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**Original research article**

# To Study the Effect of Perioperative Duloxetine for Postoperative Pain Relief in Patients Undergoing Lumbar Spine Surgery

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**Abstract**

**Introduction**: Postoperative pain management is essential for an early postoperative recovery. In spinal decompression surgery, nociceptive pain occurs due to surgical tissue injury to soft tissues and bony structures. And also manipulation of neurological tissue leads to neuropathic pain. Duloxetine (SSNRI) has an antinociceptive effect and it interfere with occurrence of chronic post surgical pain by modulating pain pathways. Duloxetine reduces acute postoperative pain as well as reduces dose of analgesic consumption.

**Material and Method** : 80 patients of ASA grade 1 and 2 were randomized into 2 groups as Group I (placebo, n=40), Group II (Duloxetine 60 mg, n=40). The patients received placebo or the study drug 1 hr before and 24 hr after surgery. Demographic data, vital signs, postoperative pain scores and any side effects were recorded.

**Results**: Time for first rescue analgesia was significantly longer in group II as compared to group I. Duloxetine 60 mg provided better analgesia (similar NRS score) as compared to placebo.

**Conclusion:** Our data suggest that Duloxetine 60 mg provides better post operative analgesia than placebo in patients undergoing Lumbar Spine Surgery.

**Keywords**: Duloxetine, postoperative pain, spine surgery

## Introduction

**S**pine surgery often results in severe acute post-operative pain, which has been challenging to manage.

The risk of Chronic Post Surgical Pain (CPSP) increases with the inadequate management of postoperative pain in first 48 hrs after the surgery. Adequate postoperative pain management is essential for an early postoperative recovery. The primary aim of postoperative pain management is to provide adequate pain relief with minimal use of drugs and to reduce any possible side effects of the administered drugs. [(1)]

Inadequate postoperative pain management can lead to multisystem effects such as tachycardia, hypertension, myocardial ischemia, myocardial infarction, decrease in vital capacity, pneumonia, poor wound healing, insomnia and transition to chronic pain have been observed in various studies.[2] Prolonged post-anesthesia care unit (PACU) stays, late hospital discharge, and readmissions have been recorded in numerous studies due to inadequate postoperative pain relief.[3]

In spinal decompression surgery, nociceptive pain occurs due to surgical tissue injury to soft tissues and bony structures. And also manipulation of neurological tissue leads to neuropathic pain.[4]

Central sensitization occurs due to surgical incision which results in significant postoperative pain. Analgesic treatment given to prevent establishment of altered central processing, results in reduction of acute postoperative pain and chronic pain development.[5]

The chronic use of opioids for treatment of moderate to severe postoperative pain increases the risk of perioperative opioids induced hyperalgesia and chronic post surgical pain.[1,7] Adjuncts are used in combination with opioids to decrease opioid consumption and to reduce opioid-related side effects in postoperative period.[5]

Postoperative pain arising from various sites in the central and peripheral nervous system can be managed with Multimodal analgesia combining opioids and non-opioids [6] Some of the adjuvants like ketamine, gabapentanoids (gabapentin,pregabalin) and clonidine have proven to be useful in perioperative pain management.[6,7]

Duloxetine (SSNRI) with its antinociceptive effect and ability to modulate pain pathways,it could interfere with chronic post surgical pain occurrence.[1] SSNRI antidepressants have been used for pain relief in various chronic pain syndromes including post herpetic neuralgia, diabetic neuropathy, and fibromyalgia. Duloxetine redues acute postoperative pain as well as reduces dose of analgesic consumption.[6]
The present study has been designed to study the effect of perioperative duloxetine for postoperative pain relief in patients undergoing lumbar spine surgery.

## MATERIAL AND METHODS

The study was conducted on patients undergoing lumbar spine surgery. Patients received duloxetine 60 mg or identical placebo orally one hour before surgery, and then again the medication was administered 24 hours later. The medication was given by the nurses. The tablets were identified by a number, which at the end of the study was revealed by opening the packets in which it was registered whether it was duloxetine 60 mg or placebo. The substances (duloxetine 60mg or placebo) were kept in 80 packets with 2 tablets each. Patients included in the study were of ASA Physical Grade I and II, between the age group 20 to 60 years and of either sex. The patients excluded from the study were: Patient's refusal, uncooperative patients, history of significant cardiovascular, pulmonary, renal, hepatic, neurological or metabolic disease, patients who are unable to understand pain assessment test, patients having severe obesity (BMI > 35 kg/m2), coagulation disorder, patients with history of drug allergy to duloxetine, paracetamol or tramadol.

