Randomized Trial

Transforaminal Versus Parasagittal Interlaminar Epidural Steroid Injection in Low Back Pain with Radicular Pain: A Randomized, Double-Blind, Active-Control Trial

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Background: Epidural injections are the most common minimally invasive intervention used to manage low back pain with lumbosacral radicular pain. It can be delivered through either transforaminal (TF), interlaminar, or caudal approaches. The TF approach is considered more efficacious than the interlaminar approach probably because of ventral epidural spread. However, catastrophic complications reported with the TF approach have raised concerns regarding its use. These concerns regarding the safety of the TF approach lead to the search for a technically better route with lesser complications with drug delivery into the ventral epidural space. The parasagittal interlaminar (PIL) route is reported to have good ventral epidural spread. However, there is a paucity of literature comparing the effectiveness of PIL with TF.

Objectives: To compare effectiveness of PIL and TF epidural injections for managing low back pain with lumbosacral radicular pain.

Study Design: Randomized, double-blind, active-control study.

Setting: Interventional pain management clinic in a tertiary care center in India.

Methods: Sixty-two patients were randomized to receive fluoroscopically guided epidural injection of methylprednisolone (80 mg) either through the PIL (n = 32) or TF (n = 30) approach. Patients were evaluated for effective pain relief (≥ 50% from baseline) by 0 – 100 visual analogue scale (VAS) and functional improvement by Modified Oswestry Disability Questionnaire (MODQ) at 2 weeks, 1, 2, 3, 6, 9, and 12 months. Patients who failed to respond to the treatment or when the patient's response deteriorated received additional injection of same injectate, dose, and approach. Only if the pain returns should there be a maximum of 3 injections. Other outcome measures were overall VAS and MODQ, number of injections, and presence of ventral and perineural spread.

Results: Effective pain relief (≥ 50% pain relief from baseline on VAS) was observed in 76% (90% CI 60.6 – 88.5%) of patients in the TF group and 78% (90% CI 62.8 – 89.3%) of patients in the PIL (P = 1.00) group at 3 months. The pain relief survival period was comparable in both groups (P = 0.98). Significant reduction in VAS and improvement in MODQ were observed at all time points post-intervention compared to baseline (P < 0.001) in both groups. On average, patients in the PIL group received 1.84 and patients in the TF group received 1.92 procedures annually. The majority received injection at L4-L5 intervertebral level (24 in TF and 23 in PIL). Ventral epidural spread was comparable in both groups (PIL – 91.6% and TF – 89.6%). No major complications were encountered in either group; however, initial intravascular spread of contrast was observed in 3 patients in the TF group.

Limitations: Limitations included lack of documentation of adjuvant analgesic drug therapy and procedures performed by a single experienced interventionalist.

Conclusions: Epidural injection delivered through the PIL approach is equivalent in achieving effective pain relief and functional improvement to the TF approach for the management of low back pain with lumbosacral radicular pain. The PIL approach can be considered a suitable alternative to the TF approach for its equivalent effectiveness, probable better safety profile, and technical ease.
Trial registration: CTRI/2012/08/002938.

Key words: Low back pain, lumbosacral radicular pain, interlaminar, parasagittal, transforaminal, epidural steroid injection, epidural steroids, equivalence clinical trial

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Low back pain (LBP) with or without involvement of extremities is the most common of all spinal, and even chronic, pain problems (1). Health care expenditure on its management continues to rise at an unsustainable rate (2-7). It is the most common of the diseases for the largest number of years lived with disability in 2010 in US (3). Intervertebral disc herniation (IDH) is the common etiology of lumbosacral radicular pain (1,2,8,9).

There have been explosive increases in spinal interventional techniques for spinal pain in the US is in past decade (10,11). Epidural steroid injection (ESI) for management of lumbosacral radicular pain is minimally invasive, effective, and is the most commonly performed procedure (1,2,10,11). ESI has been associated with substantial debate in reference to effectiveness, appropriate medical necessity, and indications. According to critics the available evidence suggests that ESIs offer only short-term relief of leg pain and disability for patients with sciatica (12). The small size of the treatment effects, however, raises questions about the clinical utility of this procedure in the target population (12). Proponents argue that there is at least moderate evidence based on the literature that properly evaluates evidence-based medicine principles (1,2,10,11,13,14). It is also shown that local anesthetic with or without steroids is equally effective and thus, many clinicians may even avoid steroids (15-18). In addition, a recent systematic review by Bicket et al (19) shows an equal or even superior effect of non-steroid injections into the epidural space. On the contrary, in a proper placebo design Ghahreman et al (20) showed a lack of effectiveness of epidural local anesthetic and sodium chloride injection when it was injected in or away from the epidural space. They reported substantial outcome in epidural steroid group and ruled out simply a placebo effect (20).

Most IDHs are located posteriorly in the ventral epidural space, hence it is suggested that ESI would be more effective if delivered close to this targeted site (1,14,21,22). The epidural space in the lumbar spine can be accessed through interlaminar (IL, either midline or parasagittal), transforaminal (TF), and caudal approaches (1,2,12-18,21,22). Though the IL approach is widely used, its efficacy was reported to be limited (22-24). This was mainly ascribed to the use of the midline interlaminar (MIL) approach: lack of target specificity and distribution of injectate into the dorsal rather than ventrolateral space (25,26). The TF approach is considered as target specific (delivering injectate into the ventrolateral epidural space near nerve root) and in the past was reported to be more effective than the IL route (22-24).

However, recent studies (15,27-29) and recent systematic reviews (30,31) show that IL epidural injections are as effective as TF injections and equally as effective as caudal (16) when performed in contemporary interventional pain management settings utilizing fluoroscopy.

Transforaminal ESI is associated with a multitude of serious complications; the most catastrophic are spinal cord infarction and permanent paralysis due to intra-arterial drug injection and paraplegia (32). Increasing instances of intradiscal drug injections (33) and even death with cervical spine TF injection (34) have also been reported. The concerns regarding the safety of TF ESI led to the search for a technically better route with lesser complications and with drug delivery into the ventral epidural space.

