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Original Article

Comparison of Pregabalin and Tramadol for Post-operative Pain Management in Patients Undergoing Lumbar Laminectomy

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Abstract

Introduction: Prevention and treatment of post-operative pain continue to be a major challenge in post-operative care. Opioid analgesics, with their well-known side effects, continue to represent a cornerstone in post-operative pain control.

Aim: Aim of this study is to assess and compare the efficacy and safety of pre-operative administration of pregabalin and tramadol in patients undergoing elective lumbar laminectomy.

Materials and Methods: Group 1 was received a placebo capsule orally 1 h before anesthetic induction. Group 2 was received a tramadol capsule 100 mg orally 1 h before anesthetic induction. Group 3 was received a pregabalin capsule 150 mg 1 h before anesthetic induction.

Results: The pain scores in Group 2 are less than Groups 1 and 2 preoperatively, after extubation and 1, 2, 4 and 6 h postoperatively, and this difference is significant ($P < 0.05$). The sedation score in Group 2 is greater than that of Group 3 which is greater than that of Group 1 preoperatively, after extubation and 1, 2, 4 and 6 h post-operatively. Fentanyl requirement is more in Group 1 compared to Group 3, which itself is more than Group 2. These differences are statistically significant. Adverse effects such as nausea, vomiting, and drowsiness are less than that of Groups 1 and 2.

Conclusion: Pregabalin has a statistically significant effect when compared to placebo, but this effect is less when compared to tramadol. The need for rescue analgesia is in the least in tramadol patients followed by pregabalin, and it increases maximum in the placebo group.

Key words: Lumbar laminectomy, Post-operative pain, Pregabalin, Tramadol

INTRODUCTION

Post-operative pain is one of the most feared problems among patients coming for surgery. Post-operative pain management includes pain management, prevention, and treatment of post-operative complications and restoring pre-operative function.[1,2] Prevention and treatment of post-operative pain still remain a major challenge in post-operative care despite significant advancements in pain assessment and therapy.[3] By early mobilization of the patient, it improves his or her well-being. It has been reported that roughly 80% of patients undergoing surgical procedures experience post-operative pain. Post-operative pain at rest is responsive to opioids.[4] However, movement-evoked pain is considerably less responsive and is related to post-operative pulmonary, cardiac, and thromboembolic complications.[5] The guidelines for post-operative pain treatment have been revised, and drugs such as S-ketamine, pregabalin, metamizole, and oxycodone are used as new methods of preventing post-operative pain. Prolonged chronic pain after surgery has been under recognized until recently which is actually a very common phenomenon. A number of risk factors and predictors including the age, gender, surgical procedure, pre- and post-operative pain, genes, psychosocial factors,

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and pain modulation variables have been identified. Together with increased knowledge about the pathophysiology of chronic pain after surgery, it may be possible to develop successful drugs and interventions in the near future. Post-surgical pain is normally perceived as nociceptive pain.[4] Surgical trauma causes central and peripheral sensitization and hyperalgesia which when untreated can lead to chronic post-operative pain after surgery. Indeed pain is one among the three most common causes of delayed discharge after ambulatory surgery next to drowsiness and nausea/vomiting. Antihyperalgesic drugs improve the post-operative pain by preventing the development of central sensitization.[6] The recent advance in post-operative pain management includes finding exact molecular mechanisms, new drugs and other routes and modes of analgesic delivery. For years opioids have been the cornerstone of post-operative pain management in spite of their side effects. Hence, the search for newer analgesics and combination of analgesics and other non-opioid drugs continues to improve post-operative analgesia and reduce opioid-related side effects.

In this context, the gabapentinoids (gabapentin and pregabalin) have been targeted by the researchers. The early success in the treatment of trigeminal neuralgia with gabapentinoids has led to many studies that have assessed their analgesic potency in treating neuropathic pain associated with diabetic peripheral neuropathy and postherpetic neuralgia.[7] Furthermore, their analgesic efficacy after a variety of surgical procedures has also been studied. This study was thus taken up to test the hypothesis of the utility of pregabalin for the relief of post-operative pain in lumbar laminectomy.

