Comparison of two doses of corticosteroid in epidural steroid injection for lumbar radicular pain

Owlia M B, Salimzadeh A, Alishiri Gh, Haghighi A

ABSTRACT

Introduction: Low back pain and lumbar radicular pain are the leading causes of job loss worldwide. Therapeutic approaches to lumbar radicular pain, including sciatica and spinal canal stenosis, are diverse. Many clinicians use 80 mg long-acting glucocorticoids in epidural steroid injections (ESI). The aim of this study is to compare the clinical response of 80 mg versus 40 mg methylprednisolone in ESI.

Methods: 84 patients with newly exacerbated lumbar radicular pain were randomly allocated into two groups. 43 patients underwent ESI with 80 mg Depo-Medrol and 41 age- and sex-matched cases received 40 mg Depo-Medrol as the comparison group. The pain in the second week, and every month thereafter was assessed using a visual analogue scale (VAS).

Results: Remarkable improvement in one month VAS occurred in 64 cases (75 percent) from both groups. VAS values between 80 mg and 40 mg groups were comparable in the two-week (p-value is 0.827) and three-month (p-value is greater than 0.746) post-injection periods. Slightly better results were shown in patients in the 40 mg group after one month.

Conclusion: In the case of lumbar radicular pain, ESI with low dose (40 mg) methylprednisolone is as effective as high dose (80 mg) with comparable results and less adverse profile.

Keywords: epidural injection, glucocorticoid, herniated disc, radicular pain, steroid injection

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Department of Internal Medicine, Shahid Sadoughi University of Medical Sciences, Shahid Sadoughi General Hospital, Safaeieh, Yazd, Iran

Owlia MB, MD
Rheumatologist and Assistant Professor

Department of Internal Medicine, Tehran University of Medical Sciences, Sina Hospital, Imam Khomeini Street, Tehran, Iran

Salimzadeh A, MD
Rheumatologist and Assistant Professor

Department of Internal Medicine, Baghiyatollah University of Medical Sciences, Baghiyatollah Hospital, Molla-Sadra Street, Tehran, Iran

Alishiri Gh, MD
Rheumatologist and Assistant Professor

Department of Internal Medicine, Shahid Mohammadi Hospital, Hormozgan University of Medical Sciences, Jomhoori Blvd, Bandar-abbas, Iran

Haghighi A, MD
Rheumatologist and Assistant Professor

Correspondence to:
Dr Mohammad Bagher Owlia
Tel: (98) 913 153 2954
Fax: (98) 351 822 4100
Email: mbowlia2@yahoo.com

INTRODUCTION

Low back pain (LBP) is one of the most common causes of medical visits either as outpatients or hospital admissions. It is estimated that 80% of people experience LBP during their life, and LBP is considered as the fifth cause of referrals to medical centres.[1] Both sexes are involved and individuals have this problem more frequently between ages 30 and 50 years. Smokers and people with sedentary or active jobs are at increased risk.[2–4] LBP is the leading cause of job loss and the issue of compensation.[3,5] Sciatica (sciatic nerve root entrapment) and spinal canal stenosis are among the most common causes of chronic LBP.

Apart from the inflammatory causes of LBP, inflammation and fibrinolytic defect have some critical role in the pathophysiology of some mechanical LBP, notably acute disc herniation.[6] Studies in both humans and animals indicate that pro-inflammatory cytokines (mediators of inflammation), including tumour necrosis factor alpha (TNF-alpha), are produced by macrophages in the nucleus pulposus.[3,6] When TNF-alpha contacts a nerve root, pathophysiological changes occur within the nerve, including reduced blood flow, intravascular coagulation, myelin splitting, and decreased conduction velocity, which are associated with pain. Subsequent sensory changes may then ensue as TNF-alpha impairs transmission along injured nerves.[8]

Therapeutic approaches to lumbar radicular pains include bed rest, non-steroidal anti-inflammatory drugs, muscle relaxants, even opioids and finally corticosteroids administered by oral or epidural route.[9] Intravenous infusion of Infliximab (Remicade) or subcutaneous perispinal administration of Etanercept (Enbrel) was associated with a dramatic response.[8,13] Injecting either anaesthetics, steroids, or both, is one of the methods used to treat patients with chronic or subacute LBP which needs evaluation with respect to effectiveness and optimum choice of procedure.

