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Original Research Article

COMPARISON OF PREEMPTIVE ANALGESIA WITH TWO DOSES OF PREGABALIN IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY

Vijaya Durga S[1], Muneer Ahmed T[2], Chalapathy P[3] , Lakshmi Praveena B[4], Sunil C[5]

[1,2]*Assistant Professor, Department of Anaesthesiology, GMC&GGH, Kadapa, Andhra Pradesh, India.*
[3,4]*Associate Professor, Department of Anaesthesiology, GMC&GGH, Kadapa, Andhra Pradesh, India.*
[5]*Professor & HOD, Department of Anaesthesiology, GMC&GGH, Kadapa, Andhra Pradesh, India.*

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Corresponding Author:
Dr. Lakshmi Praveena B
Associate Professor, Department of Anaesthesiology, GMC&GGH, Kadapa, Andhra Pradesh, India.
Email: praveenadoc4all@gmail.com

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ABSTRACT

Background: Management of post-operative pain has become inevitable with focus on newer methods of pain relief, and one among such methods is preemptive analgesia. Preemptive analgesia with different drugs as a part of a multimodal approach in cases of laparoscopic cholecystectomy is in vogue. This study focuses on the pre-emptive analgesic effect of different doses of Pregabalin on patients posted for laparoscopic cholecystectomy given in the pre-operative period.

Material and Methods: A total of 60 ASA grade I and II patients of either sex posted for laparoscopic cholecystectomy were randomly divided into two groups. GROUP A patients received 150mg oral pregabalin, and GROUP B patients received 225mg oral Pregabalin 1.5 hours before surgery. We monitored postoperative VAS scores, intubation response, first rescue analgesia time, total analgesic requirement, RAMSAY sedation score, perioperative hemodynamics, side effects.

Results:

We have found that there is a significant difference between the two groups with respect to post-operative VAS scores($p<0.05$). Though there is a difference between Heart Rate, MAP, Ramsay sedation score, and side effects, the difference is non-significant.

Conclusion: Preemptive analgesic effect with 225mg oral pregabalin is a better alternative to pregabalin 150mg with comparable side effects.

Keywords: Preemptive analgesia, Pregabalin, VAS score, MAP, Ramsay sedation score.

INTRODUCTION

Postoperative analgesia in laparoscopic surgery is an area of continued interest. Postoperative pain has significant impact on the surgery outcome due to many adverse effects like tachycardia, hypertension, ischemia, reduced alveolar ventilation, poor wound healing and patient discomfort.[1] Hence, the alleviation of pain has been the priority of the medical profession and health authorities since time immemorial. Pain after Laparoscopic Cholecystectomy is multifactorial. Also, it can be curtailed by a multimodal approach, which has been popular today. A better understanding of the pain pathways and physiology led to the emergence of a new regimen known as preemptive analgesia. Preemptive analgesia was a concept developed by Crile, and it is a method of administration of medications before surgery to prevent the establishment of central sensitization of pain, thus reducing the intensity and duration of postoperative pain.[2]

Pre-emptive analgesia focuses on reducing postoperative opioid consumption and pain levels, decreasing the incidence of adverse events, and improving patient satisfaction quality of life and reducing financial burden in the post-op period. Pregabalin, (S)-3-(aminomethyl)-5-methylhexanoic acid, is a pharmacologically active S-enantiomer of a racemic 3-isobutyl gamma amino butyric acid analogue. Pregabalin is used for various neuropathic

pain syndromes. Pregabalin is an antagonist of voltage-gated Calcium channels and specifically binds to alpha-2-delta subunit to produce antiepileptic and analgesic action. Its postsynaptic binding to the alpha-2-delta subunit of the dorsal horn neurons' voltage-dependent calcium channels causes a decrease in the entry of calcium into the nerve endings and thus decreases the release of neurotransmitters such as noradrenaline. The efficacy of perioperative pregabalin administration in the prevention of acute postoperative pain has been studied by various authors.[3]

Several studies have used different doses of pregabalin (75mg,150mg,300mg,600mg) for pre-emptive analgesia. The incidence of side effects profile increased with an increase in the dose of pregabalin.[4,5,6,7]

