Original Article

A prospective randomized comparative study of analgesic efficacy of epidural Methylprednisolone and Bupivacaine with epidural Triamcinolone and Bupivacaine in treatment of refractory low back ache with or without radiculopathy

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Abstract

This prospective, randomized, comparative, active control, study was done to compare the efficacy of the two commonly used steroid preparations, methylprednisolone acetate and triamcinolone acetonide for patients with refractory low back ache. A total of Sixty patients suffering from recurrent episodes of Lumbar radicular pain > six months but < one year with failure of at least twelve weeks of conservative therapy were included in the study. Thirty patients were assigned in one of the two groups (Group M or Group T) randomly. Group M patients received epidural injection containing 0.25% Bupivacaine, 8 mL, mixed with Inj. Methylprednisolone (80 mg). In contrast, Group T patients received epidural injection of 0.25% Bupivacaine, 8 mL, mixed with Inj. Triamcinolone (80 mg). Outcome was measured using changes in pain scores obtained on the Visual Analog scale and in SLR measured at each follow up interval up to 4 weeks. 23 out of 26 patients (88.5%) in the group M and 21 out of 27 patients (77.8%) in the group T, with positive SLR showed improvements in the degree of their SLR at 4 weeks follow up with no significant difference in the number of patients showing improvement between the two groups (p value 0.582). The degree of pain relief obtained on the Visual Analog Scale was in favor of triamcinoline group up to two hours post procedure. However, after 2 hours there was no statistically significant difference observed in the VAS scores between both the groups. This study confirmed the efficacy and safety of the depot preparations of methylprednisolone and triamcinolone for their use in lumbar epidural steroid injections for the treatment of refractory low back ache. No definitive conclusions however, could be made with regards to the relative efficacy of these two drugs.

Keywords: Chronic low back pain, epidural injections, local anesthetic, steroids.

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INTRODUCTION

Spinal pain is associated with significant economic, societal, and health impact.[1] Low back ache refractory to a trial of conservative treatment is frequent in clinical practice[1,2] with the pathological basis of such a pain usually being disc herniation with or without radiculitis, degenerative disc disease and/or spinal stenosis. Effective treatment based on rehabilitation or interventional techniques, for this intractable pain remains a challenge with the problem compounded by a lack of standard guidelines.[3-7] Epidural injection based on the concept of inflammatory pathology for pain[8-10] is one of the most commonly performed interventions for refractory low back ache secondary to multiple pathologies with multiple studies and systematic reviews[7,8,11-18] showing that evidence exists for short term relief especially in

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lumbar radicular pain in a selected group of patients, thus providing a reasonable alternative to surgical intervention. Epidural injections appear to speed the rate of recovery and return to function, allowing patients to reduce medication levels and increase activity while awaiting the natural improvement expected in most spinal disorders[12,14-16,19-21] Controversies exist regarding the optimal approach, type and dose of steroids, volume of injectate and frequency of administration[3,8-12,16] Steroid preparations differ significantly in their pharmacological properties in terms of relative anti-inflammatory and mineralocorticoid potency, elimination half-life, duration of action, particle size and tendency to aggregate and the neurotoxicity of various preservatives used[22-24]. A number of synthetic particulate (e.g. methylprednisolone acetate, triamcinolone acetonide, compound betamethasone) and nonparticulate (e.g. dexamethasone) steroids have been used for these epidural spinal injections with the choice of the steroid often being based on physician preference rather than strong clinical evidence. Given the paucity of literature, comparative clinical efficacy and safety of these steroid preparations with different pharamacological profiles needs to be determined which will help in choosing the steroid preparation most suited for a given patient and disease profile. The aims of this study were to[1]. assess the short term clinical and functional outcomes following interlaminar lumbar epidural steroid injections with two commonly used synthetic particulate steroid preparations methylprednisolone acetate and triamcinolone acetonide for patients with refractory low back ache using straight leg raising (SLR) and visual analog scale (VAS) scores as measures of disability; and[2] to compare the outcomes between the two agents so as to determine the indications for choosing the either. The null hypothesis assumed was that these two agents had equal efficacy and safety.

