A comparative study between interlaminar nerve root targeted epidural versus infraneural transforaminal epidural steroids for treatment of intervertebral disc herniation

ABSTRACT

Background: Low back pain (LBP) is one of the most common musculoskeletal abnormalities. Epidural corticosteroid injections (ESIs) have been used long time ago for treatment of lumbar radiculopathy or discogenic back pain in case of failed medical and conservative management. Different techniques for ESIs include the interlaminar, the caudal, and the transforaminal approaches.

Purpose: The aim of our study is to compare between the efficacy of infraneural transforaminal ESI and lumbar paramedian nerve root targeted interlaminar steroid injection in reduction of unilateral radicular pain secondary to disc prolapse.

Patients and Methods: This prospective double-blind randomized study was performed on 40 patients randomized into two equal groups, each of 20: the infraneural transforaminal ESI (IN group) and the interlaminar parasagittal ESI (IL group). Patients with backache without leg radiation, or with focal motor neurological deficit, previous spine surgery, S1 radiculopathy, lumbar ESI in the past month, systemic steroid used recently within 4 weeks before the procedure, allergy to any medication or addiction to opioids, and pregnancy were excluded from the study. The duration and efficacy of pain relief (defined as ≥40% reduction of pain perception) by 0–10 visual analog scale (VAS) is the primary outcome. Functional assessment using Modified Oswestry Disability Questionnaire (MODQ) and possible side effects and complications are the secondary outcomes.

Results: The VAS and MODQ scores were significantly lower in both groups in comparison with the basal values. There was also a lower VAS in the infraneural group than the parasagittal (IL) group up to 6 months after injection.

Conclusion: The infraneural (IN) epidural steroid is more favorable than the parasagittal (IL) interlaminar epidural steroid owing to its long-term improvement in physical function than the parasagittal technique with no serious side effects.

Key words: Infraneural transforaminal; low back pain; parasagittal interlaminar; steroid

Introduction

Low back pain (LBP) is one of the most common musculoskeletal abnormalities. It affects more than 70% of people during their life. LBP may persist after 12 months from the onset, which have a negative impact on healthcare. Variations in occurrence of LBP is likely due to variable risk factors such...
as age, education, occupation, culture/ethnicity, lifestyle, and psychosocial issues. The higher age and male gender are the most important risk factors and important predictors of pain and disability.

The most common clinical presentation of a lumbosacral radiculopathy is radicular leg pain below the knee level with neurological deficits in the distribution of the lumbosacral nerves. Radicular pain has a typical lancinating, shocking, or electric quality traveling into the lower limb along a narrow band. In approximately 90% of cases, radiculopathy is caused by a prolapsed disc involving nerve root impingement.

The clinical course of back pain and lumbosacral radiculopathy has been assessed in many cohort studies, which often follows a pattern of general improvement that starts rapidly and plateaus over time. Conservative treatment for LBP is primarily aimed at pain reduction, using pure analgesics or nonsteroidal antiinflammatory drugs (NSAIDs), or more specific drugs against neuropathic pain. Other treatment options are epidural steroid injections (ESIs).

ESIs have been used a long time ago for the treatment of lumbar radiculopathy or discogenic back pain. The traditional approaches are the midline interlaminar and the caudal approach. Midline interlaminar injection is unilateral in the majority of patients and only 36% of the injectate reach the ventral epidural space. Most of the lumbar interlaminar injections appear unilateral, mainly owing to the limitation to the flow dorsally by the plica mediana dorsalis; ventrally by the median raphe between the posterior longitudinal ligament and the disc. In pathologic conditions, adhesions will further decrease the flow of the injectate. The most recent approach is the transforaminal, which is used to target a predetermined nerve root with medications for diagnostic as well as therapeutic purposes.

In transforaminal injections there is a ventrolateral contrast spread along the segmental nerve. The target is the segmental nerve (and dorsal root ganglion) within the radicular canal.

The aim of this study is to compare between the efficacy of the newly implemented infraneural transforaminal ESI and lumbar paramedian nerve root targeted interlaminar steroid injection in a reduction of unilateral radicular pain secondary to disc prolapse. We hypothesize that infraneural ESI may be more effective than paramedian nerve root targeted ESI.

