Open Access

SCHOLARENA

Journal of Anaesthesia and Therapeutics

RESEARCH ARTICLE

ISSN: 2639-7242

Epidural Adhesiolysis in the Management of Chronic Low Back Pain in Failed Back Surgery Syndrome and in Lumbar Radicular Pain: First Year of Experience in General Hospital Pula - Croatia, A Randomized Trial

Kalagac FL[1*], Šuput A[1], Gusić N[2] and Mamontov P[2]

[1]*Departement of Anesthesiology and Pain Therapy, General Hospital Pula, Pula, Croatia*
[2]*Departement of Surgery and Neurosurgery, General Hospital Pula, Pula, Croatia*

[*]**Corresponding author:** Kalagac FL, MD PhD, Departement of Anesthesiology and Pain Therapy, General Hospital Pula, A.Negri 6, 52100 Pula, Croatia, Tel: +38598728151, E-mail: lada1966@gmail.com

Citation: Kalagac FL, Šuput A, Gusić N, Mamontov P (2018) Epidural Adhesiolysis in the Management of Chronic Low Back Pain in Failed Back Surgery Syndrome and in Lumbar Radicular Pain: First Year of Experience in General Hospital Pula - Croatia, A Randomized Trial. J Anaesth Ther 1: 102

Article history: Received: 10 April 2018, **Accepted:** 05 July 2018, **Published:** 06 July 2018

Abstract

Objective: To evaluate the efficacy and the feasibility of percutaneous adhesiolysis to reduce pain, to improve daily functions and reduce drugs intake in patient with chronic pain.

Chronic radicular pain can be caused by scar tissue, compression, inflammation, swelling disks. Adhesiolysis by placement of a wire-bound catheter into the ventrolateral aspect of the epidural space at the site of the exiting nerve root enables precise application of steroids, hyaluronidase, local anesthetics and saline for the purpose of achieving pain relief.

Methods: Standard percutaneus epidural adhesiolysis was preformed in 54 patients who were divided into two groups: pain from FBSS versus chronic radicular pain without previous spine surgery.Visual analog score (VAS), change in pharmacotherapy intake, subjective satisfaction and evaluation of the lysis procedure were observed in pretreatment, in the 4th and 12th week after the intervention.

Results: VAS scores for pain were significanty reduced in both groups in the 4th and 12th week. Statistically significantly decrease was expressed in the Radiculopathy group (VAS^{0} =7.5 0.87 / VAS^{12th}= 4.6 1.05) versus the FBSS group (VAS^{0} = 7.6 0.85 / VAS^{12th}= 5.0±1.58) ($p<0.001$) Improvement in short-term pain relief resulted in significant reduction in pharmacotherapy intake ($p<0.001$) and clinical effectivenes rate of >50% was achieved in 27% patients of FBSS and 25% of patient with chronic radicular pain without surgery experience.

Conclusion: Considering our small sample, our results in short-term pain relief, suggests that epidurolysis can be an effective method in the treatment of patients with chronic radicular pain like in the patients with FBSS.

Keywords: Adhesiolysis; Failed Back Surgery Sindrome; Chronic Radicular Pain; Hyaluronidase; Clinical Outcome

Introduction

Radicular pain is a type of pain which radiates into the lower extremity directly along the course of a spinal nerve root. The most typical symptom of radicular pain is sciatica (pain that radiates along the sciatic nerve). Leg pain can be accompanied by numbeness and tingling, muscle weakness and loss of reflexes. Radicular pain is caused by compression, inflamation and /or injury to a spinal nerve root, arising from common conditions including herniated disc, foraminal stenosis, peridural fibrosis and spinal stenosis [1]. Many times, the duration of painful symptoms (such as leg pain; pain at rest, at night and on coughing), consumption of analgesics and inefective conservative treatments are indicators which point to the need of using contrast-enhanced fluoroscopic epidural steroid injections [2].

The *International Association for the Study of Pain* defined failed back surgery syndrome (FBSS) as the phenomenon of persistent or recurrent pain, mainly in the lower back and/or legs, even after previous anatomically successful spinal surgeries. A recent systematic literature review of discectomies for lumbar disc herniation in patients under the age of 70 years demostrated a frequent recurrent back or leg pain in 5%-36% of the patients, 2 years after the operation [3,4].

