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Original Research Article

Comparative Analysis of Pregabalin with Gabapentin on Post-Operative Pain in Patients Undergoing Laproscopic Cholecystectomy

Shuaib Ahmed M Mulla[1], Disha Khanapure[2]

[1]Assistant Professor, Department of Anaesthesiology, Belagavi Institute of Medical Sciences, Belgavi, Karnataka, India

[2]Assistant Professor, Department of Anaesthesiology and Critical Care, Belagavi Institute of Medical Sciences, Belgavi, Karnataka, India

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Corresponding author: Dr Shuaib Ahmed M Mulla

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Abstract:

Background and Aim: Opioids were still being considered as conventional drugs for post-operative analgesia; however its use leads to longer duration of ICU stay, negating the advantages of laparoscopic surgeries. Hence using an alternative analgesic in the place of opiods can facilitate faster post-operative recovery. The present study aims to evaluate the effects of the addition of Pregabalin and Gabapentin in reducing post-operative pain in patients undergoing laparoscopic cholecystectomy

Material and Methods: A prospective comparative study was conducted for a period of 12 months in the department of anesthesiology of medical college hospital. The entire study subjects were randomized into three groups of 50 each. Group B subjects received 3 tablets of Beplex forte (as placebo), Group G subjects received 3 tablets of Gabapentin 300mg (total 900mg) and Group P subjects received 3 tablets of Pregabalin 50mg (total 150mg). . Post-operatively degree of pain, requirement for rescue analgesia, sedation score and adverse events occurred was monitored and analysed between the three groups.

Results: Pain score was less in the pregabalin group at all intervals compared to gabapentin and placebo group and the difference was found to be statistically significant ($p<0.05$) Similarly Sedation score was significantly high among the gabapentin group particularly at 6t h hr and 12t h hour post-operatively compared to pregabalin and placebo group ($p>05$). Postoperatively tramadol in the form of injection was used for attenuation of pain and it was observed in our study that maximum amount of tramadol requirement was seen in the placebo group followed by gabapentin group and minimal dose requirement was needed for pregabalin group and the difference was found to be statistically significant.

Conclusion: Pregabalin given in the form of oral dose of 150 mgs as pre-anaesthetic agent is very effective in managing post-operative pain as patients in this group required lesser dose of rescue analgesic compared to gabapentin given in the dosage of 900 mgs. Further, pregabalin and gabapentin had a similar type of hemodynamic and adverse events.

Keywords: Gabapentin, Pregabalin, Rescue analgesia, Sedation score.

Introduction

Postoperative pain prevention and treatment continues to be a major challenge in postoperative care and plays an important role in allowing the patient to move and feel better. Although opioid drugs are commonly used in postoperative pain management, they are accompanied by side effects such as nausea, vomiting, drowsiness, itching, and urinary retention, leading to restriction of their use.[1] Other methods such as epidural analgesia are effective, but require extra effort and are associated with serious complications. Non-steroidal anti-inflammatory drugs (NSAIDs) are also used for postoperative analgesia, but may be accompanied by damage to gastrointestinal mucosa, bleeding, renal toxicity, allergic reactions, and heart failure. Selective cyclooxygenase-2 NSAIDs have pro-thrombotic properties and increase the risk of stroke and myocardial ischemia.[2]

The use of laparoscopy for Cholecystectomy surgery has become a common practice because of its better patient satisfaction and faster recovery time. Opioids were still being considered as conventional drugs for post-operative analgesia, however its use leads to longer duration of ICU stay, negating the advantages of laparoscopic surgeries.[3] Hence using an alternative analgesic in the place of opiods can facilitate faster post-operative recovery. Currently most of the anesthetist prefer the usage of multimodal analgesia technique, like using NSAID's, paracetamol, gabapentinoids, local anesthetic drugs, clonidine and dexmedetomidine either alone or in combination which acts via different mechanisms to improve the degree of pain relief without inducing any side effects.[4] Recently, there is growing interest in use of Pregabalin and Gabapentin because of their novel target site of action.[5,6] As the advances progress using pregabalin and gabapentin in acute postoperative pain has been studied and the results were favorable as both these drugs have been found to reduce the opioid requirement in the post-operative period.[7]