MATERIALS AND METHODS

The prospective, randomized, comparative, active control, single center study was conducted in department of anaesthesia at SMS Medical College Jaipur and was based on Consolidated Standards of Reporting Trials (commonly known as CONSORT) guidelines[25]. This study was conducted with the internal resources of the center without any external funding, either from industry or from elsewhere. The study protocol was approved by the Institutional Ethical Review Board and written informed consent was obtained from all subjects.

Patients

Sixty ASA grade I-II patients who presented to the pain clinic for low back ache with or without leg pain not responding to an adequate 3 months trial of conservative approaches like bed rest, exercise, NSAIDS etc were enrolled in the study and were assigned to one of 2 groups. They were given the approved protocol and informed consent which described in detail all aspects of the study and withdrawal process.

Interventions

Of the 60 patients, 30 patients were assigned to Group M, who received lumbar interlaminar epidural injection containing a preservative free local anaesthetic 0.25% Bupivacaine, 8 mL, mixed with 2 mL of Inj. Methylprednisolone acetate (80mg). The other 30 patients were assigned to Group T and received lumbar interlaminar epidural injection containing 0.25% Bupivacaine, 8 mL, mixed with 2ml of Inj. Triamcinolone acetonide (80 mg).

Pre-enrollment Evaluation

Demographic data, medical and surgical history with co-existing disease(s), radiologic investigation findings, physical examination findings including vital physiological parameters and derangement in the SLR test and pain rating scores using the VAS were assessed prior to enrollment.

Inclusion and Exclusion Criteria

Eligibility criteria included (a) age 20-70 years inclusive, at the time of informed consent (b) body mass index (BMI) between 18-30 kg/m' (c) low back ache with or without radicular pain > six months but < one year with failure of, at least, twelve weeks of conservative therapy (d) patients willing to give their consent for the study. Patients were excluded if they had: (a) symptoms requiring early surgical treatment (severe motor weakness, cauda equina syndrome, hyperalgic sciatica) (b) structural spinal deformities (non degenerative scoliosis or spondylolisthesis) (c) back pain secondary to malignancy or infection (d) uncontrolled medical illness, either acute or chronic or any condition that could interfere with the interpretation of the outcome assessments (e) received any spinal injection in the past year (f) undergone low back surgery, or any other intervention (g) history of recent spinal trauma (h) pregnancy (i) known allergy to corticosteroids or local anaesthetics (j) known bleeding disorders (k) uncontrolled psychiatric disorders or those on tricyclic antidepressants or lithium or with history of substance abuse.

Description of Interventions

All injections were performed under strict aseptic precautions with the patient in a sitting position, by the same anesthesiologist under fluoroscopy in an ambulatory care setting with appropriate monitoring and resuscitative equipments kept on standby. Intervertebral space associated with the pathology was identified by digital palpation and entry into the lumbar interlaminar epidural space was assessed utilizing the loss of resistance

technique and confirmed by an injection of non-ionic contrast medium and steiroid injections were given to the patient according to his/her group. Patient was then positioned supine with pillow under the shoulders and continuous monitoring was done in the recovery room for at least 16 hrs post-procedure. The patient was then discharged and re-examined weekly for one month. All patients were advised to carry out their normal activities but avoid acute bending, lifting heavy loads or engage in vigorous physical activity. All patients continued their previously directed exercise programs, their employment, and medications. Based upon an individual patient's medical necessity and improvement or lack thereof, these medications were either discontinued or the dosages increased. However, no specific physical therapy, occupational therapy, bracing, or interventions, other than the assigned study intervention, were offered.