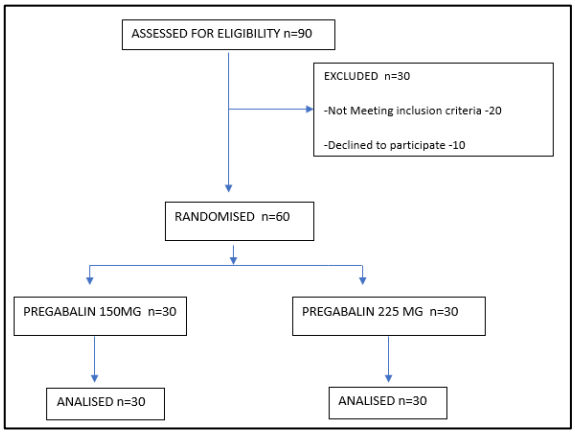
This study is done to find out if pregabalin 225 mg is a better alternative to pregabalin 150mg in improving preemptive analgesic effect with the most diminutive side effect profile on patients posted for laparoscopic cholecystectomy. The primary objective was to assess and compare Pregabalin 150mg and pregabalin 225mg about VAS score for post-operative pain in 24 hours, intubation response, the time to first rescue analgesia, and total analgesic requirement in the 24-hour post-operative period. The study's secondary objective was to look for Ramsay sedation score, other side effects, and hemodynamic response in the post-operative period.

MATERIAL AND METHODS

A randomised, double-blind study was conducted on 60 American Society of Anaesthesiologists (ASA) physical status I and II patients of age 18-60 years, of either sex undergoing elective laparoscopic cholecystectomy under general anaesthesia. Patients with ASA status III and IV, patients with a difficult airway, patients with a history of allergy to Pregabalin, patients who were prescribed Pregabalin for other indications, patients having a history of chronic pain and chronic daily intake of analgesics, those with a history of epilepsy and other neurological disorders, pregnant women, breast feeding mothers, and patients with liver or renal disease were excluded from the study. Patients were assigned to two groups, Group A (pregabalin 150mg) and Group B (pregabalin 225mg), 30 each using computer-generated random numbers. The drug was administered one and half hours before surgery by oral route, which was kept in a sealed opaque envelope by a person who was unaware of the group details. Neither the patients nor the anaesthesiologist who gathered the data during the post-operative period were unaware of the group details.

The incidence of VAS at 4–8 h was taken as a parameter for calculating the sample size. We took a power of 0.90, an effect size of 0.90, a 10% chance of error with $\alpha = 0.05$, $\beta = 0.20$, and a confidence interval of 95%. Our sample size came out to be 30 subjects per group. The study was conducted for two months.

FLOW DIAGRAM OF STUDY DESIGN



Preanesthetic checkups and basic investigations were done for every patient before the surgery. Informed written consent was obtained from the patient after providing complete details regarding the study protocol and the procedure during the preanesthetic visit. The patient was familiarized with the VAS for pain assessment during preanesthetic checkup. One and a half hours before the induction of anaesthesia, the patients of

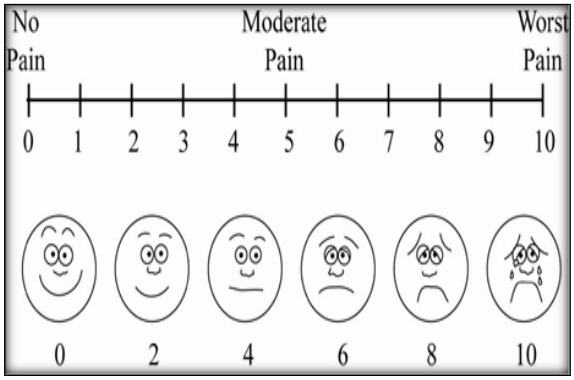
Group A (Pregabalin 150 mg) - were given oral two capsules of 75 mg with sips of water.

