A Randomized Clinical Trial of Three Different Steroid Agents for Treatment of Low Backache through the Caudal Route

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Abstract

Background: Although epidural steroids are commonly used for conservative management of sciatica, controversies exist regarding optimal approach, type and dose of steroids, volume of injectate and frequency of administration. This randomized comparative blinded study was undertaken to compare the efficacy of caudal methylprednisolone acetate with triamcinolone acetonide and dexamethasone acetate, for pain relief for sciatica associated with lumbar-disk herniations.

Methods: A Total of 163 patients with radicular pain due to lumbar-disk herniations, between 27-70 years of age were randomly divided into four groups: three were given epidural steroid injection therapy (methylprednisolone acetate, triamcinolone acetonide and betamethasone acetate) with bupivacaine; one group received bupivacaine alone via caudal approach. Injections were repeated every three weeks till a total of 210 mg of methylprednisolone (and equivalent) or three injections. Pain relief, disability and activity levels were assessed at 3, 6, 9 and 12 weeks interval.

Result: Pain relief was present in all four groups by three weeks with no difference between the groups ($p=0.006$; 0.005 ; 0.0045 ; 0.005 respectively to baseline). By the 6 and 12 week, the three steroid groups had significant pain relief ($p<0.001$). Among these, both methylprednisolone and triamcinolone groups showed greater improvement in the finger-to-floor distance ($p=0.006$). A smaller proportion of patients in this group had residual sensory deficits ($p=0.03$) as compared to dexamethasone but difference was statistically insignificant. Overall pain relief was significantly better at all follow-up evaluations in the steroid group than in the control group ($p<0.001$ at all evaluations).

Conclusion: Short-term improvement in leg pain and sensory deficits was observed in patients with sciatica due to a herniated nucleus pulposus with both epidural bupivacaine and steroids. All long-acting steroids had no statistically significant difference between their efficacy in pain relief but methylprednisolone and triamcinolone were more effective by the second injection as compared to dexamethasone which required a third injection in a significant number of cases. Differences between methylprednisolone and triamcinolone were insignificant. Complications were negligible and temporary.

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Key Words : Epidural steroid injections; Methylprednisolone; Triamcinolone; Dexamethasone; Sciatica

Introduction

Chronic low back pain (LBP), defined as pain persisting >12 weeks, is commonly caused by nerve-root inflammation with/ or without mechanical factors secondary to extrusion of nucleus pulposus. Theories for this induced inflammation include mechanical compression from the herniated disc, direct chemical irritation of the nucleus pulposus of the herniated disc, autoimmune response to material of extruded nucleus pulposus or combination [1]. Suppression of the biochemical factors of inflammation is the rationale behind the use of corticosteroids in LBP leading to reduction in soft-tissue swelling, oedema, pressure, soft adhesions and slow regression of disc herniation [2,3].

Epidural steroid injections (ESIs) localize the drug

around the area of affected nerve roots, thereby decreasing systemic effects and side-effects. Caudal route with or without fluoroscopy is a popular approach for the lumbar region [4]. Agents commonly used are methylprednisolone acetate, triamcinolone acetonide and betamethasone acetate [5,6]. Hydrocortisone and prednisolone have significantly less anti-inflammatory potency and higher mineralocorticoid effects (sodium retention with a tendency for hypertension). Hydrocortisone is additionally irritant to the nerves, meninges and can precipitate grand-mal epilepsy [7,8].

ESIs are administered with or without dilution using local anesthetics or isotonic saline solution. Local anesthetics are advantageous in providing temporary pain relief by means of analgesic effects exerted by blocking nerve conduction and suppressing ectopic signal

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generation in injured nerves. Prolonged benefits may occur by putatively interrupting the spasm-ischemia-pain cycle, thus favoring muscle relaxation. These also help in confirming whether the steroids have reached the clinical site [6].

In the Armed Forces, a number of backache patients are admitted every year leading to high bed occupancy. The aim of this study was to determine the efficacy and safety of ESIs given through the caudal approach for out-hospital management of sciatica, thereby avoiding hospital admission for the treatment of sciatica. Also, the comparative efficacy of available steroid formulations keeping the availability and cost-effectiveness of the three drugs with the null hypothesis that these are of equal efficacy was determined.

