**Randomized Trial**

**Anatomical Flow Pattern of Contrast in Lumbar Epidural Space: A Human Study with a Midline vs. Parasagittal Interlaminar Approach under Fluoroscopy**

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**Background:** Epidural injections for managing chronic back pain are one of the most commonly performed interventions; however, controversy continues regarding the most effective method of epidural injections. A ventral distribution of epidural injected drug plays a significant role in its effectiveness.

**Objective:** To determine the distribution of a drug in the epidural space after parasagittal and midline epidural injection.

**Setting:** Academic hospital.

**Study Design:** In randomized double-blind clinical trial, patients with a diagnosis of low back pain (LBP) and unilateral lumbosacral radicular pains were randomized to receive drug through either parasagittal or midline approach.

**Methods:** Patients were assessed for anterior epidural spread of contrast under fluoroscopy in anteroposterior and lateral views. After epidural space confirmation, triamcinolone (80 mg) plus bupivacain was injected and patients were followed up for 2 weeks.

**Results:** Fifty-six patients enrolled in the study. Successful infiltration of the drug into the ventral epidural space was successfully achieved in 75% of cases in the parasagittal group but in only 25% of the cases in using a midline approach. Effective pain relief (numeric rating scale [NRS] < 3) was observed in 76.5% of patients in the parasagittal group and 24.5% of patients in the midline group (P = 0.001) at 2 weeks. Number of patients with improved disability (measured by Oswestry Disability Index [ODI] < 20%) was significantly higher in the parasagittal group (78%) compared to the midline group (26%) at 2 weeks (P = 0.002).

**Limitations:** The results of the current study should be interpreted in relation to the study design and future studies should include larger patient numbers and longer follow-up time. However, the results are consistent with previous studies.

**Conclusion:** Parasagittal epidural injection showed higher infiltration of the drug to the ventral epidural space compared to the midline approach. The higher infiltration of the ventral epidural space provides better improvement of clinical disability and pain in the parasagittal group.

**Key words:** Epidural, midline, parasagittal, ventral distribution, disc herniation

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Intervertebral disc herniation is a common cause of low back pain (LBP). Epidural steroid injection (ESI) is a minimally invasive intervention commonly used to manage lumbosacral radicular pain (1,2). Epidural injection can be delivered through transformaminal (TF), interlaminar midline, paramedian, parasagittal, or caudal approaches (3). However, there is lack of evidence to determine the most effective method of epidural injections. The interlaminar entry can be directed more closely to the assumed site of pathology, requiring less volume than the caudal route (4). The TF approach is target-specific and requires the smallest volume to reach the primary site of pathology; specifically, the anterior-lateral epidural space as well as the dorsal root ganglion. The TF approach is considered more efficacious than the interlaminar approach probably due to better ventral epidural spread (5). The concerns regarding the safety of the TF approach lead to the search for a technically better route with lesser complications.

The efficacy of midline epidurals to deliver drugs into the ventral epidural space is debated. Patients with radicular LBP vary tremendously in their response to interlaminar midline ESI, and its effectiveness has therefore been called into question. The majority of evidence suggests that ESIs offer back pain relief only in part due to the lack of exact distribution of drugs to the ventral epidural space where the pathology exist (6). The parasagittal interlaminar route could have good ventral epidural spread with fewer complications than TF (7). However, there is a paucity of literature showing the effectiveness of the parasagittal with midline approach.

**Objectives**

To determine the distribution of drugs in the epidural space after parasagittal and midline epidural injections.

**Methods**

The study was reviewed and approved by the University Review Board and hospital ethics committee. Information about trial was given comprehensively both orally and in written form to the patients. All patients gave their written informed consent prior to their inclusion in the study according to the University Hospital Ethics Board Committee.

In a prospective, randomized, double-blind, clinical trial, patients admitted to the pain clinic, aged 18 to 65 years, with a diagnosis of LBP and unilateral lumbar or sacral radicular pain, with a minimum of 3 months duration not responding to medications and physical therapies were enrolled.

The diagnostic criteria for lumbosacral radicular pain were discussed previously (8). 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 women, or those having an ESI within 30 days of trial were also excluded.