Group B (Pregabalin 225 mg) - were given three capsules of 75 mg pregabalin with sips of water. In the operation theatre, intravenous access was obtained, and a fluid infusion was started. The baseline heart rate, peripheral oxygen saturation (SpO2), mean blood pressure, and respiratory rate were recorded. This was followed by the intravenous injection of glycopyrrolate 0.2 mg and fentanyl two µg/kg. After preoxygenation with 100% oxygen for three minutes, the patient was induced with an injection of Propofol 2 mg/kg intravenously slowly, and intubation was facilitated with an injection of vecuronium 0.1mg/kg intravenously. Intubation response was assessed by noting the Heart rate and Mean arterial pressure before and immediately after intubation. Anesthesia was maintained with 50% oxygen, 50% nitrous oxide, sevoflurane 2% titrated according to blood pressure (BP) readings, and vecuronium 0.025 mg/kg. The vital parameters, including heart rate, systolic BP, diastolic BP, mean arterial pressure, SpO2, and end-tidal carbon dioxide (EtCO2) levels, were monitored continuously and recorded every 15 minutes. Intravenous paracetamol 1gm was administered towards the end of the surgery, and the patient was reversed with intravenous Neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg. The patient was extubated when fully awake. After extubation, the patient was shifted to the recovery room when fully awake, which was considered zero hours. VAS scores were assessed in the immediate

postoperative period hourly for the first four hours and at 8,12, and 24 hours. Rescue analgesia was administered with intramuscular Diclofenac sodium 1 mg/kg. Time of administration of first analgesic given was noted and also total dose of inj Diclofenac required in first 24 hours was noted. Hemodynamic parameters were also noted while VAS scores were being assessed. Patients were also monitored for side effects like nausea, vomiting, skin rash, somnolence, headache, dizziness, drowsiness, visual disturbances, peripheral oedema and respiratory depression (respiratory rate < 10 breaths/minute and oxygen saturation <90% without oxygen supplementation).

All results were tabulated and analyzed using analysis of variance (ANOVA) and Tukey's Post Hoc test. For qualitative data, a Chi-square test was used. The data was analyzed using Statistical Package for Social Sciences software (SPSS) (version 25; IBM SPSS Statistics for Windows, Armonk, NY) and the Microsoft Excel program. Descriptive statistics was used for all data, which were reported in terms of mean, standard deviation, and percentages. Appropriate statistical tests of comparison were applied. A p-value of < 0.05 was considered statistically significant, and a P-value of < 0.001 was considered highly significant.

VAS SCORES



Index for VAS and Ramsay scores

Table 1: The Ramsay Sedation Scale

CLINICAL SCORE	PATIENT CHARACTERISTICS
1	Awake; agitated or restless or both
2	Awake; cooperative, oriented, and tranquil
3	Awake but responds to commands only
4	Asleep; brisk response to light glabellar tap or loud auditory stimulus
5	Asleep; sluggish response to light glabellar tap or loud auditory stimulus
6	Asleep; no response to glabellar tap or loud auditory stimulus

Adapted from Ramsay MA, Savage TM, Simpson B, et al: Controlled sedation with alphaxalone-alphadolone. *British Medical Journal* 22;2(5920):656–659. doi: 10.1136/bmj.2.5920.656

RESULTS

The demographic data concerning age, gender, BMI and duration of surgery was similar in both groups . The P-value is not significant (P-value > 0.05), so both groups were comparable. [Table 2]

The mean heart rate values of GROUP B are less than GROUP A at each hour. However, the difference is statistically not significant. (P-value > 0.05). [Table 3]

The mean arterial pressure of Group B is less than that of Group A. However, both groups were comparable as the P value is not significant (p-value >0.05). [Table 4]

The mean VAS scores of group B were less than group A, with statistically significant p-value (<0.05) at 0, 1, 2, 4th, 6th, 8th, 12th, and 24th hr postoperatively. [Table 5]

The Ramsay sedation scores of Group B were higher than those of Group A at each hour postoperatively. However, the difference is statistically not significant(p>0.05). [Table 6]

The patients of group B reported a higher incidence of nausea and vomiting than group A. However, the p-value is not significant (more than 0.05). Concerning other side effects, the data was comparable between both groups, as the p-value is not statistically significant. [Table 7]

The mean value of time to first rescue analgesia of group B is more than that of group A, but the difference between the groups is not statistically significant. The mean values of total analgesic consumption (IM Diclofenac) between the two groups depicted a statistical change (p-value < 0.05). [Table8]

Table 2: Demographic data

		GROUP A	GROUP B	P VALUE
1	AGE	42 ±1.26	46± 1.34	0.74
2	SEX (M%)	78 ± 1.23	84 ±1.45	0.38
3	BMI	22 ± 1.54	24.8 ± 1.45	0.74
4	DURATION OF SURGERY	82 ± 1.28	88 ±1.46	0.48

Table 3: Hemodynamics (Heart Rate)

