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Randomized Trial

The Dosages of Corticosteroid in Transforaminal Epidural Steroid Injections for Lumbar Radicular Pain Due to a Herniated Disc

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Background: Intervertebral disc herniations are the most common cause of lumbosacral radiculopathy, and transforaminal epidural steroid injection (TFESI) is an important tool in treating lumbosacral radiculopathy. But the ideal dose of corticosteroid in the epidural management of lumbosacral radiculopathy has yet to be determined.

Objective: The aim of this study was to determine the effective dose of steroids in TFESI for pain reduction in patients with lumbosacral radiculopathy.

Study Design: A randomized, double blind, controlled trial

Setting: An interventional pain management practice center.

Methods: A total of 160 participants received 2 epidural injections of either 5 mg, 10 mg, 20 mg, or 40 mg of triamcinolone in one week intervals via TFESI. The degree of participant satisfaction and verbal numerical rating scale (VNRS) were assessed at pretreatment, one week, and 2 weeks after the first TFESI.

Results: The number of participants experiencing pain relief was significantly less than in other groups in the 5 mg triamcinolone group at one week after the first TFESI. There were no significant differences among the groups at one week after the second TFESI. VNRS decreased in the other groups except the triamcinolone 5 mg group at one week after the first TFESI. VNRS decreased in all groups at one week after the second TFESI.

Limitations: The limitations include lack of placebo control group and lack of long-term follow-up.

Conclusions: We recommend a minimal effective dose of corticosteroid (triamcinolone 10 mg) in TFESI for patients with lumbosacral radiculopathy.

Key words: herniated disc, steroid, transforaminal epidural steroid injection, triamcinolone.

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Intervertebral disc herniations are the most common cause of lumbosacral radiculopathy; 10% to 15% of these patients eventually require surgery (1). Therapeutic approaches for treating lumbar radicular pains include bed rest, drug therapy, acupuncture, physical therapy, spinal cord stimulation, cryotherapy, radiofrequency thermocoagulation, psychotherapy, and surgery (2-6). Epidural injection of corticosteroids is one of the most commonly used interventions in managing spinal pain (3-15). The transforaminal route to the lumbar epidural space for corticosteroid injection has gained widespread acceptance for the treatment of lumbar and leg pain (3-7,9-14). A number of studies and systematic reviews have demonstrated that fluoroscopically guided transforaminal epidural steroid injection (TFESI) is an important tool in the non-surgical management of lumbosacral radiculopathy due to a herniated disc, even though debate continues (3-7,12-23).

Epidural injection of corticosteroids has some advantages over systemic therapy, such as delivering higher concentrations of the drug to the diseased area and having a notably lower rate of systemic adverse effects (16,17). Injecting medication precisely at the site of the presumed pathology allows the use of lower dose corticosteroids (3,4,11,18,20). However, there are only a few well-designed, randomized, controlled studies that have been performed to determine the effectiveness of epidural injections according to the steroid dosages. The ideal dose of corticosteroid in epidural management of lumbar radicular pain has yet to be determined (3,4,11,24,25). Thus, practitioners currently empirically determine the dose of the drug used. However, to avoid potential adverse effects from an excess of exogenous corticosteroids, a minimal effective dose of corticosteroids needs to be determined for successful use in patients (25-28).

The aim of this study was to determine the effective dose of corticosteroids in TFESI for pain reduction in patients with lumbosacral radiculopathy due to herniated discs.

Methods

In an interventional pain management practice center, after patient written informed consent was obtained in accordance with the Declaration of Helsinki, 160 patients aged 18-60 years old were randomly assigned to one of 4 groups to participate in a prospective, double blind trial. Patient assignments were generated from a randomization table.

Each participant in this study had a history and physical examination done prior to the initiation of steroid injection therapy. The diagnosis of lumbar intervertebral disc herniations was based on clinical manifestations and magnetic resonance image (MRI) findings.