Material and Methods

Two hundred seven patients in ASA grade I-II who presented to the Pain Clinic in a tertiary care service hospital for sciatica were included in this double blind, randomized, comparative study after taking approval from hospital ethical committee and an informed consent. Sciatica was defined as the presence of constant or intermittent pain in one or both legs, radiating below the knee.

Eligibility criteria included (a) age 20-70 years inclusive, at the time of informed consent (b) body mass index (BMI) between 18-30 kg/m² (c) recurrent episodes of sciatica > four weeks but < one year with failure of, at least, six weeks of conservative therapy (including all the episodes) (d) computed tomographic (CT) evidence of a herniated nucleus pulposus at a level corresponding to symptoms and clinical findings (e) >20 score on the Roland-Morris Disability Questionnaire [9, 10]. CT scan was chosen over MRI because the service hospital had only a CT scan.

Patients were excluded if they had: (a) symptoms requiring early surgical treatment (severe motor weakness, cauda equina syndrome, hyperalgesic sciatica) (b) structural spinal deformities (scoliosis >40°, spondylolisthesis) (c) symptoms from causes other than herniated nucleus pulposus (d) received any spinal injection in the past year (e) undergone low back surgery, chemonucleolysis, or nucleotomy (f) pregnancy (g) known allergy to corticosteroids (h) ongoing treatment with tricyclic antidepressant drugs or lithium.

A sample size calculation was done to look for clinically relevant difference of 30% between the success rate of steroid groups (70%) Vs. control group (40%) keeping a two-sided alpha of 5% and power of 80%. A sample size of 39 per group was calculated; keeping in mind a 10% loss to follow up it was decided to enroll 50 patients in each group.

Patients fulfilling criteria were randomly allocated to the four groups using block randomization sequence generated by the computer and instituted by the study nurse using sealed envelopes:

Group A - Caudal injection of 10-15 ml 0.125% bupivacaine alone.

Group B - Caudal injection of 10-15 ml 0.125% bupivacaine and 80 mg methyl prednisolone.

Group C - Caudal injection of 10-15 ml 0.125% bupivacaine and 80 mg triamcinolone.

Group D - Caudal injection of 10-15 ml 0.125% bupivacaine and 15 mg dexamethasone.

The initial level of pain and functional disability was monitored using a Visual Analogue Scale (VAS) and Roland Morris low-back-pain disability questionnaire (Table 1). Nerve-root irritation and/or compression were evaluated by Lasègue's sign (reproduction of radicular pain by elevation of the leg) and the angle of leg noted by a goniometer for Straight Leg Raising (SLR) test. Finger-to-floor distance (FTFD) was also measured. Presence or absence of paraspinal muscle spasm was documented. Motor and/or sensory deficits were recorded.

The caudal block was performed under strict aseptic precautions with all resuscitative equipments kept standby. 2cc of air was injected through the caudal hiatus and area over the thoraco-lumbar spine auscultated for a 'swoosh' (modified 'Whoosh Test') [11]. The anaesthesiologists making the assessments were not the same as those giving the injections.

Follow up: Patients were discharged after an hour of observation following ESI. Re-evaluation was done after 1

Table 1

The Roland - Morris Disability Questionnaire

- I stay at home, most of the time because of my back.
- I change position frequently to try and get my back comfortable.
- I walk more slowly than usual because of my back.
- Because of my back, I am not doing any of the jobs that I usually do around the house.
- Because of my back, I use a hand rail to get upstairs.
- Because of my back, I lie down to rest more often.
- Because of my back, I have to hold on to something to get out of an easy chair.
- Because of my back, I try to get other people to do things for me.
- I get dressed more slowly than usual because of my back.
- I only stand for short period of time because of my back.
- Because of my back, I try not to bend or kneel down.
- I only walk short distances because of my back.
- I sleep less well on my back.
- Because of my back pain, I get dressed with help from someone else.
- Because of my back pain, I am more irritable and bad tempered with people than usual.
- Because of my back, I go upstairs more slowly than usual.
- I stay in the bed most of the time because of my back.
- I sit down for most of the day because of my back.
- I avoid heavy jobs around the house because of my back.
- I find it difficult to get out of chair because of my back.
- My back is painful almost all the time.
- I find it difficult to turn over in the bed because of my back.
- My appetite is not very good because of my back pain.
- I have trouble putting on my socks (stocking) because of pain in my back.

Total = The score is the total number of the items checked and will range from 0 to 24.

Fig. 1 : Flow chart of patients

Numbers in dark circles did not require the next injection. Numbers after each injection denote the patients lost with reasons. Final figures are mentioned in rectangular blocks.