Lately, good ventral epidural spread (VESp) of contrast is reported while using a modified interlaminar approach, i.e. parasagittal interlaminar (PIL) (35) or lumbar interlaminar ventral epidural (LIVE) injections by placing an epidural catheter at the ventrolateral side of the nerve root (36). However, these studies investigated contrast spread as the primary outcome. The clinical significance was either not elucidated (36) or was limited by the observational uncontrolled nature (35), as Candido et al (35) only controlled the first intervention for each patient and additional treatment decisions were made on a case to case basis, limiting their ability to evaluate the efficacy of one technique over another. While assessing the clinical outcome of PIL with a MIL approach of ESI, our group has recently reported more effective pain relief at 6 months and better VESp of injectate (89.7% versus 31.5% in MIL) with a PIL approach compared to MIL (21).

There is a paucity of literature regarding the head to head comparison of PIL with TF ESI for the management of chronic LBP (CLBP) with radicular pain. Thus in view of this, the current study was conducted to compare the effectiveness and safety of fluoroscopically guided TF ESI with PIL ESI for managing CLBP with unilateral lumbosacral radicular pain secondary to IDH not responding to conservative management.

Methods

Study Design

This was a prospective, single center, randomized, double-blind, active-controlled parallel group clinical trial. The study was conducted in accordance with the

Consolidated Standards of Reporting Trials (CONSORT) guidelines (37) and following the principles of the Declaration of Helsinki. The study was approved by the PGIMER institutional review board (Chandigarh, India), and all patients provided written, informed consent. The trial was registered with the Clinical Trial Registry of India (CTRI) with an assigned number of CTRI/2012/08/002938.

Patients

The study setting was a public sector interventional pain management specialty referral clinic in a tertiary care hospital in India. Adult patients of either gender, aged 18 to 65 years, with a diagnosis of CLBP and unilateral lumbosacral radicular pain, with a minimum of 3 months duration not responding to medications and physical therapies, having a pain score of at least 50 as assessed on 0 – 100 Visual Analogue scale (VAS) at baseline were eligible for study recruitment. The diagnostic criteria for lumbosacral radicular pain were discussed previously (1,38). Patients were clinically examined including straight leg raising test. Magnetic resonance imaging (MRI) was performed to correlate the symptomatology and exact disc level protrusion.

Patients were excluded if they had any clinically significant or unstable medical or psychiatric illness, previous surgery on the lumbar spine, facet joint arthropathy, spinal canal stenosis, unstable neurological deficits, or cauda equine syndrome. Those having received lumbar ESI in the past, corticosteroids or anesthetics allergy, taking anticoagulants or bleeding diathesis, taking systemic corticosteroids, pregnant and lactating women, or those being treated with investigational drug within 30 days of trial were also excluded.

Randomization and Masking

Patients were randomized to receive ESI through either the TF or PIL approach. Randomization was performed by an independent pharmacist using a computer generated randomization schedule (Software Random-Randomizer, blocks of six). Random numbers were kept in opaque sealed envelopes and opened by an independent anesthesiologist at the time of injection. None of the study investigators, including the outcome assessor, had access to the randomization sequence. All procedures were performed by single investigator (BG) and followed by other investigators (DB/JPK). Study cases were kept in between clinical non study cases during the procedure as well as for follow-up. It was done to enhance the blinding and allocation concealment.

Study Interventions and Procedures

Before the intervention, intravenous access and standard monitoring was established. The intervertebral level was determined by clinical examination and MRI studies. All procedures were performed under C-arm fluoroscopic guidance. Initial anteroposterior (AP) images were obtained to identify the level and interlaminar space in a prone position with a pillow of 10 cm height kept under the abdomen.

In the PIL group, an 18-gauge, 3.5 inches, Tuohy needle was introduced at the level of disc pathology and advanced in a posterior to anterior direction. The needle was introduced into the most lateral epidural space of the affected side, using the loss-of- resistance to saline technique and this parasagittal orientation of the needle was maintained throughout the procedure (21) (Fig. 1A).

In the TF group, a 22-gauge, 3.5 inch Quincke's needle was introduced at the level of disc pathology using first an AP and, subsequently, an oblique orientation (15 – 30^0) of the fluoroscopy C-arm to achieve the "Scotty Dog" appearance of the lumbar spine and then directed until the needle tip was in the posterior and superior aspect of the intervertebral foramen as checked in the lateral imaging, and in line with the pedicle on AP view (39) (Fig. 1B).

In both groups, once the needle was in position, and after negative aspiration for cerebrospinal fluid and blood, 0.5 mL Iohexol (300 mg/mL), (OMNIPAQUE™, GE Healthcare, UK) was injected to confirm the epidural space in the AP view. This was followed by further injection of 3.5 mL of contrast under continuous fluoroscopy to confirm the spread of the contrast as well as to verify that no contrast medium attained the intra vascular, subarachnoid, subdural, or intra-discal spread (Figs. 2A, 2B). Lateral images were taken to evaluate the ventral epidural space. Ventral spread was defined as present if contrast travelled along the posterior longitudinal ligament or abutted the posterior aspect of the contiguous vertebral body at the level of needle insertion (Figs. 3A, 3B). Perineural spread and segmental spread was also noted on AP view (Figs. 2A, 2B). After epidural space confirmation, 2 mL of methylprednisolone acetate (l mL = 40mg) (DEPO-MEDROL™ injection, Pfizer products India Pvt. Ltd, Mumbai) with 2 mL sterile normal saline were injected.

All the patients were kept under observation for at least 30 minutes post-procedure.

