Randomized Trial

Effect of Different Volumes on Pain Relief in Patient Receiving Fluoroscopic Guided Interlaminar Lumbar Epidural Steroid Injection

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Background: Epidural steroids injections (ESI) are frequently used to treat lumbar radicular pain. Although different volume have been used for interlaminar ESI in adults, there is no controlled trial comparing the effect of different volumes on pain relief for the same dose of steroid .

Objective: To compare the effect of increase in volume of epidural drug on pain relief in lumbar ESI .

Study design: Randomized double blind trial

Settings: Pain OR of a tertiary care centre

Methods: Sixty patients were randomly allocated to 1 of 3 groups: Group A (4 mL), Group B (6 mL), and Group C (8 mL). Pain was evaluated using visual analog scale (VAS) and improvement in disability using modified Oswestry Disability Questionnaire scores (MODQS) at 2, 4, 8, 12, and 24 weeks. Patients having less than 50% pain relief from baseline received an additional epidural injection of the same volume with a maximum of 3 injections at least 15 days apart. The primary objective of the study was incidence of patients attaining more than 50% pain relief at 6 months. Secondary outcome included MODQS and pattern of spread of iodinated contrast on fluoroscopy.

Results: At the end of 6 months, there was no significant difference in the effective pain relief between the 3 groups (Group A-16/22 (72.7%), Group B-15/20 (75%), Group C-13/18 (72.2%); $P = 0.98$, chi- square test). All groups demonstrated a significant reduction in mean VAS scores. There was no significant intergroup difference in VAS sores and MODQS at all the time intervals. The pattern of contrast spread did not differ between the 3 groups.

Limitation: Not a placebo controlled trial

Conclusions: An increase in volume of the injectate from 4 mL to 8 mL did not increase the efficacy of interlaminar ESI.

Key words: Epidural steroid, volume, low back pain, interlaminar**:**

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Epidural steroid injections (ESI) are commonly used to treat chronic radicular low back pain secondary to disc herniation. Steroids act by inhibiting production of inflammatory markers (phospholipaseA2) at the interface of the epidural space. Also they inhibit the occurrence of ectopic discharge from unmyelinated C fibers and relieve central sensitization (1,2).

Several factors, like site of needle insertion, direction of bevel of the needle, speed of injection, epidural space contexture, age, weight, height, and volume of drug, might affect the distribution of the drug administered in the dorsal epidural space (3). The volume in which a drug is administered is a major factor in determining the range of spread of injected solution. Although different volumes have been used for interlaminar ESI in adults, only limited trials exist assessing the effect of volume on efficacy of interlaminar ESI (4,5).

The aim of the present study was to compare therapeutic efficacy of the same dose of steroid in different volumes in patients receiving interlaminar ESI for lumbosacral radicular pain.

Methods

The institutional ethics committee approved this randomized double blind trial (NK 1098/MD/13542-543 dated 8-11-13, CTRI/2016/02/006675; registered on 24/02/2016). Fifty-eight patients between the ages of 30 to 60 years, with unilateral lumbosacral radicular pain for a minimum of 3 months duration, not responding to medications and physical therapies, were enrolled. Patients with lumbar canal stenosis, facet joint arthopathy, allergy to contrast or steroid, previous surgery on the lumbar spine, and those who received lumbar ESI in the past 3 months were excluded.

Written informed consent was acquired. Patients were randomly divided into 1 of 3 groups using a computer generator random number sequence. Random numbers were kept in sealed envelopes and opened by an anesthesiologist uninvolved in the study. Group A received 80 mg of methylprednisolone acetate (MPA) with a total volume of 4 mL (2 mL of MPA + 2 mL of 2% lidocaine). Group B received the same dose of MPA with a total volume of 6 mL (2 mL of MPA + 2 mL of 2% lidocaine + 2 mL saline) and Group C with a total volume of 8 mL (2 mL of MPA + 2 mL of 2% lidocaine + 4 mL saline). One investigator performed the lumbar ESIs. Another investigator then followed the patient in a pain clinic. This investigator and patient were unaware of the group they had been assigned to. The intervertebral level for intervention was selected based on clinical examination and the results of a magnetic resonance imaging (MRI) study. The intervertebral level, which was maximally affected, was selected for intervention.

