Original Research Article

Study of preoperative oral pregabalin and gabapentin with respect to postoperative pain relief and postoperative analgesic requirement in patients undergoing laparoscopic cholecystectomy

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Abstract

Background: Pregabalin and gabapentin share a similar mechanism of action, inhibiting calcium influx and subsequent release of excitatory neurotransmitters; however, the compounds differ in their pharmacokinetic and pharmacodynamic characteristics. We aimed to study the analgesic efficacy of preoperative oral pregabalin and gabapentin with respect to postoperative pain relief and postoperative analgesic requirement in patients undergoing laparoscopic cholecystectomy. **Material and Methods:** Present study was hospital based, double blind, randomized, prospective, comparative clinical study, conducted in patients 18-70 years, of either sex, with ASA grade I-II, undergoing Laparoscopic cholecystectomy surgery. 60 patients were randomly divided Gabapentin group (Gabapentin 600 mg orally with sips of water, two hours prior to surgery) and Pregabalin group (Pregabalin 150 mg orally with sips of water, one hour prior to surgery). **Results:** In present study, there was no substantial difference among the two groups with regard to age, weight, sex and ASA grade. In present study, patients receiving Pregabalin (14.7 ± 4.1) had a statistically significant lower mean first hour post operative visual analogue scale score as compared to patients receiving Gabapentin (32.8 ± 9.6). The mean time of rescue analgesia in the pregabalin group was 4.33 hours and that in the gabapentin group was 1.75 hours and difference was statistically significant. Pain was lower in the Pregabalin group when compared with the Gabapentin group, during the entire observation period. Mean Ramsay sedation score was higher in gabapentin group during the first 8 hours post operatively as compared to pregabalin group and difference was statistically significant. **Conclusion:** Pregabalin is superior to gabapentin as: it decreases post operative pain for the first 24 hours, reduces the requirement of rescue analgesia and is associated with low incidence of side effects.

Keywords: Pregabalin, gabapentin laparoscopic cholecystectomy, rescue analgesia

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INTRODUCTION

Laparoscopic cholecystectomy results in less postoperative pain and/or reduced analgesic consumption as compared with open cholecystectomy.1,2,3 Nonetheless, pain after laparoscopy may be moderate or even severe for some patients, and may require opioid treatment. Interestingly, the type of pain after laparoscopy differs considerably from that seen after laparotomy. Early pain after cholecystectomy is reduced by minimizing residual pneumoperitoneum and by giving incisional local anaesthetics, epidural analgesia, and non-steroidal anti-

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inflammatory drugs.[2] Different treatments have been proposed to relieve pain after laparoscopy. Opioids, NSAID's, antidepressants and anticonvulsants are used as pharmacological agents to treat pain. However, no single class of drug has been found to be effective in all types of pain, presumably because pain syndromes involve different mechanisms.[3] With increasing evidence of efficacy of Pregabalin and Gabapentin in a wide variety of pain syndromes, especially neuropathic pain, both may be potentially useful because of their relative freedom from serious adverse effects, lack of interactions with other drugs and lack of potential for causing drug dependence.[4] Pregabalin and gabapentin share a similar mechanism of action, inhibiting calcium influx and subsequent release of excitatory neurotransmitters; however, the compounds differ in their pharmacokinetic and pharmacodynamic characteristics.[4] We aimed to study the analgesic efficacy of preoperative oral pregabalin and gabapentin with respect to postoperative pain relief and postoperative analgesic requirement in patients undergoing laparoscopic cholecystectomy.

MATERIAL AND METHODS

Present study was hospital based, double blind, randomized, prospective, comparative clinical study, conducted in Department of Anaesthesia, Dr.Vasantrao Pawar Medical College, Hospital And Research Centre, Adgaon, India. Study duration was of 2 years (July 2018 to June 2019). Study was approved by institutional ethical committee.

INCLUSION CRITERIA: Patients 18-70 years, of either sex, with ASA grade I-II, undergoing Laparoscopic cholecystectomy surgery.