Table 2

Outcome criteria after 3 months

	Roland - Morris disability score*	Mean consumption of Diclofenac tablets/week	Positive straight leg raising	Finger-to-floor distance
Success	>5 points	<6/week	Increase by 20°	>15 cms
Failure	<5 points	>6/week	Decrease by 20°	<15 cms

*Primary criteria

week, 3, 6 and 12 weeks after the first injection. At each visit, pain and functional disability was monitored as in the first visit. Information on use of analgesics and Non-steroidal Anti Inflammatory Drugs (NSAIDs) was recorded on individual patient's cards. If still symptomatic, ESI were repeated till a maximum of 210 mg/year of methylprednisolone and triamcinolone and 40 mg of dexamethasone or a total of three injections.

Patients in all four groups were permitted to take Diclofenac (50 mg tablets, up to four times daily) at any time during the study and to change the frequency as necessary. Patients were asked to keep a daily diary of their use of Diclofenac. The use of oral narcotic or non-narcotic analgesics other than Diclofenac was prohibited and no intrathecal, epidural, or neurolytic nerve blocks were administered during the entire follow-up period.

As per the VAS score, patients were divided into 3 groups at the end of the three month trial group: Complete pain relief (those requiring <6 Diclofenac tab/ week); Incomplete pain relief but satisfactory (those requiring >6 Diclofenac tab/ week, no other medication and not considering surgery as treatment option); Incomplete pain relief and unsatisfactory (those requiring >6 Diclofenac tab / week, other medications and/ or considering surgery as treatment option).

Statistical analysis (analytical software SPSS Version 10.0): The primary outcome for power analysis was RM score at three months (Table 2). Data was analyzed according to the intention-to-treat principle. Missing data were given a value by applying the last observation carried forward (LOCF) procedure. An analysis according to protocol was also performed for the main end point excluding (a) subjects wrongly included (b) subjects for whom data were not

Table 3**Baseline characteristics of patients**

	Group A (n=55)	Group B (n=50)	Group C (n=52)	Group D (n=50)
Age (in year) (mean; range)	43 + 7.4 (34-68 years)	40 + 5.6 (38-58 years)	39 + 6.8 (28-63 years)	42 + 9.2 (27-70 years)
Sex (M/F) (190:17)	50/5 (90.9%)	46/4 (92%)	49/3 (94.2%)	45/5 (90%)
Weight (in kgs) (Average, range)	78 + 7.3	79 + 5.9	77 + 8.1	77 + 7.3
Median duration of leg pain (weeks)	16 + 9	16 + 3	17 + 5	16 + 3
Mean consumption of Diclofenac tablets/ week	48	51	49	47
Discs involved as per CT scan				
One	47/55 (85.5%)	41/50 (82%)	45/52 (86.5%)	44/50 (88%)
Two	7/55 (12.7%)	8/50 (16%)	7/52 (13.5)	5/50 (10%)
>Two	1/55 (1.8%)	1/50 (2%)	0/52 (0%)	1/50 (2%)
Discs involved				
L ₁₋₂	1/55	0/50	1/52	1/50
L ₂₋₃	1/55	2/50	2/52	1/50
L ₃₋₄	40/55	41/50	38/52	42/52
L ₄₋₅	35/55	39/50	39/52	40/50
L ₅ -S ₁	9/55	6/50	7/52	5/50
Motor deficit (% of patients)	15/55 (27.3%)	14/50 (28%)	15/52 (28.8%)	14/50 (28%)
Sensory deficits (% of patients)	35/55 (63.6%)	34/55 (61.8%)	33/52 (63.5%)	31/50 (62%)