Post-operative scar formation is a natural part of the process of tissue healing after any surgery. Naturally, spine surgery will result in the formation of fibrotic adhesions within the epidural space. By compressing the nerve roots and consequently decreasing

the range of motion in the back and inducing pain with movement, these adhesions may cause back and leg pain. Adhesions may contribute to, or cause, 20-36% of FBSS cases and may also, by creating septations within the epidural space that prevent steroid from acting on its intented target, compromise the efficacy of ESI [5]. Adhesions can theoretically be lysed by delivering hyaluronidase, thereby improving baseline pain scores and improving steroid effect [6,7].

Treatment options for FBSS are limited, because neither reoperation nor conservative treatment has been shown to be effective.

Most authorities agree that the conservative treatment in cases of chronic low back pain and FBSS should be physical therapy, anti-inflammatory medication, injection prolotherapy for enthensopathies and analgesics drugs (opiates, antiepileptic drugs such as gabapentin), and cognitive behavioral modification [8,9]. However, even many of the patients who have been treated so have persistent pain and seek further intervention.

An alternative method to reduce fibroplasias and to remove barriers between tissues, to induce resolution of scar tissue or epidural adhesiones and for delivering steroids to inflamated nerve tissue, is the use of a technique developed at Texas Tech Health Sciences Pain Center, published in 1989 [10].

Epidural lysis of adhesiones (LOA), also known as epidural neuroplasty, is a minimally invasive technique for the treatment of axial spine or radicular pain when epidural steroid injections or when conservative therapy has failed. The technique involves the introduction of an epidural radiopaque navigable catheter into the epidural space via the sacral hiatus. The catheter is then guided to the area of obstruction, which is believed to be the source of nociception. Once proper position is confirmed by the injection of contrast (which can also be used to map the fibrosis and obstruction) hyaluronidase, local anaesthetic, steroids, and other fluids are administered [11].

Regardless of whether the epidural scar tissue was created by a surgical procedure or a non-surgical phenomenon, the common premise for treating FBSS and painful radiculpathy (disc hernia, disc protursion, spinal stenosis) with LOA is that the presence of epidural fibrosis can both cause pain and prevent delivery of medications for relief. The relationship between the presence of scar tissue and pain has been examined by multiple studies, and is still being debated. Kuslich, *et al.* first described pain sensitive structures in the spinal canal while performing surgical laminectomies. Specifically, they found that nerve roots may become painful when inflamed or restricted by scar tissue [12]. Few years later the study of Ross, *et al.* showed that nerve roots exiting the spinal canal in the lateral reces are 3.2 times more likely to produce radicular pain if surrounded by scar tissue [13].

Another proposed mechanisam of action for epidural LOA is the wash out of inflammatory cytokines from the affected area. Rabinovitch, *et al.* found the relationship between the amount of volumen injected and the magnitude of pain relief. The mechanisms they proposed, of increasing the total amount of volume ensure a broad lavage of epidural space, suppression of ectopic discharge from injured nerves, and enhancing blood flow to ischemic nerve roots [14].

We hypothesize that LOA may be useful in patients with chronic lumbar radicular pain and low back pain. The aim of this study was to compare FBSS versus lumbar radicular pain, and the role of hyaluronidase when added to fluroscopically guided steroid and local anesthetic epidural injectate.

Methods

Subjects

After the approval of the Investigational Review Board, informed consent was obtained from patients participating in the study. The clinical subjects were 54 patients, of who some with previous back surgery who were compared to the others who didn't go through spine surgery but expressed radicular low back pain in wich there was failure of conservative therapy (pharmacotherapy plus physical therapy) and failure of conventional epidural steroid injection, chronic low back pain for at least 6 month duration, positive Laseque test (over 105^0) , and had a minimum visual analog pain core of 6/10.

This study included patients that showed magnetic resonance imaging findings of fibroplasias around nerve roots, central spinal canal stenosis, recurrent herniation of intervertebral disc or disc fragments remaining after surgery. Excluded from the study were individuals with spondylolisthesis, with facet joint lesions or sacroilitis, unstable or heavy opioid use, uncontrolled psychiatric disorders, hemostatic disorders, infection, and systemic steroids use.

Methods

The 54 patients, that partecipated in this study between January and December 2017, considering that the main criteria was post-surgical experience (FBSS – 33p.) or without any surgical experience (radiculopathy- 21p.), were divided into two groups.

All procedures were performed in the operating room under appropiate sterile conditions utilizing fluoroscopy. The procedure included appropriate preparation with intravenous access, antibiotic administration, and appropriate sedation using midazolam (2 to 3mg i.v.); patient were sedated but conscious. Patients were placed prone on a horizontal operating table. Pillows were placed under the abdomen to facilitate the entry of the sacral hiatus.