Inclusion criteria for the study were: 1) signs and symptoms consistent with entrapment of the nerve root exiting the adjacent neural foramen, radicular leg pain and a positive straight leg raising test; and 2) at least a single level disc herniation shown on recent MRI corresponding with patient clinical symptoms. Exclusion criteria were: 1) lumbar spinal stenosis; 2) history of an allergic reaction to local anesthetics or corticosteroids; 3) known contra-indications for epidural steroid injections; 4) history of lumbar epidural steroid injections within 6 months; 5) previous lumbar spine surgery; and 6) unstable neurological deficits or cauda equina syndrome.

Injections were performed at the level that best matched the participant's clinical presentation. For the transforaminal technique, a pillow was placed under the lower abdomen with the participant lying prone, while the fluoroscopic tube was rotated obliquely to an ipsilateral oblique angle with respect to the suspected nerve root. The goal of positioning was to allow a perpendicular needle track toward the classic injection site underneath the pedicle in the so-called safe triangle, which is defined by the pedicle superiorly, the lateral border of the vertebral body laterally, and the outer margin of the spinal nerve medially (16,26). The participant's skin was disinfected and 1% lidocaine (Lidocaine HCL, Huons, Korea) was administered to the area where the needle would be inserted. With fluoroscopic guidance, an 8-cm, 22-gauge epidural needle (Tuohy epidural needle 22G, Tae-Chang Industrial Co, Korea) was then advanced into the "safe triangle." The needle position was confirmed using anterior-posterior and lateral views of fluoroscopy, followed by an injection of approximately 1 mL of contrast material (Telebrix 30, Guerbet, France). Anteroposterior and lateral views were obtained to identify contrast material distribution. After correct needle confirmation was obtained, each participant received a total volume of 3 mL of 1% lidocaine containing triamcinolone (Triam, Dongkwang, Korea).

Participants received 2 epidural injections of either 5 mg, 10 mg, 20 mg, or 40 mg triamcinolone in one week intervals by TFESI. The epidural steroid injections were performed by one physician, who administered 2 injections one week apart per participant. Group as-

signments were blinded to the medical personnel who administered the interventions. The injectates used for the 4 groups were indistinguishable from one another. Additionally, the participant and evaluating physician were blinded to group assignment.

All participants were evaluated by one physician who did not perform the injections and did not know the type of injections used in each participant. All participants were evaluated individually using the verbal numerical rating scale (VNRS) and the degree of participant satisfaction at pretreatment, one week and 2 weeks after the first treatment. VNRS measured the pain experienced with 0 representing no pain and 10 representing the worst pain. Participants also provided their degree of satisfaction. They were asked to choose from one of the 4 possible responses based on their satisfaction with treatment. Results after injections were assessed according to the rate of improvement and were classified according to a 4-grade scale: excellent, 90% improvement; good, 67-89% improvement; fair, 34-66% improvement; and poor, below 33% improvement. Participants rating the improvement as "excellent" or "good" were considered as having successful treatment. Those rating the improvement as "fair" or "poor" were considered as having failed treatment. All participants were screened thereafter for any major or minor complications.

Statistical analysis

The data were presented as the mean ± standard deviation (SD). One-way analysis of variance (ANOVA) test was used to compare differences in gender, age, weight, height, and duration of symptoms among the groups. Success rates were compared by a chi-square test. Data were analyzed by performing repeated measurements of ANOVA for the serial comparisons before and after the treatment in VNRS within the group and ANOVA among the groups, followed by Scheffe test. In all comparisons, a P value less than 0.05 was considered statistically significant. The statistical analyses were performed using SPSS 12.0 (IBM Corporation, Somers, New York).

Sample size

On the basis of a pilot study, we determined that a sample size of 40 participants per group was sufficient for this study using a desired power of 0.8 and a α level of 0.05. The primary outcome for power analysis was the pain score. The calculations were made for back and leg pain based on the VNRS, using a clinically significant difference among the groups with a rating of a 25% reduction in VNRS and assuming a standard deviation of 15%.

Results

A total of 160 patients were enrolled; the demographic data are presented in Table 1. There were no statistically significant differences among the groups with respect to gender, age, weight, height, and duration of symptoms.