	GROUP A	GROUP B	P VALUE
Baseline	84±1.36	83± 1.46	0.70
Immediately After intubation	94±1.11	90±1.31	0.37
15 min	92±1.12	88±1.31	0.40
30min	90 ± 1.44	89 ± 1.34	0.70

45min	88± 1.09	86± 1.07	0.92
1hr	89± 1.99	85 +- 1.87	0.73
1.5 hr	86± 1.56	84± 1.66	0.74
0 postop	85±1.36	83± 1.46	0.70
1hr	84±1.23	82±1.16	0.75
2hr	90 ± 1.44	89 ± 1.34	0.70
4hr	88±1.23	90±1.04	0.37
8hr	92±1.31	88±1.05	0.24

Table 4: Hemodynamics (MAP)

TIME	GROUP A	GROUP B	P VALUE
baseline	96±6.335	94.43±9.302	0.449
Immediately After intubation	96.6±4.598	94.83±6.878	0.2496
15 min	96.73±4.689	94.7±7.423	0.2112
30min	97.06±5.619	94.7±6.454	0.1362
45min	96.66±5.188	95.16±5.663	0.2874
1hr	98.8±5.115	96.2±4.254	0.037
1.5 hr	95.53±5.649	94.8±4.978	0.5978
0 postop	85.93± 1.45	88± 1.34	0.67
1hr	92±1.25	90± 1.22	0.89
2hr	88± 1.23	86± 1.35	0.61
4hr	86± 1.33	84± 1.23	0.67
8hr	88± 1.11	86± 1.21	0.64
12hr	86± 1.31	84± 1.53	0.40
24hr	84± 1.21	82± 1.33	0.61

Table 5: VAS SCORE

TIME	GROUP A	GROUP B	P VALUE
0 hr	1.76± 0.34	1.2 ± 0.21	0.01
1hr	2.1± 0.12	1.8±0.21	0.003
2hr	2.46± 0.22	2.1± 0.31	0.06
4hr	3.54±0.12	2.3± 0.08	0.03
6hr	2.96± 0.08	3.2± 0.12	0.03
8hr	2.1± 0.25	2.09± 0.16	0.01
12hr	1.96± 0.04	1.4 ±0.06	0.03
24hr	1.16± 0.21	0.71± 0.14	0.03

Table 6: Ramsay sedation score

TIME	GROUP A	GROUP B	P VALUE
0 hr	1.9± 0.77	2.2± 0.88	0.47
1hr	1.2± 0.67	1.5±0.65	0.87
2hr	1.5± 0.11	1.8±0.13	0.37
4hr	1.4± 0.21	1.6±0.2	0.79
8hr	1.3±0.22	1.4±0.25	0.49
12hr	1.13± 0.23	1.5±0.27	0.39
24hr	0.8±0.19	1.1±0.21	0.59

Table 7: Side Effects in Percentage

	GROUP A	GROUP B	P VALUE
Nausea	4±0.19	6±0.21	0.59
vomiting	30±2.34	40±3.34	0.06
headache	6±0.55	8±0.65	0.37
Visual disturbance	8±0.99	14±0.85	0.41
Dizziness	6.8±0.45	14.6±0.56	0.24

Table 8: The mean value of time to first rescue analgesia

	GROUP A	GROUP B	P VALUE
Time of first rescue analgesia	7.1hrs± 0.66	7.9 hrs± 0.73	0.59
Total diclofenac IM consumption	71 mg ±15.11	65±10.31	0.04

DISCUSSION

Perioperative anxiety and postoperative pain remain problems for many outpatients during the perioperative period. Benzodiazepines are effective in reducing preoperative anxiety in the ambulatory setting[8], but the anxiolytic effect is frequently accompanied by undesirable sedation. The prevention and treatment of postoperative pain with opioid analgesics contributes to postoperative nausea and vomiting and can delay recovery of

bowel function, as well as adversely affect many other organ systems in the body.[9] Opioid-related side effects contribute to delayed discharge and recovery of activities of daily living after ambulatory surgery.[10] Recently, an increasing emphasis has been placed on the use of non-opioid analgesic drugs as part of a multimodal regimen for preventing pain in the perioperative period.[10,12]

Pregabalin is an analogue of gabapentin, which has been alleged to possess anxiolytic, analgesic, and antiepileptic activity.[13] By altering calcium currents, pregabalin reduces or modulates the release of several excitatory neurotransmitters, including glutamate, norepinephrine, substance P, and calcitonin gene-related peptide, producing inhibitory modulation of "over-excited" neurons and returning them to a "normal" state.[13,14]