In each group the cutanues entry site was infiltrated with 2% lidocaine, and the lysis precedure was performed using a caudal approach. After a 16 gauge RX-2 Coude needle was placed into the sacral canal via the sacral hiatus and confirmed in the lateral

and antero-posterior views under fluoroscopy, 10ml of radiopaque contrast material (Omnipaque 300 MgIodine /Iohexol/,GE Healthcare) was injected to confirm epidural placement and identify any filling defects suggestive of epidural adhesions. Next a TUN-L-Kath, 20 G- catheter (Epimed International, USA) was inserted through the epidural needle and advanced to the antero-lateral area of filling defect and confirmed by 5 ml of radiopaque contrast material. Then 10ml of normal saline was injected through the catheter followed by 10ml of normal saline containing 1500 IU hyaluronidase. At the end another volume of 10ml saline with local anesthetic ropivacaine (3ml of 0.75% Ropivacaina Molteni, Italy) and 8 mg dexamethasone was slowly injected. After the synchronous withdrawal of the needle and of the catheter, the local skin was covered with a piece of aseptic compress. In addition, patient were asked to lie in bed on the treated/dependent side for at least half hour before turning on back.

During the recovery time patient were encouraged to perform standard physical therapy for lumbar neural flossing.

Evaluation

All patients were evaluated for demographic data (age, gender, Oswestry Disability Indeks – ODI, Visual Analog Score-VAS) duration of pain in months/years, segmental level of surgery, medical and surgical history, physical examination, and radiographic examinations (MR).

Follow-Up and Outcome

The primary outcome measure of this study was to identify if pain relief can be achieved in the same way between FBSS and chronic low back pain patients with the procedure of epidural lysis of adhesions.

The secondary outcome measures were reduction in painkiller intake, improvement in functional status, and the satisfaction with the improvement.

The effects of the procedures were evaluated by measuring the Visual Analog Score (VAS), level of LOA efficacy, and level of satisfaction with pain control before the procedure, in the 4th and the 12th week after the procedure. Each patient underwent a standard physical examination and was asked to complete a 100mm visual analogue scale (VAS) questionnaire, in wich 0mm represented no pain and 100mm the worst imaginable pain, for low back pain and leg symptoms on movement during activities of daily living.

The efficacy of the LOA procedure at the 4th and at the 12th week was valued using the modified Macnab evaluation standard in wich:

1. point – dissappointed, no any changes
2. point – poor - insufficient improvement to enable increase in activities
3. point - fair – improved functional capacity, but handicapped by intermittent pain of sufficient severity to curtail or modify work or leisure activities
4. point – good – occasional back or leg pain of sufficient severity to interfere with the patients normal work or daily work or leisure activities
5. point – excellent – no pain, no restriction of activity

In the 4th and the 12th week, after physical examination each patient was asked to estimate on his/her own, the percent value of the subjective improvement of pain reduction and the increase of the quality of daily life after the epidurolysis experience.

The pharmacotherapy intake was recorded during the time before the procedure and evaluated during the follw-up at the 4th and 12th week. By proper instructions the patients were allowed to slightly modificate the core pain therapy.

Level of pharmacotherapy intake was assessed as none, basic (NSAID), mild (tamadol <200mg/dy or oxycodone <20mg/dy), neuropathic (mild therapy plus pregabaline <150mg/dy), moderate (tramadol >300mg/dy, oxycodone >20mg/dy, pregabalin >150mg/dy), heavy (transdermal fentanyl, buprenorphine, morfine) based upon dosage, frequency and schedule.

Any potential complications (infection, rush, reaction, subarachnoid blockade) were also evaluated at each visit.

Statistics

The SPSS 18.0 statistical program for Windows was used for all analysis. Demographic and clinical characteristics are reported using descriptive statistics. Each treatment arm was assessed by comparing the results to the baseline results using repeated measures reapeted measures ANOVA. Between-groups comparison was done by using ANOVA. Global impression of pharmacotherapy intake was analized using non parametric Friedman test for within-subject effect, Chi-square test, and the p value of less than 0.05 was considered statistically significant.

Results

54 patients were included in our sample, of which 33 FBSS and 21 radiculopaty. Patients' characteristics were similar in the 2 groups regarding the demographic data (age, sex), duration of pain, ODI scores, segmental level of spine disease, average time from the last surgery (Table 1).

