

# The Epidural Steroids in the prevention of epidural fibrosis: MRI and clinical findings

Martin HÄCKEL<sup>1</sup>, Václav MASOPUST<sup>1</sup>, Martin BOJAR<sup>2</sup>, Youssef GHALY<sup>4</sup>,  
and Daniel HOŘÍNEK<sup>1,3</sup>

1. Department of Neurosurgery, 1st Medical Faculty, Charles University, Central Military Hospital;
2. Department of Neurology, 2nd Medical School, University Hospital Motol, Prague; Czech Republic
3. Department of Neurosurgery, Medical Faculty, Philipps University, Baldingerstraße, 35033, Marburg, Germany.
4. Institute of Pathological Physiology, Laboratory for Neuroimaging Research, Second Faculty of Medicine, Charles University, Plzenska 130, Praha 5, 158 00, Czech Republic.

*Correspondence to:* Daniel Hořínek, MD, Ph.D.  
Department of Neurosurgery, Central Military Hospital, First Faculty of Medicine,  
Charles University, U Vojenské nemocnice 1200, Prague 6, 160 00  
TEL/FAX: +420 973202963, EMAIL: daniel.horinek@uvn.cz

*Submitted:* 2008-06-16 *Accepted:* 2008-10-12 *Published online:* 2009-03-12

*Key words:* epidural steroids; epidural fibrosis; prevention; discectomy; pain

Neuroendocrinol Lett 2009;30(1):51–55 PMID: 19300380 NEL300109A03 ©2008 Neuroendocrinology Letters • www.nel.edu

## Abstract

**BACKGROUND:** Epidural fibrosis (EF) represents a frequent and poorly manageable complication of lumbar disk surgery.

**OBJECTIVES:** To investigate the influence of perioperative Epidural Steroid (ES) application on the development of EF.

**METHODS:** One hundred and seventy eight patients underwent L4/5 or L5/S1 discectomy. The study group receiving ES comprised of eighty five patients, and a further control group comprising eighty two patients received a placebo. At a 12 month follow-up, all subjects underwent contrast magnet resonance imaging of the lumbosacral spine.

One hundred and sixty seven patients filled in a predetermined questionnaire containing the Visual Analogue Scale (VAS; pain scale) during the first postoperative days and 12 months after. Intergroup differences were analysed and a correlation between the extent of EF and VAS was examined.

**RESULTS:** The groups did not differ regarding the extent of EF. There was a statistically significant correlation between the degree of fibrosis and VAS ( $p < 0.05$ ). However, there was no significant difference in subjective pain assessment between both groups 12 months postoperatively. The application of ES did not influence their return to work.

Patients receiving ES experienced less pain on the first and third days after surgery. The average hospital stay after surgery was shorter in the steroid treated group (4.5 days) compared to 5.2 days in the control group ( $p < 0.05$ ).

**CONCLUSIONS:** The application of ES did not prove to be useful in the prevention of Failed Back Surgery Syndrome and epidural scar formation. Postoperative pain was decreased in the steroid treated group during the first postoperative week, but not 12 months postoperatively.

## INTRODUCTION

The introduction of microneurosurgery and overall improvement of the diagnostic therapeutic processes reduced the rate of postoperative complications in the management of degenerative spine disease. In contrast to the decrease of diagnostic and surgical pitfalls (poor patient selection, improper/inadequate surgery), there has been a relative increase in what is a poorly manageable complication – epidural fibrosis (EF). EF is likely to develop in 5–33% of cases after surgery for lumbar disk herniation, with the rate varying depending on the type of surgery (Benoist *et al.*, 1979).

Devulder (1998) demonstrated that the current treatment of EF is not optimal, in that hyaluronidase application may exceed three months in 55% patients. Much evidence lends support to the hypothesis that the mechanisms of pain in lumbar disc disease are more complicated than simple nerve root compression, and that inflammation is an important mediator of pain in these patients (Grönblad *et al.*, 1994; Olmarker *et al.*, 1995; McCarron *et al.*, 1987). Lumbar disc herniation may lead to a local inflammatory response, the cytokines and growth factors may enhance the presence of sciatic pain (Specchia *et al.*, 2002; Brisby *et al.*, 2002). The main goal of perioperative ES application is to relieve postoperative pain and to prevent late scar tissue formation. The application of nucleus pulposus fragments on nerve roots has been shown to reduce nerve conduction velocity, and that this process could be avoided by the early administration of steroids (Olmarker *et al.*, 1994).

