

# Comparative Analysis of Oral Pregablin vs Oral Flupertine as Premedication for Laparoscopic Gall Bladder Surgeries

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## ABSTRACT

**Background:** Cholecystectomy is one of the most common intraabdominal surgical procedures performed in the present era. Acute pain in post-operative period affects patient significantly as it may cause adverse effects. Hence; we planned the present study to assess and compare the effect of oral Pregablin and oral Flupertine given as premedication in patients undergoing Laparoscopic gall bladder surgeries.

**Materials & Methods:** The present investigation included 60 patients scheduled for Laparoscopic surgery under general anesthesia. All the patients were explained about visual analogue scale (VAS) for postoperative pain assessment. '0' means no pain and '10' means maximum pain. On the day of surgery, patients were randomly selected and given either oral Pregablin 150 mg or oral Flupertine 200 mg one hour before surgery. Group P- Received 150 mg Pregablin one hour before surgery, Group F- Received 200 mg Flupertine one hour before surgery. Patient was given i.v. paracetamol and was reversed and extubated. Postoperative pain was assessed by Visual analog score (VAS). All the results were recorded in Microsoft excel sheet and were analyzed by SPSS software.

**Results:** Non- significant results were obtained while comparing the mean hemodynamic parameters in between the

two study groups at different intraoperative and postoperative time interval. Higher level of satisfaction was observed among subjects of Pregablin group. However; while comparing the occurrence of nausea among subjects of both the study groups, non-significant results were obtained.

**Conclusion:** More satisfactory results occur when Pregablin is used as a premedication agent in patients undergoing laparoscopic cholecystectomy.

**Key Words:** Flupertine, Pregablin, Laparoscopic.

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## INTRODUCTION

Cholecystectomy is one of the most common intraabdominal surgical procedures performed in the present era. In cases where cholecystectomy is indicated, Laparoscopic removal the procedure of choice.<sup>1-3</sup> Ever since its introduction in 1990s, Laparoscopic cholecystectomy (LC) has essentially replaced the open technique for routine cholecystectomies. Indications for LC include patients with cholecystitis (acute/chronic), symptomatic cholelithiasis, biliary dyskinesia, acalculous cholecystitis, gallstone pancreatitis, and gallbladder masses/polyps.<sup>4-6</sup>

Acute pain in post-operative period affects patient significantly as it may cause effects such as tachycardia, hypertension, cardiac problems, decrease respiratory reserve, poor wound healing and discomfort. It is essential to control this pain for early mobilization, better recovery and shorter hospital stay. Pregablin, a gabapentinoid class drug has been used for premedication which not only attenuates the laryngoscopic response but also decrease

the postoperative analgesic requirement.<sup>7, 8</sup> Flupertine is non-opiate, non NSAID. It is a central acting analgesic and N-methyl D aspartate (NMDA) receptor antagonist.<sup>9</sup>

Hence; we planned the present study to assess and compare the effect of oral Pregablin and oral Flupertine given as premedication in patients undergoing Laparoscopic gall bladder surgeries.

## MATERIALS AND METHODS

The present investigation was commenced in the department of Anaesthesiology over a period of 6 months during July 2017 to December 2017 in 60 patients scheduled for Laparoscopic surgery under general anesthesia. Ethical approval was obtained from institutional ethical committee and written consent was obtained from all patients after explaining in detail the entire research protocol. Patient of ASA grade I and II, between 18 - 65 years were included in the study. Exclusion criteria for the present

study included patients with cardiovascular disorder, any hepatic or renal insufficiency, drug allergy, and pregnancy. A detailed preanaesthetic assessment was done one day prior to surgery. All the patients were explained about visual analogue scale (VAS) for postoperative pain assessment. '0' means no pain and '10' means maximum pain. On the day of surgery, patients were randomly selected and given either oral Pregablin 150 mg or oral Flupertine 200 mg one hour before surgery.

Group P- Received 150 mg Pregablin one hour before surgery

Group F- Received 200 mg Flupertine one hour before surgery.