The patients were randomly allocated into the following 2 groups (n=40 each) Group I (control) included 40 patients who received a placebo tablet 1 hour before surgery and another tablet the next morning. Group II (duloxetine 60 mg) included 40 patients who received 60 mg duloxetine

1 hour before surgery and again the next morning. Upon arrival of the patient in the operation room, intravenous 500 mL of crystalloid infusion was started through the 18G cannula. All the baseline vital parameters like NIBP, pulse oximeter, electrocardiography were connected and basal reading recorded. Patients were preoxygenated with 100% oxygen for 3 minutes by facemask. All patients were premedicated with inj. Glycopyrrolate 0.005-0.01 mg/kg IV, inj. Pentazocine 0.3-0.6 mg/kg IV. Anaesthesia was induced with inj. Thiopentone 3-5 mg/kg IV and muscle relaxant Inj. Succinylcholine 1- 1.5mg/kg IV. Endotracheal intubation was done with appropriate sized cuffed endotracheal tube. Anaesthesia was maintained with $N_2O$: $O_2$ (67:33) and isoflurane gas mixture along with Loading dose (0.5 mg/kg IV) and maintainance dose (0.1 mg/kg IV) of Inj. Atracurium. After completion of the surgery, neuromuscular blockade was reversed with inj. Neostigmine 0.04-0.08 mg/kg IV and inj. Glycopyrrolate 0.5mg IV once adequate reversal was obtained. During postoperative period pulse rate, blood pressure, respiratory rate and severity of pain on NRS scale was noted at 1 hr, 6 hr,12 hr, 24 hr and 48 hr after surgery. The adverse effects such as headache, nausea, vomiting, dizziness, and drowsiness if present were also noted. Pain management during postoperative period consisted of I/V paracetamol infusion 1 gm (100 ml over 30 minutes) 8 hourly, starting from $6^{th}$ postoperative hour, till 48 hours after surgery. Inj. tramadol 2 mg/kg IV was given as rescue analgesic whenever the patient requested for analgesia or when NRS was $\geq 4$.

The observations recorded in the two groups were tabulated and statistical analysis was carried out by using statistical software SPSS 20.0. $p>0.05$ and $p<0.05$ were considered as statistically insignificant and significant respectively.

**RESULTS**

On comparing demographic data such as age, weight, sex and duration of surgery (min), no statistically significant difference was seen between the two study groups as shown in table 1 .

**Table 1: Demographic profile and duration of surgery among two groups**

| Parameters (Mean±SD) | Group I | Group II | p value |
|---|---|---|---|
| Age (yrs) | 43.40±12.23 | 44.2±9.11 | >0.05 |
| Weight(in kgs) | 60.12±8.67 | 58.8±7.14 | >0.05 |
| Sex (M:F ratio) | 2.43 | 2.17 | >0.05 |
| Duration of surgery(min) | 134±40.60 | 133±41.65 | >0.05 |

Time for rescue analgesia was significantly prolonged in duloxetine 60mg group (105.18±10.44) as compared to placebo group (40.13±8.57).

On hemodynamic parameters, significant changes ($p<0.05$) were present at $1^{st}$ hour in pulse rate, systolic blood pressure and diastolic blood pressure among the two groups and non significant at all other points of time.

NRS score was lower in duloxetine 60 mg group as compared to placebo group but the difference was statistically non significant.

Total 8(10%) patients suffered with nausea and vomiting. 6 (15%) patients in duloxetine 60 mg group as compared to only 2(5%) patients in placebo group.

In duloxetine 60 mg group, 5(12.5%) patients had drowsiness but in placebo group none of the patients had drowsiness. Thus it was seen that duloxetine causes more drowsiness than placebo.