Two pathophysiological mechanisms are responsible for pain generation in epidural fibrosis. The pressure from the fibrous scar, and the mediators of inflammation are responsible for the alteration of vascular supply to the nerve root and the myelin sheath. Blood accumulation in the epidural space further enhances scar formation (Rydevik *et al.*, 1981). Whereas the risk of direct damage to the nerves or profuse bleeding may be minimized by adequate surgical technique and skill, the release of a number of pro-inflammatory substances may be inhibited by ES application (King *et al.*, 1976).

Methylprednisolone is indicated for treating inflammation of soft and articular tissues, and is approved for epidural uses. Synthetic derivatives of cortisone with anti-inflammatory effects are noted for inhibiting locally the production of one's own antibodies, resulting from the production and deposition of autoimmune complexes. Methylprednisolone enters the cycle of the inflammatory reaction inhibiting scar formation.

The aim of this study is to investigate the influence of perioperative ES application on the development of EF. Furthermore, to assess the relationship between the extent of EF on MRI, and the intensity and character of postoperative pain experienced by patients after surgery for lumbar disk herniation.

## MATERIAL AND METHODS

### Study sample

One hundred and seventy eight patients were enrolled into the study. All were surgically treated for lumbar disk herniation from 2001 to 2003. All participants signed an informed consent form and the study design was approved by the local ethical committee. This study was devised as a prospective randomised study.

### Methods

Subjects underwent elective procedure, e.g. simple L4/5 or L5/S1 discectomy. In L5/S1 discectomy a transligamental approach was performed, in L4/5 discectomy a limited partial hemilaminectomy and foraminotomy were performed. Larger decompression was considered as an exclusion criterion for the study. The instructions for the use of steroids or placebo were enclosed in a closed envelope, which was opened at the end of the surgery. The identification number was then entered into patient's clinical records.

After the nerve root decompression and disk hernia removal, four little prism-shaped pieces of spongostane; 1x1x2 cm in size; were soaked in a mix of 80 mg methylprednisolone acetate (2 ml of 40 mg each) and 1 ml fentanyl dihydrogenocitrate (78,5 µg in 1 ml solution), and then inserted into the surgery site. They were inserted into the region of the posterior ligament, laterally to the nerve root and dorsally to the region of the flaval ligament. The control group received sodium chloride as an alternative.

After surgery the patients received standard postoperative care including rehabilitation, and were verticalized by day 2 in most cases. As an analgesic treatment, patients received pethidine hydrochloride (100 mg) every eight hours for the first two days, after which the treatment was changed to non-steroid antiphlogistics.

The group receiving ES comprised of 85 patients, and the control group receiving placebo comprised of 82 patients. The study group (85 patients) comprised of 42 women and 43 men, aged from 27 to 47 years, with a mean age of 49.5 years. The control group comprised of 44 women and 38 men, ranging from 24 to 70 years, with a mean age 44.5. All subjects underwent native MRI and also with Gadolinium of the lumbosacral spine within 12 months. A total of 167 patients were examined by both methods and filled in the predetermined questionnaire. From the initial group, 11 patients failed to keep in touch due to unforeseen circumstances (i.e. change of domicile etc).

All patients' VAS were taken during the first postoperative week. The early postoperative course was divided into three periods: day 1, days 2–3, and days 4–5. The results for each period were then averaged. All patients were examined 12 months postoperatively during outpatient visits, undergoing lumbar spine MRI with Gadolinium, and also filling in the questionnaire with the VAS pain scale (0–10).



**Figure 1:** shows the T1 weighted image with the post-contrast enhancement at the site of epidural fibrosis. The extent of the epidural fibrosis corresponds to the grade 4 according to Ross scale (Ross et al., 1998).

