

The adjuvant effect of Hyaluronidase to Lumbar Interlaminar Epidural Steroid injection in Central Spinal Stenosis: A Randomized Controlled Trial.

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Abstract:

Introduction: Lumbar spinal canal stenosis is a common cause of lower extremity and low back pain. Interlaminar epidural steroid injection is commonly used for pain relief in spinal stenosis. In this study we evaluated the adjuvant effect of hyaluronidase to epidural steroid in increasing duration of pain relief and functional outcome in patients with central spinal stenosis.

Material and methods: In this study 80 patients were randomly allocated to two groups. Group D received lumbar interlaminar epidural injection with 5ml Bupivacaine (0.25%), 2ml methylprednisolone (40mg/ml), 1 ml normal saline. Group DH received 5ml Bupivacaine (0.25%), 2ml methylprednisolone (40mg/ml), 1 ml hyaluronidase 1500 IU. The effects were evaluated by Numeric pain rating scale (NPS) and Oswestry disability index (ODI) at 2, 6 and 12 weeks after intervention.

Results: Result of 30 patients in each group was assessed. Pain relief and improvement in ODI was observed in both groups 2 weeks after injection. Group DH had significantly better pain relief and ODI improvement as compared to group D 12 weeks after intervention. 40% patients in group DH had more than 50% pain relief after 12 weeks as compared to 3% patients in group D.

Conclusion: Addition of hyaluronidase to lumbar interlaminar epidural injection of methylprednisolone improves its efficacy by increasing the duration of pain relief and functional improvement.

Keywords: Hyaluronidase, Interlaminar Epidural Injection, Steroid, Central spinal stenosis.

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I. Introduction

Low backache is common cause of disability in India. Lumbar canal stenosis is a common cause of lower extremity and low back pain leading to neuropathy and disability. Canal stenosis is defined as narrowing of spinal canal leading to encroachment of neural structures by surrounding tissues¹.

Multiple modalities of treatment including decompressive surgery with or without fusion and conservative treatments as analgesics, nonsteroidal anti-inflammatory drugs, orthosis, rehabilitation, physical therapy, exercise, heat and cold, transcutaneous electrical nerve stimulation, ultrasound and epidural steroids have been recommended in the treatment of symptomatic central spinal stenosis.²

Lumbar interlaminar epidural injection of local anesthetic with steroid is beneficial in patients with lumbar central spinal stenosis³. It is a commonly performed nonsurgical intervention that can bring symptomatic and functional improvement in patients of central spinal stenosis. Primary symptoms can be relieved by epidural steroids thus reducing the need of surgery. It is the only option in patients who are not candidates for surgery or after failure of conservative treatments and surgery. Steroids relieves the radiculopathy and pain by its anti inflammatory effect through reduction of prostaglandins and phospholipases, increases micro-circulation and also reduces of edema surrounding nerve roots.⁴ But the duration of analgesia provided by epidural steroid injection differs among patients and is short lived.

Hyaluronidase has been used as adjuvant to epidural steroid to increase its efficacy and duration of action by reducing the fibrosis and edema in tissues and lysing the adhesions thus facilitating the spread of injected steroid.⁵ Studies have been done to determine additional effect of hyaluronidase in interlaminar epidural steroid injection for failed back surgery syndrome⁶ and low back pain and sciatica⁷ but there is paucity of literature regarding its adjuvant effect in central canal stenosis.

In this context this study was done to evaluate adjuvant effect of hyaluronidase to interlaminar lumbar epidural steroid injections in increasing the pain relief duration and functional improvement in patients with lumbar central canal stenosis.

II. Material and methods

Study Design: Prospective randomised controlled clinical study.

Study Location: This study was conducted at tertiary care teaching hospital in department of Anaesthesia.

Study Duration: January 2016 to December 2017.

Inclusion criteria: Patients over 30 years old with MRI confirmed central lumbar canal stenosis suffering from chronic lower leg and back pain of at least 6 months duration were included in study.

Exclusion criteria: Patients with foraminal stenosis without central spinal stenosis, uncooperative, psychiatric, coagulopathy, localized skin sepsis, history of allergy or adverse reaction to local anaesthetic, steroid or hyaluronidase were excluded from study.

