

Effect of transforaminal hypertonic saline on the treatment of lumbar herniated discs: A prospective, randomized, controlled study

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Abstract

Aim: The aim of the study is to evaluate the effect of adding hypertonic saline to conventional transforaminal epidural steroid injections (TFESIs) in the management of patients with lumbar disc herniation (LDH) with radicular pain.

Material and Methods: The study included 57 patients with L4–L5 LDH treated with TFESI. The patients were divided into two groups: the hypertonic (n = 29) and conventional groups (n = 28). The conventional group was administered with triamcinolone, bupivacaine, and isotonic saline. Subsequently, the hypertonic group was administered with triamcinolone, bupivacaine, and 10% hypertonic saline. The patients were followed up using the numeric rating scale (NRS) and Oswestry disability index (ODI). Substantial and moderate responder ratios were achieved using NRS. Outcome measurements were performed at baseline, one, three, six, and nine months. Complications were recorded in both groups.

Results: TFESI with or without adjuvant hypertonic saline was found to be effective by achieving a significant reduction in NRS and ODI scores during the overall follow-up period. Reduction of NRS scores at six- and nine-month follow-up and ODI scores at nine-month follow-up in the hypertonic group were significantly higher than those in the conventional group. Moreover, substantial response in the hypertonic group was significantly higher than that in the conventional group. Both groups had no complications.

Conclusion: The administration of adjuvant 10% hypertonic saline to transforaminal injections enhances the treatment efficacy by increasing pain reduction and improving the quality of life in the late follow-up period.

Keywords: Lumbar disc herniation; low back pain; radicular pain; transforaminal epidural steroid injection; hypertonic saline.

INTRODUCTION

Lumbar disc herniation (LDH), affecting 1% to 3% of the population, is the most commonly diagnosed degenerative disorder of the lumbar spine and is the primary cause of lumbar spine surgery in adults (1,2). LDH is formed by the displacement of the intervertebral disc material (nucleus pulposus) toward the outer membrane (annulus fibrosus) usually at its posterolateral area (3,4). Typical clinical presentation of LDH includes initial low back pain (LBP), followed by radicular pain called sciatica (5). Symptoms usually improve within four to six weeks in the natural course of LDH (6). However, a small portion of individuals with LDH tend to present chronic symptoms and may require medical interventions, such as injections and surgeries (7).

One of the frequently preferred treatment modalities for relieving chronic symptoms of LDH is epidural steroid injection (ESI) (8,9). ESI is considered to relieve sciatica and lumbago symptoms by decreasing nerve root inflammation and ischemia (8). Transforaminal epidural steroid injection (TFESI), an ESI modality, has been applied in LDH and lumbar stenosis treatment with good to fair results (10–14). Although TFESI is reportedly effective in the early period, this effect tends to be diminished in the mid- and long-term period (10,15). Epidural adhesions considered responsible for causing the short duration of this effect by preventing the diffusion of medicines in the surrounding tissue of the nerve root, which can occur in patients with LDH without a history of surgery (16–18).

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Adhesiolysis is performed to resolve epidural adhesions, and hypertonic saline is a commonly used adjuvant for adhesiolysis, but the efficacy of adjuvant hypertonic saline is still controversial (19–21). A prospective, randomized, controlled study showed that the use of hypertonic saline in spinal stenosis obtained better pain relief in the early period, but results were similar in the mid- and long-term periods (22). Besides, a retrospective analysis showed that adjuvant 10% hypertonic saline in TFESI is more superior and provides durable pain relief in patients with LDH (23). However, no prospective study has been published that analyze the effect of adjuvant hypertonic saline in patients with LDH. In this randomized controlled study, we aimed to evaluate the effect of adding hypertonic saline to TFESI on the symptomatic LDH treatment.

MATERIAL and METHODS

The Institutional Review Board of the Erzincan University (date: 12.12.2017 number: 17-17/05) approved this study, and informed consent was obtained from all participants. Between December 2017 and May 2018, patients with unilateral radiculopathy were screened for compatibility.