EXCLUSION CRITERIA: Patients with known history of hypersensitivity to the drug. History of ischemic heart disease. Patient refusal to participate. Patients with uncontrolled concomitant medical disorders. History of peptic ulcer or of bleeding diathesis or taking antacids. Impaired kidney or liver functions. Ingestion of analgesics within 24 hours before scheduled surgery. Antidepressant and calcium channel blocker use.

After getting approval from the ethical committee the study was started. The patients in the study group were explained about nature of study and informed consent was obtained for participation in the study. Patients were educated about Visual Analogue Scale (V.A.S.) for grading of pain.

All patients were investigated including Hemoglobin, Complete blood counts, Urine analysis, Bleeding time, Clotting time, Liver function tests, Renal function tests, Chest X-Ray and ECG as appropriate.

The patients were randomly divided in two groups as -

Gabapentin group- Patients receiving Capsule Gabapentin 600 mg orally with sips of water, two hours prior to surgery.

Pregabalin group– Patients receiving Capsule Pregabalin 150 mg orally with sips of water, one hour prior to surgery. On the day of the surgery, patients were administered the drug (either gabapentin or pregabalin) orally with sips of water according to the number allocated to the patient approximately two hours and one hour prior to surgery respectively. Once inside the operation theatre, routine monitors were attached using cardioscope, non-invasive blood pressure monitoring, pulse oximeter and capnometer. Preoxygenated with 100% oxygen with face mask for three minutes. Premedication was done with Inj. Glycopyrrolate 0.004 mg/kg, Inj. Ranitidine 1 mg/kg, Inj. Ondansetron 0.08mg/kg, Inj. Midazolam 0.03 mg/kg and Inj. Fentanyl 1-2mg/kg intravenously. Anaesthesia was then induced with Inj. Propofol 2-3 mg/kg IV in titrated doses. Intubation was facilitated with Inj. Atracurium 0.5 mg/kg. Anaesthesia was maintained with 50% air with 50 % oxygen and inhalational isoflurane(0.8-1%) and infusion of atracurium 25 mg /hr to maintain adequate depth of anaesthesia. Normocapnia was maintained. Intra operatively additional analgesia was provided with Inj. Diclofenac 75 mg immediately after intubation. After completion of surgery Inj. Neostigmine 0.05 mg/kg with Inj. Glycopyrrolate 0.01 mg/kg was given to reverse neuromuscular blockade. Tracheal extubation was performed after adequate and regular spontaneous ventilation was established and adequate tone, power and reflexes were regained.

Postoperatively patients were observed in recovery room where monitoring was done for a period of 24 hours by an anaesthesiologist blinded for the drug. The anaesthesiologist recorded vital parameters, V.A.S. score on arrival in recovery room(immediately after the surgery=0 hour) and every 2 hourly till 24 hours. V.A.S. score of pain was used where 100 mm scale marked with '0' at one end represented 'no pain' and marked '100' at other end represented 'worst possible pain'. When asked, patient was told to point out his assessment of pain at that time on the multiple points of this visual analogue scale. When V.A.S. score was ≥30 , rescue analgesia was given with Inj. diclofenac 1.5 mg/kg IV. The time to first rescue analgesia was recorded and total analgesic requirement over 24 hours was assessed. The side effects of the drugs were also studied.

The visual analogue scale (VAS) is a common method for the quantification of pain severity. It is a continuous outcome measure consisting of a 100-mm scale from 0 to 100 with low and high end points of no pain and worst pain.

RSS (Ramsay sedation score): The Ramsay Sedation Scale (RSS) was the first scale to be defined for sedated patients and was designed as a test of arousability.

Ramsay Sedation Scale: Patient is anxious and agitated or restless, or both. Patient is cooperative, oriented and tranquil. Patient responds to commands only. Patient exhibits brisk response to light glabellar tap or loud auditory stimulus. Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus. Patient exhibits no response.

The data was collected. Demographic parameters were analysed by student's t-test. The binary data like sex and ASA grading were analysed by chi-square test. Postoperative visual analog scale score and Ramsay's sedation score was analysed. For finding statistical significance between the groups, t-test was applied to ascertain the pattern and magnitude of differences. A p value of 0.05 was considered as significant.