The Anaesthesia technique was standardized for both groups with I/V Fentanyl 2µg/Kg, Midazolam (0.05mg/kg), Propofol (1-2mg/kg) in titrated doses, Vecuronium bromide (0.08-0.1mg/kg). Patient was intubated after 3 minutes of ventilation with oxygen and

maintained on 60% air and 40% oxygen and isoflurane 1%. Monitoring of oxygen saturation (Spo<sub>2</sub>), End tidal carbon dioxide (ETCO<sub>2</sub>), systolic blood pressure (SBP), Diastolic blood pressure (DBP), Heart rate (HR), was monitored preoperatively, after intubation at one minute, 5 minutes and thereafter every 15 minutes. Patient was given i.v paracetamol and was reversed and extubated.

Postoperative pain was assessed by Visual analog score (VAS). Patient was given rescue analgesia on demand and time for first analgesic and total requirement of analgesic was recorded for 24 hours. All the results were recorded in Microsoft excel sheet and were analyzed by SPSS software. Chi-square test and Mann-Whitney U test were used for assessment of level of significance. P-value of less than 0.05 was taken as significant.

**Table 1: Mean age of the subjects of both the study groups**

Group	N	Mean age (years)
Pregablin	30	43.26
Flupertine	30	44.43

**Table 2: Distribution of subjects according to gender**

Group	Gender	
	Males	Females
Pregablin	10	20
Flupertine	11	19

**Table 3: Hemodynamic parameters at preoperative time**

Parameter	Pregablin	Flupertine	P- value
Mean preoperative SBP	127.66	135.833	0.04*
Mean preoperative DBP	80.76	83.63	0.03*
Mean preoperative arterial pressure	84.83	84.76	0.956
Mean preoperative pulse rate	83.23	80.16	0.515

\*: Significant

**Table 4: Hemodynamic parameters at pre-intubation time**

Parameter	Pregablin	Flupertine	P- value
Mean pre-intubation SBP	123.56	130.36	0.48
Mean pre-intubation DBP	81.16	82.46	0.35
Mean pre-intubation arterial pressure	80.40	79.93	0.10
Mean pre-intubation pulse rate	81.00	82.60	0.22

**Table 5: Hemodynamic parameters after intubation time**

Parameter	Pregablin	Flupertine	P- value
Mean SBP after intubation	122.86	130.66	0.79
Mean DBP after intubation	80.90	83.63	0.35
Mean arterial pressure after intubation	120.00	83.96	0.47
Mean pulse rate after intubation	85.70	87.10	0.18

**Table 6: Hemodynamic parameters at intraoperative time**

Parameter	Pregablin	Flupertine	P- value
Mean intraoperative SBP	118.83	129.16	0.28
Mean intraoperative DBP	80.36	82.50	0.84
Mean intraoperative arterial pressure	76.00	73.10	0.00*
Mean intraoperative pulse rate	82.43	81.10	0.36

\*: Significant

**Table 7: Hemodynamic parameters at one minute of intraoperative time**

Parameter	Pregablin	Flupertine	P- value
Mean intraoperative SBP _ 2	122.50	130.63	0.80
Mean intraoperative DBP _ 2	79.86	82.26	0.91
Mean intraoperative arterial pressure _ 2	78.10	92.40	0.00*
Mean intraoperative pulse rate _ 2	81.60	82.76	0.10

\*: Significant

**Table 8: Hemodynamic parameters at five minute of intraoperative time**

Parameter	Pregablin	Flupertine	P- value
Mean intraoperative SBP _ 3	117.10	130.06	0.08
Mean intraoperative DBP _ 3	76.33	80.46	0.25
Mean intraoperative arterial pressure _ 3	84.80	90.10	0.61
Mean intraoperative pulse rate _ 3	79.56	81.00	0.60

**Table 9: Hemodynamic parameters at fifteen minute of intraoperative time**

Parameter	Pregablin	Flupertine	P- value
Mean intraoperative SBP _ 4	119.23	129.86	0.08
Mean intraoperative DBP _ 4	77.90	80.90	0.25
Mean intraoperative arterial pressure _ 4	76.96	87.30	0.61
Mean intraoperative pulse rate _ 4	78.83	81.33	0.06