Patients and Methods

After approval of the local Institutional Review Board (IRB) at Mansoura Faculty of Medicine, Mansoura, Egypt, with IRB code number (M15.9.45) and clinical trial registration online at Pan African clinical trial registry (code number PACTR201611001878318).

This prospective randomized study was conducted on 40 patients. The sample size was calculated using G’Power 3.1 program based on effect size 0.8 to achieve a power of 80%. Patients were divided according to the way of injection into two equal groups (20 patients each):

1. Infraneural transforaminal ESI (IN group)
2. Interlaminar parasagittal ESI (IL group).

A written consent was taken from all patients. The randomization was performed via sealed opaque envelopes. All procedures were performed by one investigator during the period between 1/2016 and 10/2017.

This study included patients with unilateral radicular pain chosen according to American Society of Anesthesiologists (ASA) physical status grade I and II, who had a single or multiple levels lumbar disc prolapse with unilateral radiculopathy over a single dermatome with a minimal duration of 4 weeks, and pain does not improve markedly by either medical treatment or physiotherapy.

Patients with backache without leg radiation or with focal motor neurological deficit were excluded from this study. Also, previous spine surgery, patients with S1 radiculopathy, lumbar ESI in the past month, a systemic steroid used recently within 4 weeks before the procedure, allergy to any medication used, addiction to opioids, pregnancy, and patients with any other neurological deficit were excluded from the study.

All patients were subjected to clinical evaluation including history, clinical examination, and lumbosacral spine magnetic resonance imaging (MRI). The degree of pain was assessed using the visual analog scale (VAS) score. Patients were evaluated for effective pain relief (defined as ≥40% reduction of pain perception by 0–10 VAS postprocedure).

Functional assessment is done using Modified Oswestry Disability Questionnaire (MODQ), which is formed of 10 sections, including pain intensity, personal care, lifting, walking, standing, etc. This questionnaire has been designed to give us information about how back or leg pain is affecting the ability to manage in everyday life, and the higher the
score, the worse the situation. Both VAS and MODQ were evaluated at 1 day then at 1, 3, and 6 months after the procedure. We used nerve stretch test as an objective method for improvement after injection. The femoral nerve stretch test is used for upper lumbar radiculopathy from L2 to L4 where the patient lies prone, whereas a hand is put on the pelvis to prevent movement and the other hand flexes the knee for 4 s. We compared the degree of pain before and after injection using VAS to evaluate the pain improvement after the procedure on the first day then at 1, 3, and 6 months after the procedure. For lower lumbar radiculopathy at L4-S1, we used sciatric stretch test (straight leg raising test) where pain below the knee is produced with raising the leg on the affected site up to a certain degree. This was performed before the procedure and after it.

The intervertebral level affected and right versus left sides of radiating pain was determined. An intravenous (IV) cannula was inserted with initiation of ringer’s lactate at 10 ml/kg to guard against hypotension and emergency medications such as atropine and ephedrine were prepared. All patients were monitored throughout the procedure by ECG, noninvasive blood pressure, and pulse oximetry throughout the procedure and during the postprocedure period for 1 hour. Mild sedation was carried out with 0.03 mg/kg of midazolam intravenously. Patients were placed in a prone position with a pillow under their abdomen (between the iliac crests) to decrease the lumbar lordosis, despite this sometimes may be uncomfortable for patients with a large belly. The procedures were performed under fluoroscopy guidance. The affected nerve root was chosen according to a bond between clinical examination and radiological findings. After fluoroscopic detection of the desired intervertebral level, the site of injection was identified and the skin was anesthetized with local infiltration of 3 ml of lidocaine 1%.

