EVALUATION OF SINGLE PREOPERATIVE DOSE OF PREGABALIN IN TERMS OF POSTOPERATIVE PAIN AFTER LAPAROSCOPIC CHOLECYSTECTOMY

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ABSTRACT

Objective: Evaluation of single preoperative dose of pregabalin in terms of postoperative pain after laparoscopic cholecystectomy.

Study Design: Randomized controlled trial (RCT).

Place and Duration of Study: Study was conducted in Surgical Department of Military Hospital Rawalpindi over a period of one year fromJan 2013 to Dec 2013.

Material and Methods: One hundred patients (50 in each group) were included in this study. They were divided into two groups. Group-A was given pregabalin and group-B was given placeboafter laparoscopic cholecystectomy.

Results: Mean age was 38.2 ± 11.0 years in group A and 36.9 ± 11.7 years in group B. Regarding distribution of gender, 14 patients (28.0%) in group-A and 17 patients (34.0%) in group-B were males while 36 patients (72.0%) in group-A and 33 patients (66.0%) in group-B were females. Mean visual analogue score at 24 hours was 4.98 ± 1.87 and 6.58 ± 2.03 in group-A and B, respectively. The difference between two group was statistically significant (p<0.001). Analgesia was required in 17 patients (34.0%) in group-A and 37 patients of group-B.

Conclusion: A single preoperative oral dose of pregabalin 150 mg was found very effective method for reducing postoperative pain in patients undergoing laparoscopic cholecystectomy.

Keywords: Laparoscopic cholecystectomy, Postoperative pain, Pregabalin.

INTRODUCTION

Gallstones disease is prevalent worldwise and has incidence of 1-3% per year[1]. Laparoscopic cholecystectomy is amongst most commonly performed surgical procedure for symptomatic gallstones and has become gold standard in recent times. Postoperatively pain is the most common complaint after laparoscopic cholecystectomy. Where laparoscopic cholecystectomy has greatly decreasedmorbidity, hospital stay and[2] convalescent time, the post operative pain still remains a major problem needing intravenous[3] analgesia. Various drugs ranging from simple NSAIDs to patient controlled analgesia are in use. few other treatment options like intraperitoneal administration of local[4,5] anaesthetic agents have been studied but still remain a controversial issue. Pregablin and its predecessor gabapentin were initially used as antispasmodic agents and adjuncts for treatment of seizures resistant to conventional therapy. Pregabalin has a definative role in treating neuropathic pain, however, evidence supporting the analgesic effectiveness of pregabalin in postoperative period is limited to randomized controlled trials in patients undergoing[6] spinal fusion surgery, dental surgery, laparoscopic hysterectomy[7] and day case laparoscopic gynaecological surgery[8,9].

A single preoperative dose ofpregabalin150 mg has proved to be beneficial in controlling post operative pain after laparoscopic cholecystectomy[10]. Its oral route of administration, good safety profile[11], single dosage, make it a useful agent in controlling postoperative pain. In a recently published study, Peach and colleagues[12] concluded that a single preoperative dose of 100 mg pregabalin was ineffective in reducing acute post operative pain

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The rationale of this study was to evaluate the efficacy of single preoperative dose of pregabalin for elimination of postoperative pain after laparoscopic cholecystectomy. Pregabalin is less commonly used in tertiary care hospitals and there is a need to evaluate its effectiveness as verylimited data is available.

PATIENTS AND METHODS

This was a randomized controlled trial (RCT) carried out over a period of one year from Jan 2013 to Dec 2013. Study was conducted in Surgical Department, Military Hospital, Rawalpindi. Inclusion criteria included patients undergoing elective laparoscopic cholecystectomy for symptomatic cholelithiasis between the ages of 20-60 years, American Society of Anesthesiology (ASA) I and II status. Patients of either sex were included. Exclusion Criteria included conversion to open cholecystectomy, acute cholecystitis, choledocholethiasis, pancreatitis, bile leakage during surgery, patients not willing for surgery and previous major abdominal surgery. One hundred patients fifty for each group were recruited. Total number of patients required for the study were calculated with the help of World Health Organization (WHO) sample size calculator using two mean formula on the basis of 80% power to detect a significant difference in the postoperative pain requiring analgesia consumption at a 5% significant level. Permission from hospital ethical committee was sought. One hundredpatients undergoing laparoscopic cholecystectomy fulfilling the inclusion criteria randomly alloted two equal groups, A and B. Informed written consent was obtained from all the patients. Hospital registration number, name, gender, age, address and phone number (optional) were recorded. Subjects were randomly divided into two groups of 50 each. Group A was given pregabalin 150mg administered orally 1 hr before surgery and group B received a matching placebo.

Induction was done with fentanyl, propofol and atracurium with dosage adjusted according to the weight of patient. Maintenance anaesthesia was with mixture of air sevoflurane and oxygen. Pneumoperitonem was created with Veress needle through periumbilical incision and a pressure of 12mm of mercury was maintained throughout the procedure. All of the surgeries were performed using standard four port laparoscopic cholecystectomy technique. Postoperative analgesia was controlled by administering intravenous ketorolac 30mg at 12 hours and then at 24 hours after recording VAS. Patients in both groups were kept in hospital forduration of at least 24 hours. Pain in postoperative period was assessed and scored by trainee researcher in both the groups using visual analogue score from 0-10 at 24 hours. Whole of the information was recorded on a specially designed proforma. Data analysis was computer based with the use of SPSS version 12. The variables to be analyzed were included quantitative data like age, postoperative pain and qualitative data like gender. Mean and standard deviation was calculated for quantitative data like age and VAS at 24 hours. Independent sample t-test was used to compare mean pain score between two groups at 24 h. A *p*-value <0.05 was considered significant. Results were explained with the help of tables.