Procedure

All epidural injections were administered in the operating room (OR) in the prone position. An initial anteroposterior fluoroscopic image was obtained to identify the interalaminar space at the desired level of intervention. Local infiltration was done with 1% lidocaine down to the lamina. An 18-gauge Tuohy needle was inserted into the skin at this level aiming towards the base of the spinous process in the interalaminar space. Midline orientation of the needle was maintained between the 2 spinous processes. Once the needle touched the lower border of the lamina, the same was redirected into the epidural space using the loss-of-resistance to saline technique. The bevel of the needle was directed towards the symptomatic side. After a negative aspiration for blood and cerebrospinal fluid, 0.5 mL of iohexol dye (300 mg/mL), (Omnipaque, GE Healthcare, London, UK) was injected to confirm the epidural space. Following this, the equivalent volume of contrast, according to group assignment, was injected to evaluate for unilateral or bilateral spread. Lateral images were taken to see the ventral epidural spread, defined as presence of contrast along the posterior longitudinal ligament or abutting the posterior aspect of the contiguous vertebral body at the level of needle insertion, caudal spread, and segmental spread. The test drug (2 mL of MPA + 2 mL of 2% lidocaine in different volumes) was then injected into the epidural space according to the designated group. Total fluoroscopy time was recorded for each procedure.

Assessment

Assessment for pain relief and disability was done using the visual analog scale (VAS) from 0 (no pain) to 100 (maximum pain) and Modified Oswestry Disability Questionnaire (MODQ), respectively. Patients were also assessed for any postural headache, motor weakness, newly developed pain, paraplegia, or paresthesia.

Primary and Secondary Outcomes

The primary outcome of the study was to compare the effect of different volumes of lumbar ESI (4 mL, 6 mL, and 8 mL) on therapeutic efficacy in patients with lumbosacral radicular pain, defined as the number of patients attaining more than 50% pain relief at 6 month. Secondary objective measures were to study VAS scores, MODQ scores, and the pattern of spread of iodinated contrast on fluoroscopy.

Follow-up

All patients were followed for a period of 6 months at an interval of 2, 4, 8, 12, and 24 weeks. Patients who reported < 50% pain relief from baseline received an ad-

ditional injection with the same approach and volume at least 15 days apart for a maximum of 3 injections. Those patients who reported > 50% pain relief received a subsequent epidural injection during the study period, only if pain increased to > 50% of baseline again.

Statistical Analysis

A sample size of 20 patients in each group was required based on a standard deviation (SD) of 2.5 at a power of 80% to detect a difference of 2 in mean VAS scores between baseline and at any follow-up period.

Data were presented as mean + SD or median (range) with 95% confidence interval where necessary. Numerical variable were assessed for normality. Analysis of demographic data was done by student t- test and chi-square tests. Continuous data like VAS and MODQ were analyzed using 2 way repeated measures of analysis of variance (ANOVA), and with post hoc test when indicated. Categorical data (presence of anterior spread, perineural spread, and complication) were analyzed using chi-square test.

