Prospective Study

Comparison of Pain Reduction and Changes in Serum Cortisol and Glucose Levels to Different Doses of Lumbar Epidural Dexamethasone: A Prospective Study

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Background: Lumbar epidural steroid injection (LESI) is an effective treatment for low back pain. However, it may result in increased blood glucose levels, decreased plasma cortisol concentrations, and suppression of the adrenocorticotropic hormone axis.

Objective: We investigated the effects of 4 mg and 8 mg of dexamethasone as an LESI on back pain and the resulting changes in serum cortisol and glucose levels.

Study Design: Prospective study.

Setting: Department of Anesthesiology and Pain Medicine, Neurosurgery at Daegu Wooridul Spine Hospital.

Methods: Sixty-three patients were randomized into 2 LESI groups: one received 4 mg of dexamethasone (n = 25) and the other received 8 mg of dexamethasone (n = 28). Visual analog scale (VAS) scores and the Oswestry Disability Index (ODI) were determined. In addition, serum cortisol and glucose concentrations were measured before treatment, at the second LESI (one month follow-up), and at 2 months. All patients received LESI.

Results: Blood glucose and serum cortisol concentrations were not significantly different within a group and between groups. There was no difference in serum cortisol and glucose levels, VAS, and ODI between the first LESI and second LESI in both groups. The VAS and ODI were reduced in both groups and the difference between groups was not statistically significant.

Limitations: The dexamethasone dosage was not variable; hence, we could not use larger doses of dexamethasone. Secondly, the blood draw interval was longer in this study than in previous studies.

Conclusion: After the first lumbar epidural injection of either 4 mg or 8 mg of dexamethasone, there was a reduction in pain in both groups. There was no significant difference in serum cortisol and glucose levels before treatment and during follow-up. Therefore, 4 mg or 8 mg of dexamethasone can be considered a treatment for patients who have low back pain.

Key words: Epidural steroid, dexamethasone, dosage, cortisol, glucose, VAS, ODI

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Corticosteroids inhibit the synthesis and release of several proinflammatory substances that relieve pain by reducing inflammation around the nerve. Lumbar epidural steroid injection (LESI) is utilized to treat chronic low back pain with radicular pain (1). Chronic low back pain can be due to failed back surgery syndrome, lumbar degenerative disc disease, herniation of intervertebral discs, arthritis, or spinal stenosis. When nerve roots exiting the spinal column are compromised, low back pain that radiates

into the lower extremities may occur, also known as lumbar radiculopathy (2). Steroids are administered by injection and are thought to be integral in decreasing inflammation around the affected nerve tissue (3), leading to a reduction in pain.

However, steroids increase blood glucose levels, decrease plasma cortisol concentrations, and suppress the adrenocorticotropic hormone (ACTH) axis (4-9).

Kay et al (6) measured plasma cortisol and ACTH in patients receiving a lumbar epidural injection of 80 mg triamcinolone acetate and found that plasma ACTH and cortisol levels were significantly suppressed 7 days after the first epidural steroid injection. By the end of the second week, the plasma ACTH and cortisol levels were suppressed further. Another study reported that 80 mg methylprednisolone acetate markedly suppressed plasma cortisol levels for up to 3 weeks after the injection (7-10). Maillefert and Aho (8) reported that 9 patients given a single epidural injection of 15 mg of dexamethasone acetate had markedly decreased levels of cortisol in the serum and urine, and lower ACTH levels at 2 and 7 days postinjection. These levels normalized by 21 days postinjection.

The recommended doses or types of epidural steroid are variable (11,12). Which steroid is more effective for pain relief is controversial (11,12). Recently, particulate steroids were not recommended for epidural injection (13).Therefore, nonparticulate steroids are used for LESI (14-17). However, the optimal dose of nonparticulate steroid (e.g., dexamethasone) is unclear (12,14,16-18).

This study aimed to investigate the effects of different doses (4 mg versus 8 mg) of dexamethasone as an LESI on back pain and the resulting changes in serum cortisol and glucose levels.

Methods

This study was approved by our institutional review board. Patients who received a lumbar epidural steroid injection from January 2017 through December 2020 and who had their blood drawn postinjection were included.

A total of 63 patients were enrolled in our study, which was a randomized single center study with a 2-month follow-up period. The inclusion criteria were: 1) a diagnosis of herniated lumbar disc, spinal stenosis, and/or spondylolisthesis; 2) presence of magnetic resonance imaging; 3) aged 18-80 years; and 4) undergoing a 2-course LESI treatment. The exclusion criteria were: 1) diabetes mellitus; 2) use of oral steroids; 4) failed back surgery syndrome; 4) pregnancy; and 4) history of bleeding disorders.

