Prospective Randomized Comparative Study to Evaluate Epidural Fibrosis and Surgical Outcome in Patients Undergoing Lumbar Laminectomy with Epidural Autologous Free Fat Graft or Gelfoam: A Preliminary Study

Abstract

**Introduction:** Epidural fibrosis (EF) contributes to unsatisfactory relief of symptoms and failed back syndrome after spine surgery. EF around the nerve root can be more refractory to treatment than the original disc herniation itself. Reoperation on the scar can produce more scarring. Few studies have been conducted regarding the type of material to be used for decreasing EF. **Materials and Methods:** The prospective randomized comparative study was conducted in the Department of Neurosurgery and Radiodiagnosis, of a tertiary care hospital. Informed and written consent was obtained. Patients previously unoperated with symptoms and radiological features of lumbar spinal canal stenosis were included in the study. Fifteen patients were assigned to Group A (free fat graft) and 15 patients in Group B (Gelfoam group). Postoperatively, at 3 and 6 months, clinical outcome was evaluated and EF was assessed on CE-MRI. **Results:** Age and sex were comparable in both groups. The pain relief at 3 and 6 months was more in Group A as compared to Group B. In Group A, on CEMRI at 3 months, 87% of patients had none to mild fibrosis, with none had extensive fibrosis. The CEMRI at 6 months showed no increase in fibrosis. In Group B, 80% of patients had none to mild fibrosis at the end of 3 months. At 6 months, 13.3% patients had extensive fibrosis. The extent of EF was found to be statistically significant at 6 months postsurgery. **Conclusion:** Use of free fat graft at laminectomy site helps in reducing EF.

Keywords: Contrast-enhanced magnetic resonance imaging, epidural fibrosis, free fat graft, Gelfoam

Introduction

Epidural fibrosis (EF) significantly contributes to unsatisfactory relief of symptoms and failed back syndrome after spine surgery. EF can tether the dura mater which can adversely affect the outcome and make the nerve roots vulnerable to injury, with dural tears occurring during a reoperation. EF around the nerve root can be more refractory to treatment than the original disc herniation itself. This is in addition to the fact that a reoperation on the scar can produce more scarring. Few studies have been conducted till date regarding the type of material to be used for decreasing EF.

Materials and Methods

The study was conducted in the Department of Neurosurgery and Department of Radiology, in a tertiary care hospital attached to Medical College after obtaining clearance from hospital ethics committee. Informed and written consent was obtained from each patient. The study was a prospective, randomized comparative study. Patients previously unoperated with symptoms and radiological features of lumbar spinal canal stenosis (primary and secondary spinal canal stenosis) were included in the study. A total of 30 patients were enrolled in the study. Fifteen patients were randomized to Group A (free fat graft), and 15 patients were placed in Group B (Gelfoam group). Postoperatively, clinical outcome and EF were assessed on contrast-enhanced magnetic resonance imaging (CEMRI) at 3 and 6 months postoperatively.

Randomization technique

Block randomization with sealed envelope system was used (In this, ten randomly generated treatment allocations within sealed opaque envelopes were prepared).
assigning A and B in 5 envelopes each, where A represented Group A receiving free fat graft and B represented Group B receiving epidural gel foam). Once a patient gave consent for the study, an envelope was opened, and the patient was then offered the allocated group.

Procedure
All patients were operated under general anesthesia. The patient was made to lie supine on table and then rolled over to the prone position. Operative field was cleaned and draped. The skin incision was made. Length of incision depended on how many laminectomies had to be performed. Back muscles were split down the middle and subperiosteal dissection was done. Muscles were moved to either side exposing the lamina of each vertebrae. After localization using C arm, bony spinous process and lamina were removed with bone biting tool; thickened ligamentum flavum was also removed. The facet joints are directly over the nerve roots and were undercut to give the nerve roots more room in case of nerve root compression. Discectomy was done in case of herniated disc causing compression. Gelfoam or free fat graft taken from same incision site was placed over the dura mater after laminectomy. Four layer closure (muscle, fascia, subcutaneous tissue and skin) was done with vicryl and nylon.

Clinical outcome assessment
It was done at 3 and 6 months. Activity related pain, backache and radicular pain and straight leg raising (SLR) examinations and assessments were done. Pain intensity, assessed both pre-and post-operatively, was evaluated by the numeric verbal rating (NVR) scale, with 0 meaning no pain while 10 meaning worst possible pain and patients were categorized as 1 - pain free (0); 2 - improved pain (1–4); 3 - fair (5–7); and 4 - bad (8–10). Significant pain relief group included patients in pain free and improved pain categories, i.e. pain relief of 50% or greater. Nonsignificant pain relief group included patients in the fair and bad categories, i.e., pain relief <50%. The patient’s functional clinical outcome was measured according to the clinical improvements in SLR test.