Outcomes

Outcome measures utilized included changes in vital physiological parameters (heart rate, systolic blood pressure and diastolic blood pressure) based on their sequential recording along with calculation of pain scores obtained on the Visual Analog scale and derangement in SLR measured at each follow up interval which was 0.5, 1, 2, 16 hrs post procedure and 1, 2, 3 and 4 weeks thereafter. Visual Analogue Scale (VAS) scale is a 100 mm. horizontal line labeled as "no pain" at one end and "worst pain imaginable" on the other end which are given a score of 0 and 100% respectively (26). Depending on the degree of pain relief as measured by serial VAS scores results were categorized into 5 groups

Excellent: Pain relief => 80%
Good: Pain relief => 60% and < 80%
Fair: Pain relief => 40% and < 60%
Poor: Pain relief < 40%
No relief: 0% pain relief.

Straight Leg Raising Test (SLR) test indicates nerve root compression and is said to be positive when pain radiating to the lower extremity is elicitated between 30 to 70 degrees. The angle was measured using a hand held goniometer and performed according to published instructions[27]. Decrease in the angle of SLR was calculated as 70 degrees – the angle at which patients' SLR was positive[28]. With regards to the choice of outcome measure used, SLR has been shown to be reliable measure correlating with measures of self reported disability[29,30] SLR has been used successfully as outcome measures in patients with radiculopathy after lumbar transforaminal epidural steroid injections also[31]

Randomization

Sixty patients meeting the inclusion criterion were invited to participate. Thirty patients were enrolled and assigned to each group randomly using a computer-generated simple random allocation sequence. Patient randomization was done by a study nurse without knowledge of the patient, physician or other personnel.

Blinding (Masking)

The patients were blinded to group allocation and the study patients were mixed with routine treatment patients. Due to lack of personnel the physician perfoming the intervention and those involved in follow up assessments could not be blinded.

Statistical analysis

Data was recorded in Microsoft Excel and analyses were carried out using the Statistical Package for Social Sciences version 15 (SPSS Inc, Chicago, IL, U.S.A.). An intent to treat analysis was done. Data was initially analyzed descriptively, with frequencies and percentages for categorical data and means and standard deviations for continuous data. For categorical data, Chi-squared statistic and Fisher's exact test were applied while for continuous data Mann Whitney U statistic was used for comparison. Because the outcome measures of participants were recorded at 8 different time intervals, repeated measures analysis of variance with post hoc analysis was performed for comparison. A p value of less than 0.05 was considered significant.

RESULTS

Table 1: Illustrates demographic and clinical features of patients in each group

	Methylprednisolone (n=30)	Triamcinolone (n=30)	Level of significance (p value)
M:F (no. of patients)	11:19	14:16	
Mean Age in yrs (±SD)	43.6 ± 18.8	39.0 ± 13.0	0.186
Mean Body Weight in kg (±SD)	59.0 ± 8.6	59.0 ± 7.5	0.987
Number of patients with sensory deficit	5	5	
Number of patients with positive SLR	26 (14R/ 3L/ 9 bilateral)	27 (10R/ 5L/ 12 bilateral)	0.095
Mean Baseline VAS score (±SD)	74.0 ± 12.2	73.7 ± 11.6	0.914
Mean Baseline SLR (R) in degrees (±SD)	57.0 ± 9.4	50.8 ± 24.0	0.115
Mean Baseline SLR (L) in degrees (±SD)	71.7 ± 23.6	62.5 ± 23.6	0.156
Mean Baseline SBP in mm Hg(±SD)	124.2 ± 17.3	122.9 ± 9.8	0.584
Mean Baseline DBP in mm Hg (±SD)	75.9 ± 6.2	75.5 ± 7.9	0.857
Mean Baseline Heart rate/min (±SD)	76.2 ± 8.7	75.9 ± 8.2	0.927
MRI diagnosis (no. of patients)			0.249