Parasagittal interlaminar approach

The fluoroscopy is centered and the targeted vertebra was squared with the appropriate cranio-caudal tilting of the C-arm. Under complete aseptic precautions an 18G 3.5-inch Tuohy needle was inserted at the midpoint of the interlaminar space with a slight lateral direction toward the paramedian epidural area near the most affected nerve root. This is achieved with a slight oblique tilt of the fluoroscopy toward the affected site. It was further advanced gradually in the lateral view and guided into the epidural space using loss of resistance to saline. This is followed by injection of 2 ml (80 mg) of methyl prednisolone (depomedrol), plus 4 ml of bupivacaine 0.125%, plus 9 ml of normal saline, 0.9 percent in a total volume of 15 ml after confirmation of epidural space using 3 ml of nonionic contrast iodine dye (Ultravist 300) before the procedure on the first day then at 1, 3, and 6 months after the procedure.

Infraneural transforaminal approach

Similarly, for the infraneural (IN) transforaminal approach the targeted nerve root was determined and the fluoroscopy was directed in the antero-posterior view before obtaining the trajectory view. A caudal or cephalic tilt was used to line up both the superior endplate (SEP) and the inferior endplate of the adjacent lumbar vertebrae (preferentially line up the SEP interior to the target). The C-arm then obliqued approximately 10–30° toward the affected side. The target point is the junction of the superior articular process and the SEP of the inferior vertebral body. Then a (Quincke 22G) 3.5-inch spinal needle with a 10° bend tip directed to the target in a tunnel vision where the tip and the hub of the needle appear like a dot. The needle is placed as low as possible in the lower third of the foramen. After negative aspiration, 1 ml of nonionic dye iopromide 300 (Ultravist 300) was injected to assess the contrast spreading in the epidural space and to exclude intravascular injection using real-time fluoroscopy, then another 1 ml of contrast is injected for delineation of the nerve root with a filling of the epidural space medially is confirmed [Figure 4]. After confirmation of the needle position, an injection of 2 ml (80 mg) of methyl prednisolone plus 3 ml of bupivacaine 0.12% in a total volume of 5 ml was performed.

The incidence of intravascular injection and possible complications were evaluated with both techniques, such as fever, headache, or neurological injury for a period of 1 week after the procedure where the patient is instructed to report any fever or headache after the procedure and to take a course of antibiotic for 3 days.

Data analyses were performed using SPSS statistical package version 20.0 (SPSS, Inc., Chicago, IL, USA). The data were examined for normality of distribution using Kolmogorov–Smirnov test. The parametric data reported as mean and standard deviation, whereas the nonparametric data reported as median and the range. The categorical data were summarized as percentages. The unpaired Student’s t-test was used for comparisons of parametric variable, Mann–Whitney U-test for nonparametric, and Chi-square test for categorical variables. The statistical significance level was set at $P < 0.05$.

Results

This study included 48 patients, eight were excluded [Figure 1]. There was no significant difference between the demographic data of both groups [Table 1]. The median duration of disease was not significantly different between both groups [Table 1].
The VAS and MODQ scores were significantly lower in both groups in comparison with the basal values [Figures 2 and 3]. Significantly, there was also lower VAS in the infraneural group in comparison to the parasagittal (IL) group at day 1, 1 month, up to 6 months after. Also, the MODQ score was lower in the infraneural than the parasagittal (IL) groups after injection from the first day till 6 months after injection [Figure 3].

As regards the side effects, hypotension was higher in the parasagittal (IL) group (10.0%) compared to the infraneural (IN) group [Table 2].

**Table 1: Demographic data of studied groups**

|                      | Infraneural group (IN) | Parasagittal group (IL) | P    |
|----------------------|------------------------|-------------------------|------|
| Age (years)          | 55.2±8.82              | 49.4±11.37              | 0.07 |
| Complaints duration (months) | 10 (4-12)              | 12 (4-40)               | 0.07 |
| Affected discs in (MRI) |                        |                         |      |
| L2-3                 | 5%                     | 10%                     | 0.14 |
| L3-4                 | 15%                    | 20%                     |      |
| L4-5                 | 50%                    | 45%                     |      |
| L5-S1                | 30%                    | 25%                     |      |

Values in mean±SD, in median (min-max), or number (percent); n=20

Discussion

The present study aimed to compare the efficacy of infraneural (IN) transforaminal versus parasagittal interlaminar ESI (ILESI) using a single injection of local anesthetics and steroids regarding effective pain relief and functional improvement in patients with unilateral radicular pain secondary to disc prolapse over 6 months period.