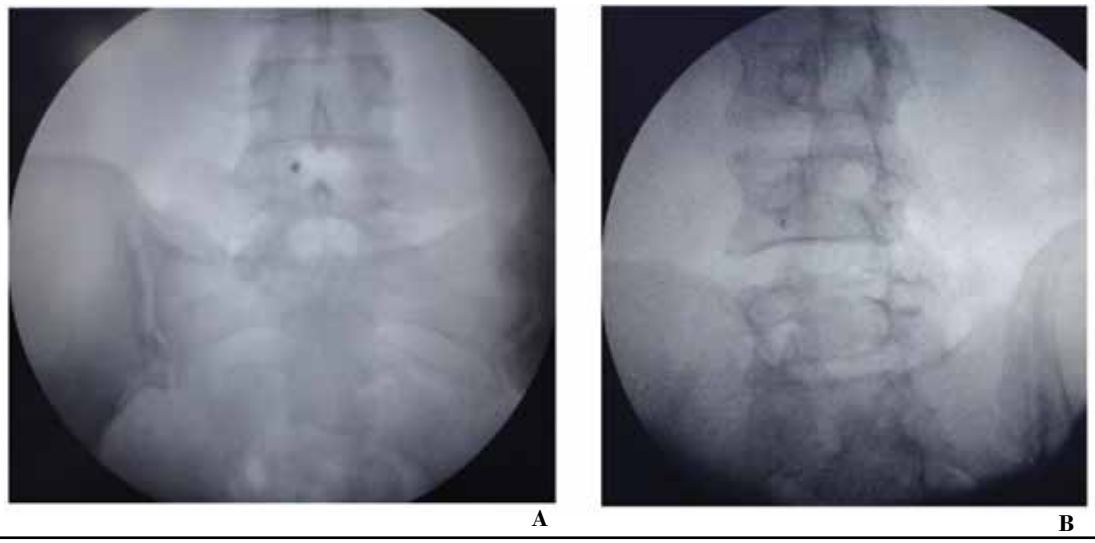


Fig. 1. *A. Parasagittal interlaminar approach. AP view showing the needle placement at the lateral most part of L4-L5 interlaminar area. B. Oblique view showing "Scotty Dog" appearance of vertebra and needle insertion for transforaminal approach between L4-L5.*

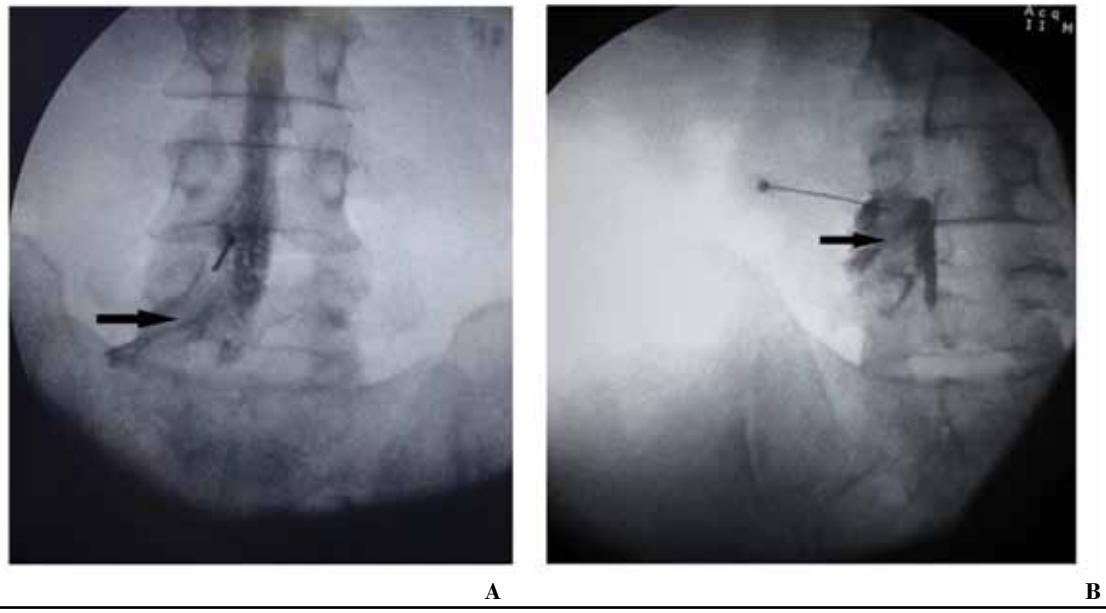


Fig. 2. *A. Confirmation of needle with parasaggital interlaminar approach. AP view of contrast showing epidural as well as perineural spread of contrast of the same side (arrow). B. Confirmation of needle with transforaminal approach. AP view of contrast showing epidural as well as perineural spread of contrast of the same side (arrow).*

Assessment and Follow-up

Patients were assessed for pain by VAS on a horizontal 0 (no pain) to 100 (worst pain possible) scale and for functional impairment using modified Oswestry Disability Questionnaire (MODQ) (40) at 2 weeks, 1, 2, 3, 6, 9, and 12 months post-intervention. We defined the approach as "effective" when pain relief was a ≥ 50% reduction from baseline on VAS. The primary endpoint was effective pain relief at 3 months. However, pain relief and MODQ were assessed continuously for 12