PIVD	15	21	
Spinal Stenosis	5	4	
Spondylosis	10	5	
Affected level (no. of patients)			
L2-L3	1	0	
L3-L4	5	10	0.244
L4-L5	21	15	
L5-S1	3	5	

Majority of the patients included were between 20 to 50 years of age (49 out of 60 cases i.e. 81.6%). Male patients were outnumbered by the female patients in a ratio of 5:7. No significant statistical difference was noted in the age and sex distribution between the two groups. There was no significant difference between the two groups in the distribution of various etiologies for their low back ache and the affected intervertebral levels as diagnosed on MRI. Prolapsed intervertebral disc was the most common etiology of low back pain with 36 out of 60 cases i.e. 60% diagnosed with the condition on MRI. Because of lower number of patients with different etiologies subgroup analysis was not performed. The study group patients were also comparable with regards to the pre-enrollment clinical data (heart rate, systolic and diastolic blood pressure, neurological deficits) and baseline measurements on the outcome scales (VAS and SLR) with no significant statistical difference. (Table.1) 23 out of 26 patients (88.5%) in the methylprednisolone groups and 21 out of 27 patients (77.8%) in the triamcinolone group, with positive SLR on either or both sides showed improvements in the degree of their SLR at 4 weeks follow up with no significant difference in the number of patients showing improvement between the two groups (p value 0.582).Of note, this figure includes 2 patients each in both the groups with bilateral involvement on the SLR showing improvement only on one side. (Table 2) Mean angle at which SLR test was positive on each side was recorded for both the groups. There was significant improvement in this angle shown by both the groups at different follow up intervals when compared to the baseline as shown in the table. Since there was a significant difference in the absolute degree of SLR recorded at baseline between these two groups no intergroup comparisons were made at different follow-up intervals. However, mean improvement in the degree of SLR at 4 weeks follow-up as measured on the right and left sides respectively (calculated as 70 degrees – the angle at which patients' SLR was positive) was 23.5 ± 13.4 degrees and 27.9 ± 22.5 degrees in the methylprednisolone group and 18.4 ± 19.1 degrees and 19.4 ± 14.0 degrees in the triamcinolone groups with no significant statistical difference between the two groups (p values 0.116 and 0.347 on the right and left sides respectively). Paired samples t-test analysis showed significant improvement in pain recorded as early as 30 min in the triamcinolone group and 1 hr in the methylprednisolone group with the improvement sustaining at further follow-up intervals. In the mean VAS score recorded at 0.5 hour, 1 hour and 2 hours after the epidural injection significant difference was observed between the groups in favor of the triamcinolone group. However, after 2 hours there was no statistically significant difference observed in the VAS scores between both the groups.

Table 2: Mean values of pain score on Visual Analog Scale and degree of SLR on both sides in study groups

Time interval	VAS score (Mean ± S.D.)		Right SLR in degrees (Mean ± S.D.)		Left SLR in degrees (Mean ± S.D.)	
	Group M (n=30)	Group T (n=30)	Group M (n=23)	Group T (n=22)	Group M (n=12)	Group T (n=17)
Baseline	74.0 ± 12.2	73.7 ± 11.6	47.4 ± 12.5#	37.5 ± 8.9#	45.0 ± 13.1	43.8 ± 10.5
0.5 hour	72.7 ± 13.9	58.2 ± 18.4*#	49.1 ± 14.1	46.8 ± 12.0*	50.4 ± 17.4	50.0 ± 9.7*
1 hour	69.7 ± 15.0*	56.7 ± 16.9*#	51.7 ± 11.9*	47.1 ± 11.9*	55.4 ± 15.8*	50.0 ± 9.7*
2 hour	65.2 ± 16.6*	54.7 ± 19.1*#	53.9 ± 12.7*	46.8 ± 12.0*	55.5 ± 16.4*	51.2 ± 11.4*
16 hour	62.0 ± 16.5*	54.3 ± 18.5*	55.2 ± 12.7*	49.4 ± 14.1*	57.9 ± 13.7*	51.2 ± 11.4*
1 week	34.7 ± 15.3*	37.5 ± 21.7*	70.4 ± 13.6*	60.7 ± 20.1*	69.5 ± 11.8*	62.6 ± 15.2*
2 week	32.3 ± 13.2*	33.0 ± 17.9*	70.4 ± 13.6*	59.3 ± 19.0*	72.1 ± 13.4*	63.8 ± 16.5*
3 week	34.4 ± 12.7*	34.3 ± 17.9*	70.4 ± 13.6*	62.3 ± 19.7*	72.9 ± 14.2*	63.2 ± 16.5*
4 week	34.0 ± 13.0*	36.3 ± 18.9*	70.4 ± 13.6*	56.1 ± 19.7*	72.9 ± 14.2*	63.2 ± 16.5*