Radiologic evaluation assessment
Contrast MRI evaluation was done at 3 months and 6 months period postoperatively, for the extent and incidence of EF. Epidural granulation or scar tissue categorization was done for three cuts per disc level, four quadrants per level (a-d). The main assessment was done at the level passing through the neural exit foramina. Axial images covered at least one level above the operative site to one level below the site (except for L5-S1, where the caudal-most slices were to the mid S1 body). Criteria for EF identification included iso- to hypointense signal relative to intervertebral discs on T1-weighted MR images, replacing the epidural fat signal intensity. EF was fairly homogeneous. Both EF and disc protrusions may show mass effect, especially in early stages of granulation tissue formation. Aging of the EF may result in retraction of the dura toward the side of the scar. EF enhanced immediately after the injection of gadolinium, in contrast to recurrent herniation, which may need up to 20 min after contrast injection.

Epidural fibrosis grading: scale of 0–4 for each quadrant
Quadrants a–d for levels 1, 2, and 3; Grade 0 = no to trace scar; Grade 1 = trace to 25%; Grade 2 = 50%; Grade 3 = 75%; and Grade 4 = 100% [Figures 1 and 2]. Patient with a scar score of 4 in any one of the quadrants was considered as an extensive scar.

Results
All statistical analyses were performed by SPSS version 21.0, IBM corp., Armonk, NY, USA.

Demographic factors
Age and sex
Both the groups, i.e., Group A and Group B were comparable with respect to age and sex of patients. There was no statistical difference [Table 1].

Pain relief at 3 and 6 months
The pain relief at 3 months was significant in 100% patients in Group A which decreased to 86.67% at 6 months, which is possibly attributed to EF. In Group B, the pain relief was significant in 86.67% which reduced to 80% at 6 months. The pain relief at 3 and 6 months in both the groups was not statistically significant although the relief of pain was more in patients in whom free fat graft was
placed as compared to patients in whom Gelfoam was placed [Table 2].

**Straight leg raising test at 3 and 6 months**

SLR test in Group A had improved to 86º and 84.6º at 3 and 6 months which was better than Group B that showed improvement to 81º and 79º at 3 and 6 months, respectively. SLR improved in 100% patients at 3 months and 93.3% at 6 months in Group A, whereas it remained the same for Group B at 3 and 6 months, i.e., 86.7% of cases. On statistical analysis, improvement in SLR test was not statistically significant at 3 months and 6 months when compared between both groups. Improvement was more in patients in Group A, i.e., patients in free fat group as compared to Group B (Gelfoam group) [Table 3].

**Magnetic resonance imaging findings at 3 and 6 months**

In Group A, on contrast MRI at 3 months, 87% of patients had none to mild fibrosis and rest of patients had moderate fibrosis with no patient in extensive fibrosis category. The MRI done at 6 months showed no increase in fibrosis in patients in Group A. In Group B, 80% of patients had none to mild fibrosis, 6.7% in moderate, and 13.7% in extensive category at the end of 3 months which changed to 46.7% in none to mild category at 6 months, 40% patients had moderate, and 13.3% patients had extensive fibrosis. EF on CEMRI, when compared in both groups, was found to be statistically insignificant at 3 months postsurgery. On evaluation of CEMRI at 6 months after surgery, the difference of EF between the two groups was statistically significant. The amount of EF was less in free fat group as compared to Gelfoam group [Table 4].

**Complications**

Two patients developed wound infection in our study. Both patients were diabetic and were in Group B [Figures 3 and 4].

**Discussion**

Lexer[5] first reported the use of free fat grafts for prevention of scar formation in the early 1900. LaRocca and Macnab[2]

described EF as the “postlaminectomy membrane” in a canine model in 1974. In 1980, Mayfield[6] reported that fat grafts could prevent “constricting cicatrix” and can also act as space-occupying lesion leading to neural compression.

Lumbar EF has been proved to be an important cause of FBS. FBS usually occurs in 15%–60% of operated cases.[7–14] EF is reported in 10%–24% of FBS cases. The postoperative recurrence of pain after an initial pain-free period was often attributed to EF.[12] The rate of EF increases to more than 60% in reoperations with a possible
worse outcome. The fibrosis makes nerve root more susceptible to compression due to the tethering effect of the scar tissue. EF makes reoperations risky and more difficult. EF increases the risk of dural tear during reoperation.