RESULTS

In present study, there was no substantial difference among the two groups with regard to age, weight, sex and ASA grade.

Table 1: Demographic Data

Parameters	Gabapentin (n=30)	Pregabalin (n=30)	' p' Value	Significance
Age(Yrs)	47.2 ± 10.8	52.7 ± 10.3	0.058	Not significant
Weight (Kgs)	70.0 ± 8.0	70.3 ± 9.9	0.157	Not significant
Sex (M/F)	14/16	15/15	0.796	Not significant
ASA Grade(I/II)	17/13	13/17	0.302	Not significant

In present study, patients receiving Prega3qbalin (14.7 ± 4.1) had a statistically significant lower mean first hour post operative visual analogue scale score as compared to patients receiving Gabapentin (32.8 ± 9.6). Patients requiring rescue analgesia during the first postoperative hour was found to be of reduced magnitude in the pregabalin group as compared to the gabapentin group (10 vs. 0) and difference was statistically significant. The mean time of rescue analgesia in the pregabalin group was 4.33 hours and that in the gabapentin group was 1.75 hours and difference was statistically significant.

We noted a significant difference in the total number of analgesic doses required in gabapentin group (24) compared to the pregabalin group (11).

Table 2: Comparison post operative visual analog scale (VAS) score

	Gabapentin (n=30) Mean ± SD	Pregabalin (n=30) Mean ± SD	' p' Value	Significance
First (0) post operative hour VAS score	32.8 ± 9.6	14.7 ± 4.1	< 0.001	Significant
No. of patients requiring rescue analgesia in first post operative	10	0	0.033	Significant
Time o`f first rescue analgesia	1.75 ± 1.800	4.33 ± 1.670	< 0.001	Significant
No. of patients requiring rescue analgesia in 24 hour post operativ	24	11	< 0.001	Significant

Pain, as measured by the visual analogue scale score was always found to be lower in the Pregabalin group when compared with the Gabapentin group, during the entire observation period.

Table 3: Comparison of mean vas scores at various time periods

Time (Hours)	Gabapentin (n=30) Mean ± SD	Pregabalin (n=30) Mean ± SD	' p' Value	Significance
0	32.8 ± 9.6	14.7 ± 4.1	< 0.001	Significant
2	31.0 ± 8.2	16.5 ± 4.4	< 0.001	Significant
4	30.0 ± 7.1	25.5 ± 6.1	0.010	Significant
6	26.0 ± 6.6	25.2 ± 7.7	< 0.001	Significant
8	24.3 ± 6.8	24.0 ± 5.8	< 0.001	Significant
10	25.6 ± 7.2	24.5 ± 3.8	< 0.001	Significant
12	27.3 ± 6.7	24.2 ± 5.4	0.048	Significant
14	24.8 ± 5.5	19.2 ± 6.8	0.001	Significant
16	27.2 ± 6.1	18.0 ± 4.7	< 0.001	Significant
18	25.3 ± 5.4	22.8 ± 4.9	< 0.001	Significant
20	24.3 ± 5.0	22.7 ± 5.2	< 0.001	Significant
22	23.5 ± 6.5	20.2 ± 7.9	< 0.001	Significant
24	17.7 ± 5.2	17.3 ± 6.3	< 0.001	Significant

Mean Ramsay sedation score was higher in gabapentin group during the first 8 hours post operatively as compared to pregabalin group and difference was statistically significant. After post-operative 8 hours, Ramsay sedation score was comparable in both groups.