RESULTS

One hundred patients were divided into two groups. Group A received pregabalin 150 mg and group-B received placebo. Distribution of cases by age showed 13 (26.0%) patients between 20-30 years in group A and 17 (34.0%) patients in this range were present in group B. Sixteen (32.0%) patients between 31-40 years of age in group A while 14 (28.0%) patients in group B. There were 14 (28.0%) patients between 41-50 years of age in group A and 10 (20.0%) patients of this age group fall in group B. Seven (14.0%) patients between 51-60 years of age presented in group A while 9 (18.0%) patients in group B. Mean age was 38.2 ± 11.0 in group A and 36.9 ± 11.7 in group B (table-I).

Regarding distribution of the gender, 14 patients (28.0%) in group-A and 17 patients (34.0%) in group-B were males while 36 patients

(72.0%) in group-A and 33 patients (66.0%) in group-B were female. Mean visual analogue score at 24 hours was 4.98 ± 1.87 and 6.58 ± 2.03 in group-A & B, respectively. The difference between two group was statistically significant (p<0.001) (table-II).

Analgesia was required in 17 patients (34.0%) in group-A and in 37 patients of group-B (table-III).

Table-I: Distribution of cases by age n=100.

Age (Year)	Group-A (Pregabalin 150 mg) (n=50)		Group-B (Placebo) (n=50)	
	Number	Percentage (%)	Number	Percentage (%)
20-30	13	26.0	17	34.0
31-40	16	32.0	14	28.0
41-50	14	28.0	10	20.0
51-60	07	14.0	09	18.0
Total	50	100.0	50	100.0
Mean ± SD	38.2 ± 11.0		36.9 ± 11.7 p-value=0.6	

Table-II: Mean values of visual analogue score (VAS) at 24 hours n=100.

Variable	Group-A (Pregabalin 150 mg) (n=50)	Group-B (Placebo) (n=50)
	Mean ± SD	Mean ± SD
VAS at 24 hrs	4.98 ± 1.87	6.58 ± 2.03
p-value	<0.001	

Table-III:Analgesia required at 24 hours n=100.

Analgesia required	Group-A (Pregabalin 150 mg) (n=50)		Group-B (Placebo) (n=50)	
	Number	Percentage (%)	Number	Percentage (%)
Yes	17	34.0	37	74.0
No	33	66.0	13	26.0
Total	50	100.0	50	100.0

p-value=<0.001.

DISCUSSION

Postoperative pain is the commonest complaint and the major reason for prolonged convalescence after laparoscopic cholecystectomy[13]. Severe pain immediately after laparoscopic cholecystectomy might predict the development of chronic pain (e.g. post-laparoscopic cholecystectomy syndrome). Experimental models of inflammatory hyperalgesia and neuropathic pain have demonstrated that γ-aminobutyric acid analogues such as pregabalin and gabapentin possess both antinociceptive and antihyperalgesic effects[14]. The pharmacological efficacy of pregabalin result from its action as a ligand at the alpha-2-delta binding site, which is associated with the voltagegated calcium channels in the central nervous system[15]. Potent binding of pregabalin at alpha-2-delta site has proved to decrease the depolarization-induced calcium influx at nerve terminals with a consequential reduction in the release of several excitatory neurotransmitters such as norepinephrine, glutamate, CGRP, and[16] substance. The role of pregabalin in managing acute post-operative pain has been evaluated in recent studies. These studies sought to determine whether perioperative pregabalin was effective in decreasing pain during postoperative period and whether it had opioidsparing effects. However, due to differences in the dosages of pregablin and different types of surgery results are contrasting. A study evaluating pain attenuation after dental extraction showed that pregabalin administered in dosage of 400 mg after operation was more

effective than ibuprofen in reducing acute post-procedural pain[17]. In another clinical trial, Jokela *et al*[7] concluded that perioperative administration of pregabalin in dosage of 300 mg before and after laparoscopic hysterectomy reduces oxycodone consumption, but is associated with an increased risk of side effects. Jokela *et al*[8] in another study concluded that pain relief was better after premedication with pregabalin 150 mg in patients undergoing day-case gynaecological laparoscopic surgery. Reuben *et al*[6] observed that in patients undergoing lumbar laminectomy, pregabalin 150 mg before and after surgery was as effective as celecoxib in reducing postoperative pain and patient controlled morphine consumption and the combination of both drugs was the most effective.

In present study, pregabalin for attenuating pain in post operative period after laparoscopic cholecystectomy proved very effective. Mean VAS score was significantly lower in group-A (p=0.001). Findings of present study are comparable with results of other studies mentioned above. Further studies should be carried out to prove the effectiveness of pregabalin in reducing the incidence of chronic post-operative pain.

CONCLUSION

A single preoperative oral dose of pregabalin 150 mg was found an effective method for reducing post-operative pain in patients undergoing laparoscopic cholecystectomy.

CONFLICT OF INTEREST

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

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