**Randomization**

Patients were randomized to receive ESI through either the parasagittal or midline approach. Randomization was performed by computer generated accidental numbers. Random numbers were kept in opaque sealed envelopes and opened by an independent pain physician at the time of injection. Study cases were kept in between clinical non study cases during the procedure as well as for follow-up to enhance the blinding and allocation concealment.

**ESI Procedure**

An 18-gauge, 3.5 inch, Tuohy needle was introduced at the level of disc pathology and advanced in a posterior to anterior direction vertical to the body surface. After determination of the most lateral place for needle entrance in a fluoroscopic antero-posterior (AP) view, the needle was introduced into the epidural space of the affected side, using the loss-of-resistance technique and this parasagittal orientation of the needle was maintained throughout the procedure. Bevel direction was positioned toward lateral. For the midline approach, the needle was introduced from the midline interspinous space with the same method.

Once the needle was in position, and after negative aspiration for cerebrospinal fluid and blood, 1 mL contrast dye (OMNIPAQUE ™, GE Healthcare, UK) was injected to confirm the epidural space distribution in the AP view. This was followed by further injection of 2 mL of contrast under fluoroscopy to confirm the spread of the contrast as well as to verify that no contrast medium attained the intra vascular, subarachnoid, sub-
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dural, or intra-discal spread. Lateral images were taken to evaluate the ventral epidural space. Ventral spread was defined as present if the contrast travelled along the posterior longitudinal ligament or adjacent to the posterior aspect of the contiguous vertebral body at the level of needle insertion. Perineural spread and segmental spread was also noted on AP view. After epidural space confirmation, 2 ml of triamcinolone (1 mL = 40mg) plus bupivacaine (2 mL of 0.5%) and 6 mL sterile normal saline were injected. All the patients were monitored for at least 30 minutes after the procedure.

Data Recording

Fifty-six patients were randomized to receive fluoroscopically guided epidural injection either through the parasagittal or midline approach. The primary outcome measured was presence of ventral spread of contrast dye.

Patients were evaluated for effective pain relief (numeric rating scale (NRS) < 3) by 0 – 10 NRS (9) and functional improvement by Oswestry Disability Index (10) (ODI < 20%) at 2 weeks.

Results

Fifty-six patients with radicular LBP were enrolled in the study. They were randomly injected with parasagittal or midline ESIs. Demographic characteristics are listed in Table 1. There were no significant differences in age, gender, BMI, duration of pain, NRS, and ODI prior to the procedure between the 2 groups (P > 0.05).

Anatomical Distribution of Drug after Epidural Injection

Ventral epidural acquisition and distribution of the drug after epidural injection was compared in 2 groups of study. In the parasagittal epidural injection group, successful infiltration of the drug into the ventral epidural space was achieved in 75% of cases; while in midline approach group, successful ventral distribution was achieved in only 25% of cases. Successful ventral spread was significantly higher with the parasagittal approach (75%) compared to the midline approach (25%) (P = 0.001, chi-square test) (Fig. 1).

Effective Pain Relief

Effective pain relief (NRS < 3) was observed in 76.5% (95% CI: 57 – 89.5%) of patients in the parasagittal group and 24.5% (95% CI: 12.4 – 49.4%) of patients in the midline group (P = 0.001) at 2 weeks (Fig. 2). Mean NRS pain score was also compared between the 2 groups. The mean NRS was not significantly different in the 2 groups prior to epidural injection. However, the mean NRS score was significantly lower in the parasagittal group compared to the midline group at 2 weeks (P = 0.0014) (Fig. 2).

Functional Improvement during Follow-up.

The number of patients with improved disability (measured by ODI < 20%) was significantly higher in the parasagittal group (78% of cases) compared to the midline group (26% of cases) at 2 weeks (P = 0.002) (Fig. 3). Mean ODI score was also compared between the 2 groups. The mean ODI was significantly lower in the parasagittal group compared to the midline group at 2 weeks (P = 0.0033) (Fig. 3).

The schematic shows the fluid (drug) following the path of least resistance toward the ventral epidural space when the epidural injection is performed with a parasagittal approach; while with a midline approach the fluid accumulates in the posterior epidural space moving the thecal sac forward (Fig. 4).