**Table 10: Hemodynamic parameters at postoperative time**

Parameter	Pregablin	Flupertine	P- value
Mean post-operative SBP	123.7	138.7	0.82
Mean Post-operative DBP	78.96	87.36	0.65
Mean post- operative Mean arterial pressure	84.16	93.60	0.15
Mean post- operative pulse rate	80.83	86.63	0.55

**Table 11: Quantity of dose in 24 hours**

Parameter	Pregablin	Flupertine	P- value
Dose in 24 hour	1.56	2.40	0.32

**Table 12: Satisfaction among subjects of the two study groups**

Parameter	Pregablin (n)	Flupertine (n)	P- value
Satisfaction	Good	27	0.00*
	Adequate	3	
	Poor	0	

\*: Significant

**Table 13: Presence of nausea among patients of the two study group**

Nausea	Pregablin (n)	Flupertine (n)	P- value
Present	1	4	0.161
Absent	29	26	

**Table 14: VAS**

VAS	Pregablin (n)	Flupertine (n)	P- value
Pre-operative period	3	3	0.111
Postoperative period	3	4	

## RESULTS

In the present study, mean age of the patients of the pregablin and flupertine group was 43.26 and 44.43 years respectively. There were 10 males and 20 females in pregablin group and there were 11 males and 19 females in the Flupertine group respectively. Mean preoperative systolic blood pressure (SBP) and diastolic blood pressure (DBP) among subjects of Pregablin and the Flupertine group were 127.66, 135.833, 80.76 and 83.63 mm of Hg respectively. Non- Significant results were obtained while comparing the mean preoperative hemodynamic parameters among subjects of the two study groups (P- value > 0.05). While comparing the mean hemodynamic parameters between the two study groups intraoperative and one minute, five minute and fifteen minute of intraoperative time, non- significant results were obtained. While comparing the mean hemodynamic parameters among subjects of both the study groups at pre-intubation time, non-significant results were obtained (P- value > 0.05). Non-significant results were obtained while comparing the mean hemodynamic parameters in between the two study groups at different intraoperative and postoperative time interval (P- value >0.05). Also, there was more demand of total analgesics in postoperative period in first 24 hours in Flupertine group in comparison to the pregablin group. However; the results were found to be non- significant. While comparing the satisfaction levels among subjects of both the study groups, significant results were obtained. Higher level of satisfaction was observed among subjects of Pregablin group (P-value < 0.05). Nausea and vomiting was present in one subject of the Pregablin group and four subjects of the Flupertine group respectively. However; while comparing the occurrence of nausea among subjects of both the study groups, non-significant results were obtained (P-value > 0.05). In Pregablin group, VAS was 3 in postoperative period, while in Flupertine group, VAS was 4 in the postoperative period.

## DISCUSSION

An ideal premedicant drug should relieve anxiety, produce amnesia and sedation, decrease secretions, prevent nausea and vomiting, have dose-sparing effect on the anesthetic drugs and suppress pressor response to laryngoscopy and intubation. Traditionally benzodiazepines such as midazolam and diazepam have been used. Gabapentinoids, which include gabapentin and pregablin (PG), are a new class of drugs which binds to  $\alpha$ -2 $\delta$  protein subunit of voltage-gated calcium channels and inhibits the release of excitatory neurotransmitters in the central and peripheral nervous system.<sup>1,3,4</sup> In the present study, mean age of the patients of the pregablin and flupertine group was 43.26 and 44.43 years respectively. There were 10 males and 20 females in pregablin group and there were 11 males and 19 females in the Flupertine group respectively. Mean preoperative systolic blood pressure (SBP) and diastolic blood pressure (DBP) among subjects of Pregablin and the Flupertine group were 127.66, 135.833, 80.76 and 83.63 mm of Hg respectively. Non- Significant results were obtained while comparing the mean preoperative hemodynamic parameters among subjects of the two study groups (P- value > 0.05). Gupta P et al evaluated the effect of Pregablin (PG) as premedication on the perioperative anesthetic requirement and analgesia. They assessed 90 patients and allocated them to one of the three groups of thirty patients each. Group I received tablet diazepam 10 mg HS and 5 mg 1 h before