Except for the group treated with 5 mg triamcinolone, the VNRS scores decreased at one week after the first TFESI. However, the VNRS scores decreased at one week after the second TFESI in all groups. The VNRS scores (mean 5.4) at one week after the first TFESI showed no statistically significant difference in comparison before the injection (VNRS mean 7.0) in the group treated with 5 mg triamcinolone. The VNRS scores (mean 4.3, 3.9, 3.8) at one week after the first TFESI decreased in comparison before the injection (VNRS mean 7.0, 7.2, 7.3) in the groups treated with 10 mg, 20 mg, and 40 mg triamcinolone. The VNRS scores (mean 3.9) at one week after the second TFESI decreased in comparison before the injection (VNRS

Table 1. *Demographic Data*

	Group 1 (n=40)	Group 2(n=40)	Group 3 (n=40)	Group 4 (n=40)
Gender (female/male)	24 / 16	23 / 17	25 / 15	26 / 14
Age(yrs.)	47 ± 7.4	53 ± 7.2	52 ± 4.9	53 ± 5.6
Weight(kgs)	46 ± 6.4	49 ± 6.9	54 ± 5.3	53 ± 5.4
Height(cms)	156 ± 8.2	162 ± 9.2	158 ± 8.2	159 ± 7.1
Duration of symptoms (days)	37 ± 4	33 ± 7	42 ± 5	33 ± 5

Values are mean ± SD or number of patients.
Group1: triamcinolone 40 mg; Group2: triamcinolone 20 mg; Group3: triamcinolone 10 mg; Group4: triamcinolone 5 mg.

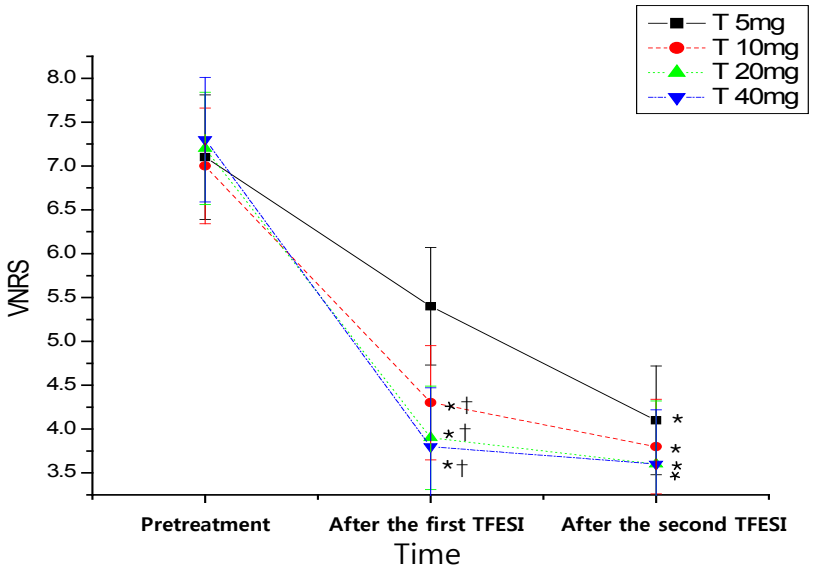

Fig. 1. *The scores for severity of back pain and sciatica, as measured on a verbal numerical rating scale (VNRS), after transforaminal epidural steroid injections (TFESI) in patients with lumbar disc herniations.*
T 5 mg: triamcinolone 5 mg (group 4)
T 10 mg: triamcinolone 10 mg (group 3)
T 20 mg: triamcinolone 20 mg (group 2)
T 40 mg: triamcinolone 40 mg (group 1)
**: P < 0.05 compared with pretreatment.*
†: P < 0.05 compared with Group 4.

mean 7.0) in the group treated with 5 mg triamcinolone. The VNRS scores (mean 3.4, 3.3, 3.2) at one week after the second TFESI decreased in comparison before the injection (VNRS mean 7.0, 7.2, 7.3) in the group treated with 10 mg, 20 mg, and 40 mg triamcinolone. The VNRS scores at one week after the first TFESI was higher in the group treated with 5 mg triamcinolone compared to the other groups. There were no significant differences among the groups at one week after the second TFESI (Fig. 1, $P < 0.05$).