Discussion

ESIs have been used to treat radicular pain from herniated discs, spinal stenosis, and disc-related spinal radiculopathy. However, the evidence for ESIs is highly variable, rated from indeterminate to strong in various publications due to many factors, mainly its anatomical

<table>
<thead>
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<th>Table 1. Demographic characteristics of the patients.</th>
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<tr>
<td><strong>Parasagittal</strong> (n = 28)</td>
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<tr>
<td>Age</td>
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<tr>
<td>Gender (Male/Female)</td>
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<td>Pre-procedure NRS</td>
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BMI: body mass index; NRS: numeric rating scale; ODI: Oswestry Disability Index
Fig. 1. Percent of patients with successful ventral infiltration of drug in the 2 groups after parasagittal and midline epidural steroid injection. Lateral fluoroscopy view of ventral contrast dye flow after parasagittal epidural injection; contrast ventral spread appears like a line in ventral space (right figure).

Fig. 2. Comparison of the proportion of patients achieving effective pain relief (NRS < 3) at 2 weeks after parasagittal or midline epidural injection (left figure). Mean pain score (NRS) during follow-up time between the 2 groups of parasagittal and midline epidural injection (right figure).
spread. In this study we have embarked on determining the anatomical spread of the drug after epidural injection through a parasagital versus midline approach. Our results showed that the parasagittal approach lead to more successful drug delivery to the ventral epidural space compared to the midline approach. Clinical pain and disability were improved more effectively with parasagittal injections compares to the midline approach.

The underlying mechanism of action of ESIs is still not well understood. It is believed that washout of inflammatory mediators, nociceptive afferent block, interruption of the pain-spasm cycle, and corticosteroid reduced inflammation are the major mechanisms (11). ESI would only be considered effective for radicular pain if it reaches the disc prolapse as the cause of the pain and if the corticosteroid is injected close to the target or the nerve root. Therefore, injections should

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**Fig. 3.** Comparison of the proportion of patients improving disability index (ODI < 20%) at 2 weeks between the 2 groups of parasagittal and midline epidural injection (left figure). Mean ODI score during follow-up time between the 2 groups of parasagittal and midline epidural injection (right figure).

**Fig. 4.** In the parasagittal approach, the drug injected into epidural space follows from high pressure to lower pressure gradient of the ventral epidural space; however, in the midline approach the drug accumulates in the posterior epidural space moving the thecal sac forward.
be fluoroscopically guided and should be aimed at the ventral part of the epidural space, near the spinal nerve root (12). Although the Food and Drug Administration (FDA) issued a letter of warning that injection of corticosteroids into the epidural space of the spine could result in adverse events, the results of a thorough review show the efficacy of epidural steroid injections (13).

The ventral epidural space is closer than the posterior space to the posterior disc margin and nerve roots, which is presumably the site of pathology in lumbar radiculopathy (14). In fact, disc herniation induces an inflammatory process in the vicinity that mostly affects close nerve roots which lies within the ventral and lateral epidural space. It is known that the annulus fibrosus is not only innervated but contains a variety of simple and complex neural structures derived from branches of the sinuvertebral nerves, gray rami communicantes, direct branches of the truncus sympathicus, and lumbar ventral ramus (15) (Fig. 5).

The most direct method to deposit medication into this region is by using a TF approach. Although the TF approach is a well-documented method for one side injections, clinicians had been disinclined to use TF due to continued debate and reports of complications (16,17). One of the replacements to the TF approach is the parasagittal approach.

In our study, parasagittal epidural injection showed a tendency to push the drug toward the ventral epidural space in 75% of our patients; while with the midline approach ventral distribution was achieved in only 25% of the cases. A similar study has depicted results similar to ours in which the ventral epidural spread of the contrast was significantly higher in the Parasagittal Interlaminar (PIL) 89.7% vs 31.7% in the midline interlaminar (MIL) group (18). Although major progress has been made in understanding the anatomy of the epidural space, the exact anatomical distribution of drugs in epidural space is more enigmatic. The succeeding paragraphs discuss the characteristics of anatomical and physical factors and then how these affect the ventral spread of drugs.