Inclusion criteria were age ≥ 20 years, dominant unilateral radicular pain with less LBP, chronic symptoms resistant to conservative management involving physiotherapy and analgesic medication, symptom duration ≥ 8 weeks, protruding or bulging disc herniation compatible with symptoms at the L4–L5 level confirmed with magnetic resonance imaging (MRI). MRI findings were assessed by an experienced neuroradiologist unaware of the study and confirmed the cases of LDHs.

Exclusion criteria were bilateral radiculopathy, history of spinal surgery and steroid injections, patients with motor weakness or neurologic deficits, extruded or sequestered disc herniations, intolerable pain > 9 on the numerical rating scale (NRS), pain < 4 on the NRS, allergies to steroids or contrasts, coagulopathy, systemic or injection site infections, unstable psychiatric or medical state, radiologically confirmed lumbar spinal stenosis and spondylolisthesis.

This study comprised two groups: the hypertonic ($n = 29$) and conventional groups ($n = 28$). The patients who agreed to participate in the study were assigned to the groups based on their order of admission. The patients were blinded to the medication used for treatment until the study was finalized.

Transforaminal epidural injections were administered under fluoroscopic guidance using a single fluoroscopy C-arm system by a single board-certified neurosurgeon. Each patient was placed in a prone position with two pillows to the lateral of the abdomen. The intervertebral foramen was identified based on the anatomic landmarks, and a blunt needle was gently advanced to the upper quadrant of the foramen located below the pedicle of the superior vertebrae. After accurate needle positioning

was validated via anteroposterior and lateral views, to be certain of that the needle tip was not located in vascular or neural structures, an aspiration was done for the presence of either blood or cerebrospinal fluid (CSF). Subsequently, contrast dye was injected via real-time fluoroscopy to avoid intravascular or intrathecal injection and to validate proper flow to the epidural space. All patients were administered 2 ml of 0.5% bupivacaine (Marcaine, Astra Zanecca, Istanbul, Turkey) and 40 mg triamcinolone acetonide (Kenacort-A, Bristol Mayers, New York, USA) mixture. Subsequently, 1 ml of 10% sodium chloride (hypertonic saline) and 1 ml of 0.9% sodium chloride (isotonic saline) were administered to the hypertonic and conventional groups, respectively.

All data were collected by an independent clinician who was blinded to the study. Baseline characteristic data included sex, age, body mass index, medical history, total pain duration, analgesic medication, and target side. Primary outcomes were measured by pain scores using NRS (0 = no pain, 10 = intolerable pain). Secondary outcomes were measured by functional disability using the Oswestry disability index (ODI) (range 0–100, 0 = no disability, 100 = bedbound state) and responder rate. Responder rate was determined in terms of the ratio of patients presenting a substantial response ($\geq 50\%$ or ≥ 4 -point decrease in NRS) or moderate response ($\geq 30\%$ or ≥ 2 -point decrease in NRS). NRS, ODI, and responder rate were measured and compared at baseline, first, third, sixth, and ninth months. Adverse events after TFESI (muscle weakness, pain, and paresthesia) were also compared.

Statistical analysis was performed using SPSS 19.0 (SPSS Inc., Chicago, IL, USA). The mean values and standard deviations of numerical variables were summarized. The chi-squared test or Fisher exact test was used to examine differences of categorical variables. Independent sample t-test was used to compare differences of continuous numerical variables between the groups. Furthermore, $P < 0.05$ was accepted as statistically significant for all analyses.

RESULTS

Both groups completed nine months of follow-up. The baseline characteristics were comparable between the groups (Table 1). Members of both groups were predominantly young adults (mean age in hypertonic and conventional groups: 34.6 and 35.4, respectively), and the female/male ratios were 1.07 and 1.15 in hypertonic and conventional groups, respectively. No difference was observed in the medical history, which reported smoking, hypertension, and diabetes mellitus, between groups. Pain duration before the procedure and medication were comparable in both groups. Disc pathology was localized at the L4–L5 level in all patients, and no significant difference was found in the side distribution (left vs. right) between groups. Besides, NRS scores for pain and ODI scores for quality of life were comparable between the groups.