Gabapentin is a structural analogue of gamma aminobutyric acid. It acts by binding with α2-δ protein subunit of presynaptic voltage gated calcium channels in both central and peripheral nervous system which results in antinociceptive, antihyperalgesic, and antiallodynic properties.[8] Pregabalin is a structural analogue of gamma aminobutyric acid but has a superior pharmacodynamic and pharmacokinetic profile.[9] It is more potent and more effective analogue of gabapentin. It is useful in the treatment of peripheral neuropathic pain, post herpetic neuralgia, partial seizures, and generalized anxiety disorder.[10,11]

There were very few clinical studies available in the literature comparing analgesic efficacy of pregabalin and gabapentin as pre-emptive analgesic for postoperative pain management for the patients posted for spine surgery. Liu et al. in his recent meta-analysis of the preoperative use of gabapentinoids for the treatment of acute postoperative pain following spinal surgery concluded that preoperative use of gabapentinoids was able to reduce postoperative pain, total morphine consumption, and morphine related complications following spine surgery. They opined that further studies should be done to determine the optimal dose and whether pregabalin is superior to gabapentin in controlling acute pain after spine surgery.[11] Most of the studies done so far used a lesser dose of prgabalin and gabapentin as pre-anesthetic medications for reducing the pain postoperatively, very few studies used a higher dose. The present study aims to evaluate the effects of the addition of Pregabalin and Gabapentin in reducing

post-operative pain in patients undergoing laparoscopic cholecystectomy

Material and Methods

A prospective comparative study was conducted for a period of 12 months in the department of anesthesiology of medical college hospital. The study was started after getting the approval from the institutional ethical committee and the informed consent was obtained from all the study subjects involved in the study. All the patients posted for elective laparoscopic cholecystectomy in the age group between 18 and 70 years with ASA score of either 1 or 2 were included as our study subjects. Patients having history of hypersensitivity to our test drugs, pregabalin or gabapentin were excluded from the study. A total of 150 study subjects were included in our study, the sample was taken following quota sampling which is a type of non-random sample technique. The entire study subjects were randomized into three groups of 50 each following a computer generated random number table and a double blinding technique was followed were both the patient and the investigator were not aware of which drug was used on the patient. Group B subjects received 3 tablets of Beplex forte (as placebo), Group G subjects received 3 tablets of Gabapentin 300mg (total 900mg) and Group P subjects received 3 tablets of Pregabalin 50mg (total 150mg). Premedication tablet Alprazolam 0.5 mg, Pantaprazole 40 mg was given to all the patients involved in the study.

Along with it 3 tablets of Beplex Forte, Gabapentin or Pregabalin depending on the group they belong to was given 60 min before the start of the surgery with sips of water. Standard monitors like pulse oximetry, NIBP, and electrocardiography were connected, and baseline heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure were recorded – before and 15 minutes after giving the premedication drugs. General anaesthesia was started with intravenous injection of Midazolam (0.02mg/Kg) and Fentanyl (2mcg/kg). Patients were pre-oxygenated with 100% oxygen for 3 minutes by anatomical face mask. Induction was done with iv propofol (2mg/kg) and vecuronium (0.08mg/kg) and after 3 minutes laryngoscopy was done and appropriate size endotracheal tube was placed in trachea. Anaesthesia was maintained with 66% N2O, 33% O2 and 1% isoflurane. Repeat dose of muscle relaxant vecuronium (0.02mg/kg) were given as and when required. Patients were mechanically ventilated with ventilator settings titrated to maintain ETCO2 at 30-40mmHg. The blood pressure, heart rate and SpO2 were measured every 5 minutes for the first half an hour after induction and then once every 15 minutes till the end of the surgery. Postoperatively degree of pain was measured based on the Visual Analogue Scale and when the patient experienced pain more than 4 on VAS, rescue analgesia was given in the form of Inj. Tramadol (1mg/kg). The pain score was recorded every 30 minutes for the first 2 hours, then hourly for next four hours, then once every two hours till 12 hours post-operatively. The total amount of rescue analgesia required in each group was noted. Sedation score was measured using Ramsay sedation Scale at hourly intervals for 12 hours. Occurrence to adverse events were recorded and documented.