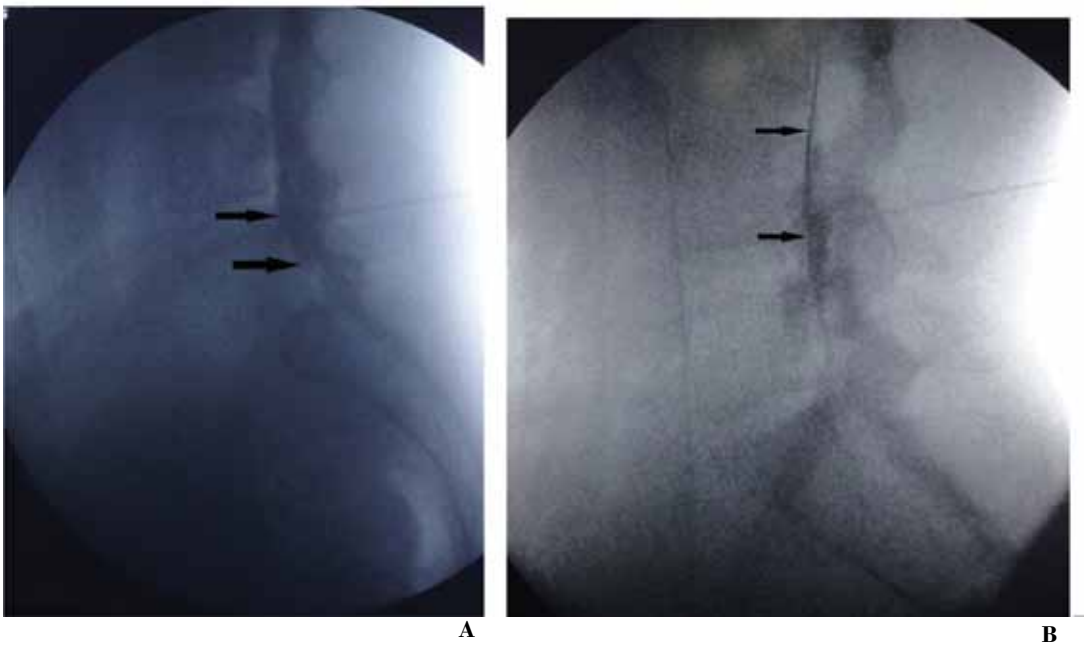


Fig. 3. *A. Lateral view of parasagittal interlaminar approach. Ventral epidural spread is indicated by arrows. B. Lateral view of transforaminal approach approach. Ventral epidural spread is indicated by arrows.*

months of follow-up at above mentioned time points. Patients' self-evaluation of overall change was done on the basis of a 7-point Patient Global Impression of Change (PGIC) (41) at 3, 6, and 12 months post-intervention. Patients were also assessed for possible neurologic complications and any newly developed pain.

Patients who failed to respond to the treatment or patients whose response deteriorated received additional injection of same injectate, dose, and approach. Only if the pain returns should there be a maximum of 3 injections. The minimum time between the 2 injections (if required) was 15 days.

Co-Interventions and Post-intervention Medications

All study patients were receiving conservative management including analgesics (adjuvant; pregabalin, opioid, or non-opioid) and/or an exercise program before joining the study. Exercise programs continued and analgesics continued/reduced/increased as per need. Job attendance continued. The only new treatment introduced was the study intervention.

Primary and Secondary Endpoints

The proportion of patients achieving effective pain relief at 3 months in each group was considered as the primary endpoint. The secondary endpoints included overall mean pain and MODQ scores at various time points, PGIC score, presence of ventral and perineural spread, segmental spread, number of injections required, treatment emergent adverse events (TEAEs), and possibly neurological complications as assessed by clinical and laboratory evaluation.

Statistical Analysis

Sample size was calculated assuming both approaches providing pain relief at 3 months to the tune of 75% (15,21,42) and largest clinically acceptable effect to be able to declare equivalence is 15% so that 90% confidence interval (CI) of proportion of effective pain relief in each group should lie between 60% and 90%. True mean difference between the 2 approaches is thought to be zero with equal group allocation, probability of type I error of 2.5% at each side, power 90%; we got a sample size of 27 patients to be recruited in each arm. We recruited 62 patients for possible drop outs.

Data are presented as mean with standard deviation (SD) or median with interquartile range (IQR). Demographic data were analyzed using either 2 sample independent student t-tests or χ 2 tests. The primary endpoint was analyzed by χ 2 test. Two-way repeated

measures analysis of variance (ANOVA) was used to analyze VAS and MODQ over time within and between groups. Greenhouse-Geisser test was used with adjustment for time × factor, time × group interaction, and between-subject effects for VAS and MODQ followed by Bonferroni correction for multiple comparisons. Effective pain relief duration was analyzed using Kaplan-Meier survival analysis. Clopper-Pearson Exact method was used to find the 90% CI of effective pain relief proportion and upper limit of 95% CI of complications. PGIC was assessed using Mc-Nemar Bowker test. Statistical software SPSS version 15.0 (SPSS Inc, Chicago, IL) was used for analysis. $P < 0.05$ was considered significant.

Results

Patient Disposition

The study period was October 2011 to April 2013. Patients' clinical characteristics, demography, and disposition through the study period are summarized in Table 1 and Fig. 4, respectively. One hundred twenty-four patients were screened and 62 patients (n = 30 in the TF group and n = 32 in the PIL group) were included in the study. All included patients were available for complete follow-up. Both groups were similar with respect to pre-procedure characteristics (Table 1).

Primary Outcome

Effective pain relief at 3 months was 76% (90% CI 60.6% – 88.5%) in the TF group and 78% (90% CI 62.8% – 89.3%) in the PIL group (= 1.00). Thus, the proportion of relief was within equivalence width in the 2 groups. The proportion of subjects achieving effective pain relief (Fig. 5) at 2 weeks, 1, 2, 3, 6, and 12 months were also comparable in both groups.

Effective Pain Relief Survival Analysis

Kaplan-Meier curves (Fig. 6) for effective pain relief survival were found to be comparable in both groups, showing that effective pain relief survival period was similarly achieved with both approaches ($P = 0.98$).

PGIC

Overall, 24 of 30 patients in the TF group and 25 of 32 patients in the PIL group improved with ESI over 52 weeks of follow-up on the PGIC scale (Table 2) ($P > 0.05$ at all time points). One in each group did not achieve any pain relief despite receiving 3 ESIs. This patient in the PIL group had surgery at 9 months.

VAS and MODQ Score Over Time

Repeated measures ANOVA revealed time × factor ($P < 0.001$ for both VAS and ODQ) interaction but no time×group interaction ($P = 0.79$ for VAS and $P = 0.68$ for ODQ). Between-group effect was not found to be significant ($P = 0.58$ for VAS and $P = 0.34$ for ODQ). Follow-up within group pairwise analysis revealed that VAS and MODQ decreased significantly at all time intervals compared with baseline in both groups ($P < 0.001$, Figs. 7 and 8). Between-group analysis revealed that VAS and MODQ scores were comparable in the 2 groups at all time intervals (Figs. 7 and 8).