Aim

Aim of this study is to assess and compare the efficacy and safety of pre-operative administration of pregabalin and tramadol in patients undergoing elective lumbar laminectomy.

MATERIALS AND METHODS

This a prospective, randomized, single blinded, placebo-controlled study was conducted in the Department of Anaesthesiology, Madras Medical College. This study was conducted in 75 patients belonging to the American Society of Anesthesiology - 1 (ASA) and ASA - 2 of either sex and age group between 20 and 60 years undergoing elective decompressive lumbar laminectomy. The patients were randomized into three groups of 25 patients each by closed envelope method. The patients were blinded to the group they belong.

Inclusion Criteria

Age – 20-60 years, weight – 40-70 kg, body mass index (BMI) – <30 kg/m^2, ASA - 1 and 2, surgery - elective lumbar decompressive laminectomy, patients who have given valid informed written consent.

Exclusion Criteria

Patients not satisfying inclusion criteria, patients posted for emergency surgery, patients with renal insufficiency, patients with liver disease, known allergy or sensitivity to the drugs used, history of seizure disorder, ongoing therapy with sustained release opioids.

The patients satisfying inclusion criteria were randomly allocated into three groups each containing 25 patients. Group 1 was received a placebo capsule orally 1 h before anesthetic induction. Group 2 was received a tramadol capsule 100 mg orally 1 h before anesthetic induction. Group 3 was received a pregabalin capsule 150 mg 1 h before anesthetic induction.

The primary outcome of the study was to measure the analgesic and anxiolytic efficacy of pregabalin and tramadol for post-operative pain while the secondary outcome was to assess the adverse effects of these drugs.

RESULTS

The study was conducted in 75 patients of either sexes in the age group of 20-60 years, belonging to ASA class - 1 and SA class - 2, undergoing elective lumbar laminectomy under general anesthesia. The mean age of patients in Group 1 is 44.04 with a standard deviation (SD) of 7.44 and in Group 2 the mean age are 44.12 with a SD of 8.52 and in Group 3 the mean age is 45.96 with a SD of 8.5. The $P = 0.645$, which is insignificant. The mean weight of the patients in Group 1 is 56.44 with a SD of 7.19 and in Group 2 are 57.44 with a SD of 7.49 and in Group 3 are 56.88 with a SD of 6.18. The *P* value is found to be 0.828 which is not significant. Therefore, the three groups are comparable in their weight. The mean height of patients in Groups 1, 2, and 3 are 1.56, 1.57, and 1.59 with a SD of 0.07, 0.07, and 0.09, respectively. The *P* value is found to be 0.404 which is not significant. This implies that there is no significant difference in height among the three groups and they are comparable. The mean BMI among Groups 1, 2, and 3 are 23.35, 23.20, and 22.53 with a SD of 1.74, 2.04, and 1.14, respectively. The $P = 0.192$ which is not significant. Therefore, the BMI is comparable among all three groups. The sex ratio (male:female) among Groups 1, 2, and 3 are 8:17, 9:16, and 8:17, respectively. The *P* value is found to be 0.942 which is not significant. The ASA class 1:2 ratios among three Groups 1, 2, and 3 are 13:12, 13:12, and 12:13, respectively. The *P* value is found to be 0.948 which is not significant. The mean duration of surgery in minutes among Groups 1, 2, and 3 are 148 ± 15, 148.80 ± 11.3, and 146.40 ± 17.29, respectively. The *P* value is found to be 0.63

which is insignificant. The spinal levels of laminectomy (1:2) in Groups 1, 2, and 3 are 12:13, 11:14, and 13:12, respectively, with a *P* value of 0.852 which shows that the groups are comparable. No significant difference was observed in the heart rate and respiratory rate recorded preoperatively (1 and 5 min after intubation), immediately after extubation (1, 2, 4, and 6 h post-operatively) among the groups ($P > 0.05$). Similarly, no significant difference was observed in the mean systolic and diastolic blood pressures preoperatively, 1 min after intubation, as well as 1, 2, 4, and 6 h postoperatively among all the three groups.

