

# Effects of Perioperative Pregabalin on Functional Outcomes 3 Month After Lumbar Discectomy: A Randomized Double Blinded Controlled Trial.

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## ABSTRACT

**Background:** Pregabalin may decrease PPSP (persistent post-surgical pain) in patients undergoing lumbar discectomy for lower back pain if given as preemptive analgesics. **Methods:** It was a randomised double blinded study involving 36 patients divided into two groups of Pregabalin and placebo, undergoing lumbar discectomy. Primary outcomes were pain, and functional outcomes at 24 hours and 3 months. **Results:** Pain scores were better in those receiving pregabalin than those of placebo. The RMDS at 3 months was less in those who received pregabalin ( $2.8 \pm 1.9$ ), than those who received placebo ( $6.5 \pm 8.4$ ). **Conclusion:** Perioperative use of pregabalin is associated with better pain scores, lesser requirement of breakthrough analgesic, and improved functional outcomes at 3 months.

**Keywords:** Lumbar Discectomy, Post-operative pain, Pregabalin.

## INTRODUCTION

Low back pain (LBP) is the most common cause of disability in patients younger than 45 years of age.<sup>[1]</sup> Lumbar disc protrusion causing radiculopathy or sciatica has a life time incidence of 2%.<sup>[2]</sup> Lumbar discectomy is the referred treatment for prolapsed intervertebral disk with neurological deficits or resistance to conservative therapy. In patients with sciatica, short-term outcome do favor early surgery than prolonged conservative therapy, after 1 year there is no differences between the groups.<sup>[4]</sup> In 10-40% of cases lumbar disk surgery are ineffective as there are the persistent symptoms of pain, motor deficit, and decreased functional status.<sup>[5-8]</sup>

Pregabalin is an analog of inhibitory neurotransmitter gamma amino butyric acid (GABA). Besides, it presynaptically binds to the  $\alpha\delta$  subunit of a voltage dependent calcium channel, and decreases the release of neuropeptides; glutamate, noradrenaline, and substance P. Tissue damage causes hyper excitation of dorsal horn neuron, and pregabalin, by decreasing this hyper-excitability, has a role in the treatment of postoperative pain.<sup>[11-13]</sup> In this study we compared the effects of adding 600 mg pregabalin perioperatively (300 mg preoperatively, and 150 mg at 12 hours and at 24 hours post

operatively) in patients undergoing lumbar discectomy, and evaluated the improvement in present pain intensity visual analog scale (PPI-VAS) score from preoperatively to 3 month postoperatively.

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## MATERIALS AND METHODS

After approval from the institutional ethical committee and having obtained written informed consent from each patients 36 ASA grade 1&2 patients, aged 18-60 years, suffering from chronic lumbar sacral radiculopathy undergoing elective lumbar discectomy were randomly allocated into one of the two groups, placebo and the pregabalin, using a computer generated random number table. Patients with spinal structural deformity, previous lumbar surgery, previous treatment with pregabalin, LBP of <3 month >12 month duration, obesity (BMI >30 kg/m<sup>2</sup>), and patients with known neurological or psychological disorders were excluded from the study.

4 questionnaires were completed by all the patients, preoperatively on the evening before the surgery.

These were

- 1) VAS pain at the rest and on the movement (VAS pain r and m)
- 2) Short-form Mc Gill pain questionnaire
- 3) Ronal Morris Disability Questionnaire
- 4) Medical outcomes study short forms (SF-36)

VAS anxiety score was recorded preoperatively, and immediately before induction of anesthesia.

Patients received either pregabalin or placebo, 300 mg at 90 minutes preoperatively, and 150 mg at 12 hours and 150 mg at 24 hours postoperatively. The anesthetist giving the medications had no further involvement in the study.

Immediately after shifting the patients in the O.T. complex, an I.V. line was secured, and hemodynamic monitors like ECG, SpO2, NIBP, Heart rate were placed and patients was induced and maintained by a common and standard anesthetic technique, by using Inj. Propofol for induction, Inj. vecuronium bromide to facilitate endotracheal intubation, and sevoflurane, intermittent vecuronium bromide for maintenance. The patients received analgesics in the form of Inj. fentanyl 2µg/kg IV in premedication, Inj. paracetamol 1 gm IV, and Inj. Diclofenec 75 mg IV. Intraoperatively, and Inj. bupivacaine 0.25% was infiltrated subcutaneously just before incision suturing.

Postoperatively in the recovery room, patients received Inj. Fentanyl 2 µg/kg, as required till a max dose of 10µg/kg.

Postoperatively in the ward, all patients received oral paracetamol 6 hourly and oral diclofenac twice a day. Intramuscular tramadol was used for breakthrough pain.

