

A Placebo Controlled Trial to Evaluate Effectivity of Pain Relief Using Ketamine with Epidural Steroids for Chronic Low Back Pain

Dr. Chashamjot Kaur Bawa¹, Dr. Ruchi Gupta², Dr. Lakshmi Mahajan³, Dr. Saru Singh⁴

Abstract: Introduction: Chronic low back pain being devastating in more than one way; shows physical, mental, social, economical and occupational impact on the patient and his family. Epidural steroid injections are the cornerstone of treatment leading to markedly improved quality of life and satisfactory pain relief. Since ketamine has been used as an adjunct for various chronic pain conditions, its efficacy with epidural steroids needs evaluation. Material & Methods: A study was conducted in 60 patients with chronic low back ache with or without leg radiation lasting for more than three months unresponsive to conservative treatment. These patients were randomly allocated into two groups of 30 each and given epidural steroids with additional 30mg ketamine in group A while Group B given steroids with normal saline as placebo under fluoroscopic guidance and epidurographic confirmation. Pain relief in terms of reduction of pain scores (VAS), improvement of quality of life (QOL) (Roland morrisdisability index, Oswestry and depression score) and patient satisfaction score (NASS) when followed at two weekly intervals upto 3 months. Results: Pain relief & Quality of life scores showed highly significant improvement in both the groups compared to baseline with no difference on intergroup comparison, thereby indicating both were equally effective. The patient satisfaction was assessed with NASSPSI, showing 60% patients were completely satisfied post block in both groups. Conclusion: Thus to conclude ketamine's advantage on long term basis in prolonging pain relief from LESI warrants further research.

Keywords: epidural, pain, ketamine, steroids

1. Introduction

Chronic low back pain is defined as a pain that persists beyond the period of healing i.e. 3 months. It has become a leading cause of disability as it interferes with quality of life and work performance, and is the most common reason for medical consultations. Few cases of back pain are due to specific causes; most cases are non-specific.

Treatment of chronic low back pain involves participation of physician, psychologist, orthopaedician and anesthesiologists in evaluating various generators of pain and treating them individually. Various modalities like pharmacotherapy, physiotherapy, cognitive behavioral therapy, TENS and recently epidural steroid injections have been researched upon with no conclusive data on the most effective treatment.

Epidural Steroid injections (ESI) are now frequently performed interventions that provide immediate and significant pain reduction with earlier return to work and rehabilitation. The rationale for ESI appears to be based on the anti-inflammatory action of steroids.¹ The analgesic effect of corticosteroid is most likely related to the following mechanisms: a) Inhibition of PLA2 and inflammation, b) inhibition of neural transmission in nociceptive C fibers and c) reduction of capillary permeability d) decrease in intraneural oedema and venous congestion thereby reducing ischaemia and improving pain. However, the long term efficacy of epidural steroids remain a matter of debate.

Also, intractable backaches arising out of intricate neuronal circuits and multiple pathophysiologicals may result in failure of epidural steroids when given alone. Such intractable pains lead anesthesiologists to device adjuvants like hyaluronidase, ketamine, clonidine etc for providing superior

pain relief and functional status to steroids alone with no clear consensus.

Ketamine by its NMDA receptor antagonism and weak opioid receptor action has been used keenly in chronic persistent pains as an adjuvant. This study evaluates the efficacy of ketamine with LESI (lumbar epidural steroid injection) for prolonging pain relief in chronic low back pain.

2. Materials and Methods

A prospective randomized placebo controlled blinded study was proposed to be conducted on 60 patients attending the pain clinic at a tertiary care centre after obtaining approval from hospital ethics committee and a prior written informed consent.

Patients in the age group 18 to 70 years, history of low backache with or without radiculitis of minimum 3 months duration and no relief with conservative treatment were included in the study.