Table 4: Comparisons of mean post operative Ramsay Sedation Score

Time (Hrs.)	Gabapentin (n=30) Mean ± SD	Pregabalin (n=30) Mean ± SD	' p' Value	Significance
0	3.20 ± .805	2.83 ± .699	.045	Significant
2	3.30 ± .702	2.80 ± .484	.002	Significant
4	3.50 ± .572	2.97 ± .414	<0.001	Significant
6	2.87 ± .629	2.33 ± .547	.001	Significant
8	3.00 ± .371	2.73 ± .450	.068	Not Significant
10	2.47 ± .507	2.07 ± .254	.102	Not Significant
12	2.73 ± .521	2.17 ± .379	.34	Not Significant
14	2.23 ± .430	2.03 ± .183	.23	Not Significant
16	2.37 ± .490	2.07 ± .254	.42	Not Significant
18	2.17 ± .379	2.00 ± .000	.019	Not Significant
20	2.20 ± .407	2.03 ± .183	.45	Not Significant
22	2.10 ± .305	2.00 ± .000	.078	Not Significant
24	2.03 ± .183	2.00 ± .000	.321	Not Significant

There was no significant difference in the individual incidences of dizziness, nausea and sedation between the comparison groups. A significant difference does exist if the total incidence of all the side effects is considered.

Table 5: Comparison of side effects between two groups

Adverse Effect	Gabapentin (n=30)	Pregabalin (n=30)	'p' Value	Significance
Dizziness	4	2	0.667	Not significant
Nausea	4	0	0.121	Not significant
Sedation	4	0	0.121	Not significant
Total	**12**	**2**	**0.006**	**Significant**

DISCUSSION

Acute pain after laparoscopic cholecystectomy does not resemble the pain after other laparoscopic procedures, suggesting that the analgesic treatment might be procedures specific and multimodal.[5] Pre-incisional preemptive analgesia has been shown to be more effective in control of post operative pain by protecting the central nervous system from deleterious effects of noxious stimuli and resulting allodynia, and increased pain. Gabapentin and pregabalin both have antiallodynic and anti-hyperalgesic properties useful from treating neuropathic pain and may also be beneficial in acute postoperative pain.[6,7] Gabapentin was shown to be effective in treating a variety of chronic pain conditions, including post herpetic neuralgia, diabetic neuropathy, complex regional pain syndrome, inflammatory pain, HIV related neuropathy and headaches.[8] Gabapentin appears to be a useful adjunct for the management of postoperative pain by providing analgesia through a different mechanism than opioids and other available analgesic agents (e.g., nonsteroidal anti-inflammatory agents, tramadol, or epidural analgesia).[8] Ho *et al.*,[9] in their systematic review suggested that perioperative administration of gabapentin was effective in reducing pain scores, opioid requirements and opioid-related adverse effects in the first 24 hours after surgery. Their analysis also demonstrated a statistically significant prolongation to the time of first request for rescue analgesics. The incidence of postoperative vomiting and pruritus were also found to be significantly lower in the gabapentin group. Though sedation was associated with the use of gabapentin, no serious adverse effects were observed. Seib *et al.*,[10] noted that when given preoperatively, gabapentin is effective in reducing postoperative opioid consumption in the first 24 hours after surgery and, to a lesser extent, reducing pain scores. They also found out that dosing may play a role, with doses of 1200mg being more effective in reducing analgesic consumption than doses of 300 or 400mg. Pregabalin was developed and launched for treating partial epilepsy and neuropathic pain. Studies evaluating the appropriate dosage of pregabalin as a preemptive analgesic agent have suggested that a dose of 150 mg is ideal, with higher doses being associated with dizziness and somnolence.[11] Agrawal *et al.*,[12] evaluated the efficacy of a single preoperative dose of pregabalin for attenuating postoperative pain and fentanyl consumption after laparoscopic cholecystectomy. Postoperative pain (static and dynamic) and postoperative patient-controlled

fentanyl consumption were reduced in the pregabalin group compared with the placebo group (P<0.05). A single preoperative oral dose of pregabalin 150 mg is an effective method for reducing postoperative pain and fentanyl consumption in patients undergoing laparoscopic cholecystectomy.