VAS pain score (VAS pain r and m), Mc Gill pain Questionnaires responses, the total amount of the rescue analgesic requirement, and any adverse effects were recorded 24 hours postoperatively.

After completion of 3 months, all the patients completed the above mentioned 4 questionnaires again, in the presence of the same investigator.

Data were analyzed using SPSS 12.0. p value <0.005 was considered statistically significant.

## RESULTS

Demographic and clinical parameters were similar in both the groups [Table 1&2].

**Table 1: Showing Demographic parameters.**

Demographics features	Placebo Group	Pregabalin Group
Age(y)	38(10.3)	41(7.8)
Sex(M/F)	7/11	8/10
BMI	30.7(2.3)	29.4(4.5)
ASA Physical status (1/2)	12/6	13/5

**Table 2: showing clinical features.**

Clinical features	Placebo Group	Pregabalin Group
Site of pain (back and leg/leg only)	14/4	15/3
Duration of pain (months)	6.7(2.1)	7.9(3.0)
VAS Pain at rest (mm), at time 0	55.9(23.5)	60.7(45.7)
VAS pain at movements (mm), at time 0	64.7(16.9)	68.7(56.8)
PPI-VAS (mm), time 0	37.4(11.8)	44.6(23.8)
RMDS, time 0	17.8(4.0)	15.6(5.8)
SF-36 MOS physical function, time 0	31.8( 23.0)	35.7(11.8)

**Table 3: Showing pain scores, analgesic consumptions and outcomes at 24 hours and 3 months interval.**

Results	Placebo Group	Pregabalin Group
VAS pain rest at 24 hours	24.7(11.2)	15.3(8.9)
VAS pain movement 24 hours	40.1(23.2)	34.8(15.7)
Patients requiring breakthrough analgesia	10/18	2/18
RMDQ 3/12	6.5(8.4)	2.8(1.9) p 0.030
SF-36 Physical functions 3/12	60.8(30.7)	84.7 (9.6) p 0.005

VAS = visual analogue scale, PPI-VAS= present pain intensity visual pain analogue, RMDS = Ronald Morris disability questionnaire, SF-36 MOS= medical outcome study short forms 36. Data are absolute values or mean (SD).

There was improvement in the PPI VAS score in all the patients 3 months post operatively, compared with preoperative values, and these changes were more marked in the pregabalin group [Table 2 & 3].

RMDQ score was lower at 3 months postoperatively in the pregabalin group as compared to the placebo group [Table 2&3]. SF-36 physical function at 3 months was higher in the pregabalin group [Table 2&3].

At 24 hours postoperatively, although the VAS pain scores were similar in both the groups, there was less analgesic consumptions in the pregabalin group as compared to tht of placebo group [Table 2&3].

At 3 months postoperatively, all the patients in the pregabalin group were at work, compare to only 80% in the placebo group, and the postsurgical outcome as defined by RMDQ was better in the pregabalin, as compared to the placebo group.

## DISCUSSION & CONCLUSION

This was a double blinded randomized controlled trial aimed primarily at the evaluating the role of pregabalin as a therapeutic agent that causes improvement in present pain intensity visual analog

scale (PPI-VAS) score from preoperative to 3 months postoperative in patients undergoing lumbar discectomy.

A total of 3 doses of pregabalin, or placebo (sucrose) were given perioperatively in 24 hours period, 300 mg at 90 minutes preoperatively, and 150 mg at 12 and 24 hours postoperatively.

It was found that perioperative addition of pregabalin in patients undergoing lumbar discectomy in for LBP in a window period of 3-12 months causes improvement in pain as measured by PPI-VAS score, functional outcome as measured by medical outcome study short form (SF-36), and quality of life outcomes as measured by RMDQ score, than those who receive placebo, and also it caused better pain perception threshold in the lower limb 24 hours postoperatively.

Our study reconfirmed the findings of earlier studies of Hill et al, Jockel et al. and Burke et al (present).

In this study we used pregabalin also in the preoperative period as preemptive analgesic to improve the pain score in the acute postoperative period, and also to decrease the incidence and severity of persistent post-surgical pain (PPSP). PPSP results from central sensitisation resulting from nerve injury either due to an acute surgical insult, or nerve injury secondary to the chronic nerve compression due to disk protrusion.

The role of preemptive analgesia by using gabapentine in decreasing analgesic consumption, improvement in pain scores and decreased incidence of PPSP, is well established.

Although we didn't follow back the patients for more than 3 months, also the number of enrolled patients was quite small, still the study do recommend in using the pregabalin in the perioperative period, by improving pain, functional and quality of life outcomes, in patients undergoing lumbar discectomy for LBP. Further studies are recommended to assess duration of these beneficial outcomes as the study was terminated in 3 months post operatively

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