*p < 0.05

Table 4**Comparison of clinical parameters**

Time of observation (Parameter & groups)	Group A (n=55)	Group B (n=50)	Group C (n=52)	Group D (n=50)
Presence of paralumbar muscle spasm				
Baseline	44/55 (80%)	41/50 (81%)	42/52 (80.8%)	42/50 (84%)
At 3 weeks	n=42 32/42 (76.9%)	n=39 19/39 (48.7%)	n=42 21/42 (50.0%)	n=40 25/40 (62.5%)
At 12 weeks	28/42 (66.7%)	12/39 (30.7%)	15/42 (35.7%)	14/40 (35%)
Finger-to-floor distance (cm)				
Baseline (average value)	43.4	45.6	42.8	43.8
Average value after 3 weeks	28.4	31.4	29.2	28.6
(p value as compared to baseline)	(p=0.018)	(p=0.022)	(p=0.025)	(p=0.016)
Average value after 12 weeks	36.5	20.3	22.8	29.7
(p value as compared to baseline)		(p=0.006)	(p=0.005)	(p=0.014)
Straight Leg Raising				
Baseline				
15°–30° (20.8%)	11/55 (20%)	12/50 (24%)	11/52 (21.2%)	09/50 (18%)
35°–60° (54.6%)	30/55 (54.5%)	27/50 (54%)	31/52 (59.6%)	25/50 (50%)
65°–90° (24.2%)	11/55 (20%)	14/50 (28%)	13/52 (25%)	12/50 (24%)
Average value after 3 weeks	30/42	31/39	32/42	30/40
(p value as compared to baseline)	71.4% (p=0.043)	79.5% (p=0.046)	76.2% (p=0.041)	75.0% (p=0.044)
Average value after 12 weeks	22/42	18/39	14/42	12/40
(p value as compared to baseline)	(52.4%) (p=0.025)	(46.2%) (p=0.019)	(33.3%) (p=0.008)	(33.3%) (p=0.009)

collected any time till 12 weeks and (c) subjects non-compliant with the assigned treatment.

Success rates were compared using χ^2 analysis (Fisher's exact test) and a 95% Confidence Interval (CI) around the

difference in success rates was also estimated. $p \leq 0.05$ was required to reject the null hypothesis. Secondary outcomes (presence of paralumbar muscle spasm, FTFD and degree of SLR) were also estimated but remained exploratory in nature

Table 5**Comparison of Patient Feedback Scores**

Time of observation (Parameter & Groups)	Group A (n=55)	Group B (n=50)	Group C (n=52)	Group D (n=50)
Roland - Morris Questionnaire Score				
Baseline	21.67 + 1.582	21.40 + 1.52	22.33 + 1.37	21.12 + 1.84
		(p=0.4892)	(p=0.5924)	(p=0.3912)
Percentage improvement after 3 weeks (p value as compared to baseline)	n=42 38.09% (16/42) (p=0.047)	n=39 41.02% (16/39) (p=0.043)	n=42 40.47% (17/42) (p=0.045)	n=40 35.0% (14/40) (p=0.041)
Percentage improvement after 12 weeks (p value as compared to baseline)	n=42 23.81% (10/42) (p=0.056)	n=39 69.23% (27/39) (p=0.017)	n=42 71.43% (30/42) (p=0.018)	n=40 62.5% (25/40) (p=0.023)
Visual Analogue Scale				
Baseline	7.2 + 0.79	7.4 + 0.95	7.4 + 0.57	7.3 + 0.65
Average value after 3 weeks (p value as compared to baseline)	6.8 + 0.79 (p=0.036)	6.3 + 0.79 (p=0.028)	6.3 + 0.79 (p=0.026)	6.4 + 0.79 (p=0.035)
Percentage improvement after 12 weeks (p value as compared to baseline)	6.18 + 0.79 (p=0.029)	4.9 + 1.29 (p=0.016)	4.8 + 0.92 (p=0.018)	5.2 + 1.59 (p=0.021)

Table 6**Comparison of adjuvant therapy**

Time of observation (Parameter & Groups)	Group A	Group B	Group C	Group D
Consumption of Diclofenac tablets				
Baseline: Mean/ day	5.68	6.02	5.86	5.98
Range/ week	(21-45)	(24-44)	(22-46)	(24-42)
At 3 weeks: Mean/ day	4.82	3.78	3.28	4.02
Range/ week	(21-37)	(16-41)	(18-39)	(16-34)
(ANOVA) (p value as compared to baseline)	(p=0.3543)	(p=0.2401)	(p=0.2724)	(p=0.3084)
At 12 weeks: Mean/ day	26	18	17	18
Range/ week	(6-30)	(0-24)	(0-21)	(3-21)
(ANOVA) (p value as compared to baseline)	(p=0.4879)	(p<0.004)	(p<0.003)	(p<0.011)
Use of Physiotherapy				
Baseline	76.2% 32/42	76.9% 30/39	76.2% 32/42	77.5% 31/40
Percentage use of physiotherapy upto 6 weeks (p value as compared to baseline)	45.3% (19/42) p<0.003	25.0% (9/39) p<0.001	16.7% (7/42) p<0.001	30.0% (12/40) p<0.001
Percentage use of physiotherapy from 6 weeks to 3 months (p value as compared to baseline and to 6 weeks)	38.1% (16/42) p<0.001 p=0.592	15.4% (6/39) p<0.001 p=0.021	11.9% (5/42) p<0.001 p=0.026	25.0% (10/40) p<0.001 p=0.034

with no requirement of Bonferoni correction.