Only one prospective study,[18] and two retrospective studies,[20,21] found no difference between transforaminal ESI (TFESI) and parasagittal ILESI, regarding both short- and long-term outcomes. These studies compared the supraneural approach, which is a little bit different from our technique of infraneural (IN) approach. Up to our knowledge, this is the first randomized controlled trial comparing the
Our study revealed that the infraneural (IN) approach for TFESI was more favorable regarding the faster onset of pain relief, better functional improvement with longlasting effects compared with parasagittal ILESI. This was based on VAS score and MODQ score before injection and up to 6 months after injection.

These results support our hypothesis that infraneural (IN) approach provided a more precise and accurate delivery route with the delivery of a higher dose of steroids at the target site than the parasagittal (IL) technique. The injectate primarily becomes distributed at the disc level in the epidural space which allow rapid onset of action and effective short-term pain relief with a better long-term pain and functional improvement compared with the parasagittal approach. This is confirmed by performing epidurography of such injections, which showed that this approach covers both the disc responsible for nerve irritation and the affected segmental nerve.[22]

Lumbar radicular pain is thought to result from mechanical compression on the nerve root with the liberation of inflammatory materials at the affected intervertebral disc.[23]

Causes of nerve root irritation includes leakage of irritating substances such as phospholipase A2 from the intervertebral disc, mechanical compression, vascular compression, and a combination of these factors.[24]

Epidural administration of local anesthetics provides a sympathetic blockade with vasodilation, hence increasing blood flow to the neural tissues.[25] Moreover, local anesthetic agents inhibit the release of neurotransmitters involved in pain pathways with inhibition of neuronal sensitization also.[26] Administration of epidural corticosteroids reduces the inflammatory edema around the affected nerve root, with inhibition of sensitization of the dorsal horn neurons, and suppression of impulse transmission at the nociceptive C fibers.[27]

Yang et al.[28] supported the idea that in TFESI, by using infraneural approach, the injectate can be placed closer to the site of neural impingement and allow the delivery of medicine more directly to reduce inflammation and relieve pain. Moreover, Glaser and Falco[29] proved that an infraneural (IN) epidural steroid has more safety and better delivery of injectate to the ventral epidural space than the supraneural epidural steroid approach.

In agreement with Lutz et al.[30], patients with lumbar radiculopathy due to herniated disc who responded well to TFESIs showed that the delivery of medications into the anterior epidural space is the reason for good clinical effect. Yang et al.[28] concluded that infraneural (IN) was more superior in short-term effect with the alleviation of lumbar radiculopathy, which is attributed to disc prolapsed than did supraneural TFESI. Also, Ridley et al.[31] reported that the therapeutic benefits of single TFESI disappeared within 6 months of treatment.

Our hypothesis contradicts Candido et al., who evaluated contrast flow pattern with the parasagittal (IL) interlaminar approach and transforaminal approach and showed that there is 100% ventral epidural spread with parasagittal interlaminar approach versus 75% ventral spread with the transforaminal approach. Actually, Candido et al. were implementing the supraneural transforaminal technique.
which is not the same as our retrodiscal technique for transforaminal epidural. Candido et al. showed a similar pain relief with equal functional changes when compared to parasagittal TFESI.\(^\text{[18]}\) Also, Ghai et al.\(^\text{[32]}\) reported that ventral epidural contrast spread in the parasagittal interlaminar epidural approach was around 90%. This contradicts Schaefe et al.,\(^\text{[28]}\) who found no significant difference in pain scores postprocedure between TFESI and ILESI. However, they reported the superiority of TFESI for long-term pain relief during a follow-up of 12 months. This conclusion is uncertain owing to the repeated and uncontrolled use of additional epidural steroids or the surgical interventions during this 12 months period.