Table 1. Baseline characteristics of study groups

Variables	Hypertonic Group (n = 29)	Conventional Group (n = 28)	p values
Age (years)	34.6 ± 9.9	35.4 ± 10.4	0.446
Gender (F / M)	15 / 14	15 / 13	0.888
Smoking	8 (27.6%)	6 (21.4%)	0.589
Hypertension	3 (10.3%)	4 (14.9%)	0.650
Diabetes Mellitus	3 (10.3%)	4 (14.9%)	0.650
Body-mass index	24.5 ± 2.4	25.5 ± 2.6	0.192
Pain interval (month)	8.8 ± 5.8	8.1 ± 4.5	0.557
Medication			
Opioid	4 (13.8%)	6 (21.4%)	0.448
NSAID	24 (82.8%)	25 (89.3%)	0.478
Target Level			
L4-L5	29 (100%)	28 (100%)	1.0
Side			
R / L	16 / 13	18 / 10	0.483
Preoperative Status			
NRS	6.93 ± 1.08	6.78 ± 1.16	0.630
ODI	47.7 ± 8.5	46.3 ± 7.9	0.517

F: female, M: male, NSAID: non-steroid anti-inflammatory drug, L:lumbar, R: right, L: left, NRS: numerical rating scale, ODI, Oswestry disability index

Table 2. Pain and disability scores during follow up and differences from baseline for hypertonic and conventional groups

Time	Actual scores		Difference from baseline		p-value compared to baseline	
	Hypertonic Group (n=29)	Conventional Group (n=28)	Hypertonic Group (n=29)	Conventional Group (n=28)	Hypertonic Group (n=29)	Conventional Group (n=28)
NRS						
Baseline	6.93 ± 1.08	6.78 ± 1.16	0	0		
1 month	3.10 ± 1.09	3.32 ± 0.94	3.83 ± 1.57	3.46 ± 1.75	< 0.001	< 0.001
3 months	3.40 ± 1.21	3.85 ± 0.89	3.53 ± 1.27	2.92 ± 1.46	< 0.001	< 0.001
6 months	3.61 ± 0.99	4.28 ± 0.89	3.33 ± 1.42	2.50 ± 1.57	< 0.001	< 0.001
9 months	4.36 ± 1.09	5.03 ± 0.96	2.56 ± 1.67	1.75 ± 1.21	< 0.001	< 0.001
ODI						
Baseline	47.73 ± 8.52	46.39 ± 7.92	0	0		
1 month	25.26 ± 8.67	27.28 ± 7.30	22.46 ± 8.67	19.11 ± 10.32	< 0.001	< 0.001
3 months	28.33 ± 6.75	30.64 ± 6.62	19.40 ± 8.72	15.75 ± 8.79	< 0.001	< 0.001
6 months	31.06 ± 5.68	32.42 ± 6.25	16.66 ± 8.53	13.96 ± 8.45	< 0.001	< 0.001
9 months	35.90 ± 6.91	38.53 ± 7.05	11.83 ± 10.72	7.85 ± 6.04	< 0.001	0.010