Results

A total of 363 patients were screened for study and only 207 were enrolled in the randomized portion of the study. A total of 163 patients completed the three month follow-up (Fig. 1). The clinical and demographic characteristics of the patients before the start of the study did not differ significantly among the four groups (Table 3). All the 4 groups showed a significant improvement from baseline by three weeks on an intention to treat analysis (95% CI for the difference -5.4 to 36.3).

The steroid groups continued complete or partial pain relief till six weeks with the difference not being statistically significant. Differences in improvements between the groups

were not significant by 12 weeks, except that the methylprednisolone group had greater improvement in the finger-to-floor distance (p=0.006) and a smaller proportion (5 as compared to 9 and 11 in group C and D respectively) of patients in this group had sensory deficits (p<0.005) (Tables 4, 5). A significant number of patients in the dexamethasone group required a third injection to achieve the level of pain relief.

In the course of the three month follow-up, three patients did not return to follow-up after the first injection and eleven after the second injection. Twelve patients took other drugs apart from Diclofenac. These were excluded from the study.

In the bupivacaine group, only 15% of the patients had pain relief at the end of six weeks and more than half of them had recurrence of pain at subsequent follow-up. Overall pain

Table 7**Final outcome of patients**

	Group A (n=42)	Group B (n=39)	Group C (n=42)	Group D (n=40)
Complete pain relief	11/42 (26.19%)	17/39 (43.48%) (p=0.451)	18/42 (42.86%) (p=0.447)	15/40 (37.5%) (p=0.438)
Incomplete pain relief but satisfactory	14/42 (33.33%)	15/39 (38.67%) (p=0.374)	16/42 (38.09%) (p=0.378)	14/40 (35%) (p=0.349)
Incomplete pain relief and unsatisfactory	17/42 (40.47%)	07/39 (17.94%) (p=0.477)	08/42 (19.05%) (p=0.486)	11/40 (27.5%) (p=0.496)
Total	99.99%	99.99%	100%	100%
Repeat Injections:				
At 3 weeks	59.5%	33.3%	25.7%	35.5%
At 6 weeks	22.5%	58.5%	68.5%	58.0%
At 9 weeks	3.5%	12.4%	5.5%	6.5%
Motor Deficit	23.4%	13.8%	16.3%	16.1%
Sensory deficits (% of patients) at 3 months	20/42 (47.61%)	05/39 (12.82%) (p=0.0203)	09/42 (21.43%) (p=0.027)	11/40 (27.5%) (p=0.043)
Complications				
Local pain persisting >24 hrs	3/42	8/39	7/42	4/40
Headache	13/42	15/39	16/42	09/40
Tinnitus	03/42	01/39	04/42	01/40
Nausea	07/42	06/39	07/42	08/40
Weight gain	0/42	0/39	1/42	0/40

Table 8**Advantages of caudal approach over trans-foraminal and interlaminar approach**

- Preferential cranial flow of solutions occurs as a 'sleeve' arising non-preferentially in both, the dorsal and ventral epidural space with inflammation occurring in posterior region
- Decreased vascularity in the posterior epidural space causing lower drug washout
- Ease of entry especially in obese patients or those with post-lumbar laminectomy syndrome
- Minimal chances of inadvertent dural puncture
- Safety in patients with deranged coagulation profile
- Post-technique, this approach does not require extensive monitoring

relief was thus significantly better at all follow-up evaluations in the steroid group than in the control group ($p < 0.001$) (Tables 6, 7, 8).

No patient complained of backache following the caudal injection. A total of twenty two (13.49%) patients complained of pain at the injection site (caudal) lasting a few days (mean duration 1.6 days with a range of 0.4-3 days). Eight (4.9%) patients complained of tinnitus and one with decreased hearing (L) ear. Audiometry was done which revealed mild sensori-neural deafness. Fifty-three (32.5%) patients complained of headache after the injection, but none required medication for the same. Mild nausea was reported in twenty-eight patients but no vomiting or dizziness. There was no incidence of epidural haematoma, intravascular injection, nerve root injury, subarachnoid injection or meningitis in any of the patients.