Procedure methodology :After approval from ethical and scientific committee of hospital and after history, clinical examination, informed and written consent 80 patients were randomly divided by computer generated random allocation technique into two groups named D and DH based on drugs injected. After securing I.V. line and connecting monitors Epidural injection was given under all aseptic precautions by 18 G tuohy needle after local infiltration with 2ml of 2% lignocaine, in sitting position using Interlaminar approach at L4-L5 inter space or at the space corresponding with maximum stenosis using loss of resistance technique . After confirming the correct position of needle by fluoroscopy epidural injections were administered as follows:

Group D – received 5ml Bupivacaine 0.25%, 2ml methylprednisolone (Depo medrol 40mg/ml), 1 ml normal saline

Group DH- received 5ml Bupivacaine 0.25%, 2ml methylprednisolone (Depo medrol 40mg/ml), 1 ml hyaluronidase 1500 IU

To maintain double blinding the injectate was prepared by nurse and the intervention specialist who performed all epidurals was unaware about group of patients. Follow up of patients was conducted by another specialist who was blinded to the treatment received. To avoid confounding factors patients were maintained on same set of oral medicines.

Outcome assessment: 60 patients were included in this analysis .Outcome assessment of intervention was done utilising Numeric pain rating scale (NPS) and Oswestry Disability Index (ODI) ⁸ at pre injection and 2, 6 and 12 weeks post injection to determine long term effectiveness of hyaluronidase in reducing pain and disability. Patients who showed more than 50% reduction in pain based on NPS values at 6 weeks and 12 weeks after the intervention were calculated.

Statistical analysis: Statistical analysis of age, weight, height and comparison of mean NPS and ODI between group D and DH was done using independent T test. For gender Chi- square test was used. Comparison of mean NPS and ODI within each group for follow up was done by Repeated ANOVA (analysis of variance).

III. Results

Out of 80 patients that were enrolled for study 8 patients were excluded after 6 weeks and of remaining 72 patients, 12 patients were excluded at 12 weeks after injection due to loss of follow up. So 60 patients participated in study till 12 weeks after injection.

All groups were similar demographically and there was no significant difference with respect to age, sex, and weight, height and duration of pain (Table 1).

Table 1: Demographic data

Variable		Group D (n=30)	Group DH (n=30)	P value	Significance (S/NS)
Age (years)	Mean ± SD	52 ± 8.6	50 ± 9.2	0.54	NS
Sex	Male [n (%)]	14(47%)	15(50%)	0.79	NS
	Female [n (%)]	16(53%)	15 (50%)		
Weight (Kg)	Mean ± SD	58 ± 8.3	59 ± 7.6	0.73	NS
Height (cm)	Mean ± SD	157 ± 8.1	158 ± 8.2	0.75	NS
Duration of pain(months)	Mean ± SD	7.83± 3.1	8.03 ± 2.9	0.88	NS

S- Significant NS- Non significant

Table 2: Comparison of mean NPS in each group

NPS	Group D(n=30) Mean ± SD	Group DH(n=30) Mean ± SD	P value
Preinjection	7.17 ± 2.1	7.30± 2.2	0.86
After 2 wks	3.53± 1.8	3.70± 2.01	0.80
After 6 wks	4.13± 1.6	3.53± 1.8	0.34
After 12 wks	4.77± 2.0	3.07± 1.6	0.019
P value	0.04	0.036	

P value <0.05 - Significant

NPS was comparable in both the groups before injection ($p>0.05$). 2 weeks after injection patients in both the groups had pain relief. In group D pain relief did not improve further after 6 weeks whereas in group DH NPS decreased further after 6 and 12 weeks. There was a statistically significant difference ($p<0.05$) in NPS between both groups after 12 weeks where group DH had significantly better pain relief as compared to group D.