Table 1. *Baseline demographic characteristics.*

		TF Group (n = 30)	PIL Group (n = 32)	*P* value
Age (years)	Mean ± SD	46.1 ± 12.5	42.8 ± 9.6	0.07
Gender	Male	19 (63%)	17 (53%)	0.42
	Female	11 (37%)	15 (47%)	
Weight (kg)	Mean ± SD	67.7 ± 12.1	65.3 ± 9.3	0.68
Height (cm)	Mean ± SD	170.0 ± 7.6	168.4 ± 6.3	0.28
Body mass Index (kg/m2)	Mean ± SD	23.4 ± 3.785	23.0 ± 3.11	0.85
Duration of pain (months)	Mean ± SD Median (IQR)	30.2 ± 65.8 12 (10–24)	25.1 ± 25.9 12 (10 – 36)	0.37
Visual Analogue scale (0 – 100)	Mean ± SD Median (IQR)	73.5 ± 1.19 70.1 (70 – 80)	73.1 ± 0.99 70 (62.5 – 80)	0.57
Modified Oswestry Disability score	Mean ± SD Median (IQR)	28.93± 5.97 30 (25.75 – 30.50)	31.3 ± 7.78 31 (26.75 – 35.25)	0.27

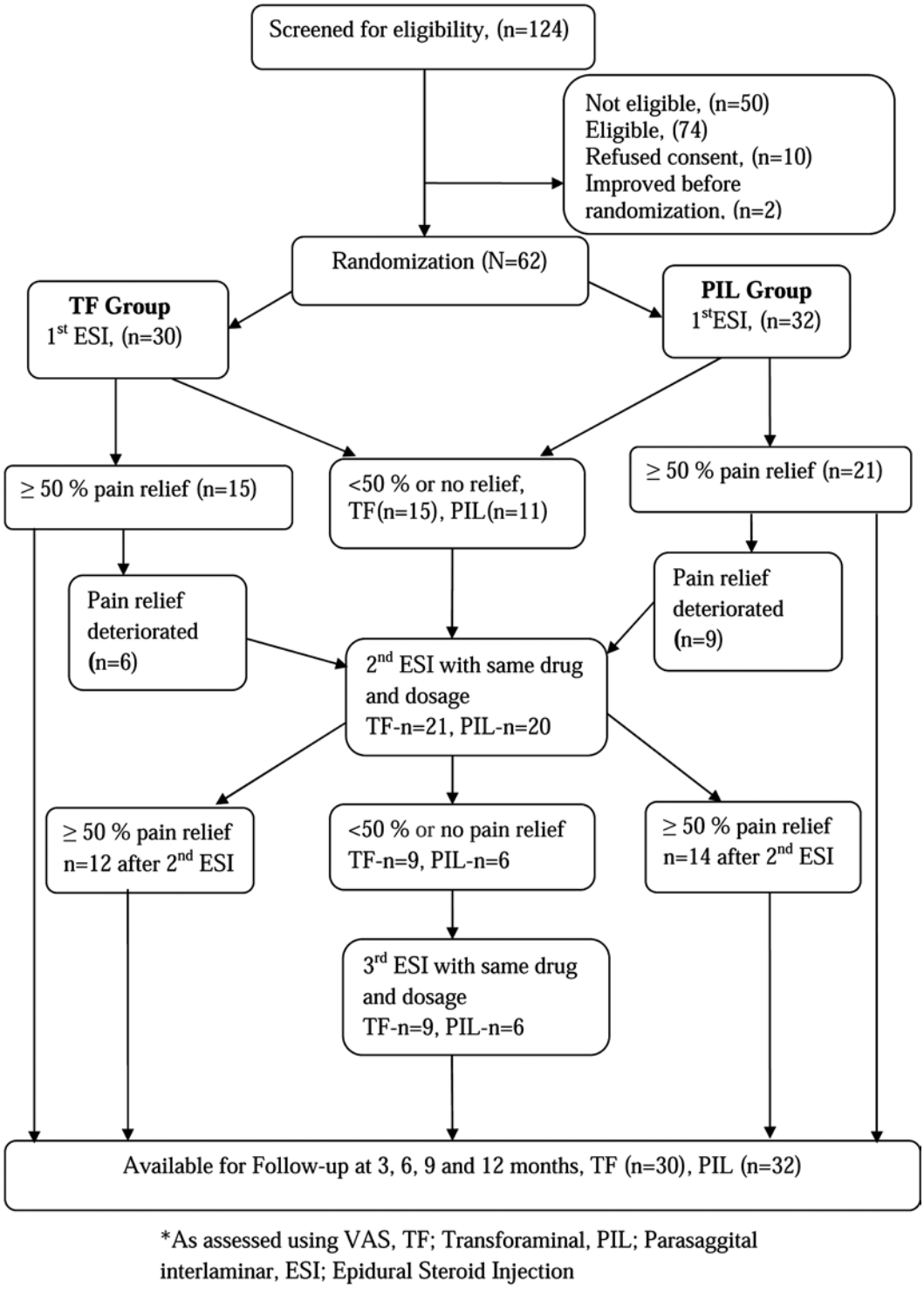
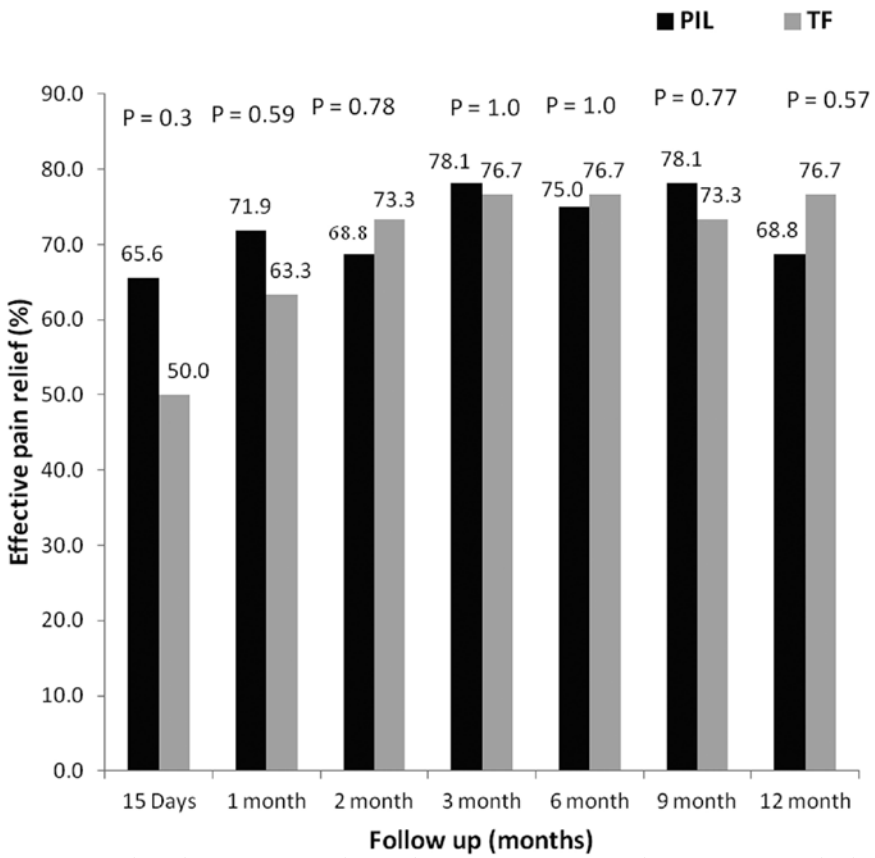


