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Original Article

Effect of Transforaminal Steroid Injection on Inflammatory Process in Lumbar Disc Herniation – Functional and Laboratory Assessment

Satish M Bobade[1], Vikrant Dhopade[2], Ambarish Mathesul[3], Amar Karale[4], Ajay Chandanwale[5]

[1]Associate Professor, Department of Orthopaedics, Government Medical College and Hospital, Baramati, Pune, Maharashtra, India, [2]Assistant Professor, Department of Orthopaedics, Government Medical College and Hospital, Baramati, Pune, Maharashtra, India, [3]Associate Professor, Department of Orthopaedics, B. J. Government Medical College, Sassoon General Hospitals, Pune, Maharashtra, India, [4]Senior Resident, Department of Orthopaedics, B. J. Government Medical College, Sassoon General Hospitals, Pune, Maharashtra, India, [5]Dean and Joint Director, DMER, Maharashtra, India

Abstract

Background: Lumbar disc herniation is major cause of low back pain with lower limb radiculopathy. Lumbar radiculopathy is the result of compression or inflammation or both, of the nerve roots exiting the spinal column. Epidural and transforaminal steroid injection is widely used for treatment of low back pain and lower extremity pain associated with lumbar disc herniation for pain relief. Steroid is administered through the injections and is thought to be integral in decreasing inflammation around the affected nerve tissue [4], hence leading to a reduction in pain. The purpose of this study was to evaluate the effect of transforaminal steroid injection over inflammatory markers such as ESR and CRP, which may demonstrate its effect over inflammation in lumbar disc herniation and also assess functional outcome measured by the Roland–Morris Disability Questionnaire and Oswestry Disability Index.

Materials and Methods: This prospective study enrolled 30 patients (male and female) who were selected with set inclusion and exclusion criteria. Serum ESR and serum CRP were assessed as markers of inflammation, functional activity was assessed by Rolland–Morris and Oswestry Disability Index scoring system. Comparison of initial (pre-procedure) and serial ESR and CRP level was done, and pre-procedure and post-procedure day 1, 2nd month, 6th week, 12 week, and then 6 months, which was done. Unpaired t- test was used for collected data.

Results: Sample size was of thirty patients. Mean age of our sample is 45 (maximum being 78 and minimum 26 years). Mean serum ESR of sample was 24.8 (maximum being 42 and minimum 12). On Follow up measurement post TFESI, Mean values were 23.4 on ppd (post-procedure day) 1, 21.5 on ppd 2 weeks, 19.9 on ppd 6 weeks and 12 weeks, and 21.2 after 6 months. On paired t-test, p value at each fallow-up was not statistically significant. Mean serum CRP of sample was 2.54 at start of study (maximum being 4.6 and minimum being 0.6). Post-TFESI mean value was 2.21 at post-operative day 1, 2.14 at post-operative 2 weeks, 2.14 at 6 weeks, 1.94 at 12 weeks, and 2.02 after 6 months. On applying paired *t* test, change in each level compare to pre-operative was not statistically significant. Functional assessment was also studied and documented.

Conclusion: This study did not reveal significant fall in serum ESR and CRP level following transforaminal steroid injection (TFSI), but showed statistically significant clinical improvement assessed by ODI and RMDQ. This study shows significant improvement in OSI and RMDQ, post-transforaminal steroid injection. As per this study, TFSI is effective tool for non-surgical management of disc radiculopathy.

Key words: Lumbar disc herniation, Transforaminal steroid injection, ESR, CRP

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INTRODUCTION

Lumbar disc herniation is major cause of low back pain with lower limb radiculopathy. Lumbar radiculopathy is the result of compression or inflammation or both of the nerve roots exiting the spinal column.[1] The causes and pathophysiology of back pain and acute radiculopathy

Corresponding Author: Vikrant Dhopade, Department of Orthopaedics, GMC Baramati Campus, Ground Floor, MIDC Area, Baramati – 413133.