Discussion

ESIs are minimally-invasive therapeutic tools, the effectiveness of which vary between 20-95% depending on route of injection and time of evaluation [5, 6, 8, 12]. This compares well with 78.53% in this study as seen by three months. The reported benefits of ESIs include relief of leg pain more than back pain, facilitating the participation in physiotherapy, reduction in analgesic consumption and improvement of quality of life. With pain reduction, patients get a feeling of control over residual discomfort and thus can avoid an operation [1,3]. A total of 19 patients out of 207 underwent laminectomy.

For accurate drug placement, ideally ESI should be performed with fluoroscopic guidance [4,13-16]. Anesthesia residents are not routinely taught to use fluoroscopy and so, although fluoroscopy is intellectually appealing, its value in improving outcomes is not proven. Ultrasonography [24,17] and epiduroscopy [14,18] have also been attempted to confirm drug placement via the caudal route. Caudal route can be verified additionally by the Whoosh test [11] and its modification, the 'Swoosh test'. The former has a sensitivity of 75-86% and the latter upto 96% [12]. All cases in this study had a positive 'Swoosh' test.

Methylprednisolone has an intermediate (12-36 hour biological half-life) duration of action. Its sodium retaining potency is half of cortisol and anti-inflammatory potency five times more. Potential problems include the cost and

the usual availability as multidose vials which increases wastage and chances of infection. The preservative used, benzyl alcohol, is a potential neuro-toxic increasing the risk of arachnoiditis or meningitis. Triamcinolone is also an intermediate drug with similar anti-inflammatory potency as methylprednisolone. However, it has no sodium retention effect. It is available in single-use ampoules without preservatives and is cheaper than methylprednisolone. It is less soluble and remains in suspension for longer periods at the injection site as compared to methylprednisolone and this has been proposed as a reason for increased local effect [5,7,15]. Dexamethasone sodium phosphate has a rapid onset and long duration of action (36-72 hour biological half-life) with higher anti-inflammatory and glucocorticoid potency as compared to other steroids (ratio of 1:5:5:27 for hydrocortisone: methylprednisolone: triamcinolone: dexamethasone). At equipotent anti-inflammatory doses, dexamethasone almost completely lacks the sodium-retaining property of hydrocortisone. It is the only non-particulate corticosteroid with no aggregation on dilution. While there are studies of its use for the cervical region [14,20,21], there are only a few studies of its use in the lumbar region [5,6].

Although steroid effects are dependant largely on the total dose and not the total injected volume, the drug should reach the affected segment. Volumes of 10 mL (for L₅ segment), 15 mL (for L₃ segment) and upto 20 mL (for upper lumbar) is recommended through the caudal approach [22]. This is in comparison to 1.5-2 mL through the transforaminal and 6-10 mL through the inter-laminar technique [6,7,23]. The theoretical disadvantage of the caudal approach i.e. the larger volume of medication required to reach the area of pathology [7,24] may actually benefit by lysing epidural adhesions [2,6,25].

Low incidence of both minor central neural sequelae such as radiculopathies (<0.05%) and serious complications such as paraplegia (incidence of 1:50,000 ESIs) has been variously reported [1,6,23]. MacKinnon et al [26] demonstrated widespread and severe axonal degeneration, affecting both the large and small fibers, maximal for hydrocortisone, intermittent for equipotent triamcinolone acetate and methylprednisolone and minimal with dexamethasone. They attributed this to direct delivery of drug within the nerve fascicle, needle injury to the nerve as well as a local allergic phenomenon [26].

Inadvertent embolization by particulate steroid into the vertebral vessels with resultant ischemia and scarring of the nerves could produce serious central neural sequelae. Methylprednisolone has uniformly sized, densely packed particles with <5% of particles >50 µm in

diameter and do not form many aggregations. Dilution of the 80 mg/mL preparation with saline results in increased proportion of aggregates >100 µm particles, an effect not seen on dilution with lactated Ringers solution or lidocaine. Particles of triamcinolone vary greatly in size and are densely packed. When diluted with bupivacaine, triamcinolone may coalesce into large (>100 µm) aggregates causing clouding of the solution. Based upon dimensions (artery >50 µm, metarteriole 20-50 µm, arteriole 10-15 µm, and capillary 5-8 µm), both methylprednisolone and triamcinolone sludge could block smaller arteries and arterioles and result in ischemia. Dexamethasone has particulate size <5 µm with the lowest density and the least tendency to aggregation among all the steroid preparations. Theoretically, dexamethasone should have minimal neurological sequelae and a short duration of action [27-29].