In our study the parasagittal (IL) interlaminar approach showed a long-term improvement in pain score, which may be attributed to the delivery of medications in the ventral epidural space at the targeted nerve root and disc pathology. This is in agreement with Manchikanti et al.,\(^\text{[33]}\) who evaluated the efficacy of lumbar interlaminar local anesthetics with or without steroids for managing chronic pain attributed to either disc prolapse or radiculopathy.

Manchikanti et al. noted a significant pain improvement (>50%) in 74% of patients treated with local anesthetics and 86% of patients treated with local anesthetics and steroids up to 12 months period. On the contrary, another study\(^\text{[34]}\) showed that midline approach for ILESI was effective for short-term but it did not reduce the long-term relief or the need for surgery. The failure of long-term success with ILESI can be attributed to the lack of delivery steroid into the ventral epidural space at the interface of the inflamed nerve root and disk problem.\(^\text{[34]}\)

In the present study, we did not observe any serious complication from either infraneural (IN) approach or parasagittal (IL) approach apart from one case in infraneural (IN) group showed intraoperative spinal neural contact by needle due to marked difficulty in the needle placement, which may be attributed to severe foraminal stenosis, the patient complained of transient paresthesia at the corresponding dermatome, which has been resolved completely after 3 days. Also, another patient in the parasagittal group had a transient headache, which was of mild intensity and resolved 1 week after the procedure with NSAID in the form of paracetamol 500 mg tablets/6 h standard. Hypotension occurred in three patients after the procedure and improved well by 10 mg of ephedrine and normal saline bolus intravenously 5 ml/kg over 10 min.

The supraneural approach for transforaminal injection is associated with more devastating complications, such as intravascular steroid injection, arterial vasospasm after direct needle injury, and spinal cord ischemia owing to embolism.\(^\text{[29]}\) The infraneural (IN) approach may have a greater margin of safety.\(^\text{[22]}\) This agreed with Windsor et al., who suggested that placement of the transforaminal needle in the inferior aspect of the foramen can reduce the risk of vascular injury.\(^\text{[35]}\) Also, Park et al.\(^\text{[36]}\) showed a higher incidence of neural contact with the supraneural approach than neural contact with the Kambin’s triangle approach because the needle was placed in the inferior–posterior location to reduce neural penetration. These findings support the idea that the infraneural approach may be considered an alternative for the conventional supraneural approach for transforaminal epidural injection as it shows greater efficacy and greater safety margin.

Our study had several limitations. First, this study did not evaluate if other factors such as patient’s mood, general health, or smoking status might influence the therapeutic effectiveness and are correlated with outcomes. Second, the follow-up and assessment were for only 6 months and is better if follow-up is prolonged up to 1 year for assessing long-term effectiveness. Also, detailed information comparing medication intake and physical therapy regimens after ESI between the two groups was not completely available. Third, subjects were recruited from only one hospital, and the sample size was relatively small. A multicenter study with higher sample size needed to be more conclusive in demonstrating the efficacy of the infraneural and parasagittal approaches.

**Conclusion**

The infraneural (IN) epidural steroid is more favorable than the parasagittal (IL) interlaminar epidural steroid, owing to its more rapid onset in reduction of pain perception in patients with lumbar disc as well as long-term improvement in physical function than the parasagittal technique with no serious side effects.

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**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Becker A, Held H, Redaelli M, Strauch K, Chenot JF, Leonhardt C, et al. Low back pain in primary care: Costs of care and prediction of future health care utilization. Spine 2010;35:1714-20.
2. Brox JI, Sorensen R, Friis A, Nygaard Ø, Indahl A, Keller A, et al. Randomized clinical trial of lumbar instrumented fusion and cognitive intervention and exercises in patients with chronic low back pain and
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1. Roeloof PD, Deyo RA, Koesc BW, Scholten RJ, van Tulder MW. Non-steroidal anti-inflammatory drugs for low back pain. Cochrane Database Syst Rev 2008;CD000396.

2. Vik A, Zwart J, Hulleberg G, Nygaard O. Eight year outcome after surgery for lumbar disc herniation: A comparison of reoperated and not reoperated patients. Acta Neurochirurgica 2001;143:607-11.