NRS: numerical rating scale, ODI: Oswestry disability index

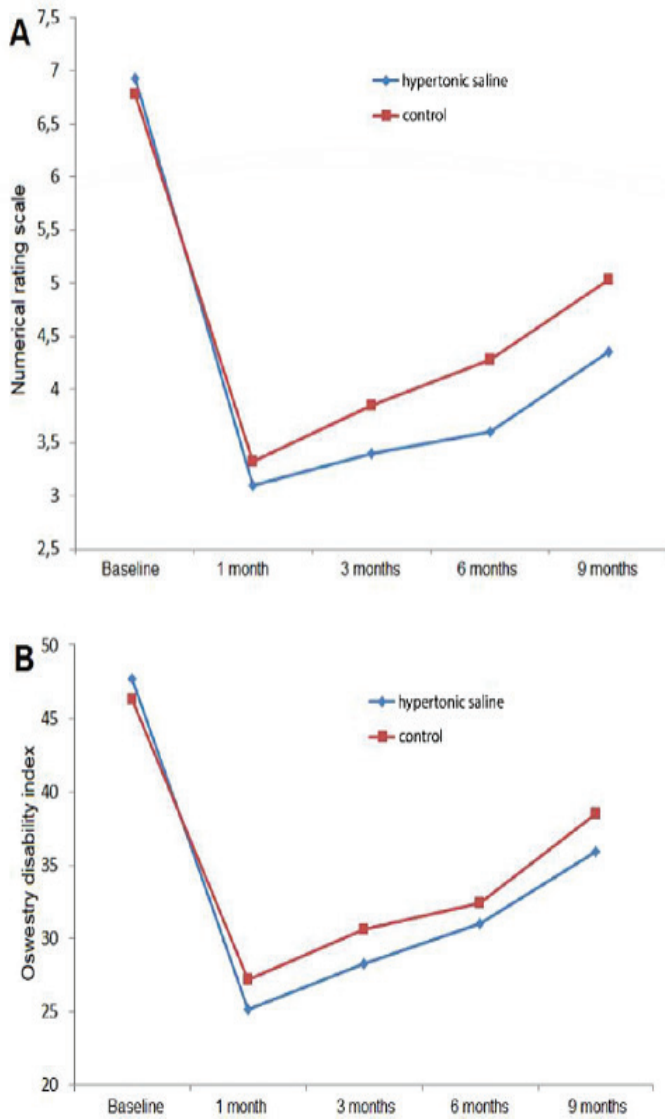


Figure 1. A.Representation of the mean baseline and follow-up values of the numerical rating scale pain score of the study groups. B. Representation of the mean baseline and follow-up values of the Oswestry disability index score of the study groups

The primary outcome of the groups was compared using NRS differences during follow-up (Table 2 and Figure 1). Although the initial NRS scores were higher in the hypertonic group (mean 6.93 vs. 6.78), no statistical difference was found between the groups. In both groups, examinations throughout the study period showed that the pain scores were significantly lower than the baseline pain scores. The NRS pain scores significantly improved in the hypertonic and conventional groups at one, third, six, and nine months ($P < 0.001$). The secondary outcomes were evaluated using ODI scores (Table 2 and Figure 1). The baseline ODI scores of the groups were comparable (mean scores in the hypertonic group: 47.73 and in the conventional group: 46.39). Similar to pain scores, ODI scores were significantly lower in both groups during the follow-up period compared with baseline scores. The ODI scores significantly improved in the hypertonic and conventional groups at one, three, six, and nine months.

The calculated reduction in the NRS score in the hypertonic group was higher than that in the conventional group during the entire research period, showing a statistically significant difference between the groups at the sixth- and ninth-month analyses (Table 3 and Figure 1). ODI scores calculated during examinations showed that the decrease during the whole study period in the hypertonic group was higher than that in the conventional group, showing a statistically significant difference at the ninth-month follow-up examinations (Table 3 and Figure 1).