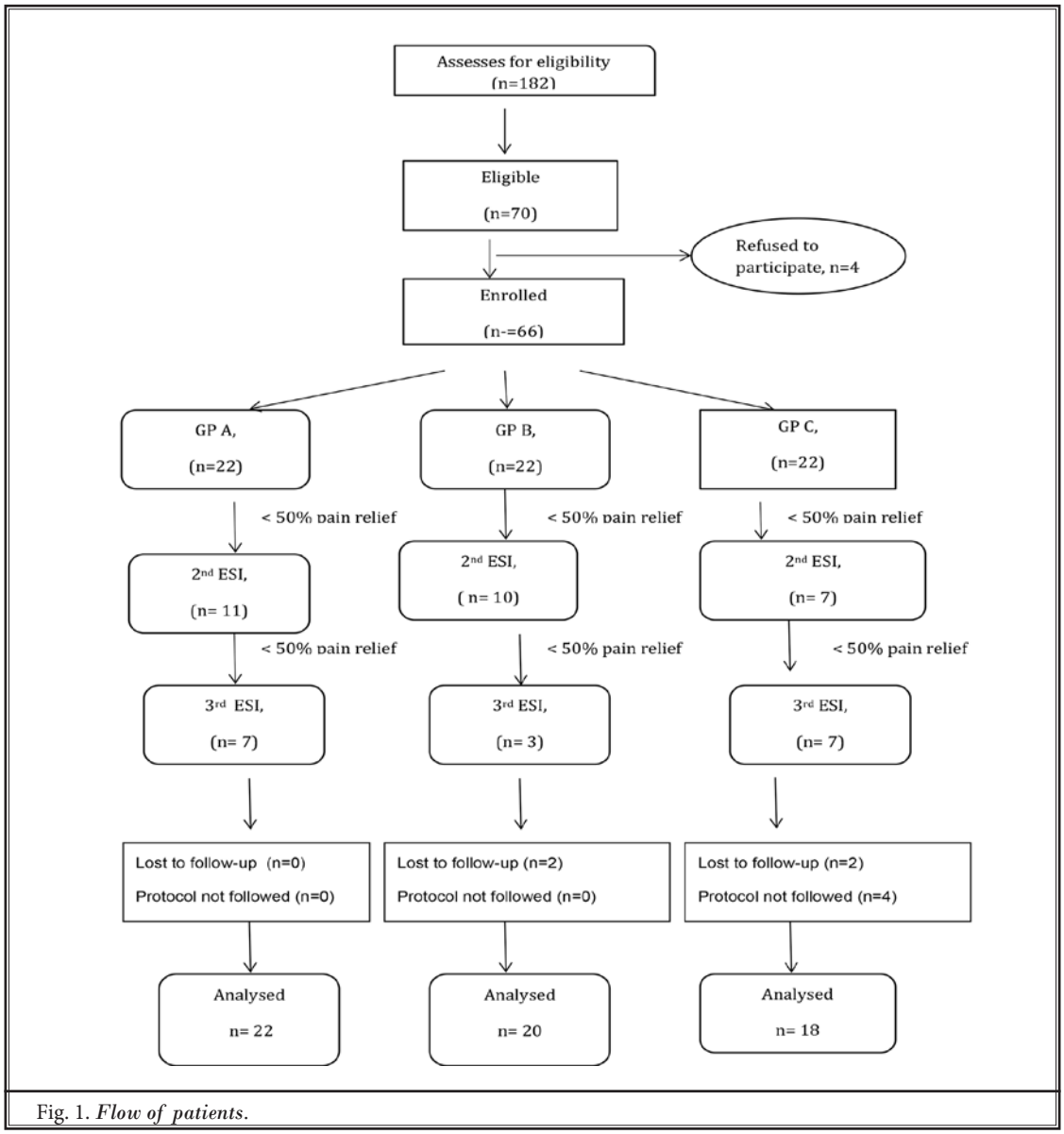

Fig. 1. *Flow of patients.*

Table 1. *Patients demographics and base line data in 3 groups.*

	Group A (n = 22)	Group B (n = 20)	Group C (n = 18)	*P* value
Age (years)¥	44.18 ± 9.116	43.85 ± 8.29	47.06 ± 8.346	0.488
Gender≠ Male Female	 10 (45.5%) 12 (54.5%)	 9 (45.0%) 11 (55.0%)	 9 (50%) 9 (50.0%)	
Height (cm)¥	162.36 ± 5.403	163.95 ± 6.03	162.69 ± 4.094	0.607
Weight (kg)¥	65.45 ± 11.979	62.35 ± 10.35	66.31 ± 10.31	0.506
Baseline VAS¥	8.50 ± 1.144	8.60 ± 1.095	8.38 ± 1.204	0.843

Data expressed as mean ± SD,≠ data analyzed using chi-square test, ¥ data analyzed using one way ANOVA, P value < 0.05 significant.