	Ep.lysis in FBSS pts. (N=33)	Ep.lysis in radiculopathy pts. (N=21)
Age	52.5±1.8	53.7±2.9
Gender (male/female)	11/22	8/13
Baseline pain score (VAS)	7.6±0.85	7.5±0.87
Duration of pain (years)	5.9±4.3	4.5±1.5
Laseque test - positive	33*pts.* (100%)	21*pts.* (100%)
ODI score	58.2±10.1	52.1±13.2
No.of spine surgery per patient	2.1±1.3	
ESI (prior to epidurolysis)	7/33 (21.2%)	4/21 (19.0%)
Previous back surgery		
fusion	7/33 (21.2%)	
total laminectomy	10/33 (30.3%)	
discectomy/partial laminectomy discectomy	5/33 (15.2%) 11/33 (33.3%)	
Level of spine disease		
L2/L3/L4	1	4
L3/L4	1	2
L3/L4/L5	11	7
L4/L5	9	2
L4/L5/S1	5	5
L5/S1	6	1

Values are means ± standard deviation

Table 1: General Characteristics of Patients

Statistical analysis revealed no group difference between epidemiological data, average baseline pain / VAS score and previous ESI experience at baseline (Table 1). Longer time of suffering the pain (years) and higher ODI score were more expressed with the FBSS group. It was not statistically significant at 5%, but it was significant at 10% (F=3.649; p=0.062). Among applied surgical methods, the discectomy and the total laminectomy were the most common. Among their spine disease injury, the most common level was L3/L4/L5 (Table 1).

All the patients completed the treatment with a sucess rate of 92.6% of epidural anterior tube indwelling. Varying degrees of adhesiones were observed in all patients when performing epidural anterior space epidurography. In four patients, two per group, the default goal of foraminal level was not reached and the predestined volumen was given at the detected level of epidural obstruction. The total volume injected in all the patients was 45 ml: 15 ml of radiopaque contrast material and 30 ml of normal saline with 1500 IU hyaluronidase, 22.5mg of ropivacaine and 8 mg of dexamethasone.

A significant reduction of pain intensity was observed in both groups after 4 weeks and 12 weeks following treatment. The results show that both groups have attained statistically significant ($p<0.05$) reduction of pain during the follow-up period, and the groups act equally related to time ($p<0.05$). According to Repeated measure methodology the tests of within-subject effects show that there are significant differences of VAS through time ($F=139.94$, $p<0.0001$) and confirm that the reduction of pain during the time is continuing to improve within each group, but between the groups the difference in VAS has no statistical significance ($F=0.770$, $p=0.384< 0.05$) (Table 2).

	Ep.Lysis in FBSS (N=33)	Ep.Lysis in Radiculopathy (N=20)	p-value
VAS			
Pretreatment	7.6±0.85	7.5±0.87	0.801
After 4 weeks	5.3±1.32	5.1±1.06	0.533
After 12 weeks	5.0±1.58	4.6±1.05	0.313
p-value	*<0.001*	*<0.001*	
Mean reduction of VAS			
After 4 weeks	-2.24±1.43	-2.38±0.92	0.712
After 12 weeks	-2.53±1.75	-2.85±0.92	0.454
p-value	0.084	**0.004**	

	Ep.Lysis in FBSS (N=33)	Ep.Lysis in Radiculopathy (N=20)	p-value
Pain relief >50% as Measured by VAS			
In the 4th week	3/33 (9.1%)	2/20 (10.0%)	
In the 12th week	9/33 (27.3%)	5/20 (25.0%)	
Level of satisfaction *(expressed in % of improvement)*			
After 4 weeks	24.3±14.35	25.3±11.47	0.806
After 12 weeks	23.0±16.10	26.6±12.47	0.387
p-value	0.299	0.388	
Evaluation of LOA procedure *(LOA efficacy)*			
After 4 weeks	2.85±1.25	3.05±1.00	0.544
After 12 weeks	2.88±1.52	3.15±1.35	0.514
p-value	0.839	0.577	

Values are means±standard deviation

Table 2: Comparison of Mean VAS, Comparison of the Mean Decrease (*in comparison with the value before the procedure - VAS*) of VAS, Pain relief >50% by VAS, Level of Satisfaction, Evaluation of LOA procedure in Each Group

The Table 2 shows decrease in VAS values in the 4th and 12th week after the procedure in comparison to the values before the procedure, respectively. As we can see the decreasing of pain is constant trough time but more expressive for the group of radiculopathy (p=0.004).

To test if the pain relief was achieved in the short time, the ratios of patients that showed at least 50% reduction in pain in the 4th and the 12th week were calculated by group.