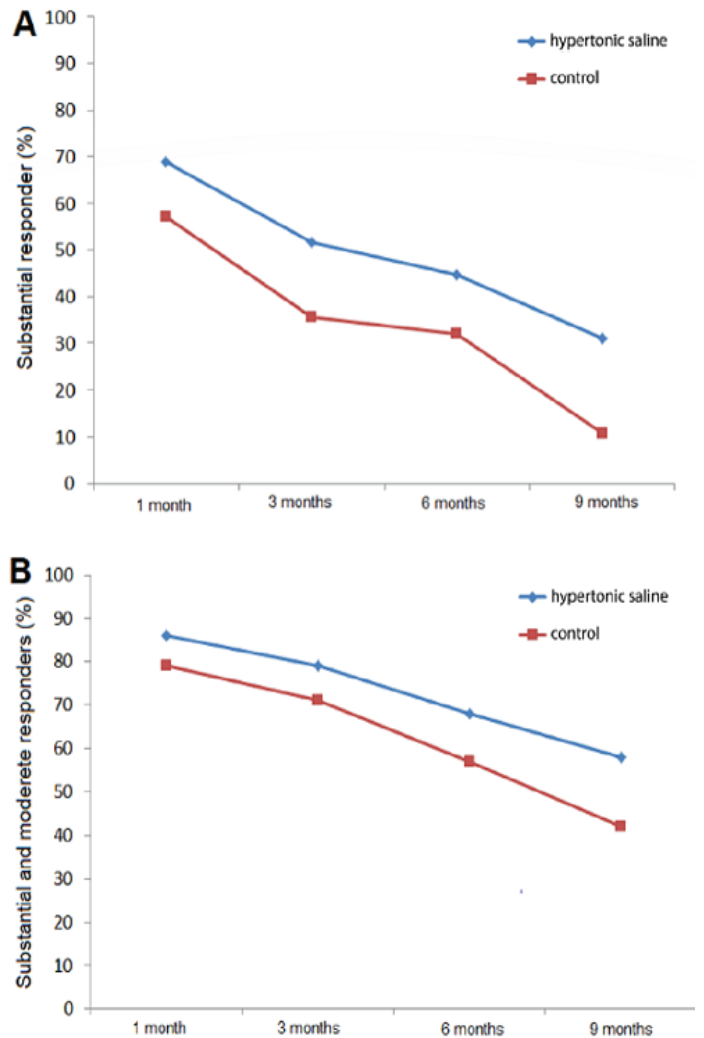


Figure 2. A.Representation of the baseline and follow-up values of the substantial responder rates of the study groups. B. Representation of the baseline and follow-up values of the substantial or moderate responder rates of the study groups

Substantial responder rates, including ≥ 4 points or $\geq 50\%$ reduction in NRS scores, in the hypertonic group were higher than those in the conventional group throughout the entire study period (Table 4 and Figure 2). The difference in substantial response rates, observed in nine and two patients in the hypertonic and conventional groups, respectively, was statistically significant in the ninth-month follow-up examinations. Besides, the significant + moderate response rate, including ≥ 2 points or $\geq 30\%$ reduction in NRS scores, in the hypertonic group

Table 3. Comparison of study groups in NRS and ODI scores decrease

Variables	Hypertonic Group (n = 29)	Conventional Group (n = 28)	p values
NRS			
1 month	3.83 ± 1.57	3.46 ± 1.75	0.233
3 months	3.53 ± 1.27	2.92 ± 1.46	0.094
6 months	3.33 ± 1.42	2.50 ± 1.57	0.031
9 months	2.56 ± 1.67	1.75 ± 1.21	0.028
ODI			
1 month	22.46 ± 8.67	19.11 ± 10.32	0.180
3 months	19.40 ± 8.72	15.75 ± 8.79	0.061
6 months	16.66 ± 8.53	13.96 ± 8.45	0.114
9 months	11.83 ± 10.72	7.85 ± 6.04	0.048

*Statistically significant values were written in bold characters, NRS: numerical rating scale, ODI: Oswestry disability index

Table 4. Comparison of study groups in response rates

Variables	Hypertonic Group (n = 29)	Conventional Group (n = 28)	p values
Substantial Responders			
1 month	20 (68.9%)	16 (57.1%)	0.354
3 months	15 (51.7%)	10 (35.7%)	0.223
6 months	13 (44.8%)	7 (32.1%)	0.116
9 months	9 (31.0%)	2 (10.7%)	0.023
Substantial + Moderate Responders			
1 month	25 (86.2%)	22 (78.5%)	0.448
3 months	23 (79.3%)	20 (71.4%)	0.489
6 months	20 (68.9%)	16 (57.1%)	0.354
9 months	17 (58.6%)	12 (42.8%)	0.233

*Statistically significant values were written in bold characters.

was higher than that in the conventional group during the whole study period (Table 4 and Figure 2). However, differences in significant + moderate response rates were not statistically significant.

No major complication was noted in the course of injections. Neither dural puncture nor inadequate drug distribution was observed during the procedure. Minor complications, including pain during the injection, which was endurable and needed no further medication, were reported in two and three patients in the hypertonic and conventional groups, respectively. No postoperative complication, such as sensory or motor function deficit, infection, or paresthesia, was recorded during the study.