MRI findings were evaluated by a radiologist and classified by the scale suggested by Ross *et al.* (1998). This scale is based on the extent of epidural fibrosis at the 5 axial levels further subdivided in four quadrants defined by perpendicular lines drawn from the central aspect of the thecal sac. The extent of epidural fibrosis was graded on a scale of 0 to 4 for posteriori epidural space filled with scar (0 = no/trace scar; 1 = 0% < filled with scar  $\leq$  25%; 2 = 25% < filled with scar  $\leq$  50%; 3 = 50% < filled with scar  $\leq$  75%; 4 = 75% < filled with scar  $\leq$  100%). Intergroup differences were assessed in EF and VAS 12 months after the procedure, and also during the first postoperative week (Mann Whitney U test). The relationship was analysed between the extent of EF and the VAS (Spearman correlation coefficient). The outcome regarding the return to work was also assessed.

## RESULTS

The study finally comprised of 85 patients receiving ES, and 82 patients receiving placebo (control group). There was no postoperative wound infection among patients receiving steroids, or in the control group.

The average grade of EF positive on MRI findings was 2.16 in subjects receiving steroids, this value is higher (but not statistically significant) than that of the control group with a value of 1.94. In the study group the incidence of massive EF (grade 4) was even higher than in the control group, see Figure 1. This showed a

statistically significant correlation between the degree of fibrosis and the VAS as showed by the Spearman correlation coefficient ( $p < 0.05$ ). The effect of epidural steroids application during the first postoperative days shows that there is a statistically significant change in the VAS between groups in both the first and third days after surgery (Table 2). However, on day 5, the difference between groups did not reach statistical significance ( $p = 0.07$ ).

There was no statistically significant difference in the subjective pain assessment between the study group and the control group at the 12 month follow-up. At this follow-up, the VAS in the study group was found to be 2.87, and in the control group was found to be 2.83. The difference between both groups did not show any statistical significance ( $p = 0.24$ ). The pain decreased after the surgery according to the VAS ( $p < 0.01$ ), as was expected.

The average hospital stay after surgery was found to be shorter in patients from the study group (4.5 days), in comparison to 5.2 days for patients from the control group ( $p < 0.05$ ).

Regarding the time taken to return to full-time work, only 158 patients out of 167 were studied; nine patients were not included because of another comorbidity other than disc herniation, because they were work disabled before the surgery, or because they were students.

The application of steroids did not significantly influence the return to work. At 12 months after the

surgery, 32 patients from the study group and 31 from the control group were still on sick leave.

## DISCUSSION

According to some previous studies, it was assumed that the perioperative application of Depo-medrol would lead to the reduction of EF in the study group. However, there was no statistically significant result, and the incidence of EF in study group was higher although not significant. The results from the VAS at 12 months after the surgery did not reach statistical significance either, and as expected there was a correlation between the extent of EF on MRI and the VAS. Although patients who received corticosteroids had a shorter hospital stay, their return to work however was not significantly different from the control group. The benefits of locally administered methylprednisolone in lumbar disc surgery still remain ambiguous. In a group of patients after discectomy the epidural methylprednisolone acetate applied perioperatively reduced the use of analgesics and shortened hospital stay (Davis and Emmons, 1990). In another study performed by Lavynne and Bilski (1992) low dose steroids failed to improve the postoperative morbidity.

Watters *et al.* (1998) investigated the effects of dexamethasone with intravenous administration during the first postoperative day followed by four daily oral doses for another 2 days. This study demonstrated that patients treated with dexamethasone experienced less leg pain and therefore required fewer narcotics than the control group. However, these patients did not have a significant decrease in postoperative back pain. Glasser *et al.* (1993) used perioperative parenteral corticosteroids and bupivacaine in microdiscectomy, thus reducing postoperative discomfort and the length of hospital stay.

By contrast, Manniche *et al.* (1994) did not find any significant effect of prednisolone treatment administered for 4 weeks in a randomized study.