3. Frost H, Lamb SE, Doll HA, Carver PT, Stewart-Brown S. Randomised controlled trial of physiotherapy compared with advice for low back pain. BMJ 2004;329:708-14.

4. Vav VB, Bhat AL, Lutz GE, Cammisa FR. Transforaminal epidural injections in lumbosacral radiculopathy. Spine 2002;27:11-6.

5. DePalma MJ, Bhargava A, Slipman CW. A critical appraisal of the evidence for selective nerve root injection in the treatment of lumbosacral radiculopathy. Arch Phys Med Rehab 2005;86:1477-83.

6. Fairbank JC, Pymsent PB. The Oswestry disability index. Spine 2000;25:2940-53.

7. Hamilton Hall M, Greg McIntosh. Passive straight leg raise test: Definition, interpretation, limitations and utilization. J Curr Clin Care Vol 2014;4:23-30.

8.发展历程。Spine 2003;28:1913-21.

9. Smith CC, Booker T, Schaufele MK, Weiss P. Interlaminar versus transforaminal epidural steroid injections for the treatment of symptomatic lumbar intervertebral disc herniations. Pain Physician 2006;9:361-6.

10. Smith CC, Booker T, Schaufele MK, Weiss P. Interlaminar versus transforaminal epidural steroid injections for the treatment of symptomatic lumbar spinal stenosis. Pain Meds 2010;11:1511-5.

11. JCR: J Clin Rheumatol 2005;11:11-5.

12. Thomas E, Cyteval C, Abiad L, Picot M, Taourel P, Blottman F. Efficacy of transforaminal versus interspinous corticosteroid injection in discal radiculalgia—a prospective, randomised, double-blind study. Clin Rheumatol 2003;22:299-304.

13. Fukusaki M, Kobayashi I, Haru T, Sumikawa K. Symptoms of spinal stenosis do not improve after epidural steroid injection. Clin J Pain 1998;14:148-51.

14. Katz WA, Rothenberg R. Section 3: The nature of pain: Pathophysiology. JCR: J Clin Rheumatol 2005;11:11-5.

15. Johansson A, Hao J, Sjölund B. Local corticosteroid application blocks transmission in normal nociceptive C-fibres. Acta Anaesthesiol Scand 1990;34:335-8.

16. Yang S-C, Fu T-S, Lai L-P, Niu C-C, Chen L-H, Chen W-J. Transforaminal epidural steroid injection for discectomy candidates: An outcome study with a minimum of two-year follow-up. Chang Gung Med J 2006;29:93-9.

17. Glaser SE, Falco F. Paraplegia following a thoracolumbar transforaminal epidural steroid injection. Pain Physician 2005;8:309-14.

18. Lutz GE, Vad VB, Wisneski RJ. Fluoroscopic transforaminal lumbar epidural steroids: An outcome study. Arch Phys Med Rehab 1998;79:1362-6.

19. Ridley M, KINGSLEY GH, Gibson T, Grahame R. Outpatient lumbar epidural corticosteroid injection in the management of sciatica. Rheumatology 1988;27:295-9.

20. Babita Ghai M, Dipika Bansal D, Vonan P, Kay M, Kaivalya Sadashiv Vadaje M. Transforaminal versus parasagittal interlaminar epidural steroid injection in low back pain with radicular pain: A randomized, double-blind, active-control trial. Pain Physician 2014;17:277-90.

21. Manchikanti L, Singh V, Falco F, Cash KA, Pampati V. Evaluation of the effectiveness of lumbar interlaminar epidural injections in managing chronic pain of lumbar disc herniation or radiculitis: A randomized, double-blind, controlled trial. Pain Physician 2010;13:343-55.

22. Ackerman III WE, Ahmad M. The efficacy of lumbar epidural steroid injections in patients with lumbar disc herniations. Anesth Analg 2007;104:1217-22.

23. Windsor RE, Storm S, Sugar R. Prevention and management of complications resulting from common spinal injections. Pain Physician 2003;6:473-84.

24. Park KD, Lee J, Lee H, Park Y. Kambin triangle versus the supraneural approach for the treatment of lumbar radicular pain. Am J Phys Med Rehab 2012;91:1039-50.