DISCUSSION

Our study showed that TFESIs, with or without 10% hypertonic saline addition, are effective in decreasing lumbar back and radicular pain and improving the quality of life in patients with LDH. Furthermore, the present study showed that hypertonic saline addition provides significantly increased pain relief at the sixth- and ninth-month follow-up examinations and improved functional capacity at the ninth-month follow-up examinations.

Moreover, hypertonic saline addition increased the rates of substantial responders, and substantial or moderate responders during the overall study period, showing a significant difference in substantial responders at the ninth-month follow-up examinations.

ESI is used in the treatment of radicular pain. The effect of steroid on pain reduction is due to the reduction of inflammatory mediators (24,25), suppression of ectopic neural discharges (26), and regulation of neuroinflammatory proteins (27). Among epidural injections, TFESI is one of the prominent intervention methods. TFESI under radiographic guidance optimizes the therapeutic effect of medicines by providing targeted delivery of these agents close to the affected nerve root and dorsal ganglion (28).

In the present study, the addition of 10% sodium chloride to conventional TFESI seemed to be a valid choice, providing a more significant amount of pain relief at the long-term follow-up. This can be clarified via two different mechanisms. The first mechanism is neuromodulation potency of elevated concentration saline solution. Hyperosmolar solutions cause blockage of nerve evoked action potential by inducing extracellular calcium removal

(29). Thus, hypertonic solutions prevent pain conduction by establishing a persistent blockade of C fibers (30). Besides, the alteration chloride ion in the intracellular matrix modulates pain pathways, resulting in the reduction of hyperalgesia and allodynia (31). Another possible mechanism is the adhesiolysis effect of hypertonic saline on perineural and epidural adhesions and fibrous tissues. Epidural adhesions, which cause deterioration in the distribution of epidural agents, are known to be detected in patients with LDH without previous surgery (17,18). A study of human fibroblast cell culture model showed the negative effect of hypertonic saline on fibroblast viability and proliferation (32). Besides, a preliminary study with a small number of patients for ventral foraminal application of hypertonic saline for low back and radicular pain due to epidural fibrosis obtained favorable results (33). The effect of the two mechanisms, separately or together, may explain why hypertonic saline increases the success rate of transforaminal injections in the late follow-up period.

Immediate complications of hypertonic saline administration include inappropriate injection, bleeding, hypotension, and severe pain. In addition, late complications include paresthesia, bowel and bladder dysfunction, sexual dysfunction, headache, infection, epidural abscess, and arachnoiditis (34-36). None of these severe complications were observed in our study.

Some precautions have been taken to prevent the occurrence of these adverse effects. First, all procedures were performed in the operating room and in compliance with sterility rules. Anterior-posterior, oblique, and lateral images were obtained to prevent inappropriate injection, and accurate agent distribution was confirmed by contrast administration in continuous fluoroscopy. Furthermore, suction was performed before the medications were administered to determine the presence of blood or CSF.

This study has several limitations. First, although our study has a control group (conventional group) in our study, this control group comprised medicine application, and our study has no placebo group. Therefore, comparisons with placebo, which are particularly relevant in the long term, could not be performed. Moreover, the results included an overall follow-up period of nine months. Although the study includes longer-term results compared to the literature, the examination of longer-term results than our study may reveal the effect of hypertonic saline more precisely. Moreover, although the number of participants in the study was sufficient for a prospective comparative study, larger series would be beneficial to obtain more accurate definitions regarding the complication rates.

CONCLUSION

In our study, the addition of 10% hypertonic saline to transforaminal injections enhanced the effectiveness of the treatment by increasing pain reduction and improving the quality of life in the late period. Moreover, transforaminal injections with or without saline addition have shown favorable results; however, better responder

rates were observed with hypertonic saline addition.

Competing interests: The authors declare that they have no competing interest.

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Ethical approval: The Institutional Review Board of the Erzincan University approved this study.(Date:12/12/2017 Number:33216249-604.01.02-E.56242).

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