Another postulate for neurological sequelae is the effect of various additives used in the formulations of steroid. Among these, polyethylene glycol causes altered compound action potentials and delayed conduction velocities but at concentrations higher than those used clinically. Intrathecal 1.5% benzylalcohol can cause neural degeneration and demyelination. Benzalkonium chloride, a triamcinolone and betamethasone additive, has been shown to be a gastrointestinal neurotoxin in much higher concentrations. EDTA, another betamethasone additive present in extremely small doses (0.1mg/mL) can induce convulsive activity in higher intrathecal doses in mice. Polysorbates and sodium phosphates have no adverse effects when given intrathecally [1,3,6,26]. Triamcinolone used for this study contained 0.9% benzalkonium while 40 mg/mL single-dose methylprednisolone contained either polyethylene glycol 3350 NF or 0.6 mg monobasic sodium phosphate; 17.46 mg dibasic sodium phosphate and 0.88% benzalkonium. No neurological deficits were observed in this study. This could be due to the higher volumes of low strength used via the caudal route thereby diluting both the steroid as well as the additives. Also the absence of both nerves and blood vessels in the caudal space prevents needle injury or ischemia to the nerves [22,25].

Since steroid remains in situ for approximately two weeks, this is logically the minimum time period to assess the patient's response and to administer a repeat injection [14,21,23]. Generally, upto 3-4 epidural injections may be performed before declaring the therapy a failure, provided the total dose not exceed 3mg/kg or 210 mg/year of methylprednisolone and equipotent doses of other steroid. Beyond this dosage, water and salt retention can occur [6]. None of the patients in this study received steroid exceeding this dose.

No explanations could be found in the reviewed

literature for headache and tinnitus. The authors hypothesize the following possibilities: (a) stress during the injection resulting in neuroendocrine alteration, (b) steroid-induced damage to the meninges with altered permeability, (c) elevated catecholamine levels to steroids resulting in cerebral vasoconstriction (d) increased CSF pressures due to rapid instillation of 20 mL.

Among the different scores available, the Roland-Morris Questionnaire (RMQ), a self-administered disability measure, was chosen as it has been shown to yield reliable measurements which are valid for inferring the level of disability, and are sensitive to change over time. The reason for inclusion of patients with a score >20 on a 24-point scale was that spontaneous significant changes over time are unusual in these patients [10].

Limitations: The natural history of prolapse of nucleus pulposus varies and therefore, lack of long-term follow-up is one limitation. Many studies reported short-term pain relief at 2- 4 weeks and conflicting results in pain-scores and operation rates by 6 and 12 months. Also, plasma levels of steroid as well as evidence of suppression of the HPA axis were not estimated. However, clinically there was no evidence of suppression or overdosage of steroid.

In conclusion, ESI is a simple, cost-effective and minimally invasive treatment for sciatica due to prolapsed disc. All long-acting steroids are effective but methylprednisolone and triamcinolone have shown to be more effective than dexamethasone which required a second or third injection to be effective. Dexamethasone is associated with more side-effects but these are minor and self-limiting. Triamcinolone is a good alternative to the more expensive methylprednisolone and is readily available in single-use vials. Hydrocortisone has not been recommended by other workers and was not evaluated in this study. The complications are negligible and temporary. ESIs are highly useful in patients who desire relief faster than waiting for natural resolution. Beneficial effects of epidural steroid, even if only for a short or medium period, justify this treatment due to the potential of decreasing pain duration, movement limitations and loss of labor-ability from weeks or months, to only a few days. It also serves as a 'water-shed' procedure and a prognosticator. Patients with poor response will most likely require surgical solutions as this indicates severe mechanical compression, swelling, oedema and/or adhesions.

Conflicts of Interest

None identified

Intellectual Contribution of Authors

Study Concept : Col Rashmi Datta

Drafting & Manuscript Revision : Col Rashmi Datta

Statistical Analysis : Col Rashmi Datta, Brig KK Upadhyay, VSM

Study Supervision : Col Rashmi Datta, Brig KK Upadhyay, VSM

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