The proportion of participants with significant pain relief of 67% or greater is illustrated in Fig. 2. The percentage of participants experiencing significant pain relief at one week after the first TFESI was significantly less, by 45% in group 4 compared with 75%, 70%, and 70% in groups 1, 2 and 3. There were no significant differences among the groups at one week after the second TFESI (Fig. 2, $P < 0.05$).

There were no major complications in this study, including epidural hematoma or abscess formation. The overall incidence of minor complications in the 4 groups was facial flushing in 2 cases and itching in one case. All events resolved without morbidity, and no participant required further hospitalization.

Discussion

The results of this 160 participant study showed that the VNRS decreased in all groups except the triamcinolone 5mg group at one week after the first TFESI in participants with lumbosacral radiculopathy due to herniated discs. In addition, the number of participants experiencing dramatic pain relief (≥67%) was significantly less than in other groups compared to the 5mg triamcinolone group at one week after the first TFESI. However, there were no significant differences among the groups in the percentage of participants experiencing significant pain relief at one week after the second TFESI. VNRS decreased in all groups at one week after the second TFESI. Our study showed that doses of at least 10 mg triamcinolone are sufficient to provide significant pain relief with one injection at one week after the block, while with the 5 mg dose we obtained

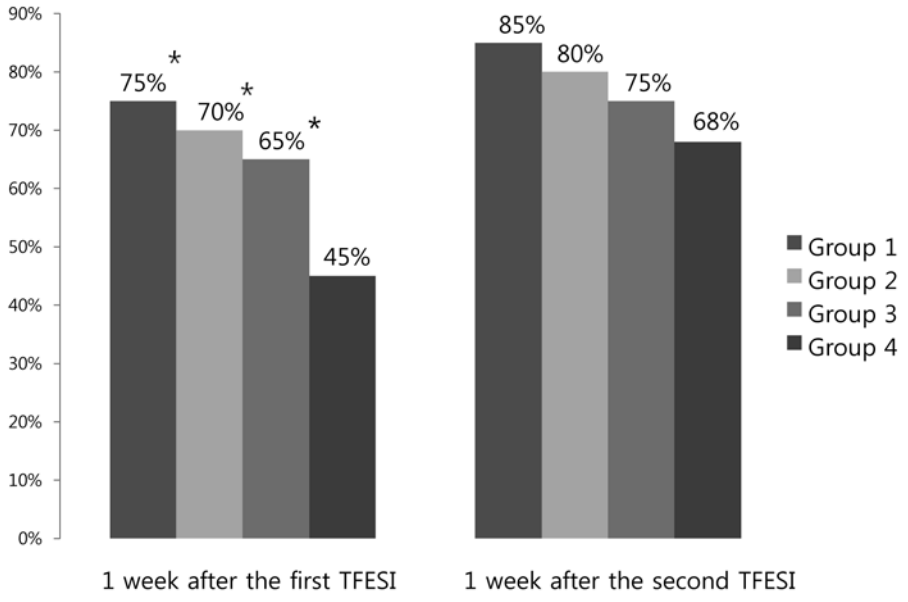

Fig. 2. *Proportion of patients with significant pain relief (≥67%). The number of patients experiencing pain relief was significantly less than in other groups in the 5mg triamcinolone group at 1 week after the first transforaminal epidural steroid injection (TFESI). There were no significant differences among the groups at 1 week after the second TFESI.*
Group 1: triamcinolone 40 mg; Group 2: triamcinolone 20 mg; Group 3: triamcinolone 10 mg; Group 4: triamcinolone 5 mg.
**: $P < 0.05$ compared with Group 4.*

similar results with 2 injections. The second injection in doses of at least 10mg triamcinolone did not affect the results.

There are various studies where pain reduction of 50% or more was considered a significant improvement. The patient satisfaction index adapted from the North American Spine Society's low back pain outcome instrument and improvement of 75% or more was considered good, in terms of successful treatment on the patient satisfaction scale, after epidural steroid injection (22,23). In the present study, participants experiencing pain relief over 67% were considered a success because patients were not satisfied with pain relief of 50% in this study.