All LESIs were performed with the patient prone and under fluoroscopic guidance. After sterile preparation, draping, and local anesthesia, a 22G, 10 cm Tuohy needle was gently advanced into the interlaminar space under an anteroposterior view. The loss of resistance method was used to detect the epidural space, and the anteroposterior and lateral fluoroscopic projections confirmed proper needle placement. Then, one-2 mL of contrast medium was injected to confirm the needle position and an adequate flow of contrast medium to the target level was verified using real-time fluoroscopy. In the absence of intravascular injection, or a subdural or intrathecal injection, the drug was administered as a total of 10 mL, mixed with 4 mg of dexamethasone (1 mL) and one percent lidocaine 2 mL and normal saline 7 mL or 8 mg of dexamethasone (2 mL) and one percent lidocaine 2 mL and normal saline 6 mL.

One month after the first LESI, the patients returned to our hospital for the second treatment (one-month follow-up). Prior to administering the second LESI, serum cortisol and glucose levels, visual analog scale (VAS) score and Oswestry Disability Index (ODI) score were measured. These same measurements were taken before LESI as a baseline. The patient visited a third time 2 months after the first LESI (2-month follow-up). At this visit the same measurements were taken. {this is redundant}

Serum cortisol was measured by a chemiluminescent microparticle immunoassay (normal = 3.7 - 19.4 μg/dL at 10 AM to 5 PM, 2.9 - 17.3 μg/dL at 5 PM to 10 AM).

Success was defined as a reduction in the VAS score of ≥ 50% or an ODI reduction of ≥ 40%.

All statistical analyses were performed using SPSS Version 25 (IBM Corporation). Pain scores within and between groups were determined by one-way analysis of variance and the Mann-Whitney Utest was used to compare changes over time. Frequency differences in the VAS and ODI were evaluated by the χ^2 test. The level of statistical significance was set when P values were < 0.05.

Results

Sixty-three patients were enrolled in this study, but 10 patients dropped out (Table 1). Neither gender nor age was associated with statistically significant differences in the pretreatment of both groups. The most frequent injection level was L4-L5.

After the first LESI, the VAS and ODI were decreased compared with baseline in both groups ($P < 0.05$) (Table 2). The VAS and ODI did not differ significantly between the 8 mg and 4 mg dexamethasone groups (Table 3). In both groups, there was no difference in the VAS and ODI between the first and second LESIs (Table 2). In the 4 mg dexamethasone group, a ≥ 50% reduction in the VAS was noted for 11 and 13 patients at one- and 2-months follow-up, respectively. In the 8 mg dexamethasone group, pain was reduced by more than 50% in 11 and 17 patients at one- and 2-months follow-up, respectively (Table 3). A reduction of > 40% in ODI change was observed in 12 and 16 patients in the 8 mg dexamethasone group at one- and 2-months follow-up, respectively (Table 4). However, there was no difference in VAS and ODI change between the first and second LESIs.

The serum cortisol and glucose levels are shown in Table 5. At one and 2 months after LESI, the cortisol and glucose levels were not significantly changed and there was no statistical difference in cortisol and glucose levels between the 2 groups (Table 5).

Table 1. *Patients characteristics.*

	Dexamethasone 4 mg (n = 25)	Dexamethasone 8 mg (n = 28)
Age (yr)	56.8 ± 9.0	55.7 ± 14.3
Gender (M:F)	16:9	11:17
Height (cm)	169.1 ± 8.4	164.5 ± 7.4
Weight (kg)	62.5 ± 17.3	65.5 ± 16.0
Duration of pain (month)	4.5 ± 8.7	4.1 ± 4.2
Level		
L3-4	2	3
L4-5	15	17
L5-S1	8	8

Table 2. *Changes of visual analog scale (VAS) and oswestry disability index (ODI) after lumbar epidural injection with different dose of dexamethasone (DXM).*

	1st epidural injection	2nd epidural at 1 month	2 months after 1st epidural injection	*P* value
DXM 4 mg (n = 25)				
VAS	7.0 ± 1.0	3.9 ± 1.0	3.6 ± 0.9	0.000
ODI	56.5 ± 8.4	31.3 ± 7.8	30.6 ± 6.8	0.000
DXM 8 mg (n = 28)				
VAS	7.0 ± 0.8	3.7 ± 0.8	3.4 ± 0.8	0.000
ODI	54.9 ± 7.6	28.3 ± 6.3	27.1 ± 5.9	0.000
P value (VAS)	0.157	0.487	0.773	
P value (ODI)	0.895	0.258	0.487	