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5% respectively.

Results

The demographic characteristics of the study subjects which includes age, gender

and weight was almost similar in all the three groups, females were more in number than males and the mean weight was 60 to 61 kgs, no statistical significant difference was observed between the three groups. Similarly ASA grading and the duration of surgery were also more or less similar between the three groups (Table 1). Heart rate for the patients was monitored from the time of intubation till 6 hours in the post-operative period.

It was found that the heart rate variation was almost similar in both pregabalin and gabapentin group, whereas in the placebo group the heart rate was found to be high and the difference was statistically significant and a similar type of observation was also seen with mean arterial pressure. Post-operatively patients pain perception was assessed using VAS scoring system, it was monitored from the first hour of the post-operative period up to 24 hours at regular intervals and it was observed that the pain score was less in the pregabalin group at all intervals compared to gabapentin and placebo group and the difference was found to be statistically significant ($p<0.05$) Similarly the level of sedation was assessed using Ramsay sedation score and it was observed that the sedation score was significantly high among the gabapentin group particularly at 6t h hr and 12t h hour post-operatively compared to pregabalin and placebo group ($p>05$) (Table 3). Postoperatively tramadol in the form of injection was used for attenuation of pain and it was observed in our study that maximum amount of tramadol requirement was seen in the placebo group followed by gabapentin group and minimal dose requirement was needed for pregabalin group and the difference was found to be statistically significant.

The occurrence of adverse events such as somnolence and dizziness was almost similar in all the three groups whereas the incidence of nausea and vomiting was less in pregabalin group compared to gabapentin and placebo group and the difference was found to be statistically significant.

Table 1: Demographic and intraoperative characteristics of the study subjects

Variables	Placebo group	Pregabalin (Group P)	Gabapentin (Group G)	P value
Age (Years)	46.2 ± 10.2	45.1 ± 9.1	44.4 ± 8.6	0.25
Gender	Male=20 Female=30	Male=17 Female=33	Male=19 Female=31	0.1
Weight in kgs	60.4 ±4.5	60.5 ± 4.8	60.3 ± 5.1	0.09
ASA Grade	Grade I = 25 Grade II = 25	Grade I = 27 Grade II = 23	Grade I = 30 Grade II = 20	0.11

Statistically significance at $p\leq0.05$

Table 2: Comparison of pain perception using VAS score between the three groups

Duration post-operatively	Placebo group	Pregabalin (Group P)	Gabapentin (Group G)	P value
1 Hr	5.22 ± 0.8	3.05 ± 0.6	3.92 ± 0.8	0.01*
2 Hr	5.10 ± 0.7	3.01 ± 0.4	3.11 ± 0.5	0.005*
4 Hr	4.23 ± 0.6	2.82 ± 0.5	3.22 ± 0.3	0.02*
6 Hr	3.87 ± 0.6	1.84 ± 0.7	3.43 ± 0.4	0.04*
12 Hr	3.84 ± 0.78	1.45± 0.6	3.12 ± 0.5	0.003*
24 Hr	3.88 ± 0.64	2.74 ± 0.6	3.23 ± 0.5	0.001*

* indicates statistically significance at $p\leq0.05$

Table 3: Comparison of Ramsay sedation score between the three groups

Duration post-operatively	Placebo group	Pregabalin (Group P)	Gabapentin (Group G)	P value
1 Hr	3.20 ± 0.8	3.49 ± 0.8	3.9 ± 0.7	0.06
2 Hr	3.10 ± 0.7	3.15 ± 0.5	3.54 ± 0.6	0.15
4 Hr	3.13 ± 0.5	3.48 ± 0.9	3.21 ± 0.4	0.20
6 Hr	2.87 ± 0.5	3.2 ± 0.8	3.44 ± 0.5	0.05*
12 Hr	2.77 ± 0.6	3.15± 0.7	3.19 ± 0.7	0.002*
24 Hr	2.45 ± 0.51	2.8 ± 0.2	2.88 ± 0.4	0.08