remain unclear. The most common causes being compression of the nerve root by protruded disc, also several studies have identified inflammatory mediators (phospholipase A2, prostaglandin E2, leukotrienes, nitric oxide, immunoglobulins, and pro-inflammatory cytokines such as interleukin [IL]-1alpha, IL-1beta, IL-6, and tumor necrosis factor alpha [TNF-alpha]) and autoimmune reaction (macrophages expressing IL-1beta and intercellular adhesion molecules) as a cause**.** An appealing hypothesis is that the leakage of these agents may produce an excitation and irritation of the nociceptors, a direct neural injury, a nerve inflammation, or an enhancement of sensitization to other pain-producing substances (such as bradykinin), leading to the nerve root pain so inflammation plays a major role in radiculopathy.[2,3] Once inflammation has been established, the nerves become exquisitely sensitive to pressure, producing prolonged, and pain-generating discharge with either gentle manipulation or pressure.[4] Such local inflammation is caused by inflammatory mediators such as interleukin-6 produced by macrophages and monocytes at the inflammatory site. High concentrations of inflammatory mediators may cause a systemic inflammatory reaction.[2,5,6] Therefore, it is believed that the levels of high-sensitivity C-reactive protein (hsCRP) are increased by low back pain. Laboratory measurement of acute phase protein is a valuable indicator of the presence and extent of inflammation and its response to treatment. Among acute phase proteins, C-reactive protein is the first to appear. It is a sensitive systemic marker of inflammation and tissue damage[5] and it also appears 6–8 h after infection. Another marker of inflammation is the erythrocyte sedimentation rate (ESR), a common hematology test that tracks the rate of red blood cell precipitation for 1 h. There are several reports in the literature regarding hsCRP and ESR levels in patients with acute and chronic lumbar radiculopathy pain.[7,8]

Epidural and transforaminal steroid injection is widely used for treatment of low back pain and lower extremity pain associated with Lumbar disc herniation for pain relief. Steroid is administered through the injections and is thought to be integral in decreasing inflammation around the affected nerve tissue,[4] hence leading to a reduction in pain.

The purpose of this study was to evaluate the effect of transforaminal steroid injection over inflammatory markers such as ESR and CRP, which may demonstrate its effect over inflammation in lumbar disc herniation. This study also aims to assess the efficacy of transforaminal epidural steroid injection in patients using pain scales. Pain is major symptom of inflammation. Hence, its variation with treatment may hint at effect over inflammation in disc herniation.

MATERIALS AND METHODS

This was a prospective and single-center study. The study was reviewed and approved by the Institutional Ethical Committee. Information about the study was given comprehensively, both orally and in written form, to the patients. Accordingly, all patients gave their written informed consent before their inclusion into the study.

The study was conducted at a tertiary well-equipped hospital (C-ARM, MRI (Magnetic Resonance Imaging) and Laboratory Facility). The study enrolled 30 patients who met the inclusion criteria.

The inclusion criteria were as follows – all patients above age of 20 years with MRI proven lumbar disc herniation with history of back pain with radiculopathy without sensory motor deficit.

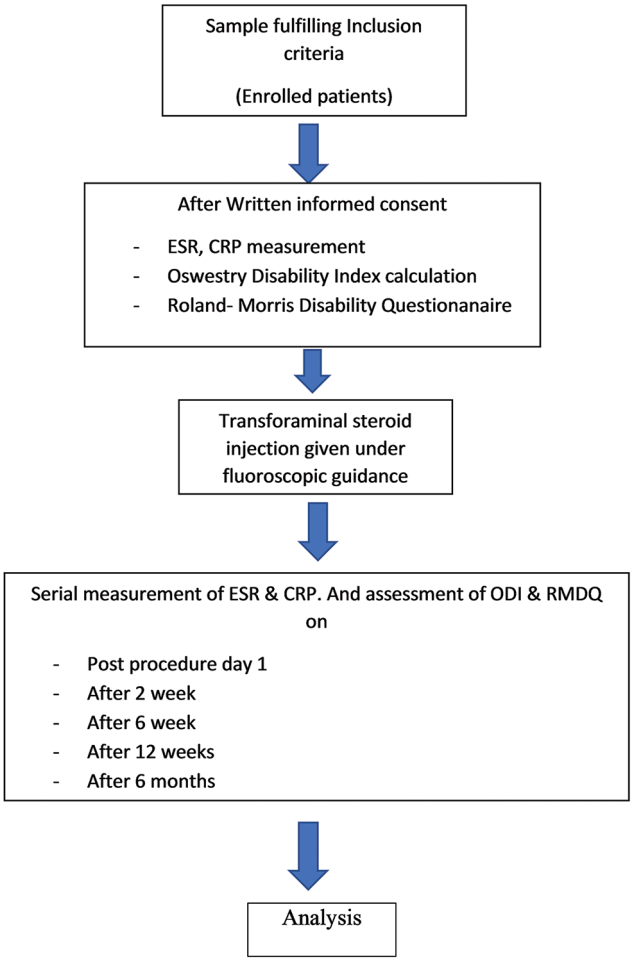
The exclusion criteria were as follows acute symptoms due to infection, compression fracture, malignancy, inflammatory diseases including rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, Reiter disease, etc., use of steroids. Body temperature > 36.5°C. Pregnancy and bleeding disorder.

