Randomized Controlled Trial

Fluoroscopy-guided Intradiscal Radiopaque Gelified Ethanol Injection Using an Anteroposterior View Compared to an Oblique View: A Randomized Controlled Trial

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Background: This study introduces a new fluoroscopy-guided intradiscal radiopaque gelified ethanol injection technique using the antero-posterior view and compare it to conventional oblique view. Intradiscal procedures, are minimally invasive techniques that aim to reduce pain associated with lumbar disc herniation by modifying the disc material and decreasing pressure on surrounding nerves.

Objectives: This study introduces a new fluoroscopy-guided intradiscal radiopaque gelified ethanol injection technique using an anteroposterior view compared to the conventional oblique view.

Study Design: This is a double blind, randomized trial.

Setting: A tertiary care center.

Methods: Patients with radicular leg pain were randomly assigned to receive a radiopaque gelified ethanol injection via an anteroposterior view or oblique view.. The primary outcomes were procedure time, complication rates, and radiation exposure.

Results: A total of 70 patients were randomized to each group (35 for each group). There were no serious complications in either group. Radiation exposure was significantly lower in the anteroposterior view group (36.92 vs 50.46 µGray/m^2 [µGy/m^2; $P = 0.007$). The procedure time was also significantly lower in the anteroposterior group (171 vs 287 seconds; $P = 0.001$).

Limitations: Limitations of our trial include the relatively small sample size, the single-center nature of the study, and the short follow-up period. We were also limited in only including patients with moderate body habitus, and patients with only L3 or L4 disc herniation, which might restrict the generalizability of the findings.

Conclusion: An anteroposterior view radiopaque gelified ethanol injection is a promising alternative to the conventional oblique view technique for radicular leg pain management. This novel approach offers a safer and more efficient treatment option, reducing radiation exposure and procedure time without compromising clinical outcomes. Its potential to minimize patient discomfort and enhance overall management of radicular leg pain warrants further investigation and widespread adoption.

Key words: Fluoroscopy, Absolute gel, anteroposterior, oblique, radicular, sciatica, intradiscal, injection technique

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Low back pain encompasses 3 distinct sources of pain: axial lumbosacral, radicular, and referred pain. Radicular leg pain travels into an extremity along a dermatomal distribution, secondary to nerve irritation (1).

About 5% to 10% of people with low back pain have sciatica (2), in which the leg pain follows the sciatic nerve (3). Leg pain originating from the lumbar spine is commonly referred to as radicular pain (4).

Treatment is targeted at reducing both symptoms and the patient's recovery time. The first therapeutic approach is usually pharmacologic along with physical therapy (5). Chemonucleolysis is a minimally invasive percutaneous technique (6). Radiopaque gelified ethanol has been introduced into clinical practice (7). It is a viscous solution containing ethyl cellulose and nanoparticles of a contrast agent (tungsten) dissolved in ethyl alcohol. Clinical outcomes seem to be encouraging, with a high reduction of possible collateral effects (8).

Absolute Gel® is a chemonucleolytic agent introduced for the first time in 2021 by Elevate Scientific. Absolute Gel is injected into the nucleus pulposus with a fine spinal needle where it is converted into a flexible, permanent implant after coming in contact with the nucleus pulposus' water content, causing dehydration of the nucleus pulposus. Absolute Gel contains ethanol with cellulose derivatives and nanoparticles of tungsten (the radiopaque component) to form a radiopaque implantable medical device (9).

Absolute Gel is hydrophilic. It attracts fluid from the herniated portion of a disc toward the center of the nucleus pulposus, thereby decompressing the disc and releasing pressure on the nerve. The main action of Absolute Gel is to block nerve receptors within the annulus fibrosus by sealing cracks in it so the nucleus pulposus does not come in contact with the spinal nerve (9). This is the primary cause of pain when the nucleus flows through the weakened interior part of the annulus fibrosus, irritating the nerves within and causing inflammation. Since Absolute Gel penetrates into the damaged area of ruptured discs, it becomes a permanent prosthesis, hence there is no risk of dislocation and leakage (9).

In a number of analyses, the precise technique employed for intradiscal injection has been sparsely reported. In instances where a fluoroscope was deployed to aid in needle guidance, several investigations maintained their utilization of posterolateral access, and in other studies it was extralaminar (10), paravertebral access (11), posterior-oblique (12), or paravertebral-oblique (13) approaches that necessitated engaging an oblique view through implementing a fluoroscopic C-arm, although this detail was not mentioned in the papers.

The distinctive characteristic of our method lies in its utilizing 3 to 4 shots capturing an anteroposterior view, rather than employing an oblique perspective. This alternative approach effectively reduces the patient's exposure to radiation (14).