In a study done by Akhavan-Akbari et al., it was confirmed that even a single pre-operative oral dose of pregabalin 150 mg is an effective method for reducing postoperative pain in patients undergoing orthopaedic surgery.[15] This was even confirmed by Agarwal et al., Mishra et al., and Anand et al. in their studies, which have shown that postoperative pain was reduced with 150 mg pregabalin when compared with placebo (P< 0.05) in patients undergoing laparoscopic cholecystectomy.[4,16,17] Entezary et al. and Sattari et al., in their studies, have also shown that preemptive use of 300 mg of pregabalin reduced postoperative pain after abdominal hysterectomy and thoracotomy, respectively.[18,19] Jokela et al. also compared Pregabalin 150 mg ×2 with placebo in laparoscopic hysterectomy,[6] Iippana EM et al. studied pregabalin 300 mg ×2 in their study.[2]

Our purpose in choosing 225mg was to find whether a dose below the already tested 300mg could be equally efficacious and have fewer side effects. We compared the efficacy of 150mg and 225mg doses of pregabalin in patients undergoing laparoscopic cholecystectomy for postoperative pain relief.

There was no substantial difference among the groups regarding demographics like age, sex, BMI, and duration of surgery (P>0.05). The hemodynamic parameters are an indirect reflection of pain control. Intraoperatively, group A showed a mean HR that was higher than that observed in group B throughout the surgery. The lower heart rates in groups A and B correlate well with the analgesic effects and can also be attributed to the anxiolytic effect of pregabalin. The mean heart rate in group B is low compared to group A, which was seen throughout the surgery, corresponding with the higher dose of pregabalin used in group B. Postoperatively, mean arterial pressure readings in our study were higher in group A than in group B; however, the intraoperative and postoperative heart rate and mean arterial pressure P values were not statistically significant (P>0.05). With respect to intubation response, the difference between mean Heart rate and mean arterial blood pressure between the two groups did not show any statistical Significance (p>0.05).

Our findings also correlate with those of Sahu et al., who found no statistically significant difference in mean systolic blood pressure, mean diastolic blood pressure, and mean respiratory rate in patients receiving two 150 mg pregabalin doses 12 h apart as compared to the placebo in patients undergoing below umbilical surgeries under spinal anaesthesia.[21]

The mean VAS values were lower in group B compared to group A at 0,1st,2nd, 3rd,4th,8th, 12th, and 24 hours of the postoperative period, and the difference was statistically significant (p<0.05). This signifies that 225mg pregabalin is a better preemptive analgesic than 150mg pregabalin.

The time required to request the first rescue analgesia was longer in Group B (7.9 hrs.) than in Group A (7.1 hrs.), but the difference was not statistically significant (p>0.05).

The time of request for first rescue analgesia for group B of our study is less than that of group B patients(8.37hrs)of a study done by Simritkaur et al. where 300mg oral pregabalin was used for preemptive analgesia.[22]

The total rescue analgesic (Diclofenac) consumption was more with group A (71mg) when compared to group B (65mg), which was statistically significant (p<0.05). In our study, patients were satisfied with rescue analgesia of Diclofenac IM injection (50mg), and the need for fentanyl injection did not arise as the VAS scores were lower after diclofenac injection. This signifies the good quality of the preemptive analgesic effect of Pregabalin, and it also reduces the financial burden of analgesic needs in the postoperative period.

These findings are compatible with most of the studies carried out in this respect. In a study done by Ittichaikulthol and colleagues [23], they found that 300 mg given 1 hr before surgery significantly reduced pain scores and morphine consumption after abdominal hysterectomy. Mathiesen et al. [24] concluded that Pregabalin resulted in a 50% reduction in 24-hour postoperative morphine requirements. Likewise, Jokela et al.,[6] found that peri-operative use of Pregabalin 600 mg (300 mg one hour before surgery and 12 hours after the first dose) was associated with a reduction in postoperative oxycodone consumption.

Somnolence and dizziness are the two most common side effects associated with pregabalin [20]. Sedation scores were higher in Group B than in Group A in the postoperative period. This is mostly due to the larger dose of pregabalin used in Group B compared to Group A. However, the difference between the groups is not significant (p >0.05).