All consenting individuals were enrolled into the study. The pre-determined protocol was used to either include or exclude consented patients from the study. MRI was conducted of all patients. To rule out other systemic inflammation USG abdomen pelvis, urine analysis and chest radiographs were done. Functional assessment of patients was done by Rolland–Morris Disability Questionnaire (RMDQ) and Oswestry Disability Index (ODI) scales provided to patients in vernacular languages. Serum ESR (Erythrocyte Sedimentation Rate) and CRP (C-Reactive Protein) level were the inflammatory markers which were done in the hospital, which was measured 1 day before procedure.

Enrolled patients were then given transforaminal steroid injection under fluoroscopic guidance, a single transforaminal epidural 40 mg triamcinolone acetonide injection along with 1% of lidocaine was given. The patient was monitored for an hour post-procedure.

Follow-up of such patients was done at next day, 2nd week, 6th week, 12 week, and then 6 months. On every visit, ESR and CRP counts were done and documented. Similarly, patients were asked to fill up both questionaries. At the end of 6 months comparison of initial (pre procedure) and serial ESR, CRP level was done, and functional activity was assessed by Rolland–Morris and Oswestry Disability Index scoring system.

Study Method



RESULTS

In this prospective study, 30 patients with back pain with radiculopathy were included in the study. Serial ESR and CRP measurements done. Minor reduction in its values occurred in patients, but no statistically significant difference was found among pre-operative levels and post-operative level.

Unpaired *t*-test was used for collected data.

Sample size was of 30 patients. 63% Female And 37% Male. Mean age of our sample was 45, (maximum being 78 and minimum 26 years) [Table 1 and Figures 1 and 2]. All patients underwent procedure of single TFESI (transforaminal epidural steroid injection) under fluoroscopic guidance, 40 mg triamcinolone acetonide along with 1% of lidocaine was used.

Mean serum ESR of sample was 24.8.(maximum being 42 and minimum 12). On Follow up measurement post

Table 1: Age in years

Age in years	
Mean	45.2
Standard error of mean	1.02
Standard deviation	10.106
Minimum	26
Maximum	78