Methods

This investigation was carried out through a randomized clinical trial approach, targeting individuals afflicted with chronic back pain attributable to lumbar disc herniation. The patients included in our study had endured discomfort for a minimum of 6 months since its initial occurrence. They were referred to our pain clinic from May 2023 through November 2023.

For determining the sample size, we used G* Power software (Heinrich Heine University). As per the Leoni, et al study (15), we considered the effect size as 0.06, (considering the mean radiation exposure) α as 0.05 and β (power) as 0.80. Based on these parameters, we selected a sample size of 70, with each group containing 35 patients.

All study patients gave written consent to participate.

Inclusion criteria were: at least 18 years old, a body mass index between 24 to 30 kg/m^2, a grade I or grade II herniated disc at L3-L4 or L4-L5, spinal canal stenosis of less than 30% as determined by clinical examinations and magnetic resonance imaging findings, chronic back pain for more than 6 months, symptomatic disc herniation, radial foot pain on one or both sides without any axial pain, no degenerative disc disease, had a Disco-Gel® (Gelscom) injection in the previous 6 months,not using opioids, no coagulation disorders, not pregnant, no history of malignancy or psychiatric problems, no spinal deformities or decreased disc height, no prior spine surgeries, no traumatic injuries causing vertebral fractures, and no vertebral infections.

Each patient in our study had a lumbar disc herniation in one or 2 levels and met the criteria set forth above. It is important to note that these patients lacked any history of neurological impairments in order to be eligible for the study. If the patient had a complication, such as an epidural hematoma or disc infection during or after the procedure, or it was not possible to inject the disc while using the fluoroscope, it was reported.

Blood pressure and heart rate were measured and recorded for all patients in the operating room after connecting noninvasive monitoring and a pulse oximeter. All the procedures were performed by a pain physician with more than 15 years of experience in interventional pain procedures.

Patients were randomized to treatment groups using a blocked randomization scheme with block sizes of 4. A nurse anesthetist generated the random allocation sequence and measured the outcomes for patients in this trial.

During the course of their procedure, paients were positioned prone on a surgery bed. After prepping the skin with chlorhexidine gluconate to ensure sterility, a sterilized gown was employed to cover the area at the back of the patient. Before treatment commenced, patients refrained from consuming any food or drink for 6 hours. Additionally, they were administered one mg of midazolam and 50 µg of fentanyl as a means to achieve light sedation. In administering anesthesia, both superficial and deep local anesthesia were provided using a solution containing 1% lidocaine. A careful patient examination took place under the guidance of the Compact Ziehm 8000 C-arm (Ziehm Imaging). Its purpose was to identify and establish both the anatomical contours surrounding the injection site as well as determine an optimal path for introducing the needle.

In the anteroposterior (AP) view technique, the entry point at which the needle penetrates was measured using a ruler in the magnetic resonance images software. In the axial image, a line was drawn from the center of the disc, passing the ateral border of the superior articular process of the inferior vertebrae, to the surface of the skin, then the distance between the entry point and midline was measured with the software (Fig. 1).

In our anteroposterior technique, the desired injection level was determined using an AP view with a C-arm. The procedure took place under local anesthesia, with 1% lidocaine administered to numb the area. An 18G Chiba needle was then inserted into the designated point at a distance of approximately 8 cm-10 cm from midline (in accordance with the magnetic resonance image measurement), with a 45° angle. After skin penetration, the needle was advanced until the tip touched the inferior vertebra's superior articular process. Then the needle was walked off over the superior articular process, through Kambin's triangle. We then advanced the needle until encountering slight resistance, and then penetrated through the disc. We cautiously advanced the needle using stepwise movements until the tip of the needle passed the medial border of the superior articular process in the AP view. The C-arm was then rotated for a true lateral view to assist us in controlling the needle's depth. The needle was then advanced until the tip was centered in the intervertebral disc.

In the oblique technique, in order to ascertain precise accuracy throughout the process, every patient's injection site anatomy, as well as the needle's trajectory path, are determined through guidance provided by C-arm imaging. Once these factors have been identified, we proceeded by aligning the superior end plate and the fluoroscope beam at the targeted level, then utilizing an oblique view. Within this viewpoint, we selected an appropriate point on the skin for needle insertion before introducing an 18G Chiba needle into the target disc. As soon as we reached beyond the medial border of the pedicle in an AP view, confirmation was sought via lateral view analysis. Upon receiving confirmation through this approach and having successfully located our target within the center of the intervertebral disc, we stopped advancing the needle at that particular point of penetration with regards to needle tip placement.