surgery, Group II received capsule PG 75 mg HS and 150 mg 1 h before surgery, and Group III received capsule PG 75 mg HS and 300 mg 1 h before surgery. Perioperative requirement of thiopentone sodium, opioid, and inhalational agent was significantly less in Group II and III when compared with Group I. Maximum number of patients required postoperative rescue analgesia within 0–2 h of surgery in Group I, 2–4 h of surgery in Group II, and 6–8 h after surgery in Group III. Patients were more comfortable and asleep with a longer pain-free postoperative period in PG groups. PG premedication effectively reduced the consumption of all anesthetic agents during induction and maintenance of anesthesia as compared to diazepam.<sup>10</sup>

In the present study, while comparing the mean hemodynamic parameters among subjects of both the study groups at pre-intubation time, non-significant results were obtained (P- value > 0.05). No- significant results were obtained while comparing the mean hemodynamic parameters in between the two study groups at different intraoperative and postoperative time interval (P- value >0.05). In one of the previous study conducted by Yadav G et al, authors analyzed the role of flupertine as a preemptive analgesic for postoperative pain relief in patients undergoing above surgery. A total of 66 cases were randomly assigned to two groups to receive capsule flupertine (200 mg) or capsule vitamin B complex administered orally, 2 h before the laparoscopic cholecystectomy surgery. Time to first analgesic requirement, assessment of postoperative pain in terms of visual analog score, and analgesic requirement postoperatively were measured as a primary outcome. Time to first analgesic requirement was significantly prolonged in the flupertine group as compared with the placebo group. There was significant pain reduction in early postoperative period (up to 4 h), but no changes occurred thereafter. Total analgesic requirement (including rescue analgesia) and side-effects were comparable between the groups except for higher sedation in flupertine group. Flupertine is effective as a preemptive analgesic in providing adequate pain relief during the immediate postoperative period after laparoscopic cholecystectomy surgery.<sup>11</sup>

In the present study, there was more demand of total analgesics in postoperative period in first 24 hours in Flupertine group in comparison to the pregablin group. The results were however, found to be non-significant. Also, while comparing the satisfaction levels among subjects of both the study groups, significant results were obtained. Higher level of satisfaction was observed among subjects of Pregablin group (P-value < 0.05). However; while comparing the occurrence of nausea among subjects of both the study groups, non-significant results were obtained (P-value > 0.05). In Pregablin group, VAS was 3 in postoperative period, while in Flupertine group, VAS was 4 in the postoperative period. Yadav G et al in another previous study, 124 counseled patients were randomized to receive 5 sequential doses of capsule flupertine 100 mg (F Group) or physically similar starch capsules (C Group), at 12 h intervals during preoperative hospitalization. Primary outcome included various aspects of patient anxiety measured by visual analog scale (VAS) just before preoperative counseling and 2 h after the completion of drug regimen under trial. Baseline VAS scores were higher for fear of surgical harm, being at the mercy of medical staff, and not awakening after surgery. A significant decline in VAS scores was observed after the completion of drug regime, but to a higher extent in flupertine-

treated patients; it achieved statistical significance in comparison to Group C. No side effects were observed in any patient. Flupertine is a useful premedication in conjunction with behavioral therapy to alleviate patient anxiety during the preoperative period.<sup>12</sup>

In comparison to some other agents like gabapentin, pregablin has a more favourable pharmacokinetic profile with better, faster, and more predictable absorption. It is rapidly and extensively absorbed after oral dosing, with maximal plasma concentration at 1 h after single or multiple doses. The oral bioavailability is 90% and is independent of dose. These properties offer some advantages over gabapentin as a perioperative medication.<sup>13</sup> However, we further research is directed for better exploration of the results.

## CONCLUSION

Under the light of above obtained data, the authors conclude that more satisfactory results occur when Pregablin is used as a premedication agent in patients undergoing laparoscopic cholecystectomy. However; further studies are recommended.

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