Some studies report lumbar disc herniation regression after successful epidural steroid injection (ESI).[10] Patients who were successfully treated non-operatively and whose pain decreased significantly within the first six weeks were found to have a larger number of resorbed extruded and sequestered disc herniations on follow-up magnetic resonance imaging (MRI). Carette et al showed a slightly better improvement in leg pain over six weeks in a randomised controlled trial of ESI in patients with sciatica due to herniated discs.[11] Another study by Cluff R et al pointed out the dosage of corticosteroid in epidural

management of lumbar radicular pain. He emphasised the the ideal dose and type of steroid have yet to be determined.[12] The aim of the present study is to compare the visual analogue scale (VAS) improvement scores of two doses of methylprednisolone in epidural management of lumbar radicular syndromes.

METHODS

84 patients with lumbar radicular pain were randomly allocated into two groups, which were treated with 80 mg and 40 mg Depo-Medrol, respectively. All of the patients had lumbar intervertebral disc herniation with or without canal stenosis confirmed with MRI. Of 84 patients, 75 (89%) had L5–S1 disc pathology and the remaining nine patients had problems at the L4–L5 level. None of our patients had previous low back surgery. All had tried full tolerable dose of non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen 2–3 g/day with or without codeine phosphate for at least two weeks and physical modalities had failed to show an acceptable response.

Our comparative study was conducted in rheumatology clinics in the Yazd province, Iran, from April 2003 to March 2005. The study was approved by the institutional review board. All lumbar epidural injections were done by a single operator using a stainless steel 18-gauge needle, after obtaining written consent and ruling out any clotting disorder or back soft tissue infection.

Inclusion criteria were: patients with lumbar radicular pain of more than two weeks duration after ruling out infectious or neoplastic causes, and who have had magnetic resonance imaging-proven intervertebral disc herniation and refractory pain, even after a full dose of NSAIDs, opioids and physical therapies for more than two weeks duration. Exclusion criteria were: patient's reluctance and lack of compliance and/or signs or symptoms denoting any underlying infection, bleeding tendency or malignancy. Patients with previous back surgery and radiologically-proven facet syndrome were excluded from the study.

After completing the history-taking and careful neurological examination, the patient was asked to lie in a lateral recumbent position with fully-flexed hip and knee joints and the head on a pillow 7–10 cm high. The skin was cleaned thoroughly with application of Betadine and was anaesthetised at the level of L4–L5 interspinous space to epidural space which is normally between 2–7 cm long. A stainless steel 18-gauge epidural needle (Touhy Epimed, NY, USA) was inserted into the skin and advanced while a syringe containing a bubble of air was attached to it. Epidural space was sensed using "loss of resistance" method and confirmed after sensory (numbness) or even motor (paresis) evidence of the proper injection site. This was achieved following the injection of 2–4 ml of 2% lidocaine.

The primary target for injection was at the L4–L5 level, unless any technical problems pushed the operator to the L3–L4 level. A prepared syringe of long-acting methylprednisolone acetate (Depo-Medrol, Upjohn NV/SA, Puurs, Belgium) with either 40 or 80 mg, which were diluted with normal saline in a total volume of 8–10 ml, was separately injected. After withdrawal of the needle, the patient lay on a supine position with knees and hips

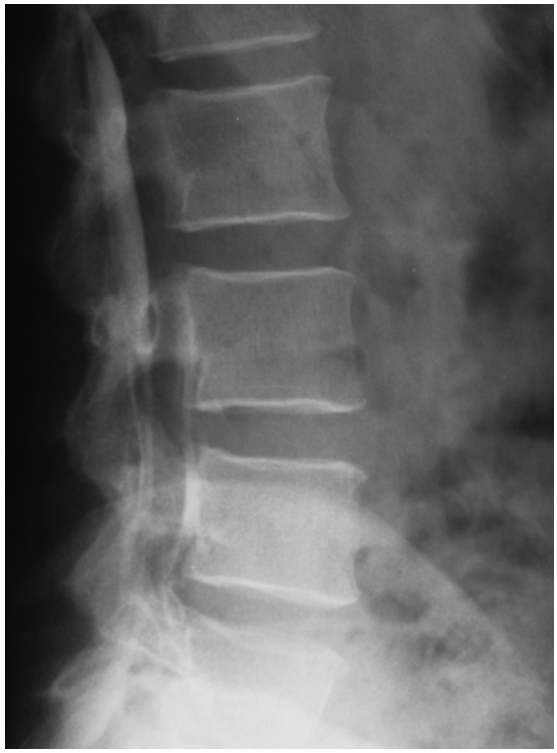

Fig. 1 Epidurogram shows access of the corticosteroid to the lumbar epidural space.

Table I. Pre-intervention characteristics of the two patient groups.