On days 3 and 4 after the surgery there has been significant improvement in this study group. In a study of Chaddock *et al.* (1999), a significant reduction in postoperative pain was noted in patients who received a methylprednisolone-soaked piece of macerated autologous fat over the nerve root at the end of the procedure. In addition patients were given an injection of bupivacaine into the paravertebral muscles and subcutaneous tissues. The authors reported that bupivacaine was not beneficial in controlling postoperative pain in contrast to ES administration. Patients who received steroids were in the early postoperative period subjectively more satisfied, this is in line with the finding of this study. Early pain relief after surgery is important with regard to the ability of early ambulation and shorter convalescence. Several papers have reported the use and efficacy of percutaneous ES injection for the treatment of back pain and radiculopathy (Johnson *et al.*, 1991; Nelson

1993). However, during the percutaneous application up to 6% accidental dural punctures may occur. The intradural application carries a significant risk of arachnoiditis (Johnson *et al.*, 1991). The perioperative application with the use of Depo-Medrol soaked spongostan or fat graft avoids the risk of intrathecal administration and ensures the safety of epidural placement.

In a study of Lundin *et al.* (2003) eighty adult subjects with lumbar disc herniation assessed by MRI, and clinical findings corresponding to the radiological level underwent microdiscectomy to investigate the outcome of perioperatively administered corticosteroids in a prospective randomized double-blind study. In this study, the postoperative hospital stay was significantly shorter in the treatment group (1.7 days) compared to the group receiving placebo, which is comparable to the findings of this study. On the other hand the time taken to return to full-time work was also significantly shorter in patients with ES treatment in this study.

The comparison between the two groups with regard to the resultant effect that the steroids had on the number of sick-leave days at one year after the surgery did not show any level of statistic significance. It cannot be entirely ruled out the patient's apprehension of legal and socioeconomic consequences of filling in a questionnaire containing their personal data. Over a period of twelve months any surgical patient is likely to encounter a number of other factors bound to influence both the perception and interpretation of their state of health. The lack of any significant difference between the study group and the control group could be explained by disability claims between the two groups. It has been shown in the past that patients with minor disk herniations tend to return to work later and the results of pain are worse in this group (Schade *et al.* 1999, den Boer *et al.* 2006). With the passage of time and with prolonged disability before surgery, psychosocial factors become increasingly important in determining outcomes.

There was a correlation between the degree of EF and the intensity of pain reported by patients after the surgery. Scarring and adhesions in the epidural space probably contribute to the patient's symptoms, although establishing a definitive association between the pathologic changes found and the symptoms is very difficult. There may be a relationship between the extent of surgery and the subsequent degree of fibrosis and adhesion formation, but this is unproven. Moreover, the patient groups with lumbar disc disease comprise a broad scale of injury including both, patients with ligamental and subligamental herniations with various degrees of injury to the adjacent nerve root.

## CONCLUSION

In conclusion this study demonstrates the significant association between the extent of epidural steroids on MRI and the intensity of postoperative pain. The VAS was significantly different in favour of the steroid



treated group for the first postoperative week but not for the 1 year follow-up. These findings indicate the application of ES did not prove to be effective in the prevention of Failed Back Surgery Syndrome and epidural scar formation.

## ACKNOWLEDGMENT

The paper is supported by a grant from IGA – MZ (NR-8848).