In both techniques, after negative aspiration, Absolute Gel was injected in 0.1 mL incremental doses. A 0.6-0.8 mL dose of gellified ethanol was injected slowly into the nucleus pulposus at room temperature.The

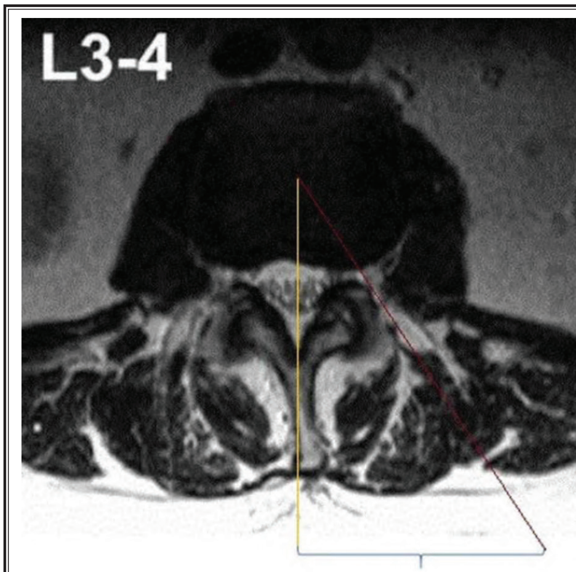

Fig. 1. *Approach to determine needle entry point, the blue bracket shows the entry point distance from the midline.*

antibiotic 10 mg of cefazolin (0.1 mL) was also injected into the disc. After 3 minutes, we removed the needle.

Assuming no unforeseen circumstances have arisen, the patient was released from medical care after 2 hours. In order to alleviate any discomfort, patients are advised to consume the prescribed pain medication and curtail their physical mobility for a 14 days wile accommodating a semi-rigid lumbar support brace. It is essential that the patient notify their physician if they undergo symptoms such as fever accompanied by chills, a sensation of pain and numbness in the lower limbs, persistent headaches and vertigo, or any other unanticipated complications that may manifest.

Dose area product (DAP) meters are utilized to evaluate patient doses by employing an ionization chamber positioned on the collimator of the x-ray tube. The chamber is designed as a sealed, parallel plate type with square plates, ensuring a larger area than the maximum beam size at its mounting position. This sealed design prevents calibration discrepancies due to variations in temperature and pressure. The ionization produced within the chamber is directly proportional to both the dose and the beam's area. Thus it is measuring the product of dose and area with a unit of Gy/cm^2. Different submultiples may be used by different manufacturers; 2 common examples being cGy/cm^2 and µGy/m^2. In the event that complications arise during or after the procedure, the specific type of complication was duly recorded (16).

The procedure time (PT) was carefully measured using a chronometer, beginning when the first fluoroscopic image was taken and ending only when the needle tip accurately reached its intended target point within the nucleus pulposus.

There were no changes to the methods after trial commencement, which means that the trial design and methods were well-defined. The patients and the nurse anesthetist responsible for outcome assessment were blinded to the intervention.

Pertinent details obtained are then meticulously documented and inputted into IBM SPSS Statistics 19.0 (IBM Corporation).

Results

Baseline and demographic characteristics of the entire cohort were analyzed. Seventy patients with LDH were enrolled in our study (35 men and 35 women). Their average age was 58.57 years old, ranging between 38 and 88 years old. Their average body mass indexwas 26.9 kg/m^2 (between 24 and 30), their DAP was 43.69 µGy/m^2 (between 30.1 to 61.33) and their PT was 229 seconds (between 110 seconds and 367 seconds).

In the group which the procedure was done with the AP technique, 35 patients (15 men and 20 women), were enrolled. Their average age was 60.4 years old, ranging between 41 and 79 years old. Their average of body mass index was 27.11 kg/m^2 (between 24 and 30), their DAP was 36.92 µGy/m^2 (between 30.1 to 47.94), and their PT was, 171 seconds (between 110 seconds and 276 seconds).

In the group which the procedure was done with the oblique technique, 35 patients (20 men and 15 women) were enrolled. Their average age was 56.74 years old, ranging between 37 and 88 years old. Their average of patients body mass index was 26.68 Kg/m^2 (between 20 and 30), their DAP was 50.46 µGy/m^2 (between 33.89 to 61.33) and their PT was 287 seconds (between 135 seconds and 367 seconds), respectively (Table 1).

The average DAP and PT in the oblique technique group was significantly greater than the AP technique group which was significantly different ($P < 0.05$).

There were no patients who had root contact, dural puncture, or experienced postprocedure paresthesia. Furthermore, every procedure was performed successfully.