Characteristics	80 mg group (n = 43)	40 mg group (n = 41)
Male/female ratio	22/21	27/14
Mean age	38.2	36
Mean body mass index	27	29
Mean duration of symptoms (weeks)	12	9
Limitation in daily activity	12	20
Radiation (left/right)	13/9	15/5
Positive SLR test	20	27
Claudication	5	2
Decreased Achilles tendon reflex	14	12
Decreased muscle force	7	12
Cauda equina syndrome	0	0
Sensory deficit	10	2

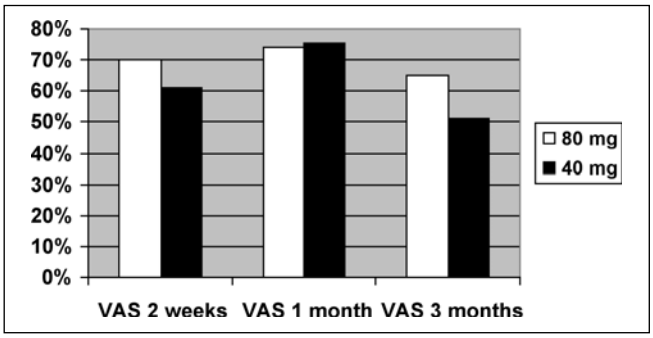

Fig. 2 Bar chart shows comparison of VAS improvement scores between the 40mg and 80 mg groups in the different post-injection periods.

in 90º and 45º flexion, respectively. The patient was trained to change his or her position every ten minutes after injection for better access of the drug to the diseased area. Control epiduralography proved the access of the drug (Fig. 1).

After the second week, and every month thereafter, the pain was assessed using VAS. Any decrement in VAS of more than two scales was defined as a significant VAS improvement (Table I). All the patients were screened thereafter for any major or minor complications, and blood glucose was assayed 24 hours after the procedure to detect any episode of hyperglycaemia. All patients had rehabilitative management for at least two weeks after ESI, as recommended by many experts. Patients were allowed to have acetaminophen 500 mg as rescue medication on an as-needed basis. The data were analysed using the Statistical Package for Social Science version 11.5 (SPSS Inc, Chicago, IL, USA) software, and by chi-square and Fisher exact tests. p-values equal or less than 0.05 were considered statistically significant.

RESULTS

Of the 84 patients studied, 45% were female and 55% were male. The mean ages of the 80 mg and 40 mg groups were 38.2 and 36 years, respectively. The minimum and maximum times from initiation of pain to epidural injections were two weeks and four months, respectively. Table I shows the characteristics of the two groups prior to intervention. Statistical differences between characteristics of the two groups were not significant.

Remarkable improvement in one-month VAS based on radicular pain occurred in 63 (75%) patients. The overall VAS improvement for two weeks and three months after ESI were 65.4% and 58.3%, respectively (Table II). VAS values for the 80 mg and 40 mg groups were comparable at two weeks ($p = 0.827$) and three months ($p > 0.746$) post-injection periods, and slightly better results were obtained from patients from the 40 mg group after one month. Even though slightly better results were obtained in the two-week follow-up in the 80 mg group, its statistical and clinical significance were negligible ($p = 0.827$). On the other hand, differences in VAS improvement in the second week and one month follow-up was significant ($p = 0.018$). Two patients in the 80 mg group complained of pain aggravation after EPI, eight patients had improvements of less than two scores [mild (one score) to moderate (two scores)] and the remaining four patients felt neither remarkable improvement nor worsening in pain perception during the two-week follow-up period (Fig. 2).

There were no major complications including epidural haematoma or abscess formation. The overall incidence of minor complications in both groups was transient hyperglycaemia in two cases (2.4%), flushing in seven cases (8.3%), cerebrospinal fluid (CSF) hypotension secondary to dural puncture in four cases (4.8%) (four cases had headache without any evidence of CSF leak), and post-injection flare in five cases (6.0%) (Table III).

Table II. VAS improvement after ESI of different doses.

Group	Significant VAS improvement		
	2 weeks	1 month	3 months
80 mg group	30/43 (69.8%)	32/43 (74.4%)	28/43 (65%)
40 mg group	25/41 (61%)	31/41 (75.6%)	21/41 (51.2%)
Total	55/84 (65.4%)	63/84 (75%)	49/84 (58.3%)

Table III. Comparison of the complications of ESI between the two groups.