Fig. 4. *Flow chart of patients who participated in the study.*



TF: Transforaminal, PIL: Parasaggital interlaminar. Compared using chi-square test,* P <0.05 within groups compared to baseline. As assessed using VAS (≥ 50% reduction from baseline). None of the groups were significantly different at any time point.

Fig. 5. Effective pain relief incidence over the 52 weeks of follow-up.

Table 2. *Patient Global Impression of Change (PGIC).*

PGIC	TF Group (n = 30)			PIL group (n = 32)			*P* value
Months	Improved	No change	Worse	Improved	No change	worse	
3	23	4	3	25	6	1	0.49
6	24	3	3	24	7	1	0.28
9	23	6	1	25	6	1	0.99
12	24	5	1	25	6	1	0.98

PGIC is a 7-point scale on which patients rated change in overall status since study start (1 – 3 = improved, 4 = no change, 5–7 = worse). Compared by McNemar Bowker test.

Table 3. *Intervertebral disc herniation involved level and level of injection.*

Level of disc herniation and injection	TF group (n = 30)	PIL group (n = 32)	*P* value
L3-L4	3	4	0.52
L4-L5	24	23	
L5-S1	3	5	

Level of Injection

Levels of injections in both groups were comparable. The majority received ESIs at the L4-L5 level (24 in the TF group and 23 in the PIL group). Three patients in the TF group and 4 in the PIL group received injection at the L3-L4 level. Three patients in the TF group and 5 patients in the PIL group received injection at the L5-S1 level ($P = 0.52$) (Table 3).

Total Number of ESI

Total ESIs administered in the TF group (60) and the PIL group (58) were comparable ($P = 0.72$) with 1.92 procedures in the TF group and 1.84 procedures in PIL group per year. Nine (30%) in the TF group compared to 12 (37.5%) in the PIL group ($P = 0.59$) received only one injection. Twenty-one patients in the TF group and 20 patients in the PIL group received further injections. Twelve

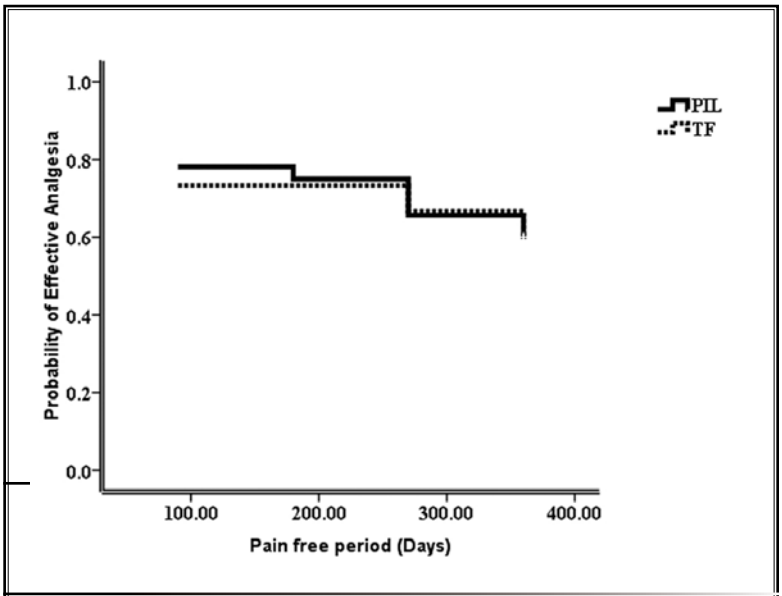
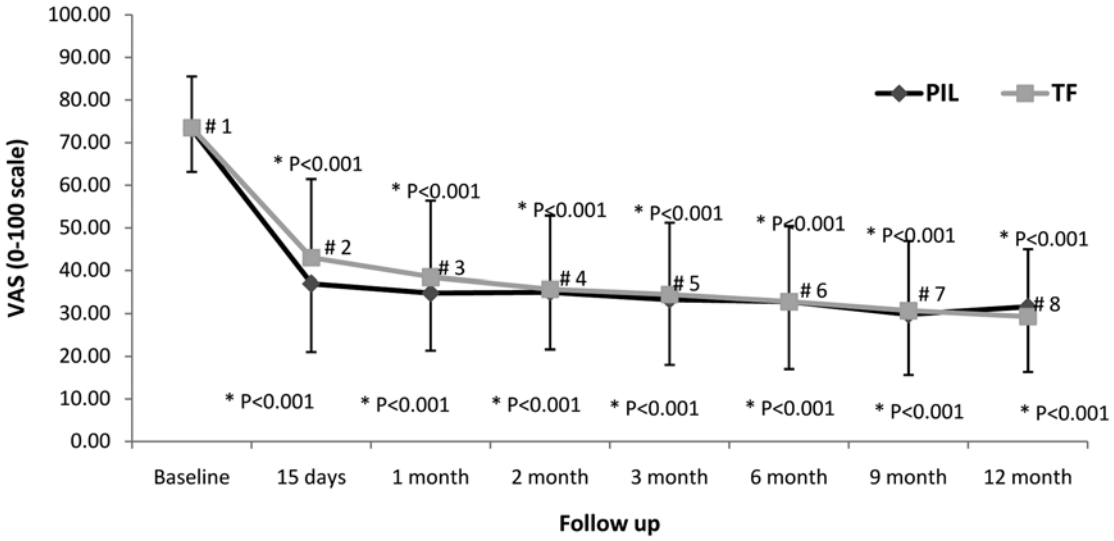
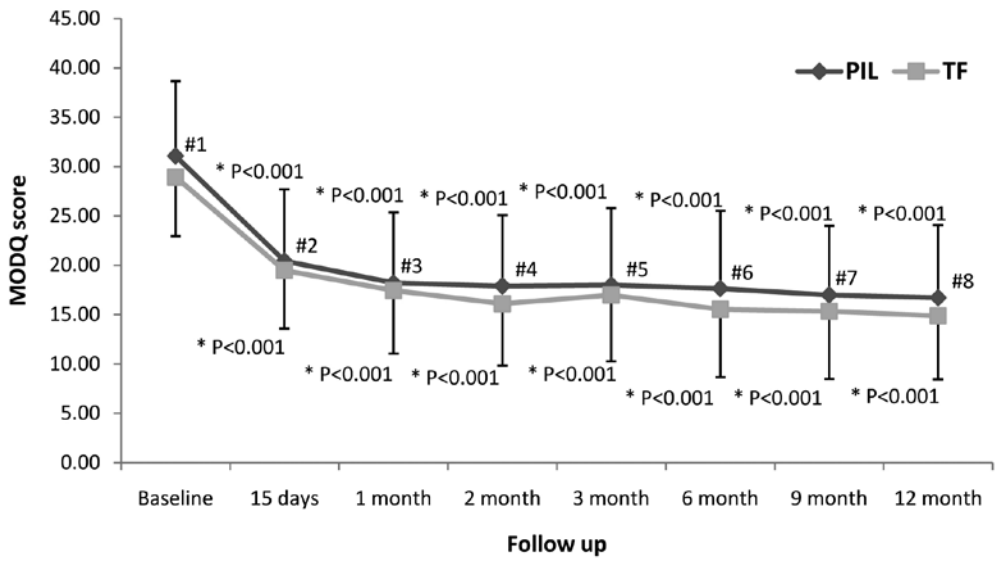