In a study by Agarwal et al., the incidence and severity of sedation were comparable in patients taking either pregabalin 150 mg or a placebo in patients undergoing laparoscopic cholecystectomy.[4] A significantly higher 24-hour sedation score was observed with pregabalin 300 mg as compared with placebo by Mathiesen et al. and Esmat et al. in their studies on patients undergoing

hip arthroplasty and laparoscopic cholecystectomy, respectively.[24,25] In a study done by Jokela et al.,[6] the degree of drowsiness was similar after perioperative administration of diazepam 10 mg, pregabalin 300 mg, or 600 mg following laparoscopic hysterectomy. In a study by Ghai and colleagues, 600 mg pregabalin was associated with excess somnolence up to 18–24 hours after surgery. Further cases were abandoned with 600 mg, though most of these cases did not require any analgesic in the first 24 hours.[26] This is usually not disabling, and the antianxiety effect has been found to be beneficial in some studies [27]. Pande et al. and Gonano et al., in their studies, have also shown that pregabalin reduces anxiety in an effective and well-tolerated manner. [28,29]

Nevertheless, the sedation that accompanies the analgesic effect of pregabalin may be beneficial because the onset of sedation indicates the reduction of anxiety. Perioperative anxiety leads to a surge of catecholamines due to the stress response, leading to tachycardia, hypertension, and hemodynamic instability.

Nausea occurred in 6 % of patients in Group B when compared to 4 % in Group A. Vomiting occurred in 40 % of patients in Group B when compared to 30 % of patients in Group A. This could be due to a higher dose of pregabalin in Group B than in Group A. The difference between the two groups with respect to nausea and vomiting was statistically not significant. ($p>0.05$). Agarwal et al. and Paechet al. also have reported similar results.[4,30] Mathiesen et al. and Esmat et al. reported a higher incidence of nausea and vomiting with 300 mg pregabalin as compared to 150 mg pregabalin and placebo.[24,25] The incidence of nausea and vomiting of group B patients of our study was less than that of patients in the above studies who received 300 mg pregabalin.

The incidence of visual disturbances in our study was 14% in Group B compared to 8% in Group A. This incidence of sedation, dizziness (14.6%), and visual disturbances(14%) in Group B of our study is less than that of the incidence in patients receiving 300mg pregabalin in the study done by Tanveersingh et al.[31] In a study by Gupta et al., Six patients reported dizziness in the pregabalin group, eight in the gabapentin group and one in the control group ($P=0.093$). [26]. In a study by Jokela et al., the incidence of dizziness and blurred vision was higher after perioperative administration of pregabalin 600 mg during the first 24 hours after surgery. [6]

This shows that the incidence of sedation, dizziness, and visual disturbances in patients who received 225 mg of pregabalin in our study is much less than that of the patients who received higher doses (300mg, 600mg) in the above studies.

Mean respiratory rate and mean SpO2 postoperatively in the recovery room were comparable in all two groups, and no significant difference was found in these values. Respiratory depression was not observed in any patient. The incidence of headache, blurred vision, peripheral oedema, and skin rash was comparable in all the groups.

We have found that oral pregabalin 225 mg, given as a preemptive analgesic one hour before laparoscopic cholecystectomy, produces good post-operative analgesia compared to pregabalin 150mg. The side effects such as sedation, nausea, vomiting, dizziness, and visual disturbances are the common side effects noted with regular doses of pregabalin. However, significant side effects were not observed in our study cases. Hence, we regard the achievement of better preemptive analgesia and anxiolysis with a single dose of pregabalin 225mg with comparable side effects to pregabalin 150 mg as a part of multimodal analgesia for managing postoperative pain.

The strength of our study lies in our study design. This was a randomized, double-blind, controlled study. We have covered a wide range of age groups in our study. We have chosen our study population as patients undergoing laparoscopic cholecystectomy, a common surgery nowadays, so our study results would be more beneficial to them. Moreover, testing for an apt dose of preemptive analgesia with acceptable side effects is an ever-interesting subject.

Our study is associated with a few limitations. Patients posted for laparoscopic cholecystectomy were taken into consideration; we have not assessed patients posted for other general anaesthesia cases, which might be one of the limitations. We have not tested the benefits of the preemptive analgesic effect of pregabalin in ASA III and ASA IV patients, where effective control of postop stress due to pain is highly beneficial. In the assessment of side effects profiles like nausea, vomiting, dizziness, and visual disturbances, there could be subjective and objective variation.