Total 8 (10%) patients suffered with shivering. 4 (10%) patients in duloxetine 60 mg group and 4(10%) patients in placebo group.

None of the patients in both the groups had tachycardia or bradycardia, hypertension or hypotension, respiratory depression and headache.

## DISCUSSION

This study was performed to assess the effect of short-term administration of duloxetine 60 mg on acute postoperative pain in patients undergoing lumbar spine surgery under general anesthesia.

Selection of duloxetine 60 mg dose in our study was based on previous studies conducted by Hoi etal[7], Bedin et al[6] and Nasr DA[8] for acute post operative pain management. Duloxetine in less than 60 mg dose has not been found to be effective in management of chronic neuropathic pain.

On comparing postoperative hemodynamic variables between the two groups, significant difference was found at 1$^{st}$ post operative hour which might be due to haemodynamic changes occuring during emergence from general anaesthesia. However no significant difference was found in hemodynamic variables at 6$^{th}$, 12$^{th}$, 24$^{th}$ and 48$^{th}$ postoperative hour. Kassim D Y et al[5] in their study of comparing the analgesic efficacy of duloxetine (with or without dexamethsaone) with placebo, found a significant difference in heart rate and mean blood pressure during first 6 postoperative hours. Our results corelated with this study.
Our study showed a significant longer time to first rescue analgesia in the duloxetine 60 mg group than the control group ( Table no.2).
Table 2:

**Time for Rescue Analgesia (TRA)(Mean±SD) among the two groups**

| Parameter | Group I (n=40) | Group II (n=40) | p value |
|---|---|---|---|
| TRA (mins) | 37.13±7.27 | 79.13±15.42 | <0.05 |

The work done by Saoud A et al[4] supports our study in which they studied the efficacy of duloxetine 60mg in patients undergoing anterior cervical microdiscectomy and fusion. Similarly Nasr D.A[8] and Altiparmak B et al[9] in their study on analgesic action of duloxetine found the same results as ours.

Similarly Attia J Z et al[10] conducted a placebo controlled study to assess the effect of perioperative use of Duloxetine in combination with Etoricoxib on postoperative pain in patients scheduled for lumbar laminectomy. Their results were in accordance with our study.

Mean Numeric Rating Scale (NRS) score at different postoperative time interval in the two groups is shown in table 3.

**Table 3: Mean Numeric Rating Scale (NRS) score at different time interval in the two groups**

| Post operative time period | Group I (n=40) | Group II (n=40) | p value |
|---|---|---|---|
| 1st hour | 2.6 | 2.3 | >0.05 |
| 6th hour | 2.7 | 2.4 | >0.05 |
| 12th hour | 2.4 | 2.2 | >0.05 |
| 24th hour | 2 | 1.8 | >0.05 |
| 48th hour | 1.9 | 1.7 | >0.05 |

Duloxetine is a selective SNRI that is used in chronic pain conditions such as painful diabetic neuropathy and fibromyalgia. The possible mechanism of action of duloxetine could be the central pain inhibitory action secondary to the potentiation of serotonergic and noradrenergic activities in the CNS. For ethical consideration, no patient in our study suffered pain with NRS≥4 and the mean NRS-pain scores in both the groups were approximately 2.5 throughout the entire study period. Any patients that suffered pain (NRS≥4) was offered rescue analgesia in form of tramadol 2mg/kg IV. All patients recieved intravenous paracetamol 1gm by infusion (100 ml over 30 minutes) every 8 hours, starting from 6th postoperative hour, till 48 hours after surgery for pain management. Thus it was expected that both the groups shall show similar NRS scores with no statistically significant difference between the groups. On statistical comparison of average NRS scores of 48 hours observation period, both the groups were comparable with no significant difference (p>0.05) seen in NRS scores of the two groups.

Few studies have evaluated the effect of duloxetine on pain scores in postoperative period. Bedin A et al[6] studied the efficacy of 60 mg duloxetine in patients undergoing spine surgery, and Ho KY et al[7] performed the similar evaluation in patients undergoing knee replacement surgery. Both the studies found no significant difference between the groups in pain scores.