Fig. 6. Kaplan-Meier graph for effective analgesia period. This figure represents probability of patients having effective analgesia at different points of time.



Error bars represents standard deviation. *P value at different time intervals as compared with baseline (within group, pair-wise comparisons with Bonferroni correction) #1 P = 0.56, #2 P = 0.63, #3 P=0.61, #4 P = 0.59, #5 P = 0.64, #6 P = 0.56, #7P=0.23 and #8P= 0.79, respectively, for between-group comparisons at specified time intervals with Bonferroni correction.
TF; Transforaminal, PIL; Parasaggital interlaminar

Fig. 7. *Mean Visual Analogue Scale score over time.*



Error bars represents standard deviation. *P value at different time intervals as compared with baseline (within group, pair-wise comparisons with Bonferroni correction)) #1 P = 0.18, #2 P = 0.29, #3 P=0.38, #4 P = 0.38, #5 P = 0.60, #6 P = 0.36, #7P=0.52 and #8P= 0.45, respectively, for between-group comparisons at specified time intervals with Bonferroni correction.
TF; Transforaminal, PIL; Parasaggital interlaminar

Fig. 8. *Mean Modified Oswestry Disability Questionnaire score over time*

of 21 in the TF group and 14 of 20 in the PIL group achieved effective pain relief after a second injection. Nine in the TF group and 6 in the PIL group received 3 injections ($P = 0.57$).

Ventral Epidural and Perineural Spread

VESp was comparable, 89.6% (52 of 58 injections) in the TF group as compared to 91.6% (55 of 60 injections) in the PIL group ($P = 0.64$). Incidence of perineural spread was significantly higher in the TF group, i.e. 95% (57 of 60 injections) compared to 62% (36 of 58 injections) in the PIL group ($P < 0.001$).

Fluoroscopy Time

Fluoroscopy time in both groups was comparable. Mean (SD) fluoroscopy time after all injections was 16.21 (5.44) seconds and 13.89 (6.7) seconds in the TF and PIL groups, respectively ($P = 0.25$).

Monitoring of the Complications

No intrathecal, intradiscal, or subdural contrast placement was encountered. Intravascular spread of contrast was noted during 3 injections (5.1%) in the TF group. Ninety-five percent CI was 0.0% – 10.8% in the PIL group and 0.0% – 11.6% in the TF group, and 0.0% – 5.8% for both groups together. Needle relocation at the desired site was required in both groups. In the TF group it was required in 3 patients due to intravascular spread and in the PIL group it was required during 3 injections as the needle was not at the lateral-most site. No patient reported any swelling, redness, or persisting pain at the injection site. Un-masking was not required for any patient.

Discussion

The study revealed comparable health benefits with both the PIL and TF approach with respect to effective pain relief for managing patients with CLBP with unilateral lumbosacral radicular pain. Significant improvement was observed with both approaches in primary as well as secondary outcomes, including functional disability (MODQ), pain intensity (VAS), and improvement ratings (PGIC) in both groups.

Among various approaches for ESI, TF was considered as target specific and more effective as compared to IL in the past (14,22-24). This may be due to blind administration of IL or needle placement in the dorsal space under fluoroscopic guidance leading to limited

VESp of steroid (28% – 47% only) (25,26). Studies have suggested the superiority of TF ESIs for both short and long-term outcomes (14,22-24). A retrospective study by Schaufele et al (22), assessing pain improvement and surgical rates for managing lumbar IDH between IL and TF injection over 18 months, reported TF ESI's superiority in short-term pain improvement and long-term surgical interventions. Ackerman and Ahmad (23), comparing efficacy of 3 fluoroscopically guided approaches (TF, IL, and caudal ESI) in patients with IDH, demonstrated TF ESI's superiority to IL ESI for lumbar radicular pain relief. They attributed this to higher VESp while using the TF approach. An advantage of TF ESI is that it can be performed in patients with failed back surgery syndrome at the levels of surgeries.