Table 3 shows distribution of patients in the two groups depending on the degree of their pain relief obtained on the Visual Analog Scale. As is evident, 13 (43%) patients in the methylprednisolone group and 12 (40%) patients in the triamcinolone group showed excellent to good degree of pain relief after the procedure. Of note, the difference in the distribution of patients between the two groups depending on the degree of pain relief was statistically insignificant (p value 0.946).

Table 3: Distribution of patients depending on the degree of pain relief as measured on Visual Analog Scale

Degree of Pain relief	Group M	Group T
Excellent	4	4
Good	9	7
Fair	11	12
Poor	5	4
No pain relief/Worsening	1	3

No significant difference was found between the two groups in the three vital physiological parameters recorded i.e. Systolic and Diastolic blood pressure and heart rate at any time interval and also within each group when compared to the base line. (Table 4).

Table 4: Mean values of different physiological parameters in the study groups at each follow-up interval

Time interval	Systolic Blood Pressure mm Hg (Mean ± SD)		Diastolic Blood pressure mm Hg (Mean ± SD)		Heart Rate per min (Mean ± SD)	
	Group M (n=30)	Group T (n=30)	Group M (n=30)	Group T (n=30)	Group M (n=30)	Group T (n=30)
0.5 hour	122.20±9.85	122.20±9.85	75.53±7.96	75.53±7.96	76.10±8.22	76.16±8.22
1 hour	122.87±11.85	123.87±11.99	76.53±7.89	77.73±7.87	76.53±7.89	76.37±8.70
2 hour	127.93±12.33	126.87±11.89	78.00±7.91	79.13±7.50	78.00±7.91	76.63±8.33
16 hour	128.60±1.97	129.60±12.47	80.07±8.06	79.87±7.5	80.07±8.06	76.70±8.42
1 week	129.59±12.65	130.47±13.02	80.47±8.69	81.03±7.73	80.47±8.69	76.63±8.31
2 week	125.93±12.28	125.93±12.28	80.47±8.69	78.93±8.53	78.60±8.68	76.77±8.29
3 week	125.87±11.77	125.87±11.77	80.47±8.69	78.93±8.53	78.60±8.68	78.93±8.53
4 week	125.83±11.77	125.87±11.77	80.47±8.69	78.93±8.53	78.60±8.68	78.93±8.53

There were no nerve root irritations or other major adverse events. Of the 60 lumbar interlaminar epidural procedures performed, there was 1 dural puncture (0.02%); however, without post-procedural headache. One patient in methylprednisolone group and two patients in the triamcinolone group complained of headache and giddiness after injection and five patients constantly complained of back pain at the site of (8.4%) injection after 4 weeks despite relief in original pain score and improvement in SLR. Of these three patients were from the triamcinolone group and two patients were from methylprednisolone group.