Similarly, in the study by Saoud A et al[4], comparing preoperative use of duloxetine 60mg and placebo, given 2 weeks prior and 2 weeks after anterior cervical microdissectomy, non-significantly lesser pain scores were found in duloxetine 60mg group than in placebo.

In contrast to our study, Altiparmak B et al[9] found lower mean VAS scores of the pregabalin and duloxetine groups in comparison to placebo group after spinal surgery.

Nasr D.A.[8] found lower VAS scores in preoperatively administered duloxetine 60 mg group compared with placebo group in patients undergoing radical mastectomy which does not coincides with our study. Attia J Z et al[10] studied the effect of preoperative duloxetine 60 mg in patients who underwent lumbar laminectomy, and the pain scores were significantly lesser in duloxetine group in comparison to placebo group which was against our study.

In our study, the incidence of post operative nausea & vomiting and drowsiness were higher in duloxetine 60 mg group in comparison to placebo group and incidence of shivering was almost similar in both duloxetine and placebo groups. Both the groups were haemodynamically stable and showed no incidence of tachycardia or bradycardia, hypertension or hypotension, respiratory depression and headache during the study period. Previous studies on comparison of duloxetine with placebo done by Saoud A et al[4], Kassim DY et al[5], Nasr DA[8] and Altiparmak B et al[9] have also demonstrated an increased incidence of nausea-vomiting and drowsiness in duloxetine group as compared to placebo group and the difference was non significant.

There are few limitations to our study. Firstly, we took into consideration only the patients undergoing lumbar spine surgery and therefore, we cannot generalize our finding to all patients undergoing different surgical procedures. And also we have not evaluated the effect of duloxetine on chronic postsurgical pain**.**

## CONCLUSION

In our study, patients receiving duloxetine 60 mg had a prolonged duration of first rescue analgesia than those receiving placebo, although pain scores did not differ significantly between the groups. Therefore, we conclude in our study that short-term treatment by duloxetine may be a good alternative for decreasing the use of opioids in order to alleviate postoperative pain without significant adverse effects.

## REFERENCES

1. Onutu AH. Duloxetine, an antidepressant with analgesic properties- a preliminary analysis. Rom J Anaesth Int Care. 2015;22:123-128.
2. Vadivelu N, Mitra S, Narayan D. Recent advances in postoperative pain management. Yale J Biol Med 2010;83:11-25.
3. Baratta JL, Schwenk ES, Viscusi ER. Clinical consequences of inadequate pain relief: Barriers to optimal pain management. Plast Reconstr Surg. 2014 Oct;134(4 Suppl 2):15S-21S.
4. Saoud A, Elkabarity R. Effect of perioperative Duloxetine on postoperative pain relief following anterior Cervical Microdisectomy and fusion - A Pilot Study. WScJ. 2013:4:57-66.
5. Kassim DY, Esmat IM, Elgendy MA. Impact of duloxetine and dexamethasone for improving postoperative pain after laparoscopic gynecological surgeries: A randomized clinical trial.Saudi J Anaesth 2018;12:95-102.
6. Bedin A, Bedin RAC, Vieira JE, Ashmawi HA. Duloxetine as an analgesic reduces opioid consumption after spine surgery: a randomized, double-blind, controlled study. Clin J Pain. 2017;33(10):865–9.
7. Ho K-Y, Tay W, Yeo M-C, Liu H, Yeo S-J, Chia S-L, et al. Duloxetine reduces morphine requirements after knee replacement surgery. Br J Anaesth. 2010; 105(3):371–6.
8. Nasr DA. Efficacy of perioperative duloxetine on acute and chronic postmastectomy pain. Ain-Shams J Anaesthesiol. 2014;7:129-33.
9. Altiparmak B, Guzel C, Demirbilek SG. Comparison of preoperative administration of pregabalin and duloxetine on cognitive functions and pain management after spinal surgery –A randomized,double blind,placebo controlled study. Clin J Pain 2018;34:1114-20.
10. Attia JZ, Mansour HS. Perioperative Duloxetine and Etoricoxibto improve postoperative pain after lumbar Laminectomy: a randomized, double-blind,controlled study. BMC Anesthesiol. 2017;17(1):162. DOI 10.1186/s12871-017-0450-z