The exclusion criterion taken for the study- Contraindications to epidural anaesthesia, a known history of allergy to local anaesthetics, psychiatric history, patients with spinal cord deformities, history of previous LESI or spinal surgery, cauda equina syndrome, epidural lipomatosis, Opioid habituation and pregnancy.

The patients selected were randomly allocated into two groups of 30 each and given triamcinalone 40 mg, preservative free ketamine 30 mg (0.6 ml) made upto 6ml solution with 0.25% bupivacaine in group A and normal saline (0.6 ml) as placebo in group B.

It was a double blind study. The envelopes assigning the patients into groups were opened by the anesthesiologist performing the procedure who did not participate in the study. Similarly, the pre procedural and post procedural assessment was done by anesthesiologists who were blinded to the patient's assignment groups.

All patients included in the study were subjected to pre anaesthetic check-up and investigations if required were done. The patients were evaluated for their baseline VAS scores and quality of life scores.

Oral midazolam tab 7.5 mg or i/v midazolam 0.03-0.04 mg/kg was given 30 minutes before the procedure to allay anxiety. Patients were then shifted to OT and standard monitoring applied. Under all sterile conditions, lumbar interlaminar epidural block was performed in prone position according to site of lesion using fluoroscopic guidance with 18G Touhy's needle. After satisfactory needle placement as elicited by loss of resistance technique and dorsal spread by dye confirmation, drugs were given according to group allocation. Fluoroscopic findings were observed for the level of spread as well as ventral, dorsal and nerve root filling using contrast injection.

Patients were followed up at 2 weeks interval for period of three months for VAS scores. Also, the improvement in Oswestry disability score, Rolland Morris disability score, and depression scores were noted at the end of 3 months.

Patients were also asked to report any side effects, particularly those related to ketamine like blurred vision, confusion, drowsiness, increased blood pressure or heart rate, mental or mood changes, nausea, nightmares, vomiting, delirium etc.

The data thus compiled was compared & analysed statistically.

3. Observations

The sample size was determined to be adequate using desired power of 0.82 and α error of 0.05. The primary analysis of power was done with mean VAS scores in the two groups. Statistical analysis was done with chi-square test for nonparametric data. For parametric data, intragroup comparison was done with paired t test and intergroup comparison with student t test. Both the groups were comparable in terms of mean age, sex, duration of symptom, MRI findings and pre – procedure scores. (Table 1- demographics).

Table 1: Demographics

	Group A	Group B
Age (in years)	56.33±14.869	49.5 ±14.115
Sex		
Male	18	13
Female	12	17
MRI		
Disc Degeneration	3	6
Facet Arthropathy	5	9
Spinal Stenosis	12	12
Disc Bulging	18	20
Annular Tear	12	6

Chi-square test; Data in no. of patients; NS-Non significant ($p>0.05$)

Also, the periprocedural epidurographic findings in both the groups were comparable with respect to ventral, dorsal and nerve root findings.

Table 2: VAS Score and Quality Of Life Score

VAS SCORE					
	GROUP A (ketamine)	w.r.t PP	GROUP B (normal saline)	w.r.t PP	INTERGROUP ANALYSIS
Pre pr (PP)	80±12.594		79.83±16.108		NS
Post pr	34±20.611	HS	35.67±21.725	HS	NS
At 2 wks	32.33±19.772	HS	29.43±17.714	HS	NS
At 4 wks	28.5±20.475	HS	26.43±18.962	HS	NS
At 6 wks	26.33±22.702	HS	28.73±20.625	HS	NS
At 8 wks	27.67±22.657	HS	29.40±22.340	HS	NS
At 10 wks	27.67±22.922	HS	30.73±24.295	HS	NS
At 12 wks	28.00±22.152	HS	32.90±26.101	HS	NS
OSWESTRY SCORE					
		w.r.t. PP		w.r.t. PP	INTERGROUP ANALYSIS
Pre pr (PP)	55.47±14.649		56.27±6.314		NS
At 12 wks	30.23±12.795	HS	34.33±16.791	HS	NS
DEPRESSION SCORE					
Pre pr (PP)	5.73±3.667		6.27±3.012		NS
At 12 wks	3.37±2.748	HS	3.97±2.869	HS	NS
ROLLAND MORRIS SCORE					
	GROUP A	w.r.t. PP	GROUP B	w.r.t. PP	INTERGROUP ANALYSIS
Pre pr (PP)	15.07±5.884		15.37±5.391		NS
At 12 wks	8.60±5.014	HS	8.67±5.268	HS	NS