Inside the group FBSS, at the 4th week after adhesiolysis 9.1% of patients had more than 50% of pain relief and 27.3% of patients had more than 50% of pain relief at the 12th week. Inside the group without surgery - patients with the radicular pain at the 4th week after adhesiolysis 10% of patients had more than 50% of pain relief and 25% of patients had more than 50% of pain relief at the 12th week (Table 2).

In the 4th and then 12th week after the procedure, the patients from the FBSS group estimated the daily functions improvement as 24% better against the beginning, and inside the group of Radiculopathy they express satisfaction of 25% in achieving a better daily life (Table 2).

In the 4th and 12th week after the clinical examination, using the modified Macnab questionnaire, every patient was asked to independently evaluate the efficacy of the adhesiolysis procedure (LOA efficacy) (Table 2). In both groups in the 4th week more than 30% of patients had estimated the LOA as procedure with disappointing / poor improvement, but the satisfaction was expressed in 39% of FBSS and 45% of radiculopathy patients. Later in the 12th week the number of unsatisfied patients didn't grow, instead it declined inside the group of Radiculopathy (25% of the patients were disappointed/poor). In the 12th week the overall sum of satisfied patients (good/excellent) was 36.4% inside the FBSS group, and 35% inside the Radiculopathy group. In conclusion the Radiculopathy group has expressed more improvement and satisfaction after LOA procedure with higher evaluation mean score (3.15 point vs.2.88 point) (p<0.05) (Table 3).

Evaluation of LOA		**Epidurolysis**			
		Ep. FBSS		**Ep. Radiculopathy**	
		at 4th week	**at 12th week**	**at 4th week**	**at 12th week**
1. disappointed	Count (%) within Epidurolysis	8 24.2%	9 27%	1 5.0%	4 20.0%
2. poor	Count (%) within Epidurolysis	3 9.1%	5 15.2%	6 30.0%	1 5.0%
3. fair	Count (%) within Epidurolysis	9 27.3%	7 21.2%	4 20.0%	6 30.0%
4. good	Count (%) within Epidurolysis	12 36.4%	5 15.2%	9 45%	6 30.0%
5.excellent	Count (%) within Epidurolysis	1 3.0%	7 21.2%	0 .0%	3 15%
Mean score		**2.85**	**2.88**	**3.05**	**3.15**

Table 3: Evaluation of LOA procedure in the 4th and 12th week by modified Macnab questionnaire

Based on Table 4 during the follow-up period after treatment we can conclude that the level of drugs intake through time has fallen in both groups (p<0.05). The dynamically changing course of pharmacotherapy intake compared to the baseline intake is

represented in the Table 5. and is of important significance for both groups (p<0.05). Especially intake of drugs for neuropathic pain relief (gabapentin / pregabalin) has been reduced significantly in both groups.

	Ep.FBSS (n=33)	Ep.Radiculopathy (n=21)
Pre-treatment	2.52	2.48
After 4 weeks	2.03	2.05
After 12 weeks	1.45	1.48
Chi-square (p-value)	31.089(<0.001)	17.077(<0.001)

Table 4: Mean rank of drugs level with Friedman tests for within-subject effects

	Pre-treatment		After 4 weeks		After 12 weeks	
	Ep.FBSS n=33	Ep.Radiculopathy n=21	Ep.FBSS n=33	Ep.Radiculopathy N=21	Ep.FBSS n=33	Ep.Radiculopathy n=21
None	**0**	**0**	0	1	**6**	3
Basic	3	0	**10**	**5**	**10**	**8**
Mild	16	17	13	13	13	**10**
Neuropathic	8	4	7	2	**1**	**0**
Moderate	3	0	1	0	1	0
Heavy	3	0	2	0	2	0

*bold p<0.05

Table 5: Drugs intake during follow-up period compared to pre-treatment therapy

Adverse Events

Transient subarachnoid block with motor block of lower limbs and moderate blood pressure drop was identified after completion of the procedure and injection of local anesthetic and steroids in one patient from the FBSS group. The block spontaneously recovered after one hour with no repercussions on the course of recovery. There were no instances of infection, rash, arachnoiditis, paralysis, weakness, blader disturbances or other serious complications.

Discussion

In this study, varying degrees of fibrosis or adhesions, and narrowed epidural space were observed in all patients when performing epidurography. There was contrast agent surrounding neurons in the form of reduced Christmas tree and filling defects of contrast agent at adhesion segments in the epidural space.