In the confined environment of the epidural space, fluid follows a path of least resistance. Injection of drugs through a midline approach cause an increase in the gradient behind the thecal sac moving the thecal sac forward and causing the drug to accumulate in the posterior space. On the other hand, drugs injected through a parasagital approach will follow from a high pressure to lower pressure gradient of the ventral epidural space.

The anatomy of the lumbar epidural space and intervertebral disc is complex. The epidural space has areas characterized by a genuine space composed of adipose tissue, veins, and nerves, together with other areas that show a virtual space where the dural sac rests on the vertebral bodies (19). When a drug is injected into the virtual epidural space it becomes a genuine space and the dural sac is partially compressed. Its diameter is therefore reduced, displacing the cerebrospinal fluid.

The epidural fat also contributes to drug distribution in the epidural space (20). Fat is mainly located in...
the posterior part of the epidural space, in the axial plane stretching towards the intervertebral disc. Epidural fat morphology is like a pyramid and has a blunt posterior apex in contact with the ligamentum flavum, and a blunt anterior base oriented towards the posterior surface of the dural sac, limited laterally to the intervertebral foramina, wrapping around nerve roots within the dural sleeves.

With the midline interlaminar approach, the administered drug will follow a path amid the epidural fat (the real epidural content is fat and Batson’s plexus), and depending on the pressure exerted upon the dura mater, it is possible to separate it from the peristium on the internal surface of the intervertebral lamina. In this way, the virtual space may disappear and transform into a real space. Part of the volume will be dispersed among the lateral epidural fat, and most of the solution will stay in the posterior epidural space. There will be little distribution to the anterior epidural space and into the intervertebral foramen. The epidural fat is a lobular structure, fixed by small vascular pedicles (21). The injected volume is dispersed between fat lobes. When contrast dye is injected next to the root, the contour of the nerve is shown because the dye distributes between fat and the nerve. On occasions only a line of drug can enter into the foraminal canal up to the anterior epidural space. On the other hand, with the parasagittal approach, epidural fat is bypassed and ventral distribution is achieved superiorly.

A meta-analysis shows that TF ESI have been shown to be effective in the treatment of lumbar radiculopathy (22,23). However, TF ESI resulted in better short-term pain improvement and fewer long-term surgical interventions than interlaminar epidural steroid injection (24). The goal of the TF approach is to enter the intervertebral foramen, while avoiding dural puncture, vascular injection, and segmental nerve trauma. However, the complication risks of TF injections must be taken into consideration (25). There have been reports of pneumocephalus during TF (26). The complication of dural puncture is documented in the context of a lumbar TF (27). The incidence of vascular penetration during contrast confirmed fluoroscopically guided TF epidural injections have been reported as 8.9% to 21.3% depending on the level of injection (28). A previous study demonstrates a high incidence of intravascular injections in TF lumbosacral epidural injections (29). Studies have presented a case of quadriparesis and brainstem herniation after selective cervical TF (30). These fluoroscopically guided injections are commonly employed to selectively deliver medication to the epidural space near the exiting spinal nerves.

One of the most important aspects of our study was that parasagital ESI injection had a better clinical outcome than midline injections. Both pain score and disability score improved more significantly in the parasagittal group compared to the midline group. This also could be due to better infiltration of drugs to the ventral epidural space. In a similar study, in the treatment of lumbar spinal stenosis, midline interlaminar epidural injection of glucocorticoids plus lidocaine offered minimal or no short-term benefit as compared with epidural injection of lidocaine alone (31). Other tissues contributing to pain in the lumbar spine such as the posterior longitudinal ligament and ligamentum flavum and dura should also be considered. All are known to have sensory innervation and are suspected to contribute to back pain. The ligamentum flavum provides a significant contribution to LBP in patients who do not respond to TF ESI.

**Conclusion**

In conclusion, parasagittal epidural injection showed a higher infiltration of the drug to the ventral epidural space compared to the midline approach. The higher infiltration of the ventral epidural space could cause more improvement in disability and pain in the parasagittal group. Future studies should be focused on comparing parasagittal and TF approaches.

**References**