Table 2. *Level of intervention in 3 groups.*

Level of intervention	L3-L4	L4-L5	L5-S1	*P value*
Group A (n = 22)	2 (9.1%)	14 (63.6%)	6 (27.3%)	0.505
Group B (n = 20)	3 (15%)	13 (65.0%)	4 (20%)	
Group C (n = 18)	0 (0%)	10 (62.5%)	6 (37.5%)	

Data presented as numbers (percentages) and analyzed using chi-square test.

Results

Figure 1 shows the flow of patients. A total of 70 patients were included in this study. Four patients refused to give consent. Another 4 patients from group C were excluded due to breach in study protocol (noncompliance on follow-up and VAS could not be recorded). There was a loss to follow-up of one patient from group A and group B each after the first ESI. Data was analyzed for 60 patients. All 3 groups were comparable with respect to demographic data, duration of symptoms, level of disc herniation, baseline VAS, and MODQ (Table 1). The level of intervention was comparable in all 3 groups (Table 2).

There was no statistically significant difference in the effectiveness of intervention among the 3 groups at the end of 6 months (Group A-16/22 (72.7%), Group B-15/20 (75%), Group C-13/18 (72.2%); *P* = 0.98, chi-square test).

There was a significant reduction in mean VAS in each group compared to the baseline at various time intervals over the period of the 6 month follow-up. Repeated measure ANOVA revealed significant VAS time interaction within the 3 groups after epidural injection. However, there was no VAS group interaction. There was no significant difference in VAS sores between the 3 groups at any of the time intervals (Fig. 2).

Intragroup analysis showed that there was statistically significant differences in MODQ reduction within the groups as compared to baseline at various points of time. On intergroup analysis, there was no significant difference in MODQ between the 3 groups over the period of 6 months (Fig. 3).

The mean number of injections required for effective pain relief were comparable in all 3 groups (Group A 2.14 ± 0.834, Group B 1.90 ± 0.641; Group C 1.80 ± 0.77; t-test, *P* value = 0.375).

There was no statistically significant difference in percentage of patients having ventral spread of contrast or perineural spread (Table 3).

The intervention was given in the intervertebral space where maximum disc bulge was found. In case of more than one level disc herniation, the intervention was performed at the level corresponding with symptoms. The level of intervention was comparable in all 3 groups. The average number of vertebral segments of cephalic spread of contrast media in Group A was 2.82 ± 1.01, 2.29 ± 1.07, and 2.67 ± 1.16 for the first, second, and third ESI respectively. Cephalic spread in Group B was 2.95 ± 1.23, 3.06 ± 0.93, and 3.00 ± 0.71 for the first, second, and third ESI respectively. In Group C, the cephalic spread was 3.25 ± 1.39, 3.00 ± 0.95, and 3.33 ± 0.52 for the first, second, and third ESI. The average number of vertebral segments of caudal spread for Group A was 4.36 ± 1.71, 4.27 ± 1.79, and 3.33 ± 2.08 for the first, second, and third ESI. In Group B, the mean caudal spread was 4.30 ± 2.03, 4.00 ± 1.83, and 3.56 ±