Epidural fibrosis is an inflammatory reaction of the arachnoid, a fine nonvascular and elastic tissue enveloping the CNS. There are many possible etiologies of epidural fibrosis, including an annular tear, hematoma, infection, surgical trauma [15]. MaCarron, *et al.* investigated the irritative effect of material from the nucleus pulposus upon the dural sac, adjacent nerve roots, and nerve root sleeves independent of the influence of direct compression upon these structures, ultimately producing back pain [16]. Kuslich, *et al.* concluded that the presence of scar tissue compounded pain associated with the nerve root by fixing it in one position and thus increasing the susceptibility of the nerve root to tension and compression. They also concluded that sciatica can only be produced by direct pressure or stretch on the inflammatory, stretched, or compressive root [12]. Even though considerable debate exists as to whether epidural fibrosis causes pain, it is widely accepted that postoperative scar tissue renders the nerve susceptible to injury. Epidural fibrosis may account for as much as 20% to 36% of cases of FBSS [17].

Scar tissue is generally found in the 3 compartments of the epidural space. Dorsal epidural scar tissue is formed by resorption of surgical hematoma and may be involved in pain generation. In the ventral epidural space, dense scar tissue is formed by ventral defects in the disc, which may persist despite surgical treatment and continue to produce either chronic low back or lower extremity pain after the surgical healing phase. Finally, the lateral epidural space includes epiradicular structures outside the roots canals, termed sleeves, containing the existing nerve root and dorsal root ganglia, susceptibile to lateral disc defects, facet overgrowth and neuroforaminal stenosis, etc [18].

The presence or absence of epidural adhesions is difficult to demonstrate by conventionally used studies such as standard x-ray or CT or MR scans. The epidurography technique seems to be the only appropriate but it is rarely used as routine praxis, that's why the percutaneus adhesiolysis is the only suitable method that allows to inject targeted high volume mixture of hyaluronidase and steroids to open this filling defects. Hyaluronidase is used to start biological lysis of the tight cell junctions between different anatomic sheets. Its primary action is to depolymerize hyaluronic acid, chondrotin-4 and chondrotin-6 sulfate, and to disrupt the proteoglycan ground substance, thus accelerating the diffusion of injected substances. The dura, wich is composed of collagen, elastin, and surface fibroblast, is preserved [19]. The combined application of hyaluronidase, the large volume of fluid, and the

low direct mechanical effects leads to the local dissection of the anatomic structures into the region of adhesions which exist in chronic local inflamed anatomic regions as the epidural space if extruded disc material or bulged disc are present. Heavner, *et al.* concluded that patients with low back pain and radiculopathy treated with hyaluronidase obtained a higher percentage of pain relief [19]. Yousef, *et al.* were able to demonstrate that hyaluronidase has a significant long-term pain relief in patients with FBSS [18]. Corticosteroids injected epidurally are effective for chronic back pain because of their anti-inflammatory effect. They also inhibit ectopic discharge; this membrane-stabilizing effect may be responsable for symptomatic improvement in patients with severe nerve root patology. In addition, neuraxially administered steroids might have an antihyperalgesic effect in patients with central sensitization. Of great concern, however, are rare injuries to the central nervous system that occur as a result of epidural corticosteroid injections. Laboratory studies have shown that certain steroid preparations contain particles and form aggregates. Methylprednisolone has the largest particles, triamcinolone is intermediate, and betamethasone has the smallest. These particles or their aggegates can act as emboli if injected into an artery and are of sufficient size to block small terminal arterioles supplying the brain or spinal cord. Dexamethasone does not form particles or aggregates [24]. Kennedy, *et al* in their study have now shown that the effectiveness of dexamethasone is not significantly less than that of particulate steroids [25].

Neural blockade achieved with epidural local anesthetic injection alters or interrupts nociceptive input, reflex mechanism of the afferent fibers, self-sustaining activity of the neurons, and the pattern of neuronal activities [20].

The results of this study show that epidural lysis of adhesions using hyaluronidase and steroids in high volume is effective in managing chronic low back and lower extremity pain in patients who were shown to be suffering pain nonresponsive to direct epidural stereoid injections and other conservative treatments. The analysis confirms that adhesiolysis can be an effective method for treating pain conditions that are the consequence of FBSS but is succesful even among patients with chronic lumbar radicular pain. This study showed that significant pain relief was achieved in both patients that suffer the same form of pain but from different source of cause. The study showed that in the 4th week, only 9% of the patients in FBSS and 10% of the patients in radiculopathy group had >50% pain relief, but in the 12th week 27% of the patients in FBSS and 25% of the patients in radiculopathy group had >50% pain relief. The significant improvement in most patients was achieved in deffered time. Significant pain relief (>50%) was also associated with significant reduction in drugs intake early within 12weeks of the procedure (FBSS – from 2.52 to 1.52; radiculopathy – from 2.48 to 1.48) (<0.001) Less pain and less painkiller intake, for both group was associated with improvement in range of motion, functional status, physical health and menthal health. Through analysis of modified Macnab questionnaire this study also showed that the majority of all patients evaluate the procedure of adhesiolysis as successful (after 12 weeks 57% of the patients in FBSS and 75% of the patients in radiculopathy group).