Intra – group comparison- paired T-test, intergroup comparison- Student T-test; Data are Mean±SD; HS – Highly Significant (p value <0.001), NS-Insignificant ($p>0.05$), PP- Pre procedure

On each follow up when mean VAS score, Rolland Morris scores, Oswestry scores and depression scores were compared with the pre procedure (PP) values in each group;

a highly significant reduction noted in both the groups with insignificant difference on intergroup comparison (Table 2).

No major complication was seen in both the groups. However in group A, 20 out of 30 patients in Group A experienced short lasting delusions 45 ± 10 min post the block which may be due to the systemic absorption of ketamine through the epidural space and intergroup comparison being statistically highly significant.

4. Discussion

Chronic low back pain arising out of mechanical causes has become a challenge to pain physicians with various pharmacological, physical, psychological and interventional modalities being applied, some successfully while others fail. Epidural steroid injections have emerged as a very fruitful intervention causing immediate anti-inflammation at the site of nociception resulting in pain relief and rendering a better quality of life.

However, short term relief accompanied by side effects of steroids have limited its use in repeated doses when required. Various analgesic and fibrolytic adjuvants have an advantage of prolonging pain relief due to ESI, thus commanding their use in severe pains.

In this study ketamine's active enantiomer S(+) ketamine has been used epidurally in a single shot dose of 30mg. Compared with racemic ketamine, the S (+)-enantiomer has a two-fold higher analgesic potency and less neurotoxic effects. It is commercially available without preservatives.² Many studies have used comparative doses of 0.3 mg/kg to 0.5 mg/kg epidurally with or without opioids for perioperative as well as chronic pain, but a single bolus dose of 30mg gave adequate long lasting analgesia with minimal side effects.³⁻⁶ Hence, a single dose of 30mg ketamine was selected for this study.

The VAS scores did not improve significantly by addition of ketamine to epidural steroids, which can be explained by the slow binding of ketamine to NMDA receptors.⁷ Hence, a single bolus injection, as performed in the present protocol, most likely did not achieve complete receptor saturation to provide additional analgesia over and above the anti-inflammatory action of steroid.

Also, epidural ketamine gets distributed rapidly into the systemic circulation after administration, which may have caused inadequate response of single dose ketamine in chronic low back ache. This is contrary to the studies conducted by Amr YM in 2011 where addition of ketamine in a bolus dose of 30mg to 80 mg triamcinalone produced highly significant reduction in VAS with one year follow up, may be due to different study design.^{8,9} Also, improved results have been seen if ketamine was repeated given through epidural catheters.¹⁰

The quality of life scores are an integral part of pain assessment because physical as well as mental well being achieved through freedom from pain helps the patient to return to their daily normal activity. The Oswestry disability index (ODI) scores, Roland Morris scores and depression

scores showed statistically significant improvement in both the groups in our study with no intergroup difference. This could be because additionally, physiotherapy was advised to all patients, thus improving the physical and mental status of the patient.¹¹

There were some limitations in our study. Majority of patients suffered "delusions" in the ketamine group, although short lasting (45 ± 10 min), hence, blinding could not be achieved by the post-procedural assessors. Also the long term efficacy of ketamine in chronic low back ache could not be evaluated due to short period of follow up (3 months only).

Thus to conclude, ketamine serves as an adjuvant to epidural steroids for pain relief in chronic low back pain. However, its potential over epidural steroids and its long term efficacy as an epidural adjunct is a matter of research.

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