CONCLUSION

Preemptive analgesia with pregabalin 225mg is associated with lower rescue analgesic consumption, higher sedation, and a longer postoperative pain-free period than Pregabalin 150mg in patients undergoing laparoscopic cholecystectomy. Moreover, pregabalin 225 mg is associated with significantly lower total rescue analgesic consumption than pregabalin 150mg. In conclusion, a single preoperative dose of pregabalin 225 mg can be used to provide effective preemptive analgesia in patients undergoing laparoscopic cholecystectomy.

Conflict of Interest: None

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REFERENCES

1. Vadivelu N, Mitra S, Narayan D. Recent advances in postoperative pain management. Yale J Biol Med. 2010; 83:11–25. [PMC free article] [PubMed] [Google Scholar]

2. Kissin I. Pre-emptive analgesia. Anaesthesiology. 2000; 93:1138–43. [PubMed] [Google Scholar]
3. Chang CY, Challa CK, Shah J, Eloy JD: Gabapentin in acute postoperative pain management. Biomed Res Int.2014, 2014:631756. 10.1155/2014/631756
4. Agarwal A, Gautam S, Gupta D, Agarwal S, Singh PK, Singh U. Evaluation of a single dose of pregabalin for attenuation of postoperative pain after laparoscopic cholecystectomy. Br J Anaesth. 2008; 101:700–4. [PubMed] [Google Scholar]
5. Peng PW, Li C, Farcas E, Haley A, Wong W, Bender J, et al. Use of low-dose pregabalin in patients undergoing laparoscopic cholecystectomy. Br J Anaesth. 2010; 105:155–61. [PubMed] [Google Scholar]
6. Jokela R, Ahonen J, Tallgren M, Haanpaa M, Korttila K. A randomized controlled trial of perioperative administration of pregabalin for pain after laparoscopic hysterectomy. Pain. 2008; 134:106–12. [PubMed] [Google Scholar]
7. Chang SH, Lee HW, Kim HK, Kim SH, Kim DK. An evaluation of perioperative pregabalin for prevention and attenuation of postoperative shoulder pain after laparoscopic cholecystectomy. AnesthAnalg. 2009; 109:1284–6. [PubMed] [Google Scholar]
8. Shafer A, White PF, Urquhart ML, Doze VA. Outpatient premedication: use of midazolam and opioid analgesics. Anesthesiology 1989; 71:495–501
9. White PF, Kehlet H. Improving pain management: are we jumping from the frying pain into the fire? AnesthAnalg 2007; 105:10–12
10. Pavlin DJ, Chen C, Penaloza DA, Polissar NL, Buckley FP. Pain as a factor complicating recovery and discharge after ambulatory surgery. AnesthAnalg 2002; 95:627–34.
11. White PF. The changing role of non-opioid analgesic techniques in the management of postoperative pain. AnesthAnalg 2005; 101:5–22
12. White PF. Multimodal analgesia: its role in preventing postoperative pain. CurrOpinInvestig Drugs 2008; 9:76–82. f
13. Kavoussi R. Pregabalin: from molecule to medicine. EurNeuropsychopharmacol 2006;16: S128–S133.
14. Shneker BF, McAuley JW. Pregabalin: a new neuromodulator with broad therapeutic indications. Ann Pharmacother 2005; 39:2029.
15. G. Akhavanakbari, M. Entezarias, K. Isazadehfar, T. Mirzarahimi.The effects of oral pregabalin on post-operative pain of lower limb orthopedic surgery: a double-blind, placebo-controlled trialPerspectClin Res, 4 (3) (2013), 10.4103/2229-3485.115376
16. Mishra R, Tripathi M, Chandola HC. Comparative clinical study of gabapentin and pregabalin for postoperative analgesia in laparoscopic cholecystectomy. Anesth Essays Res. 2016; 10:201–6. [PMC free article] [PubMed] [Google Scholar]
17. Anand LK, Sandhu M, Singh J, Mitra S. Evaluation of analgesic efficacy of pregabalin for postoperative pain relief after laparoscopic cholecystectomy: A double blind study. Anesth Pain Intensive Care. 2017; 21:174–80. [Google Scholar