* indicates statistically significance at p≤0.05

Discussion

Gabapentin and pregabalin are useful for treating neuropathic pain and may be beneficial in acute postoperative pain.[12]Both drugs have an elimination half-life of 6–8 hours after a single dose. The bioavailability of gabapentin varies with dose and ranges from 35–60%. At our dose (900 mg), 35–40% of the drug (300–320 mg) is absorbed, while 90% of pregabalin is absorbed. Gabapentin reaches its peak effect within 2 hours, while the time to reach the peak effect for pregabalin is 30–120 minutes [13] In the modern era considering the adverse events of opioids, its usage has been minimized and instead pre-incisional analgesia has come in use which had shown some promising results in the control of postoperative pain. Pre-emptive analgesia helps in reducing the amplification of post-operative pain by protecting the central nervous system from detrimental effects of noxious stimuli and resulting hyperalgesia. [12,14]

In the current study we found the hemodynamic parameters such as pulse rate and mean arterial pressure were almost similar in both the pregabalin and gabapentin group whereas both these parameters were high in the placebo group and hence both pregabalin and gabapentin were found to be hemodynamically stable drug. Similar type of results was also shown in the studies done by Saraswat et al., Tippana et al. and Van Elstraete AC et al. [12,14,15] In the present study we assessed the perception of pain in the patients by using VAS pain scale from the first hour of the post-operative period till 24 hours and it was found that the pain score for the patients in the pregabalin group was significantly less when compared to the pain score of the patients in gabapentin and placebo group and this shows that pregabalin 150 mg given in the immediate pre-operative period is very much effective in controlling the post-operative pain for a longer duration compared to gabapentin 900 mg or a placebo drug. Our results are almost in par with the study done by Agarawal et al. in the year 2008, Sahu et al. in 2010 and Swarup Paul et al. in 2016. 16-18 Turan et al. in their study found that pain scores were significantly lower in the gabapentin (1200 mg) group compared to the placebo group in spinal surgery.[19]They concluded that preoperative oral gabapentin decreased pain scores in the early postoperative period and reduced postoperative morphine consumption, thereby decreasing morphine related side effects.

In the present study sedation was assessed using Ramsay sedation score and it was shown that no significant difference was observed in the sedation score between the three groups and it proves that the sedation property of pregabalin and gabapentin is almost similar. Previously done studies had also shown a similar type of results.

In our study the rescue analgesic used in the post-operative period is much higher in the placebo group followed by gabapentin group compared to pregabalin group and

the difference was found to be statistically significant. Mishriky et al. in their study concluded that pregabalin provided better postoperative analgesia but more sedation and visual disturbances compared to placebo but there was no significant difference in 100 mg and 300 mg of pregabalin.[20]

Saraswat et al. in their study between pre-emptive gabapentin (1200 mg) and pregabalin (300 mg) for acute postoperative pain after surgery under spinal anesthesia found that gabapentin and pregabalin both provided prolonged post spinal analgesia, but pregabalin was more potent than gabapentin.[21]

Occurrence of somnolence and dizziness was less in pregabalin group compared to gabapentin group but the difference was not found to be statistically significant, whereas occurrence of nausea and vomiting is much less in the pregabalin group compared to gabapentin and placebo and the difference was found to be statistically significant. In the study conducted by Gajraj showed that somnolence and dizziness are the most common side effects reported almost equally in both pregabalin group and the gabapentin group.[22] In another study done by Turan et al. found that the incidence of nausea and vomiting are significantly lower in pregabalin and gabapentin group compared to placebo group, for which the reason was mentioned as due to lesser dose of rescue analgesic given in these two groups, which might be the reason in the present study also.[19]

Conclusion

The results of this study revealed that gabapentin and pregabalin were effective in controlling laparoscopic cholecystectomy postoperative pain, nausea, and vomiting, and compared with the placebo group, decreased opioid consumption. Pregabalin and gabapentin have proven a potential role as post-operative analgesic agent.

Pregabalin given in the form of oral dose of 150 mgs as pre-anesthetic agent is very effective in managing post-operative pain as patients in this group required lesser dose of rescue analgesic compared to gabapentin given in the dosage of 900 mgs. Further, pregabalin and gabapentin had a similar type of hemodynamic and adverse events.

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