Significant differences were observed in the pain scores of all three groups preoperatively and after extubation and at 1, 2, 4, and 6 h postoperatively, a significant decrease in the pain scores of the patients who received tramadol and pregabalin in comparison to the placebo group was noted ($P < 0.05$) (Tabel 1).

The mean anxiety scores in Group 2 are less than Group 3 which is less than Group 1, and this difference is statistically significant. The mean anxiety scores in Group 2 is less than that of Group 1 preoperatively, after extubation and 1, 2, 4 and 6 h after extubation. The mean anxiety score in Group 3 is lesser than that of Group 1. The mean anxiety scores in Group 3 are less than that of Group 1 (Tabel 2).

The sedation score in Group 2 is greater than that of Group 3 which is greater than that of Group 1 preoperatively, after extubation and 1, 2, 4 and 6 h postoperatively. The sedation scores are greater in Group 2 than in Group 1 with a significant difference in all time intervals. The sedation score is greater in Group 3 is significantly greater than Group 2 in all time intervals. The mean sedation score in Group 2 is significantly greater than that of Group 3 preoperatively and 2, 4 and 6 h postoperatively. Immediately after extubation and 1 h after extubation sedation score in Group 3 is comparable to that of Group 2 (Tabel 3).

The mean fentanyl requirement in Group 1 is 128 ± 17.40, in Group 2 is 40.40 ± 9.17 and in Group 3 it is 60.40 ± 17.29. Fentanyl requirement is more in Group 1 compared to Group 3, which itself is more than Group 2. These differences are statistically significant (Table 4). Adverse effects such as nausea, vomiting, and drowsiness are less than that of Groups 1 and 2 (Table 5).

Table 1: Pain scores in the three groups

VAS	Mean±SD			*P* value
	Group 1	Group 2	Group 3	
Pre-operatively	1.52±0.510	0.68±0.476	1.48±0.510	<0.0001
After extubation	4.84±0.624	1.48±0.510	3.12±0.332	<0.0001
1 h	5.52±0.510	2.00±0.408	2.84±0.374	<0.0001
2 h	6.48±0.510	2.40±0.500	3.40±0.500	<0.0001
4 h	5.80±0.408	2.32±0.476	4.12±0.332	<0.0001
6 h	5.72±0.458	2.52±0.510	4.08±0.277	<0.0001

SD: Standard deviation, VAS: Visual analog scale

Table 2: Anxiety scores in the three groups

Anxiety scores	Mean±SD			*P* value
	Group 1	Group 2	Group 3	
Preoperatively	1.84±0.37	0.20±0.41	1.16±0.37	<0.0001
After extubation	1.72±0.46	0.48±0.51	1.16±0.37	<0.0001
1 h	2.80±0.41	0.40±0.50	1.60±0.50	<0.0001
2 h	3.52±0.51	0.56±0.51	1.96±0.20	<0.0001
4 h	3.32±0.48	0.60±0.50	1.60±0.50	<0.0001
6 h	3.32±0.48	0.64±0.49	1.64±0.49	<0.0001

SD: Standard deviation

Table 3: Sedation scores in the three groups

Sedation scores	Mean±SD			*P* value
	Group 1	Group 2	Group 3	
Preoperatively	1.00±0.00	2.32±0.48	1.52±0.51	<0.0001
After extubation	1.28±0.46	2.64±0.49	2.48±0.51	<0.0001
1 h	1.48±0.51	3.60±0.51	3.52±0.50	<0.0001
2 h	1.48±0.51	3.80±0.41	3.52±0.51	<0.0001
4 h	1.56±0.51	3.92±0.28	3.44±0.51	<0.0001
6 h	1.60±0.50	3.72±0.46	3.40±0.50	<0.0001