Group	Complication				
	Major	Hyperglycaemia	Flushing	Post-injection flare	CSF hypotension
80 mg group (n = 43)	none	2 (4.6%)	6 (13.9%)	2 (4.6%)	1 (2.3%)
40 mg group (n = 41)	none	none	1 (2.4%)	3 (7.3%)	3 (7.3%)
p–value	–	0.097	0.012	0.120	–

None in the 40 mg group had hyperglycaemia. Only one patient who received 40 mg Depo-Medrol complained of facial flushing. All events resolved without morbidity, and no patient required further hospitalisation.

DISCUSSION

The aetiology of LBP is diverse. However, chronic lumbar radicular pain is mostly due to discopathy. From the pathophysiological standpoint, soluble mediators of inflammation play a significant role in intractable pain or perpetuating it.[13] Accordingly, anti-inflammatory agents have a role in controlling the signs and symptoms of lumbar radicular pain. These agents can be delivered to the site (milieu) of inflammation by systemic and/or local treatment. ESI is a kind of local therapy in this regard. This type of management has, however, some advantages over systemic therapy, such as getting higher concentrations of the drug to the diseased area and notably having a lower rate of systemic adverse effects like neuro-endocrine axis suppression and hyperglycaemia along with a negative impression on bone metabolism. We must consider this approach as a semi-invasive method in the care of patients with lumbar radicular pain. Potentially hazardous events may complicate the procedure, whose low incidence may be negligible in an expert hand. These complications range from transient hyperglycaemia, hypertension crisis, central nervous system symptoms, to more serious local events such as epidural haematoma and abscess formation and arachnoiditis. Some reports of vision loss after ESI are seen in the literature.[14]

Local injection therapy is superior to systemic treatment in several other conditions in routine rheumatology practice, such as periarthritides, bursitides, and even peripheral nerve entrapments like carpal tunnel syndrome. Several investigations showed little to remarkable improvement in lumbar radicular pain after ESI on the basis of role of local immunity in disc-related LBP.[8,15] Buttermann et al showed the ESI group had better improvement with ESI, while Botwin et al practised lumbar transformational ESI in lumbar radicular pain with some success.[9,16,17]

Several investigators tried ESI for spinal canal stenosis. Delport et al reported sustained relief in one-third and sustained improvement in more than half of patients.[18] However, Buttermann showed 42%–56% effectiveness for ESI in contrast to 92%–98% for the discectomy group. But he underemphasised the rather much safer and more repeatable nature of ESI in comparison to the more sophisticated surgical discectomy and resultant persistent pain in some surgically-treated cases. On the other hand, Loy reported excellent to good pain relief in 93.35% of epidurally-treated cases.[19] An apparent bias seems to exist in reports from clinicians of different working fields. Some studies show the similar long-term outcomes of surgical and non-surgical management of sciatica after four years. In contrast to previous reports that ESI cannot reduce the need for surgical decompression, Yang et al believed that it is not so.[20]

We did not find any article dealing with dose-based response of ESI in MEDLINE. However, Inman et al referred to sex differences in response to ESI for LBP.[21] Our study showed similar results in pain and functional scores in a one-month post-injection period as showed by Loy,[19] but late improvement VAS scores after three months dropped to 45%–50% as shown by Buttermann.[16] Slightly better results after one month may be due to late response of long-acting methylprednisolone or individual variations in receptor response to Depo-Medrol. This means that maximal beneficial effect of ESI is experienced around one month after injection. Late decline in response to ESI does not mask the benefits in a substantial number of patients with this minimally-invasive technique.

Most clinicians know that one of the most common indications for surgical intervention is intractable pain within the first months after the onset of symptoms. In other words, an overall 47.5% improvement after a three-month post-injection period can offset the need for surgery in a similar percentage of patients in the absence of any progressive neurological impairment. Also, the incidence of post-injection flares, flushing, and hyperglycaemia was significantly lower among patients who received a low dose (40 mg) versus a high dose (80 mg) agent. This is in spite of non-statistically significant p-values (Fisher-exact test) due to the small number of patients complicated with these undesired events. As Table III shows, the incidence of CSF hypotension is similar in the two groups, even in our small group of complicated patients, because the complication is not dose dependent and is just a technical problem. Latham et al also believed that higher doses of steroid injected intrathecally have a higher risk of arachnoiditis.[15] Steroid myopathy is another side effect of glucocorticoid therapy which is directly related to the dosage used.

In conclusion, in patients with lumbar radicular pain, ESI with low dose (40 mg) methylprednisolone may be as effective as high dose (80 mg), with comparable results and less adverse effect profile. We recommend a minimal effective dose of corticosteroid (40 mg) in ESI for patients with lumbar radicular pain. For more detailed information regarding the complication profile of low dose and high dose ESI, we suggest complementary studies in a larger group of patients.

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