However, recent studies (15,27-29) and systematic reviews (30,31) show an equivalence of IL and TF injections. Rados et al (27), while comparing TF and IL approaches in patients with chronic unilateral radiculopathy, demonstrated significant functional and pain improvement with both approaches. Gharibo et al (28), while comparing IL and TF techniques in patients with subacute unilateral radiculopathy, reported comparable significant improvements in pain, function, and depression. The IL was entered through the epidural space with a paramedian approach and ipsilateral spread was confirmed. The authors concluded that IL could be the initial technique because of better safety and less patient discomfort. Manchikanti et al (15), while evaluating the effectiveness of a single injection of lumbar interlaminar local anesthetics (LA) with or without steroids for managing chronic pain of IDH or radiculitis, reported significant pain relief in 74% patients treated with LA and 86% with LA and steroids. The epidural space was entered at the L5/S1 level or at a level below the pathology to direct contrast flow toward herniated disc side. Furman et al (29) evaluated the effect of ESI using a paramedian IL approach for lumbar radicular pain and showed pain improvement for at least 3 months.

In these later studies, IL techniques might have outperformed previous studies due to a lateral paramedian/parasagittal interlaminar approach (leftward or right, toward the side of complaint) compared to a traditional midline approach (15,28,29). However, final position of the needle in the epidural space during an IL approach was not clearly mentioned (15,28,29), though there were attempts to have the contrast spread on affected side which could influence drug spread.

The TF approach is associated with a higher incidence of serious complications due the anatomical relation of the radicular artery accompanying nerve root (32). The most devastating complication is intravascular injection leading to spinal cord infarction and permanent paralysis. At least 18 cases of permanent paralysis are reported following TF ESI in the literature (32). On the contrary, only 2 MRI confirmed reports of spinal cord infarct are reported with lumbar IL ESI (43,44). In both cases, patients had prior surgery at the level of the IL ESI and in one a 21gauge intramuscular needle was used instead of an epidural needle (43). Post-surgical changes in the epidural space, arterial spinal vasculature (43,44), and use of an intramuscular needle (43) might have contributed to this complication. Also, overall rate of intravascular injection with lumbosacral TF ESIs is reported to be 11.2% (45) as compared to 1.9% (46) with IL ESI. Other complications reported with TF ESI are a 10-fold increased incidence of intradiscal injection, hence higher risk of discitis (33) and even death with cervical injection (34). Higher occurrence of serious complications have raised concerns regarding the safety of TF ESI and led to a search for alternative techniques for better VESp with fewer complications.

Lately, good VESp is reported when the needle was placed in the lateral most part of the epidural space (35,36). Candido et al (35) demonstrated 100% VESp with the PIL approach and 75% spread with the TF approach. Choi and Barbella (36) reported VESp in all patients using the LIVE approach of injection. However, these studies investigated contrast spread as the primary outcome. The clinical significance was either not elucidated (36) or was limited by the observational uncontrolled nature (35). We recently evaluated clinical significance of PIL with MIL approach and reported that PIL was superior to the MIL approach (21). The PIL approach provided more patients with effective pain relief (68.4% vs 16.7% at 6 months), better VESp (89.7% versus 31.7% in MIL), better functional improvement, and less number of injections (21).

In the present study, VESp with the TF approach was 89.6% and 91.6% with the PIL approach. These findings are in accordance with previous studies (21,23). Good VESp in both groups might have produced equivalent clinical outcomes. We performed all interventions under fluoroscopy and did not encounter contrast spread to the intradiscal, subarachnoid, or subdural spaces. Intravascular contrast spread was observed during 3 injections (5.1%) in the TF group requiring needle relocation.

The IL technique is a part of the anesthesia residency program in a majority of countries. However, TF

ESI requires super specialized training during a chronic pain management curriculum. This can be considered advantageous with an anesthesiologist performing interventional pain management procedures. However, this may not be relevant with other specialists such as physiatrists, neurologists, neurosurgeons, and orthopedic surgeons joining the interventional pain management specialty. Also, the S1 foramen is slightly more difficult to access technically (47). AP view of the S1 foramen is not always predictable as the more easily seen foramen is the ventral foramen (47). In the AP view, while lining up ventral and dorsal S1 foramen, accidental needle tip placement anterior to the ventral foramen is possible with gastrointestinal penetration, whereas in the oblique view, the iliac crest may obstruct the path of the S1 foramen (47). An L5-S1 IL procedure is not hampered by these difficulties. Hence in the scenario of equivalent efficacy with both approaches, with the perceived advantages of the PIL approach such as technical ease, training at specialty rather than super specialty level, and probably better safety profile, the PIL approach can be considered as an alternative to the TF approach or as the first choice for administering ESI to patients with CLBP with lumbosacral radicular pain.

Strengths and Limitations

The strengths include high internal validity; treatments provided according to protocols; effective masking of interventionialist, patients, and assessors; consistent retention of patients throughout the study; and adequate sample size for a well powered equivalence trial.

Limitations included lack of documentation of adjuvant therapies like individual patient exercise routines and analgesic drug therapy. Additional between-group variability might have remained unadjusted. Other limitations are the utilization of a high volume contrast and a high volume mixture of methylprednisolone and sodium chloride solution as well as a lack of local anesthetic injection. We used total of 4 mL of contrast which was equal to the volume of the drug used for injection. This amount of contrast and drug is within the range of volume used by previous investigators (16,17,29,35). Also, saline was added to dilute polyethylene glycol 4000 (28.6 mg/mL), the vehicle added during the manufacture of methylprednisolone that has been implicated to be associated with arachnoiditis (35). Since all procedures were performed by a single experienced interventionialist (with an experience of around 10 years), generalization of these results performed by less experienced interventionialists remains yet to be established. Wider implications of this trial can only be extrapolated by conducting a clinic based study with the interventions performed by interventionists with different ranges of experience. The challenges in the implementation of these findings in clinical services are well appreciated and that our results might not be generalized to non-specialized health care settings or non-specific LBP patients.

Conclusion

ESI is comparable with TF and PIL approaches under fluoroscopic guidance for achieving effective pain relief and functional improvement over 12 months for managing CLBP with unilateral radicular pain with the requirement of a comparable number of injections. ESI was without any complications with both approaches. The equivalent clinical outcomes with both approaches are most probably due to similar VESp. The PIL approach can either be a suitable alternative to the TF approach or the first choice for its probable better safety profile and technical ease.

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