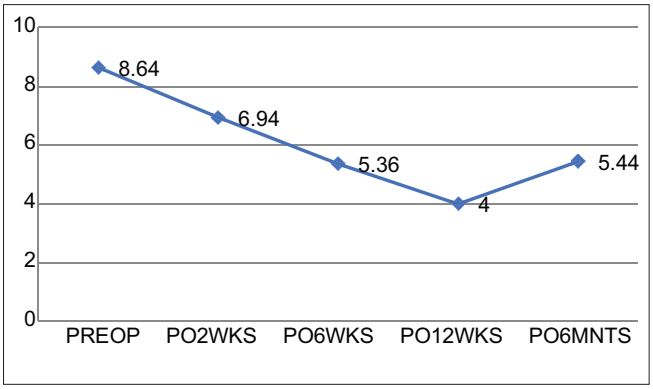


Figure 1: Gender distribution of study sample

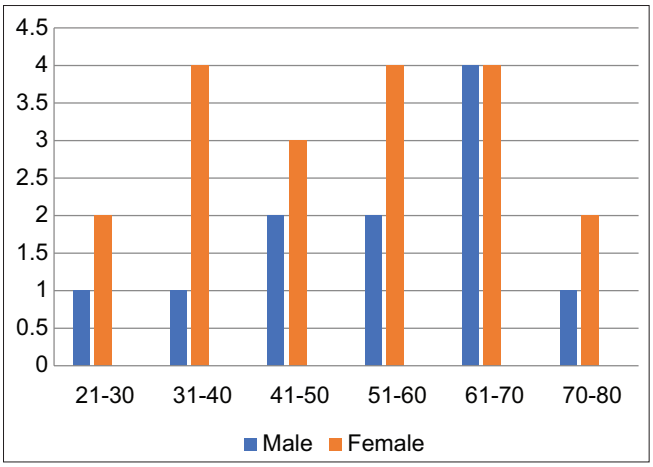


Figure 2: Age distribution of study sample

TFESI, Mean values were 23.4 on PPD (post-procedure day) 1, 21.5 on PPD 2weeks, 19.9 on PPD 6 weeks and 12 weeks, and 21.2 after 6 months. On paired *t* test, *P* value at each fallow-up was not statistically significant (Figures 3 and 5 and Table 2].

Mean serum CRP of sample was 2.54 at start of study (maximum being 4.6 and minimum being 0.6). Post-TFESI mean value was 2.21 at PPD 1, 2.14 at PPD 2 weeks, 2.14 at 6 weeks, 1.94 at 12 weeks, and 2.02 after 6 months. On applying paired t-test ,change in each level compare to pre-operative was not statistically significant [Figures 4 and 6 and Table 3].

Our study had comparable results with some studies in the literature which also suggests that there is no statistically

significant change in serum ESR, CRP level in response to transforaminal epidural steroid injection.

Significant improvement occurs in ODI and RMDQ over 3 months (Figures 7 and 8 and Tables 4 and 5).

Statistically significant difference found, hence concluding pain and general disability decreased after transforaminal steroid injection.

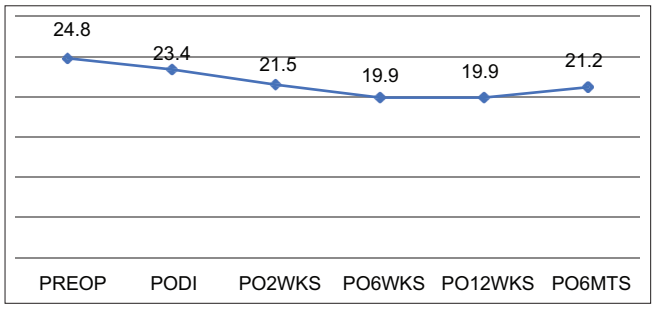


Figure 3: Analysis of serum ESR

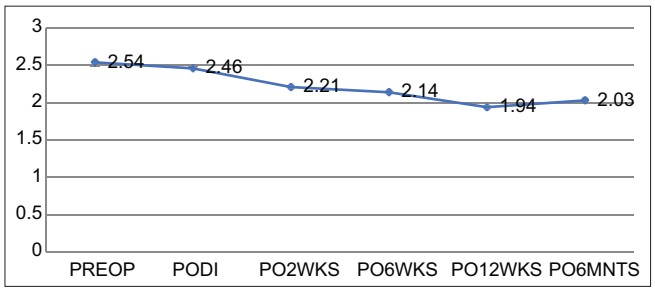


Figure 4: Analysis of Serum CRP (mg/l)