EF forms even in minimally invasive procedures. Most synthetic materials lead to more scarring and more complications compared with control groups. Autogenous barriers had better results. Preservation of the natural epidural fat is an effective barrier to reduce the occurrence of EF. It prevents the fibrous tissue invasion from the surrounding tissues. Application of a drug locally, which is known to decrease scar tissue formation, may be theoretically accepted, provided that it does not cause any harm to the patient.

Postoperative lumbar EF occurs as a result of normal wound healing. Fibroblasts infiltrate and replace the epidural hematoma and lead to granulation tissue formation. Granulation tissue leads to the formation of dense fibrous tissue which in turn leads to irritation of dura and nerve root irritation, entrapment, and compression and thus makes them more susceptible to injury.

EF formation usually takes about 6 weeks to 6 months postoperatively. EF is clearly identified on MRI by at least 3 months, stabilized by 6 months, with no further changes at 12 months. Hence, in this study, the MRI evaluation follow-up time was 6 months. EF on MRI is visualized as relatively low-signal intensity, as compared to the high-signal intensity epidural fat, and as the very low-signal intensity cerebrospinal fluid on T1-weighted images. EF usually enhances homogeneously following contrast administration.

Regarding EF and clinical recovery, Coskun et al. did not find a relation between EF and pain scores. However, in our study, we have found a good correlation between scores for the NVR scale and the grade of EF by MRI.

In our study, EF was evaluated using axial MR images, with interpretation of its extent. This helped us to study the relation between the extent of EF, patient’s symptoms, and surgical outcomes. In contrast to the grading system described by Ross et al., we have utilized three levels evaluation, centered on the level of the neural exit foramina as advised by Mohi Eldin and Abdel Razek.

Rate and grade of EF were first described by Cervellini et al., Cervellini et al. and Sen et al. found Grade II (moderate) EF predominantly. In a study done by Cinotti et al., no correlation was found between the amount of EF, as seen intraoperatively and on MR, and FBS. In this study, we have evaluated the occurrence rate and EF grades in our patients in both groups. Mohi Eldin and Abdel Razek studied the use of suction drains at operative sites to prevent EF. In a study done by Ross, patients with extensive EF were 3.2-fold more likely to experience recurrent radicular pain than those patients with less extensive EF. They found a significant association between the presence of extensive EF and the recurrence of radicular pain. In our study, we found that patients in Group A (free fat graft) developed less EF and had more relief/decrease in pain as compared to patients in Group B (Gelfoam). Our results regarding EF and its correlation to pain matched with the previous studies.