The results of present study are similar to the results of the randomized trial of Kim, *et al.,* who compared treatment outcomes in patients with FBSS and sciatica reporting that greater improvement in pain scores and function after 12 weeks was noted in the group that received hyaluronidase and steroids than those who received either drug alone [21].

A later multi-center randomized, double-blind study of Gerdesmeyer, *et al.* performed for the same indication compared epidural adhesiolysis to placebo treatment in 90 patients with lumbar radiculopathy. Three months post-procedure, the mean VAS pain score improved from 6.7 to 2.9 in the treatment group, and from 6.7 to 4.8 in the control group. Similar benefit favoring the adhesiolysis group was noted for Oswestry Disability Index scores. The statistically significant benefit favoring the treatment group was maintained throughout the 12-month follow-up [22].

A small randomized study by Yousef, *et al.* compared treatment outcomes in 38 subjects who received either fluoroscopically-guided caudal injections of 10 ml of 0.25% bupivacaine, 30 ml of 3% hypertonic saline and 80 mg of methyl-prednisolone, or the same mixture with 1.500 units of hyaluronidase added. Although significant improvements in pain and functional were noted in both groups through 3-month follow-up, only those patients who received hyaluronidase continued to experience benefit at 6 and 12-month post-procedure [18].

Although the question has not been formally addressed in randomized study, there is evidence that a significant portion of the benefit for epidural adhesiolysis can be attributed to the high volumes injected. In a systematic review by Rabinovitch, *et al.*, the researcher found a strong correlation between the volume of epidural injectate and pain relief irrespective of the steroid dose in the immediate (<6 weeks), and short-term (6 weeks- 3 months) and intermediate–term (3 months-1 year). At the same time they report that the beneficial effect that high volume confers is likely constrained by a ceiling effect [14].

The finding of this study complement positive findings of other studies that examined the safety and efficacy of epidural adhesiolysis [23].

One limitation of our study is the unknown effect of each single treatment component. Based on our findings we cannot give any recommendation if the full cycle of treatment and parameters used is necessary to achieve these results or if one of the options such as hyaluronidase, dosage of cortisone, normal saline, or just the volume injected has possibly significant effect on outcome. Further studies have to focus on these specific effects of each single parameter. We strongly believe that the epidurography and the mechanical effect of the navigable catheter have important effect on the positive outcome.

Conclusions

Percutaneous lysis of adhesiones with a mixture of hyaluronidase and steroid should be the first choice treatment option for

patients with FBSS and for patients with chronic lumbosacral radicular pain which is presented with clinical conditions similar to those of the patients enolled in our study. It is simple, safe and effective treatment almost without any adverse reaction.

References

1. Komotar RJ, Arias EJ, Connolly ES, Angevine PD, et al. (2007) Update:randomized clinical trials of surgery versus prolonged non-operative management of herniated lumbar discs. Neurosurgery 61: N10.

2. Clinical Guidelines for Multidisciplinary Spine Care, Diagnosis and Treatment of Lumbar Disc Herniation with Radiculopathy. 2012 North American Spine Society Clinical Guidelines.

3. Thomson S (2013) Failed back surgery syndrome-definition, epidemiology and demographics. Br J Pain 7: 56-9.

4. Skolasky RL, Wegener ST, Maggard AM, Riley LH (2014) The impact of reduction of pain after lumbar spine surgery: the relationship between changes in pain and physical function and disability. Spine 39: 1426-32.

5. Bicket MC, Horowitz JM, Benzon HT, Cohen SP (2015) Epidural injections in prevention of surgery for spinal pain: systematic review and meta-analysis of randomized controlled trials. Spine J 15: 348-62.

6. Rahimzadeh P, Sharma V, Imani F, Faiz HR, Ghodraty MR, et al. (2014) Adjuvant hyaluronidase to epidural steroid improves the quality of analgesia in failed back surgery syndrome: a prospective randomized trial. Pain Physician 17: E75-82.