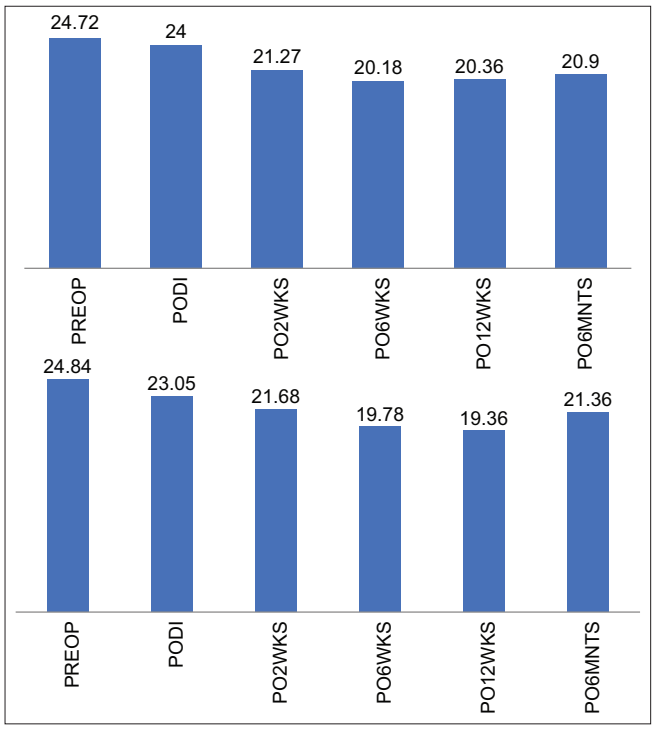


Figure 5: Assessment of ESR (male and female)

DISCUSSION

Low back pain with radiculopathy due to disc herniation has now become a real rehabilitation and management challenge in our society. Herniated lumber disc is the most common cause of radicular pain.

The pathophysiology of disc protrusion associated with low back pain with radiculopathy is incompletely understood.[9]

Table 2: Assessment of ESR

Comparison test	Mean difference	*P* value	Significant
Pre-injection versus post-operative day 1	1.4	0.030505	No
Pre-injection versus post-operative 2 weeks	3.26	0.105154	No
Pre-injection versus post-operative 6 weeks	4.83	0.019438	No
Pre-injection versus post-operative 12 weeks	5.06	0.01223	No
Pre-injection versus post-operative 6 months	3.6	0.08143	No

PPD: Post-procedure day

Table 3: Assessment of CRP

Comparison test	Mean difference	*P* value	Significant
Pre-injection versus post-operative day 1	0.08	0.7349	No
Pre-injection versus post-operative 2 weeks	0.33	0.1514	No
Pre-injection versus post-operative 6 weeks	0.41	0.0685	No
Pre-injection versus post-operative 12 weeks	0.62	0.0051	No
Pre-injection versus post-operative 6 months	0.51	0.0184	No

Table 4: Analysis of ODI

Comparison test	Mean difference	*P* value	Significant
Pre-injection versus post-operative 2 weeks	3.6	0.2227	No
Pre-injection versus post-operative 6 weeks	7.73	0.001	Yes
Pre-injection versus post-operative 12 weeks	11.46	0.0016	Yes
Pre-injection versus post-operative 6 months	4.9	0.0928	No

Table 5: Analysis of RMDQ

Comparison test	Mean difference	*P* value	Significant
Pre-injection versus post-operative 2 weeks	1.7	0.1104	No
Pre-injection versus post-operative 6 weeks	3.2	0.001	Yes
Pre-injection versus post-operative 12 weeks	4.6	1.1805	No
Pre-injection versus post-operative 6 months	3.1	0.001	Yes

