175 minutes and 18.27 ± 3.366 minutes in group A and B, respectively (p<0.001).
Conclusion: Preoperative use of pregabalin provides significantly prolonged postoperative analgesia compared to gabapentin after open cholecystectomy.

Keywords: Analgesia, Cholecystectomy, Gabapentin, Pregabalin.

INTRODUCTION

Postoperative pain is experienced by majority of patients undergoing surgery[1] and its relief is a major challenge[2]. Pain is inadequately treated in a vast majority of surgical patients[1,3]. Inadequate analgesia results in higher rate of complications and cost of treatment as a consequence of increased patient discomfort and prolonged hospital admission[4]. The goals of optimum postoperative pain management are decreased pain, better quality of recovery and early return to routine daily activities of patient[3]. Various drugs are used for intraoperative and postoperative analgesia of which opioids are most common but opioids have their own side effects. Multimodal analgesia represents an approach to decrease opioid related side effects[5]. Pregabalin and gabapentin have gained importance because of their opioid sparing effects[6]. They have shown good results in treatment of postoperative pain[2,7-9].

Gabapentin has structure similar to gamma amino butyric acid (GABA) and possesses antihyperalgesic properties. The mechanism for antihyperalgesic properties of gabapentin involves postsynaptic binding to the alpha2-delta subunit of voltage-gated calcium channels. This blocks calcium influx into nerve endings and results in decreased release of excitatory neurotransmitters[10]. Gabapentin decreases central sensitization resulting from hyper excitability of posterior horn neurons induced by lesions[10]. Pregabalin is an analog of gabapentin having similar mechanism of action but is more effective. It's pharmacokinetic profile is also better than gabapentin[11,12]. The pharmacological properties and predictable pharmacokinetics of pregabalin are a basis for its clinical use[11].

Although there are studies comparing each drug (gabapentin and pregabalin) versus

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placebo[13], there are fewer studies which compare these two drugs with each other in postoperative pain. The purpose of this study is to find a drug which can lengthen the time for analgesic requirement by the patients after open cholecystectomy. Prolongation of postsurgical pain free interval associated with use of minimal dose of analgesic drug in the preoperative period shall reduce postoperative morbidity and mortality. On the basis of the results of our study, the drug can be recommended for administration one hour before surgery in our setup for open cholecystectomy. In view of these facts we planned present study, to compare mean time duration scores from end of surgery to patient's demand for analgesic for pain relief, after open cholecystectomy with preoperative use of pregabalin and gabapentin.

PATIENTS AND METHODS

The study was carried at main operation theatre CMH Peshawar from May 2014 to November 2014. After obtaining approval of hospital ethical committee, this randomized controlled study was performed on 126 participants of American Society of Anesthesiologists (ASA) grade I and II patients between the ages of 35-65 years scheduled for open cholecystectomy. Patients gave informed consent for the study. Patients having history of chronic pain, current use of gabapentinoids or analgesics, impaired renal functions or major neurological disorders or coagulation abnormalities were excluded from the study. The results of a previous study[2] formed the basis for calculating sample size using OpenEpi, Version 3.01, open source calculator keeping a power of 90% with two sided confidence interval at 95% in two groups of equal size and with difference in mean time duration scores between group A and group B equal to 15 minutes with a sample size 63 in each group[2]. Purposive (non-probability) sampling technique was used to enroll patients for the study.

They were assigned to the two groups randomly by using lottery method. Study drugs were given one hour before surgery by mouth with group A receiving 300mg pregabalin and group B 900mg gabapentin. No other sedative premedication was given. In the operation theatre standard monitors were applied. Standard anesthetic technique was used which included nalbuphine (0.1 mg/kg), propofol (2mg/kg), atracurium (0.5mg/kg) and maintenance with isoflurane in O_2 and N_2O. After conclusion of the procedure, all patients were shifted to post anesthesia care unit (PACU).When the patient first demanded analgesic for pain relief, the time duration from completion of surgery to the time of first demand for analgesic was calculated and recorded in minutes.

All the data were recorded and analyzed in statistical package for social science (SPSS) version 20.0. Numerical values like age, body weight and mean time duration score were

Table-I: Demographic profile of the patients.