18. Entezary S, Imani, FarnadKhatibi, Ali Rezaei A. Preemptivepregabalin versus placebo for acute postoperative pain after total abdominal hysterectomy. Anesthesiol Pain. 2012; 1:59–64. [Google Scholar]
19. Sattari H, Hashemian M, Lashkarizadeh MR, Jalalifard H. Preoperative oral pregabalin reduces acute pain after thoracotomy. Maced J Med Sci. 2018; 6:1606–10. [PMC free article] [PubMed] [Google Scholar].
20. Tiippana EM,HamunenK,KontinenVK,KalsoE.Do surgical patients benefit from perioperative gabapentin/pregabalin? A systematic review of efficacy and safety. AnesthAnalg.2007; 104: 1545-1556
21. Sahu S, Sachan S, Verma A, Pandey HD, Chitra Evaluation of pregabalin for attenuation of postoperative pain in below umbilical surgeries under spinal anaesthesia. J AnaesthClinPharmacol. 2010; 26:167–71. [Google Scholar].
22. Simrit Kaur,1 SartajTurka, 2 Tripat Kaur Bindra,1 Rajan D Tuteja,1 Manoj Kumar,3 SukhminderJit Singh Bajwa,4 Madhuri S Kurdi,5 and Apoorva J Sutagatti6Comparison of the Efficacy of Pregabalin and Gabapentin for Preemptive Analgesia in Laparoscopic Cholecystectomy Patients: A Randomised Double-Blind Study. Cureus. 2023 Oct; 15(10): e46719. doi: 10.7759/cureus.46719
23. W. Ittichaikulthol, T. Virankabutra, M. Kunopart, W. Khamhom, P. Putarawuthichai, S. RungphetEffects of pregabalin on postoperative morphine consumption and pain after abdominal hysterectomy with/without salpingo-oophorectomy: a randomized double-blind trialuJMedAssoc Thai, 92 (2009), pp. 1318-1323
24. O. Mathiesen, L.S. Jacobsen, H.E. Holm, S. Randall, L. Adamiec-Malmstroem, B.K. Graungaard, et al.Pregabalin and dexamethasone for postoperative pain control: a randomized controlled study in hip arthroplastyBr J Anaesth, 101 (2008), pp. 535-541
25. Esmat IM, Farag HM. Comparative study between paracetamol and two different doses of pregabalin on postoperative pain in laparoscopic cholecystectomy. Saudi J Anaesth. 2015; 9:376–80. [PMC free article] [PubMed] [Google Scholar]
26. A. Ghai, M. Gupta, S. Hooda, D. Singla, R. WadheraA randomized controlled trial to compare pregabalin with gabapentin for postoperative pain in abdominal hysterectomySaudi J Anaesth, 5 (3) (2011), pp. 252-257
27. C. Ménigaux, F. Adam, B. Guignard, D.I. Sessler, M. ChauvinPreoperative gabapentin decreases anxiety and improves early functional recovery from knee surgeryAnesthAnalg, 100 (2005), pp. 1394-1399
28. Panda AC, Feltner DE, Jefferson JW, Davidson JR, Pollack M, Stein MB, et al. Efficacy of the novel anxiolytic pregabalin in social anxiety disorder: A placebo controlled, multicenter study. J ClinPsychopharmacol. 2004; 24:141–9. [PubMed] [Google Scholar]
29. Gonano C, Latzke D, Sabeti-Aschraf M, Kettner SC, Chiari A, Gustorff B. The anxiolytic effect of pregabalin in outpatients undergoing minor orthopaedic surgery. J Psychopharmacol. 2011; 25:249–53. [PubMed] [Google Scholar]
30. Paech MJ, Goy R, Chua S, Scott K, Christmas T, Doherty DA. A randomized, placebocontrolled trial of preoperative oral pregabalin for postoperative pain relief after minor gynecological surgery. AnesthAnalg. 2007; 105:1449–53. [PubMed] [Google Scholar]
31. Tanveer.Singh, SuneetKathuria, Richa Jain, Dinesh Sood, and Shikha GuptaJ Premedication with pregabalin 150mg versus 300mg for postoperative pain relief after laparoscopic cholecystectomy. Anaesthesiol Clin Pharmacol. 2020 Oct-Dec; 36(4): 518–523. Published online 2021 Jan 18. doi: 10.4103/joacp.JOACP_440_19. PMCID: PMC8022042.