DISCUSSION

With negligible and temporary complications ESI are a simple, cost-effective and minimally invasive treatment for refractory low back ache not responding to conservative treatment[7,8,17,14,18]. This comparative evaluation of the efficacy and safety of lumbar interlaminar epidural steroid injections in refractory low back ache patients using two synthetic particulate steroids methylprednisolone acetate and triamcinolone acetonide as the pharmacological agents and utilizing a prospective, randomized design, demonstrated significant effectiveness with improvement in pain and function with both the steroid preparations. Both these drugs have been extensively used for epidural injections in both lumbar and cervical regions in the past[19-21] with their efficacy and safety well proven. Although pharmacological differences exist between the two steroid preparations which can potentially affect their biological efficacy no similar comparative studies have been reported in order to evaluate their relative merits. Methylprednisolone is methyl derivative while triamcinolone is fluorinated derivative of prednisolone. Both of them have negligible sodium retaining potential with their anti-inflammatory potency being comparable and is five times that of cortisol[22]. In this study, although there were significant differences in the pain scores between the two groups for initial 2 hrs, the relief was comparable at further follow-up intervals. Both the drugs demonstrated a good clinical safety profile with neither any significant effects on the vital physiological parameters nor any major post-procedural complications reported. Important differences exist in the preservatives added to each steroid preparation available commercially. Methylprednisolone acetate contains 3% polyethylene glycol and 0.9% benzyl alcohol, whereas triamcinolone acetonide contains benzyl alcohol only. Both these agents have been implicated in causing neurotoxic effects[33,34]. For epidural steroid injections, the steroids are usually diluted to decrease the concentration of benzyl alcohol and polyethylene glycol and to improve the spread of the drug [33,17]. Studies [35,17] have shown that depot preparations of particulate steroids like methylprednisolone and triamcinolone are slightly more effective than nonparticulate steroids for relief of lumbar radicular pain because of their accumulative nature[22,23], whereas non-particulate steroids are rapidly cleared from the spinal canal. However as the particulate steroids have this tendency to aggregate there is higher risk of embolism[37,38,24] after their use as compared to the nonparticulate steroids. Triamcinolone has a smaller percentage of larger aggregates than

methylprednisolone.[24] Dilution with either saline or local anesthetic did not affect the distribution of the particles of triamcinolone, but increased dilution of 80 mg/ml methylprednisolone with saline resulted in an increased proportion of larger particles.[22] This potentially increases the risk of embolization with its use. This adverse effect is however less of a concern with interlaminar lumbar steroid injection[22,24]. Based on literature review, two other studies[32,39] have been reported comparing the outcomes following epidural steroid injections using these two drugs. While Huda *et al*.[32,29] reported significantly better pain scores in patients with methylprednisolone as compared to triamcinolone; Datta *et al*.[32] reported findings similar to this study with no difference in the clinical effects of these two drugs. As both these studies utilized a caudal route of injection with large volumes of injectate, dilutional effect rather than the true pharmacological effect of the drug cannot be ruled out. One of the limitations of this study was the limited duration of follow-up after the intervention. It is important to note that lumbar epidural steroids have been conclusively proven with regards to their effectiveness in pain relief only for a short term period lasting for 3-4 weeks.[7,8,11,19,20] As the purpose of this study was mainly to compare the clinical efficacy and safety of the two steroid agents, the study was designed for a short term follow-up only. Overall period of efficacy and the need for second injection for these two steroid preparations thus could not be calculated given the study design. Another significant limitation of this study was the small sample size because of which no subgroup analysis with regards to various etiologies for the pain could be performed. Also given the lack of adequate personnel the study could not be double blinded.

CONCLUSIONS

This study confirmed the efficacy and safety of the depot preparations of methylprednisolone and triamcinolone for their use in lumbar epidural steroid injections for the treatment of refractory low back ache. No definitive conclusions however, could be made with regards to the relative efficacy of these two drugs. Further studies with larger sample sizes, utilization of different approaches and longer follow-up duration need to be conducted so as to help in formulating specific guidelines regarding the choice of steroid use.

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