Discussion

In lumbar disc herniation (LDH), Volpentesta, et al (17) reported excellent and good results using RGE in 80.4% of 72 patients, despite complications in 5.45%. Theron, et al (18) also investigate effectiveness of RGE and reported a success rate of 91.4% in a group of 221 patients and a complication rate of 0.5%, while Stagni, et al (19) achieved a therapeutic success in 24 of 32 treated patients (75%) without complications.

Our study was a randomized controlled trial comparing the AP and oblique techniques for radiopaque gelified ethanol injection for LDH. Our results show that the 2 techniques are applicable, however, the oblique technique is associated with a significantly higher DAP and PT length.

The DAP is a measure of the radiation exposure to a patient during a fluoroscopic procedure. The PT is the amount of time that the patient is exposed to fluoroscopy during the procedure. Both of them are associated with an increased risk of radiation exposure.

Interventionalists and their assistants face the highest risk of radiation exposure among all occupational therapy personnel due to their close proximity to

Table 1. *Baseline and demographic characteristics of the entire cohort.*

Characteristics	Entire Cohort	AP Group	Ob Group	*P* Value
Number of patients	70	35	35	
Gender (men/women)	35/35	15/20	20/15	
Age Average (range)	58.57 (38-88)	60.4 (41-79)	56.74 (37-88)	
BMI (kg/m^2) Average (range)	26.9 (24-30)	27.11 (24-30)	26.68 (24-30)	
DAP (μGy/m^2) Average (range)	43.69 (30.1-61.33)	36.92 (30.1-47.94)	50.46 (33.89-61.33)	0.007
PT Average (seconds) (range)	229 (110-367)	171 (110-276)	287 (135-367)	0.001

AP: anteroposterior, Ob: Oblique, BMI: body mass index, DAP: dose area product, PT: procedure time

the exposure area (20). Efforts are being made to raise awareness about radiation protection and the safe utilization of radiation in the operating theater.

Other authors have also emphasized the significant positive correlation between operative time and exposure time (21,22). Ionizing radiation is significant because it has the potential to cause biological harm. The effects of radiation can be categorized as either dose-dependent (nonstochastic) or dose-independent (stochastic) (23). The biological effects of radioactivity are associated withf forming cataracts, changing thyroid function, and developing skin cancers. The radiation exposure to the chest and reproductive organs has been determined to be insignificant. Using a standard lead apron (5 mm thick) has been proven effective in protecting the chest area, shielding approximately 82% of the active bone marrow (24).

When it comes to the radiation exposure experienced by patients, particularly those with long-standing ailments who often undergo recurring medical procedures, it is crucial to recognize that even though each procedure may not entail a substantial dose of radiation individually, the cumulative effect can prove detrimental. Consequently, minimizing this dosage in each procedure emerges as the optimum approach toward preventing harm. Numerous methods exist for reducing such radiation levels; however, one of the most straightforward techniques for minimizing radiation exposure involves reducing the amount of radiation employed during imaging procedures each time.

The oblique technique tends to have a high DAP and PT values, possibly because it is a more technically demanding approach that often requires additional fluoroscopic images. The benefits of the AP technique is a lower procedure time is because fewer images are taken, hence lowering the DAP. Despite these higher values, the oblique technique is a safe and effective treatment for LDH. Neither our AP technique nor the oblique technique were associated with postprocedure complications such as dural puncture, paresthesia, or root contact, so both techniques are safe and applicable. It is also important to minimize the DAP and PT values whenever possible, regardless of which technique is used.

Limitations

All patients in our study were adults with LDH and a body mass index between 24 and 30. This new approach was assessed in some patients with a healthy weight and some who were overweight (based on their BMI), so to ensure that the results of the study would be applicable to a wider range of patients, it would be necessary for new trials to evaluate this. Other limitations are the relatively small sample size, which might restrict the generalizability of the findings, the single-center nature of the study, which could also limit generalization, and the relatively short duration of the follow-up period.

Conclusion

The AP and oblique techniques are both applicable treatments for LDH. However, the oblique technique is associated with a significantly higher DAP and PT values, which are measures of radiation exposure. It is important to minimize radiation exposure whenever possible, regardless of which technique is used. The AP technique is associated with lower radiation exposure, so it may be a better option for patients who are concerned about radiation exposure. Further research is necessary to validate the long-term effectiveness of both techniques and determine the ideal patient population for each approach. Overall, our study provides valuable information on the safety and efficacy of the AP and oblique techniques for radiopaque gelified ethanol injection for lumbar disc herniation.

Author Contributions

M.H.: Writing/manuscript preparation/invest igation

S. H. : Writing/manuscript preparation/investigation
P. D. : Manuscript preparation/investigation
M. E. M. : Manuscript preparation/investigation
S. A. : Writing/manuscript preparation/investigation

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