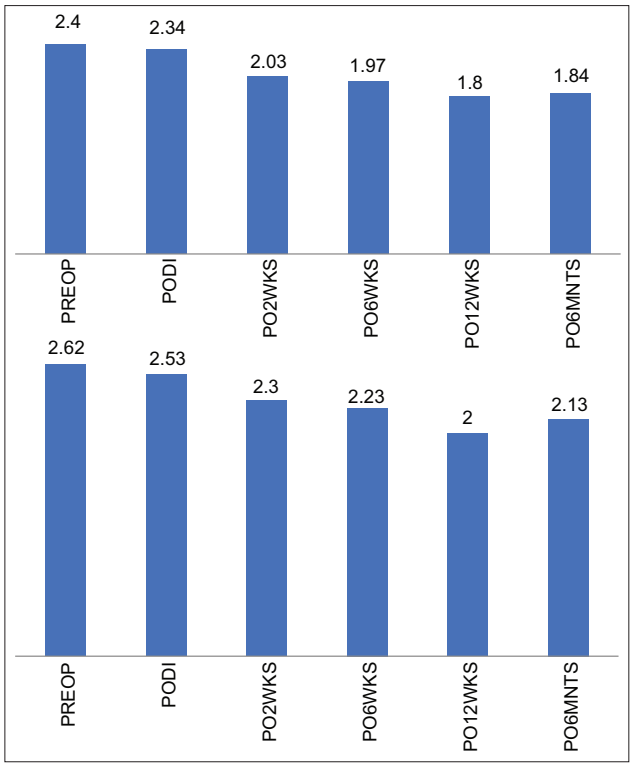


Figure 6: Assessment of CRP (male and female)

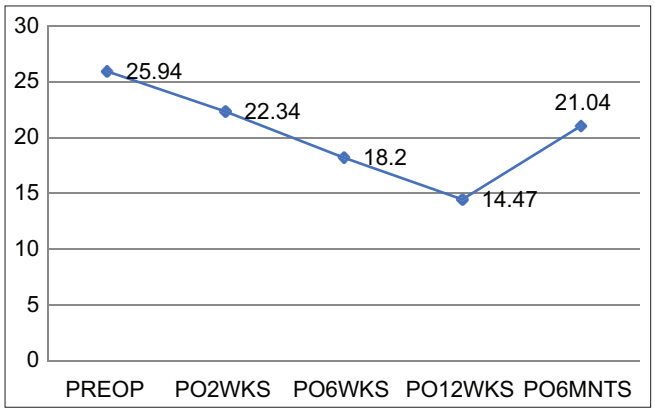


Figure 7: Assessment of ODI

The changes which occur as a disc degenerates are well documented, but are unhelpful in determining whether a degenerate disc will cause pain.[10]

It is known that disc tissue from patients undergoing discectomy for sciatica synthesizes pro-inflammatory mediators and cytokines.[11-20] Sequestrated and extruded discs produces higher levels of these mediators than specimens, in which the annulus is intact.[13,18,20,21]

In recent years, attention has begun to focus on the cellular and molecular activity of intervertebral disc tissue in the search for an understanding of the pathophysiology of sciatica and discogenic low back pain.[11-20] It is clear

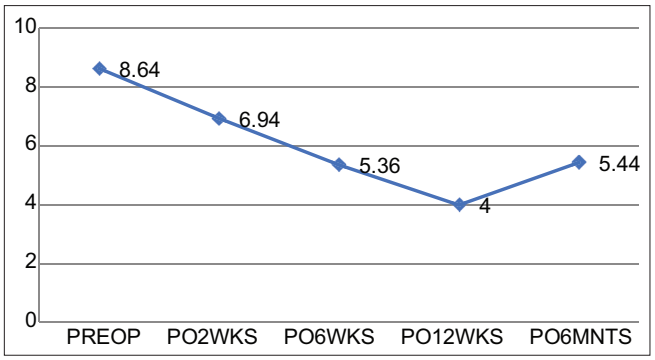


Figure 8: Assessment of RMDQ

from imaging studies that radicular pain is not simply a mechanical phenomenon.[22,23]

However, multiple studies have shown conflicting results in role of inflammation in disc pain. Transforaminal steroid injection provides relief in disc radiculopathy. In this regard, we took up our study to assess effect of transforaminal epidural steroid injection over inflammatory markers.

In this study, we measured ESR and CRP level pre- and post-TFESI, along with pain score assessment to assess effect of steroid on radiculopathy-related disability using Oswestry Disability Index calculation and Roland–Morris Disability Questionnaires.

As per the results in our study and on comparison to previous studies, most of previous studies have reached to the similar conclusions.