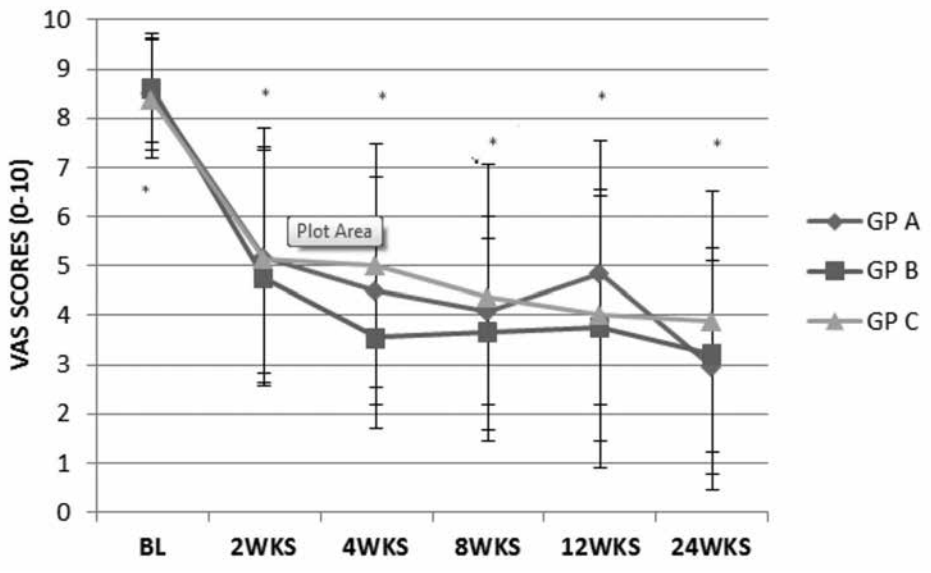

Fig. 2. *Line diagram showing mean visual analog scale in all the 3 groups at different time intervals. *represent P value 0.00 (< 0.05) within group as compare to base line at various interval (within group pairwise comparsion). Error bars represent standard deviation.*

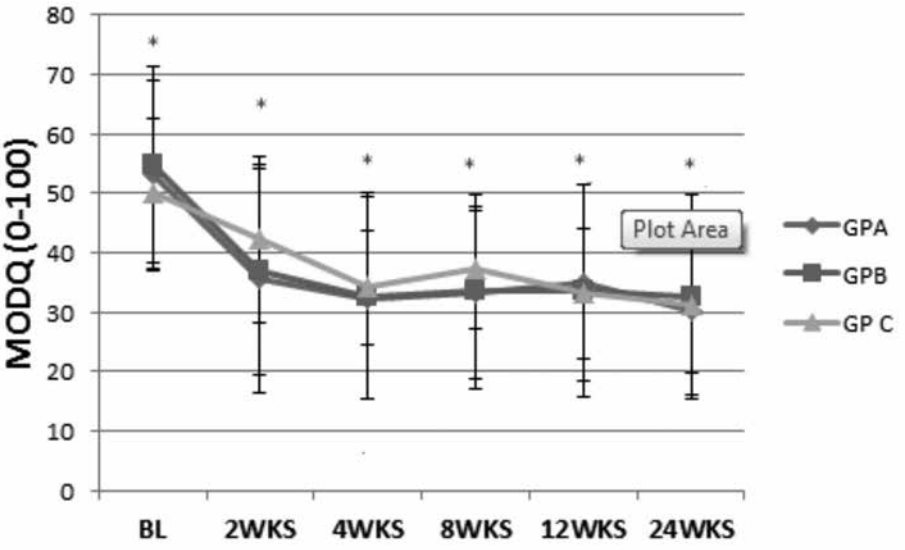

Fig. 3. *Line diagram showing mean MODQ score in all the 3 groups at various intervals. *Represent P value 0.00 (< 0.05) within group as compare to baseline, (pairwise comparison). Error bars represent standard deviation.*

1.94 for the first, second, and third ESI. For Group C, the mean caudal spread was 3.93 ± 1.94, 5.08 ± 1.24, and 3.33 ± 0.52 for the first, second, and third ESI. There was no significant difference in segmental spread between groups.

The bevel of the needle was directed towards the

Table 3. *Ventral spread in 3 groups.*

Ventral Spread	Group A	Group B	Group C
1ST ESI	9/22 (38.5%)	8/20 (40%)	6/18 (33.3%)
2ND ESI	4/11(36.3%)	4/10 (40%)	3/7 (42.8%)
3RD ESI	3/7 (42.8%)	1/3 (33.5%)	2/7 (28.5%)

Data expressed as number (percentage) and analyzed using chi-square tests.

side of pain to ensure unilateral spread. One hundred and three injections were done in total. Seventy-two patients had unilateral spread (69.9%).