SD: Standard deviation

Table 4: Mean fentanyl requirement in the three groups

Analgesic requirement	Mean±SD			*P* value
	Group 1	Group 2	Group 3	
Fentanyl requirement (mg)	128.80±17.40	40.40±9.17	60.40±17.29	0.004

SD: Standard deviation

Table 5: Adverse effects in the three groups

Adverse effects	*N* (%)		
	Group 1	Group 2	Group 3
Nausea	2 (8)	5 (20)	1 (4)
Vomiting	3 (12)	5 (20)	1 (4)
Drowsiness	1 (4)	8 (32)	1 (4)

DISCUSSION

In this study, the pain scores of the patients who received tramadol and pregabalin were significantly decreased in comparison to placebo group. The tramadol group had the least pain scores when compared to the pregabalin and placebo groups.

It was also observed that the analgesia provided by tramadol was superior to that of pregabalin, but pregabalin was more

effective in reducing the pain when compared to placebo. In study done by Kumar *et al.* pregabalin showed statistically significant analgesic effects compared to placebo, but the effect was found to be less prevalent compared to tramadol. Pain scores were low at all time intervals in the tramadol group. The need for rescue analgesia was the least prevalent in tramadol patients.[5]

Drowsiness was less frequent in the pregabalin group (4%) compared to the tramadol group (32%). Fewer patients had nausea (4%) and vomiting (4%) with pregabalin when compared to placebo (nausea 8%, vomiting 12%) and tramadol (nausea 20%, vomiting 20%). This implies that the incidence of nausea and vomiting is more with tramadol and placebo than with pregabalin. In study done by Farzi *et al.* nausea, vomiting and sedation, in the tramadol group, were higher than gabapentin group. The trends of reduction in pain score similar with both drugs.[8]

The amount of rescue analgesia required was more in control group, and hence the total dose of fentanyl given during the first 6 h of the post-operative period was relatively more when compared to tramadol and pregabalin groups. In study done by Kumar *et al.* the patients in the tramadol group required significantly less rescue analgesia than the pregabalin patients.[5]

In this study, the anxiety scores in pregabalin and tramadol groups were significantly lower when compared to the placebo group. However, the anxiety scores were significantly lower in the pregabalin group in comparison to the placebo group, whereas it is significantly higher than the tramadol group. This observation shows that pregabalin also has an anxiolytic effect additionally although it is to a lesser extent when compared to tramadol.[9,10]

The pre-operative sedation scores in my study were significantly greater in tramadol group when compared to the pregabalin and placebo groups. After extubation and postoperatively, the level of sedation increased in both pregabalin and tramadol. However, this increase in sedation in pregabalin group was more after extubation and 1 h post-operatively (but less than tramadol insignificantly); rest all time intervals, it was significantly lower than the tramadol group though the sedation was significantly higher than the placebo group. From this, we infer that pregabalin has a good anxiolytic effect without resulting in excessive sedation.

In my study, the increase in heart rate is significantly lower in tramadol group while compared to placebo at 1 and 3 min after intubation and at 30, 60 and 120 min and after extubation. The decrease in heart rate is insignificant pre-operatively and 5 min after intubation. Similarly, in the pregabalin group, the increase in heart rate is significantly lower at 1 and 3 min after intubation, at 30, 60 and 120 min and after extubation when compared to placebo group.[11]

CONCLUSION

Pregabalin has a statistically significant effect when compared to placebo, but this effect is less when compared to tramadol. The need for rescue analgesia is in the least in tramadol patients followed by pregabalin and it increases maximum in the placebo group. Pregabalin has a statistically significant anxiolytic effect when compared to the placebo group. The anxiolytic effect of pregabalin is associated with less sedation when compared to that of tramadol. Pregabalin has the lowest number of post-operative complications such as nausea, vomiting, and drowsiness when compared to tramadol.

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