Pregabalin is several times more potent than similar drug gabapentin as,[13,14,15]

1) It is rapidly absorbed orally with more than 90% bioavailability
2) Achieves peak plasma levels within 30 minutes to 1 hour.
3) Shows linear pharmacokinetics with low intersubject variability including dose independent absorption however bioavailability of gabapentin varies inversely with dose.
4) After single or multiple dosing, the maximal plasma concentration is dose proportional and absorption is independent of food intake.
5) In rodent models of chronic neuropathic pain pregabalin has showed superior analgesic potency compared with gabapentin.
6) Binding affinity of pregabalin for the alpha 2 delta subunit and potency is six times more than that of gabapentin.

In the present study, results suggested that preemptive oral Pregabalin (150 mg) as compared to oral Gabapentin (600 mg) had significant effect on reducing postoperative pain in patients undergoing laparoscopic cholecystectomy surgeries. It was also observed that the incidence of adverse effects such as dizziness, nausea and sedation were also lower in pregabalin group as compared to gabapentin group.

CONCLUSION

Pregabalin in a dose of 150 mg given in cases of laparoscopic cholecystectomy is superior to gabapentin in a dose of 600 mg as: it decreases post operative pain for the first 24 hours, reduces the requirement of rescue analgesia and is associated with low incidence of side effects.

REFERENCES

1. Grace PA, Quereshi A, Colenian J, et al. Reduced postoperative hospitalization after laparoscopic cholecystectomy. Br J Anaesth 1991;78:160-2.
2. Joris J, Cigarini I, Legrand M, et al. Metabolic and respiratory changes after cholecystectomy performed via laparotomy or laparoscopy. Br J Anaesth 1992;69:341-5.
3. Putensen-Himmer G, Putensen C, Lammer H, et al. Comparison of postoperative respiratory function after laparoscopy or open laparotomy for cholecystectomy. Anesthesiology 1992;77: 675-80.
4. Graeme J Sills. The mechanisms of action of gabapentin and pregabalin. Current Opinion in Pharmacology 2006, 6:108–113.
5. Liu J, Ding Y, White PF, et al. Effects of ketorolac on postoperative analgesia and ventilatory function after laparoscopic cholecystectomy. Anesth Analg 1993; 76: 1061-6.
6. Mujadi, Refai, Katzarov MG, Dehrab NA, Batra YK, Qattan .Preemptive gabapentin reduces postoperative pain and opioid demand following thyroid surgery. Can J Anesth 2006; 53; 268–273.
7. Pandey C K, Navkar D V, Giri P J, Raza M. Evaluation of the optimal preemptive dose of gabapentin for postoperative pain relief after lumbar diskectomy: a randomized, double-blind, placebo-controlled study. J Neurosurg Anesthesiol. 2005 Apr;17(2):65-8.
8. Turan A, Karamanlioglu B, Memis D, Hamacioglu MK, Tukenmez B, Pamukcu. Analgesic effects of gabapentin after spinal surgery. Anesthesiology 2004; 100: 935–8.
9. Kok-Yuen Ho, Tong J. Gan, Ashraf S. Habib .Gabapentin and postoperative pain – a systematic review of randomized controlled trials. Pain 126(2006) 91-101
10. Seib RK, Paul JE. Preoperative gabapentin for post operative pain relief; a meta analysis. Can J Anesth 2006; 53: 461-469.
11. Hill CM, Balkenohl M, Thomas DW, Walker R, Mathe H, Murray G. Pregabalin in patients with postoperative dental pain. Eur J Pain 2001; 5: 119–24
12. Agarwal A, Gautam S, Gupta D, Agarwal S, Singh PK, Singh U. Evaluation of a single preoperative dose of pregabalin for attenuation of postoperative pain after laparoscopic cholecystectomy. Br J Anaesth 2008; 101: 700–4
13. Gazulla J, Tintore M. The P/Q-type voltage-dependent calcium channel as pharmacological target in spinocerebellar ataxia type 6: Gabapentin and pregabalin may be of therapeutic benefit. Med Hypotheses 2007;68:131–6
14. 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. Anesth Analg 2009; 109: 1284–6
15. Arora V, Yajnik S, Rastogi S, Bhandari R. Evaluation of oral gabapentin versus oral pregabalin in acute post operative pain in surgeries under spinal anaesthesia. Indian J PAIN 2009;23: 401-406.

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