	Group-A (Pregabalin)	Group-B (Gabapentin)	*p*-value*
Gender: Male/Female n (%)	31/32 (49.2 /50.8)	27/36 (42.9/57.1)	0.475
Age (years) mean ± SD	46.68 ± 8.074	46.33 ± 8.046	0.81
Weight (kg) mean ± SD	68.54 ± 6.283	69.75 ± 5.778	0.264

*Significant *p*-value is taken as <0.05.

Table-II: Time to first requirement for analgesia (mean ± SD).

Group-A (Pregabalin)	Group-B (Gabapentin)	*p*-value*
37.48 ± 7.175 minutes	18.27 ± 3.366 minutes	<0.001

*Significant *p*-value is taken as <0.05.

expressed as mean ± standard deviation (SD). Distribution of categorical variables like gender was expressed in frequency and percentage. The mean time duration scores, age and weight between the two groups were compared by using Student t-test. Chi square test was applied for gender wise comparison. Results were presented in the form of tables. A *p*-value of less than 0.05 was considered as statistically significant.

RESULTS

There were 63 patients in each group. Patients in group A were given 300 mg pregabalin while patients in group B were given 900mg gabapentin. Mean age was 46.68 ± 8.074 years for group A and 46.33 ± 8.046 years for group B. In group A, there were 49.2% males and 50.8% females while in group B, there were 42.9% males and 57.1% females. Weight of patients was 68.54 ± 6.283 kg in group A and 69.75 ± 5.778 kg in group B respectively. The two study groups were comparable in age (p=0.81), sex (p=0.475) and body weight (p=0.264) (table-I).

Mean time duration score was 37.48 ± 7.175 minutes and 18.27 ± 3.366 minutes in group A and B, respectively. Patients in pregabalin group had significantly prolonged duration of analgesia postoperatively before they required additional analgesic as compared to patients in gabapentin group (p<0.001) (table-II).

DISCUSSION

In this study pregabalin 300 mg, given orally 1 hour before open cholecystectomy resulted in significantly prolonged postoperative analgesia compared with gabapentin 900 mg.

The therapeutic effects of pregabalin and gabapentin result from binding of the drug to the alpha2-delta subunit of voltage-gated calcium channels. They function as inhibitory modulators of excitatory neurotransmitter release which is responsible for their analgesic effects. The pharmacological properties of pregabalin are like those of gabapentin possibly with some advantages[11]. The preoperative dose of gabapentin in various studies ranges from 300 mg to 1200 mg whereas pregabalin dose ranges between 150 mg and 600 mg. We selected the doses of both the drugs for our study as used in a previous study[2].

A study by Bafna U and colleagues using oral gabapentin 600mg and pregabalin 150 mg demonstrated that effective analgesia lasted for significantly longer mean duration in pregabalin group compared with gabapentin group (p<0.001). The effective analgesia in pregabalin group had mean duration of 535.16 ± 32.86 minutes compared with 302.00 ± 24.26 minutes in gabapentin group[9]. The increase in the duration of postoperative analgesia was similar to our study.

Bekawi MS and colleagues have demonstrated safety and efficacy of 1200 mg gabapentin and 150 mg pregabalin for relieving pain after laparoscopic cholecystectomy. In their study, pregabalin and gabapentin groups had significantly lower 24-hour pethidine intake (p<0.001) compared with control group[14].

Ghai A and colleagues compared the postoperative analgesic efficacy of pregabalin and gabapentin in patients undergoing abdominal hysterectomy. They have observed that 300 mg pregabalin given as a single dose 1-2 hours before surgery provides better analgesia than 900 mg gabapentin in the course of early recovery. In their study, visual analogue scale (VAS) for pain was lower in patients in pregabalin and gabapentin groups compared to placebo after first hour of surgery. But, VAS for pain was comparable in all the groups afterwards. Patients in gabapentin group required analgesic earlier than patients in pregabalin group[2].

CONCLUSION

Preoperative use of pregabalin provides significantly prolonged postoperative analgesia compared to gabapentin after open cholecystectomy.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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