An epidural corticosteroid injection is a commonly used treatment method in patients with lumbosacral radiculopathy due to herniated discs, however there is still controversy as to its use (3-7,12-23,29-37). First, the treatment timing and therapeutic effects of epidural corticosteroid injection vary among studies (3,4,11,16,21,27,38). Because two-thirds of acute low back pain episodes resolve within 7 weeks, some practitioners advocate waiting at least that long before considering epidural steroid injection (ESI) (39). However, the present study performed the TFESI in participants that had shown poor response to a medication time course consisting of one to 2 weeks for immediate relief of pain. The argument can be made, however, for earlier intervention in the acute inflammatory phase of injury in an attempt to prevent the development of chronic pain (16). Systematic assessment of evidence showed that the evidence of lumbar transforaminal epidural steroid injections for lumbosacral radicular pain was strong for short-term and moderate for long-term improvement (3,4,11). However, positive results from ESI vary from 20% to 95% (3,4,11). Further, there is no consensus on the optimal number of injections and dose of steroid used (3,4,6,11,27). Epidural corticosteroid is used in a variety of clinical practices, however there are few well-designed, randomized, controlled

studies to determine the effectiveness of epidural injections according to the dosage of steroid. In addition, previous studies do not correlate with the current situation because larger doses (i.e., 80 mg) of corticosteroid were used compared to doses used in the present study (3,4,11,25,27). The lower dose of corticosteroids was used to avoid potential adverse effects from an excess of exogenous corticosteroids in our investigation. Therefore, corticosteroids were used from 5 mg to 40 mg to investigate the effectiveness of epidural injections according to the dosages of steroid in our study.

There is no consensus on the absolute number of epidural injections that can be performed in a year (3,4,7,11-15). If there is no effect after the first ESI injection, there is still controversy with regards to whether the administration of additional injections is warranted (3,4,7,11-15,27). In the present study, we performed 2 injections to investigate the response after the second injection in participants that had shown poor therapeutic effects after the first injection. The second injection of triamcinolone doses higher than 10 mg were performed to investigate whether the second injection would yield improved results in pain relief. In our study, there was no significant difference in the effect between the cases of performing one or 2 injections per participant when they were treated with TFESI for pain reduction except in the group treated with 5 mg triamcinolone. In this study, the group treated with 5 mg triamcinolone showed a significant difference in effect after the second injection. Hickey (40) reported an improvement in a high percentage of patients after administration of a second injection compared to the first epidural steroid injection for lumbosacral radiculopathy. These results may be due to an insufficient dose of corticosteroid used in the first injection. A significant proportion of patients with acute sciatica respond to conservative symptomatic management and resolve over a period of weeks to months (1,4,39). Since the effect of epidural steroid injection is short-lived and the therapeutic benefits of steroid peak a week after treatment, we followed-up with the participants for a relatively short period to identify the differences in therapeutic effects among the groups (3,4,27,28).

There are several approaches available to access the lumbar epidural space: transforaminal, caudal, and interlaminar (3,4,7,11-19,29-37). Substantial differences have been described among these 3 approaches, with the transforaminal approach having the advantage of being target specific and using the smallest volume, fulfilling the aim of reaching the primary site of pathology, namely the ventrolateral epidural space (3-6,11,16-19,41-43). As pain from disc disease is usually generated anteriorly in the epidural space, the ventral epidural spread is the logical target for placement of anti-inflammatory medications. TFESIs may be superior to interlaminar ESIs and caudal ESIs for radicular pain. This may be due to increased ventral spread of steroid solution providing improved contact with the herniated disk and extruded contents (3,4,11,16,41). It is logical that the closer the location of approach to the lesions, the smaller the amount of steroid that is required. Injectate is more easily delivered to the anterior epidural space to accomplish therapeutic goals using the TFESI method; thus the relatively small amounts of corticosteroid are likely to foster good results. Therefore, our study used the TFESI method for pain relief in those with lumbar radicular pain due to a herniated disc.