We did not meet any complications like intravascular injection, interathecal, or subdural injection. All of the patients were stable during and after the procedures.

Discussion

ESIs are used in combination with improved body mechanics and core muscle strengthening exercises to provide pain relief in patients with lumbar radicular pain. Optimal volume in which a steroid should be administered for lumbar ESI is debatable. Current literature suggests better pain relief with a higher volume. Several mechanisms have been proposed pertaining to this finding. Large volume leads to washing out of the inflammatory cytokines. It is also hypothesized that injecting larger volumes in the epidural space leads to lysis of neural adhesions by means of stretching along the dura and nerve roots (6,7). Further, added volume allows the lavage of epidural space, suppresses focus of ectopic discharge from the injured nerve, and enhances blood flow to the ischemic nerve roots (8).

In the absence of any randomized control trial, Rabinovitch et al (9) conducted a systematic review in 2009 to study the correlation between the volume of lumbar ESI and pain relief. These authors found a statistically significant positive correlation between the volume and pain relief and concluded that injectate volume could be a variable determining the efficacy of epidural injection.

Kim et al (10) injected a total of 50 mL in the caudal space at increments of 10 mL in 32 patients with chronic low back pain accompanied by radiculopathy. Fluoroscopic images were repeated after each 10 mL of contrast medium and drug. The authors found that the extent of spread was limited to mid and lower lumbar areas in the majority of the patients on injecting a volume of 10 mL. Further volume on subsequent injection did not increase the extent of spread. We expected to see a difference in extent of spread of contrast on using an epidural injectate volume less than 10 mL. Therefore we injected 3 different volumes of contrast at increments of 2 mL (i.e., 4, 6, and 8 mL). However, we found no difference in the extent of spread of contrast on using a volume injectate of less than 10 mL. This is probably because of the starling effect of the epidural space (11). Greater drug volumes may leak through sacral or lateral foramina in an attempt to maintain constant pressure whenever epidural space is filled over or above its capacity. This implies increasing leakage of drug from the epidural space with increasing volume.

In a single prospective trial conducted to see the effect of different volumes, Chun et al (5) recently randomized 66 patients to receive lumbar transforaminal epidural injections with either a low-volume injectate (3 mL) or a high-volume injectate (8 mL). A higher percentage of patients achieved more than 50% pain relief at one month in the high volume group. However, post procedure epidurogram were not studied in this study. Also patients in the high volume injectate group received a larger dose of lidocaine. A total dose of lidocaine was kept constant in our study.

Our decision to use 4 mL was based on the available literature on ESIs in the last 10 years, where maximum studies have used a volume ranging from 3 to 10 mL (12-14). We also wanted to evaluate whether doubling the volume to 8 mL would improve the spread and efficacy of lumbar ESIs.

We used methylprednisolone, as clinical studies evaluating the efficacy of different types of steroid injections report variable results with nonparticulate steroids (15,16). Further, methylprednisolone is acceptable for interlaminar injections (17).

Limitations

Our study has few limitations. Firstly, it is not controlled with a placebo group. However, this is justifiable as involved patients had significant pain, and so it would be unethical to have a placebo group. Secondly, contrast and drug injected have different viscosities and may therefore have different epidural flow characteristics. We assumed the contrast flow to be parallel to the drug solution flow. Thirdly, we did not define the speed of injection. Only one study has reported a positive correlation between speed of injection and cranial spread of blockade. Injections performed at a rate of 1.2 mL/s using a Tuohy needle, resulted in a 4 segments greater spread of sensory blockade compared to an injection at a rate of 0.24 mL performed using an epidural catheter (18). In contrast, the same number of dermatomes blocked after 15 min of a rapid injection of mepivacaine 8 mL over 8 seconds versus 160 seconds (19). We did not use an infusion pump and high pressure tubing to control the speed of injection fearing that this would add another source of infection. Lastly, the number of patients analyzed were not the same in each groups.

Conclusion

To conclude, our study showed no significant difference in pain relief on increasing the volume of drug in midline interlaminar approach.

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