**Conclusion**

This study demonstrated the fact that the use of fat grafts over Gelfoam application significantly improved patient outcome with respect to short-term and late pain relief and SLR. In addition, the same tools significantly reduced EF as measured by an MRI. Grading of EF with the mentioned simple MRI grading system showed a good clinical correlation between outcome on the one side and the extent of EF on the other side. Further studies with more number of patients is warranted for better statistical significance.
Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Jinkins JR, Osborn AG, Garrett D Jr., Hunt S, Story JL. Spinal nerve enhancement with Gd-DTPA: MR correlation with the postoperative lumbar sacral spine. AJNR Am J Neuroradiol 1993;14:383-384.
2. LaRocca H, Macnab I. The laminectomy membrane. Studies in its evolution, characteristics, effects and prophylaxis in dogs. J Bone Joint Surg Br 1974;56B:545-545.
3. Mohi Eldin MM, Abdel Razek NM. Epidural fibrosis after lumbar disc surgery: Prevention and outcome evaluation. Asian Spine J 2015;9:370-375.
4. Ross JS, Obuchowski N, Zepp R. The postoperative lumbar spine: Evaluation of epidural scar over a 1-year period. AJNR Am J Neuroradiol 1998;19:183-6.
5. Lexer E. New German Surgery. In: Lexer E, editor. The free transplants. Stuttgart: Enke; 1919. p. 264-545.
6. Mayfield FH. Autologous fat transplants for the protection and repair of the spinal dura. Clin Neurosurg 1980;27:349-61.
7. Annetz M, Jönsson B, Strömqvist B, Holttás S. No relationship between epidural fibrosis and sciatica in the lumbar postdiscectomy syndrome. A study with contrast-enhanced magnetic resonance imaging in symptomatic and asymptomatic patients. Spine (Phila Pa 1976) 1995;20:449-53.
8. Coskun E, Süzer T, Topuz O, Zencir M, Pakdemirli E, Tahta K, et al. Relationships between epidural fibrosis, pain, disability, and psychological factors after lumbar disc surgery. Eur Spine J 2000;9:218-23.
9. Fritsch EW, Heisel J, Rupp S. The failed back surgery syndrome: Reasons, intraoperative findings, and long-term results: A report of 182 operative treatments. Spine (Phila Pa 1976) 1996;21:626-33.
10. Gabriel EM, Friedman AH. The failed back surgery syndrome. In: Wilkins RH, Rengachary SS, editors. Neurosurgery. New York: McGraw-Hill, Health Professions Division; 1996. p. 3863-70.
11. Long DM. Failed back surgery syndrome. Neurosurg Clin N Am 1991;2:899-919.
12. Maroon JC, Abla A, Bost J. Association between peridural scar and persistent low back pain after lumbar discectomy. Neurrol Res 1999;21 Suppl 1:S43-6.
13. Songer MN, Ghosh L, Spencer DL. Effects of sodium hyaluronate on peridural fibrosis after lumbar laminotomy and discectomy. Spine (Phila Pa 1976) 1990;15:550-4.
14. Songer MN, Rauschning W, Carson EW, Pandit SM. Analysis of peridural scar formation and its prevention after lumbar laminotomy and discectomy in dogs. Spine (Phila Pa 1976) 1995;20:571-80.
15. Jönsson B, Strömqvist B. Repeat decompression of lumbar nerve roots. A prospective two-year evaluation. J Bone Joint Surg Br 1993;75:894-7.
16. Kim SS, Michelsen CB. Revision surgery for failed back surgery syndrome. Spine (Phila Pa 1976) 1992;17:957-60.
17. Dogulu F, Kurt G, Emmez H, Erdem O, Memis L, Baykaner K, et al. Topical mitomycin C-induced inhibition of postlaminectomy peridural fibrosis in rabbits. J Neurosurg 2003;99:76-9.
18. Rodgers KE, Robertson JT, Espinzoa T, Oppelt W, Cortese S, diZerega GS, et al. Reduction of epidermal fibrosis in lumbar surgery with Oxi ple粕 adhesion barriers of carboxymethylcellulose and polyethylene oxide. Spine J 2003;3:277-83.
19. Sen O, Kizilkilic O, Aydin MV, Yalcin O, Erdogan B, Cekinmez M, et al. The role of closed-suction drainage in preventing epidural fibrosis and its correlation with a new grading system of epidural fibrosis on the basis of MRI. Eur Spine J 2005;14:409-14.
20. Manchikanti L, Rivera JJ, Pampati V, Damron KS, McManus CD, Brandon DE, et al. One day lumbar epidural adhesiolysis and hypertonic saline neurolysis in treatment of chronic low back pain: A randomized, double-blind trial. Pain Physician 2004;7:177-86.
21. Porchet F, Lombardi D, de Preux J, Pople IK. Inhibition of epidural fibrosis with ADCON-L: Effect on clinical outcome one year following re-operation for recurrent lumbar radiculopathy. Neurol Res 1999;21 Suppl 1:S51-60.
22. Lladó A, Sologaistua E, Guimerá J, Marin M. Expanded polytetrafluoroethylene membrane for the prevention of peridural fibrosis after spinal surgery: A clinical study. Eur Spine J 1999;8:144-50.
23. Aydin Y, Ziyal IM, Duman H, Türkmen CS, Başak M, Sahin Y, et al. Clinical and radiological results of lumbar microdiscectomy technique with preserving of ligamentum flavum comparing to the standard microdiscectomy technique. Surg Neurol 2002;57:5-13.
24. Dullerud R, Graver V, Haakonsen M, Haaland AK, Loeb M, Magnaes B, et al. Influence of fibrinolytic factors on scar formation after lumbar discectomy. A magnetic resonance imaging follow-up study with clinical correlation performed 7 years after surgery. Spine (Phila Pa 1976) 1998;23:1464-9.
25. Cervellini P, Curri D, Volpin L, Bernardi L, Pinna V, Benedetti A, et al. Computed tomography of epidural fibrosis after discectomy: A comparison between symptomatic and asymptomatic patients. Neurosurgery 1988;23:710-3.
26. Cinotti G, Roysam GS, Eisenstein SM, Postacchini F. Ipsilateral recurrent lumbar disc herniation. A prospective, controlled study. J Bone Joint Surg Br 1998;80:825-32.
27. Ross JS. Magnetic resonance assessment of the postoperative spine. Degenerative disc disease. Radiol Clin North Am 1991;29:793-808.
28. Ross JS, Obuchowski N, Modic MT. MR evaluation of epidural fibrosis: Proposed grading system with intra- and inter-observer variability. Neurol Res 1999;21 Suppl 1:S23-6.
29. North RB, Campbell JN, James CS, Conover-Walker MK, Wang H, Plantadosi S, et al. Failed back surgery syndrome: 5-year follow-up in 102 patients undergoing repeated operation. Neurosurgery 1991;28:685-90.