7. Helm S, Racz GB, Gerdesmeyer L, Justiz R, Hayek SM, et al. (2016) Percutaneous and endoscopic adhesiolysis in managing low back and lower extremity pain: a systematic review and meta-analysis. Pain Physician 19: E245-81.

8. van Tulder M, Malmivaara A, Hayden J, Koes B (2007) Statistical significance versus clinical importance: trials on exercise therapy for chronic low back pain as example. Spine 32: 1785-90.

9. Wilkinson HA (2005) Injection Therapy for Enthesopathies Causing Axial Spine Pain and "The Failed Back Syndrome:" A Single Blinded, Randomized and Cross-Over Study. Pain Physician 8: 167-73.

10. Racz GB, Heavner JE, Diede JH (1996) Lysis of epidural adhesions utilizing the epidural approach. In: Interventional pain management. Edited by Waldman SD, Winnie AP, Philadelphia (PA), WB Saunders 339-51.

11. Trescot AM, Chopra P, Abdi S, Datta S, Schultz DM, et al. (2007) Systemic review of effectiveness and complications of adhesiolysis in the management of chronic spinal pain: an update. Pain Physician 10: 129-46.

12. Kuslich SD, Ulstrom CL, Michael CJ (1991) The tissue origin of low back pain and sciatica: a report of pain response to tissue stimulation during operations on the lumbar spine using local anesthesia. Orthop Clin North Am 22: 181-7.

13. Ross JS1, Robertson JT, Frederickson RC, Petrie JL, Obuchowski N, et al. (1996) Association between peridural scar and recurrent radicular pain after lumbar disectomy: magnetic resonance evaluation. ADCON-L European Study Group. Neurosurgery 38: 855-61.

14. Rabinovitch DL, Peliowski A, Furlan AD (2009) Influence of lumbar epidural injection volume on pain relief for radicular leg pain and/or low back pain. Spine J 9: 509-17.

15. Anderdon S (2000) A rationale for the treatment algorithm of failed back surgery syndrome. Curr Rev Pain 4: 395-406.

16. McCarron RF, Wimpee MW, Hudkins PG, Laros GS, et al. (1987) The inflammatory effects of nucleus pulposus: A possible element in the patogenesis of low back pain. Spine 12: 760-4.

17. Manchikanti L, Saini B, Singh V (2001) Spinal endoscopy and lysis of epidural adhesion in the management of chronic low back pain. Pain Physician 4: 240-65.

18. Yousef Ayman AAM, Seif El-deen A, Ead Al-deeb A (2010) The role of adding hyaluronidase to fluoroscopically guided caudal steroid and hypertonic saline injection in patients with failed back surgery syndrome: a prospective, double-blinded, randomized study. Pain Practice 10: 548-53.

19. Heavner JE, Racz GB, Raj P (1999) Percutaneous epidural neuroplasty: prospective evaluation of 0.9% NaCl versus 10% NaCl with or without hyaluronidase. Reg Anesth Pain Med 24: 201-7.

20. Abdi S, Datta S, Trescot AM, Schultz DM, Adlaka R, et al. (2007) Epidural steroids in the management of chronic spinal pain: a sistematic review. Pain Physician 10: 185-212.

21. Kim SB, LeeKW, LeeJH, Kim MA, An BW, et al. (2012) The effect of hyaluronidase in interlaminar lumbar epidural injection for failed back surgery sindrome. Ann Rehabil Med 36: 466-73.

22. Gerdesmeyer L, Wagenpfeil S, Birkenmajer C, Veihelmann A, Hauschild M, et al. (2013) Percutaneus epidural lysis of adhesiones in chronic lumbar radicular pain: a randomized, double-blind, placebo-controlled trial. Pain Physician 16: 185-96.

23. Lee F, Jamison DE, Hurley RW, Cohen SP (2014) Epidural lysis of adhesions. Korean J Pain 27: 3-15.

24. Rathmell JP, Benzon HT, Dreyfuss P, Huntoon M, Wallace M et al. (2015) Safeguards to prevent neurologic complication after epidural steroid injections. Anesthesiology 122: 974-84.

25. Kennedy DJ1, Plastaras C, Casey E, Visco CJ, Rittenberg JD, et al. (2014) Comparative effectiveness of lumbar transforaminal epidural steroid injections with particulate versus nonparticulate corticosteroids for lumbar radicular pain due to intervertebral disc herniation: a prospective, randomized, double trial. Pain Med 15: 548-55.