Values are mean ± SD

Table 3. *Frequency of visual analog scale (VAS) according to 50% pain reduction of VAS after lumbar epidural injection with different dose of dexamethasone.*

	4 mg (n = 25) dexamethasone	8 mg (n = 28) dexamethasone
Before treat vs. 1 month		
≤ 50% reduction	11	13
P value	0.379	
Before treat vs. 2 months		
≤ 50% reduction	13	17
P value	0.604	
P value	0.630	

Discussion

This study found no statistically significant differences in the serum glucose and cortisol concentrations or in the degree of pain reduction in patients receiving epidural injections of 4 mg or 8 mg of dexamethasone. Furthermore, the reduction of VAS and ODI in both groups did not differ significantly after the first and second LESI.

Epidural corticosteroids can cause a decrease in plasma cortisol concentrations (19), suppress the ACTH axis, and increase serum glucose levels (5-10). However, serum cortisol and glucose levels remained unchanged in our study. An epidural injection of triamcinolone, methylprednisolone, or hydrocortisone, significantly suppresses plasma cortisol and ACTH levels (6,7,10,19). Moreover, epidural injection of 15 mg dexamethasone significantly decreased serum and urine cortisol levels, as well as ACTH levels at 2 days and 7 days postinjection; these levels returned to normal by 21 days postinjection (8).

Generally, suppressed serum and urinary cortisol levels and ACTH levels return to normal within 21-30 days (6-8). In the our study, each patient's blood was drawn and analyzed at 4 weeks postinjection; this may explain why serum cortisol and glucose levels appeared unchanged (14,16,19). Friedly et al (19) reported that the effect on cortisol level after epidural injection of dexamethasone was not different from lidocaine injection only.

Generally, if the first ESI results in partial pain improvement, ESI may be repeated in another 1–3 weeks

Table 4. *Frequency of oswestry disability index (ODI) according to 40% reduction of ODI after lumbar epidural injection with different dose of dexamethasone.*

	4 mg (n = 25) dexamethasone	8 mg (n = 28) dexamethasone
Before treat vs. 1 month		
≤ 40% reduction	11	13
P value	0.432	
Before vs. 2 months		
≤ 40% reduction	10	16
P value	0.430	
P value	0.456	

Table 5. *Changes of serum cortisol and glucose levels of dexamethasone (DXM) injection.*

	Before treatment	1 month later	2 months later	*P* value
DXM 4 mg (n = 25)				
Cortisol (μg/dL)	7.7 ± 2.4	8.0 ± 2.5	7.6 ± 2.2	0.230
Glucose (mg/dL)	95.0 ± 5.8	95.2 ± 6.1	96.1 ± 5.0	0.474
DXM 8 mg (n = 28)				
Cortisol (μg/dL)	7.6 ± 3.2	7.8 ± 2.7	7.3 ± 2.3	0.188
Glucose (mg/dL)	95.2 ± 7.8	96.1 ± 6.2	94.9 ± 5.8	0.412
P value cortisol	0.64	0.948	0.713	
Glucose	0.561	0.911	0.433	

Values are mean ± SD

(20). However, there is no reference for optimum ESI interval. In addition, we used dexamethasone doses that were lower than that used in a previous study (8). In our study, 4 mg and 8 mg dexamethasone was used. Ahadian et al (21) reported that 4 mg dexamethasone was as effective as 8 mg or 12 mg of dexamethasone.

In our study, both 4 and 8 mg of dexamethasone reduced patients' pain, which is consistent with results of previous studies (12,15,18,21). At the 2-month follow-up (patients had received LESI twice), the reduction in the VAS was > 50% and reduction in ODI was > 40%; these were comparable to the reduction observed after the first LESI.

The optimal time interval for the injection of epidural steroids was suggested in 1999 by Abram (20). He proposed the injection of moderate steroid doses (50 mg triamcinolone diacetate or 80 mg methylprednisolone acetate) followed by a repeated injection of epidural steroids at 1-3 weeks after the first injection if there was a partial improvement in radicular signs and symptoms.

Limitations

Our study has some limitations. First, the dexamethasone dosage was not variable; hence, we could not use larger doses of dexamethasone. Second, the interval between blood draw was longer than those in previous studies. Third, diabetes mellitus patients were not included. We suggest further study on this is needed. Finally, the times of day when LESI was performed and blood draw varied.

Conclusion

In conclusion, both 4 mg and 8 mg of dexamethasone reduced pain after the first LESI. Postinjection serum cortisol and glucose levels did not change significantly from pretreatment levels. Therefore, both 4 mg and 8 mg of dexamethasone can be considered a treatment for patients with low back pain.

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