Table 3: Comparison of mean ODI in each group

ODI	Group D(n=30) Mean \pm SD	Group DH(n=30) Mean \pm SD	P value
Preinjection	24.67 \pm 6.4	23.43 \pm 7.3	0.62
After 2 wks	13.87 \pm 7.2	14.27 \pm 6.9	0.88
After 6 wks	14.70 \pm 7.4	12.97 \pm 7.6	0.53
After 12 wks	15.93 \pm 6.8	10.57 \pm 5.9	0.033
P value	0.031	0.023	

P value <0.05 – Significant

ODI was comparable in both groups preinjection ($p>0.05$). In both groups ODI decreased at 2 weeks. In group D ODI gradually increased at 6 and 12 weeks after intervention, whereas in group DH there was continuous decrease of ODI. There was statistically significant difference ($p<0.05$) in mean ODI between both groups 12 weeks after intervention. Group DH had significantly lower mean ODI after 12 weeks which implies that patients in group DH had significantly better functional improvement in long term as compared to group D.

Table 4: Pain relief > 50 % measured by NPS

	Group D [n (%)]	Group DH [n (%)]
At 6 wks	10 (33)	15 (50)
At 12 wks	1 (3)	12 (40)

To evaluate long term effectiveness of hyaluronidase, patients who had more than 50% pain relief (measured by NPS) after 6 and 12 weeks were calculated in both groups. After 6 weeks 10 patients in group D and 15 in group DH had $>50\%$ pain relief. After 12 weeks 12 patients(40%) of group DH and only one (3%) patient in group D showed $>50\%$ pain relief.

IV. Discussion

This study aimed to analyze the adjuvant effect of hyaluronidase to lumbar interlaminar epidural steroid injection in central spinal stenosis. We observed that addition of hyaluronidase increased the efficacy of epidural steroid in relieving pain, prolonged the duration of pain relief and provided more functional improvement.

Multiple studies have evaluated the role of epidural local anaesthetic and opiod in relieving lower extremity and low back pain caused by spinal stenosis. Kenneth Botwin et al studied fluoroscopically guided caudal epidural steroid injections in degenerative lumbar spinal stenosis and found that steroid reduce radicular pain and improve standing and walking tolerance⁹. Steroids are effective in pain relief but their long term effect is controversial. Laxmaiah et al in their 2 year follow up study concluded that patients may be benefitted from receiving lumbar interlaminar injections with or without steroids for lumbar central spinal stenosis³. Carette et al conducted a randomized controlled study on patients with radiculopathy and concluded that although steroids were effective in relieving early stage pain, they did not have long-term benefits¹⁰.

In this regard hyaluronidase has been used by multiple researchers to evaluate its effectiveness in increasing the efficacy and duration of pain relief of epidural steroid. Sang –Bong Ko et al studied the effectiveness of hyaluronidase in Selective Nerve Root Block (SNRB) of radiculopathy and found that the rebound pain that occurs 2-4 weeks after the injection can be reduced when hyaluronidase is added to steroid¹¹. Paupak Rahimzadeh et al reported that addition of hyaluronidase to transforaminal epidural steroid injection was effective in the management of chronic low back pain in patients with failed back surgery syndrome over a period of 4 weeks⁶. Sang BK et al reported the long term effectiveness of interlaminar epidural injection of hyaluronidase and triamcinolone to reduce pain and improve function than injection with triamcinolone or hyaluronidase alone in patients with Failed back surgery syndrome¹². Similar results were obtained in patients of low back pain and sciatica 8 weeks after interlaminar epidural injection of hyaluronidase with steroid by Sang BK et al⁷.

Results of our study correlate with above studies where group DH showed better long term pain relief over 12 weeks and reduction in disability. In group DH after 12 weeks 40% of patients had $> 50\%$ improvement in pain relief measured by NPS as compared to 3% in group D. This prolonged effect and increased effectiveness of steroid is due to reduction of edema and fibrolytic property of hyaluronidase which increases the diffusion of steroid thus increasing its efficacy.

Limitation of present study was small number of study patients and limited duration of follow up. Hence the preliminary results of this study should be confirmed by a large randomized clinical trial with a long term follow up.

V. Conclusion

From the study result it is suggested that addition of hyaluronidase to lumbar interlaminar epidural injection of methylprednisolone improves its efficacy by increasing the duration of pain relief and functional improvement in patients with central spinal stenosis.

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