## REFERENCES

- Benoist M, Ficat C, Baraf P, Massare C, Bard M, Sarre J, Cauchoix J (1979). Postoperative sciatica from epidural fibrosis and lumbar arachnoiditis. Results of 38 repeat operations. *Rev Rheum Mal Osteoartic.* **46**: 593–9.
- Brisby H, Olmarker K, Larsson K, Nutu M, Rydevik B (2002). Proinflammatory cytokines in cerebrospinal fluid and serum in patients with disc herniation and sciatica. *Eur Spine J.* **11**: 62–66.
- Chaddock JB, Sneyd JR, Pobereskin LH (1999). The role of bupivacaine in early postoperative pain control after lumbar decompression. *J Neurosurg.* **90**: 67–72.
- Cinotti G, Roysam GS, Eisenstein SM, Postacchini F (1998). Ipsilateral recurrent lumbar disc herniation. A prospective, placebo led study. *J Bone Joint Surg Br.* **80**: 825–32.
- Davis R, Emmons SE (1990). Benefits of epidural methylprednisolone in a unilateral lumbar discectomy: a matched controlled study. *J Spinal Disord.* **3**: 299–306.
- den Boer JJ, Oostendorp RA, Beems T, Munneke M, Evers AW (2006). Continued disability and pain after lumbar disc surgery: the role of cognitive-behavioral factors. *Pain.* **123**: 45–52.
- Devulder J (1998). Transforaminal nerve root sleeve injection with corticosteroids, hyaluronidase, and local anesthetic in the failed back surgery syndrome. *J Spinal Disord.* **11**: 151–4.
- Fritsch EW, Heisel J, Rupp S (1996). The failed back surgery syndrome: reasons, intraoperative findings, and long-term results: a report of 182 operative treatments. *Spine.* **1**; **21**: 626–33.
- Glasser RS, Knego RS, Delashaw JB, Fessler RG (1993). The perioperative use of corticosteroids and bupivacaine in the management of lumbar disc disease. *J Neurosurgery.* **78**: 383–387.
- Gronblad M, Virri J, Tolonen J, Seitsalo S, Kaapa E, Kankare J, Myllynen P, Karaharju E (1994). A controlled immunohistochemical study of inflammatory cells in disc herniation tissue. *Spine.* **19**: 2744–2751.
- Johnson A, Ryan, MD, Roche J (1991). Depo-Medrol and myelographic arachnoiditis. *Med J Aust;* **155**: 18–20.
- King J. S. , Gallant P. , Myerson V. , *et al* (1976). The effects of anti-inflammatory agents on the responses and the sensitization of unmyelinated c fiber polymodal nociceptors. In: Zotterman Y, ed. *Sensory Functions of the Skin in Primates With Special Reference to Man.* Oxford: Pergamon Press. p. 441–61.
- Lavyne MH and Bilsky MH (1992). Epidural Steroids, postoperative morbidity, and recovery in patients undergoing microsurgical lumbar discectomy. *J Neurosurgery.* **77**: 90–95.
- Lundin A, Magnuson A, Axelsson K, Kogler H, Samuelsson L (2003). The effect of perioperative corticosteroids on the outcome of microscopic lumbar disc Sumery. *Eur Spine J.* **12**: 625–630.
- Manniche C, Lauritsen B, Vinterberg H (1994). Perioperative prednisolone fails to improve the clinical outcome following surgery for prolapsed lumbar intervertebral disc. *Scand J Rheumatol.* **23**: 30–35.
- McCarron RF, Wimpee MW, Hukins PG, Laros GS (1987). The inflammatory effect of nucleus pulposus. *Spine.* **12**: 760–764.
- Nelson DA (1993). Intraspinal therapy using methylprednisolone acetate: Twenty three years of clinical controversy. *Spine.* **18**: 278–86.
- Olmarker K, Blomquist J, Stromberg J, Nannmark U, Thomsen P, Rydevik B (1995). Inflammatory properties of nucleus pulposus. *Spine.* **20**: 665–669.
- Olmarker K, Byrod G, Cornefjord M, Nordborg C, Rydevik B (1994). Effects of methylprednisolone on nucleus pulposus-induced nerve root injury. *Spine.* **19**: 1803–1808.
- Ross JS, Obuchowski N, and Zepp R (1998). The Postoperative Lumbar Spine: Evaluation of Epidural Scar over a 1-Year Period. *AJNR.* **19**: 183–186.
- Rydevik BL, Landborg G, Bagge U (1981). Effects of graded compression on intraneural blood flow. *J Hand Surg Am.* **6**: 3–12.
- Schade V, Semmer N, Main CJ, Hora J, Boos N (1999). The impact of clinical, morphological, psychosocial and work-related factors on the outcome of lumbar discectomy. *Pain.* **80**: 239–49.
- Specchia N, Pagnotta A, Toesca A, Greco F (2002). Cytokines and growth factors in the protruded intervertebral disc of the lumbar spine. *Eur Spine J.* **11**: 145–151.
- Watters WC 3rd, Temple AP, Granberry M (1989). The use of dexamethasone in primary lumbar disc surgery. A prospective, randomized, double-blind study. *Spine.* **14**: 440–2.