The rationale for using corticosteroids in lumbar epidural injections stems from their ability to modulate inflammation and pain (3,4,16,27,28,44-49). When inflammation occurs, the spinal peripheral nerve becomes extremely sensitive, producing prolonged pain discharges with even gentle manipulation and pressure (28). Epidural injections of steroid and local anesthetics benefit patients by inhibiting prostaglandin synthesis, stabilizing cellular membranes, suppressing immune responses, enhancing neuronal blood flow, and washing out inflammatory mediators, in addition to blocking nociceptive C fiber conduction (45,46).

Injectable corticosteroids commonly used for lumbar epidural steroid injections include dexamethasone, methylprednisolone, triamcinolone, and betamethasone. Park et al (50) reported triamcinolone to be more effective than dexamethasone in short-term outcomes in patients with lumbar radiculopathy. On the other hand, Manchikanti et al (29-37) reported that there was no significant difference in the outcomes on a long-term basis, whether steroids were used or not used and what type of steroid was used. When triamcinolone is mixed with local anesthetic and saline solution, advantages include potentially less precipitation, an evenly well distributed drug, less sodium retention, prominent anti-inflammatory effect, relatively long working times, as well as fewer side effects, for instance, vascular occlusion (51-54). For these reasons, we typically used formulations of triamcinolone.

Serious side effects or complications are rare with epidural steroid injections except for radicular spasm and spinal cord infarct (11,55-65). The most commonly

reported side effects of corticoids include insomnia, facial flushing, nausea, rash, and fever (3,4,27,28,54). In a few patients, complications may include hypothalamic-pituitary-axis suppression, elevated blood glucose, elevated blood pressure, fluid retention, and menstrual flow abnormalities. In rare cases, a patient may experience an allergic reaction to a corticosteroid preparation. In our study, there were no major complications, including epidural hematoma or abscess formation. The overall incidence of minor complications in the groups was pruritus in 2 cases in the group treated with 20 mg triamcinolone. Only one participant who received 40mg triamcinolone complained of facial flushing. All events resolved without morbidity, and no participant required further hospitalization. In our study, the side effects and complications were rare and no statistically significant differences were observed among the groups after TFESI.

This study had several limitations. We did not use a placebo control group because the participants complained of severe pain, and we did not feel that a placebo injection would be ethical in these circumstances. Another limitation of our study included not showing the long-term results with epidural steroid injections for lumbosacral radicular pain.

The issue of placebo control has been discussed extensively (3-6,29-37,66-68). In addition, in the era of evidence-based medicine, multiple control designs have been described including an active control and dose control designs (69-74). This approach has been utilized in many studies evaluating interventional techniques. Further, it is extremely difficult to design a true placebo with interventional techniques (68). The effects of sodium chloride solution, local anesthetics, placement of a needle in the closed space, and injection of any type of material into closed spaces or close to the nerve root where pain generators exist has been shown to result in significant therapeutic activity, despite the disagreement of the experts (3,4,7,66-68,75-90).

The next issue relates to short-term follow-up; however, the study was designed to evaluate dose effectiveness rather than long-term follow-up of steroids.

In this study, the groups treated with 40 mg, 20mg and 10mg triamcinolone showed an improvement in the degree of participant satisfaction and reduction of the VNRS since the initial injection was performed. However, the group treated with 5mg triamcinolone showed no significant reduction of the VNRS and less improvement of the degree of participant satisfaction compared to the other groups after the primary injection. But, the VNRS scores decreased and the degree of participant satisfaction increased at one week after the second injection in all groups. Patients with lumbosacral radiculopathy due to herniated discs often complain of severe pain. Based on these observations, when practitioners perform TFESI on their patients, they would be better off using a steroid dose of sufficient strength for immediate pain relief. In this study, the group treated with 40 mg triamcinolone and the group treated with 10 mg triamcinolone did not differ in the degree of participant satisfaction and pain relief. However, when considering the side effects of steroids, low dose steroid use is thought to be desirable. Therefore, corticosteroid should be used at a suitable dose to induce sufficient effects in pain relief along with minimal side effects after TFESI in patients with lumbosacral radiculopathy.

Conclusion

We recommend a minimal effective dose of corticosteroid (triamcinolone 10 mg) for immediate pain relief in TFESI for patients with lumbosacral radicular pain due to a herniated disc.

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