Benny *et al.*[24] showed that in patients with radicular pain that there is insufficient and conflicting evidence that either supports or refutes prognostic accuracy of hs-CRP in determining epidural steroid outcomes (two Class III studies). Chan Hong Park *et al.*[25] came to conclusion that there was no correlation between pre-treatment hsCRP and post-treatment VAS. Choi *et al.*[26] concluded there were no significant differences of inflammation markers (ESR and CRP) between responders and non-responders after CIES. Chan Hong *et al.*[27] found normal ESR levels in chronic back ache patients indicated that inflammatory processes were not occurring in low back pain patients.

However, post-TFESI, the patient showed improvement in pain relief. Pain assessment was done with the Roland–Morris Disability Questionnaire and Oswestry Disability Index at start of study mean ODI that was 25.94 and among Male 23.45 and 27.36 In Female. After TFESI, it was 22.34 at 2 weeks, 18.2 at 6 weeks, 14.4 at 12 weeks, and 21.01 at 6 months. On applying paired *t* test, improvement in score compare to pre-injection score is statistically significant at 6 weeks and 12 weeks.

Similarly, mean RMDQ score at start of study was 8.64. among men 8.81 and female 8.52. After TFESI, it was 6.94 at 2 weeks, 5.36 at 6 weeks 4 at 12 weeks, and 5.44 at end of study. On applying paired *t* test, difference with pre-injection is statistically significant at 6 weeks and 6 months.

Ghahreman *et al.*[28] reported favorable results from a prospective randomized controlled trial assessing the efficacy of transforaminal injection of steroid to local anesthetic, local anesthetic alone, normal saline alone, intramuscular injection of steroid, or normal saline on radicular pain secondary to lumbar disc herniation. Outcomes were assessed at 1 month and 12 months using Numeric Rating Scale, Roland–Morris, SF-36, and proportion of patients who underwent each treatment who obtained complete relief or at least 50% relief of pain for at least 1 month after treatment This outcome was statistically significant compared to the transforaminal normal saline, transforaminal local anesthetic, intramuscular normal saline, and intramuscular steroid groups. Robert *et al.* showed that there is fair evidence supporting TFESIs as superior to placebo for treating radicular symptoms.[29]

Mondal *et al.* concluded that transforaminal epidural steroid injection is an effective adjunct to usual conservative treatment protocol. It causes improvement not only in numerical rating scale of pain intensity measurements and Modified Oswestry Disability Index scores significantly but also improved walking pattern by changing pelvic angulations significantly.[30]

Some other studies have also demonstrated the efficacy of epidural steroid injections for the treatment of radiating pain in patients with lumbosacral disk herniation, leading to improvement in various rating scales.[29,32,33]

In our study, it was observed that there was no effect of TFESI over laboratory markers of inflammation ESR and CRP in disc radiculopathy patients, but TFESI found to be effective therapy for pain management in disc radiculopathy.

Our study had some limitations. Although ESR and CRP are markers of inflammation, these are relatively non-specific. Perhaps evaluation of more markers involved in disc inflammation such as IL-1, IL-6, and TNF-alpha may present more actual picture of effect of TFESI over disc inflammation and its response to steroid injection.

This study did not reveal significant fall in serum ESR and CRP level following transforaminal injection, but showed statistically significant clinical improvement assessed by ODI and RMDQ. This study shows significant improvement in OSI and RMDQ, post-transforaminal steroid injection. As per this study, TFSI is effective tool for non-surgical management of disc radiculopathy.

CONCLUSION

In this prospective study, conducted in Tertiary Hospital, with sample size of 30, all. All patients were having MRI diagnosed disc hernia with symptoms of radiculopathy. According to several studies cause of pain in disc herniation is local inflammation of nerves and compression of the nerves. This local inflammation leads to rise in certain markers of systemic inflammation. More easily measurable being serum ESR and CRP levels.

The study aimed at assessing effect of transforaminal steroid injection over improvement in symptoms of radiculopathy. Following conclusions were drawn from study – No effect of TFESI over ESR and CRP levels in Lumbar disc herniation and radiculopathy, However there was Improvement in functional outcome following TFESI as measured by the Roland–Morris disability questionnaire and Oswestry Disability Index.

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