EPIDURAL ADHESIOLYSIS IN THE MANAGEMENT OF CHRONIC LOW BACK PAIN IN FAILED BACK SURGERY SYNDROME AND IN LUMBAR RADICULAR PAIN: FIRST YEAR OF EXPERIENCE AT PULA GENERAL HOSPITAL, PULA, CROATIA – A RANDOMIZED TRIAL

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Aim. The aim was to evaluate the efficacy and feasibility of percutaneous adhesiolysis to reduce pain, improve daily functions and reduce drug use in patients with chronic pain. Chronic radicular pain can be caused by scar tissue, compression, inflammation, or 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 to achieve pain relief. ***Methods***: Standard percutaneous epidural adhesiolysis was performed in 54 patients divided into two groups: pain from failed back surgery syndrome (FBSS) *versus* chronic radicular pain without previous spine surgery. Visual analog scale (VAS) score, change in pharmacotherapy used, subjective satisfaction and evaluation of the lysis procedure were observed in pretreatment, and then in the 4th and 12th week of the intervention. ***Results:*** VAS scores for pain were significantly reduced in both groups in the 4th and 12th week. A statistically significant decrease was expressed in the radiculopathy group (VAS^{0}=7.5±0.87/VAS^{12th}=4.6±1.05) *versus* 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 use (p<0.001) and clinical effectiveness rate of >50% was achieved in 27% of FBSS patients and 25% of patients with chronic radicular pain without surgery experience. ***Conclusion:*** Considering the small sample size, our results in short-term pain relief suggested that epidurolysis could be an effective method in the treatment of patients with chronic radicular pain as in patients with FBSS.

Key words: epidural adhesiolysis, failed back surgery syndrome, chronic radicular pain, hyaluronidase, clinical outcome

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INTRODUCTION

Radicular pain is a type of pain that radiates into lower extremity directly along the course of the 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 numbness and tingling, muscle weakness and loss of reflexes. Radicular pain is caused by compression, inflammation and/or injury to 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), use of analgesics and ineffective conservative treatments are indicators that point to the need of using contrast-enhanced fluoroscopic epidural steroid injections (ESI) (2,3).

The International Association for the Study of Pain defined the failed back surgery syndrome (FBSS) as a phenomenon of persistent or recurrent pain, mainly in the lower back and/or legs, even after previous ana-

tomically successful spinal surgeries. A recent systematic literature review of discectomies for lumbar disc herniation in patients under the age of 70 years revealed frequent recurrent back or leg pain in 5%-36% of patients 2 years after the operation (4,5).

Postoperative 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 the intended target, compromise the efficacy of ESI (6). Adhesions can theoretically be lysed by delivering hyaluronidase, thereby improving baseline pain scores and improving steroid effect (7,8).

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

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

An alternative method to reduce fibroplasias and remove barriers between tissues, to induce resolution of scar tissue or epidural adhesions, and to deliver steroids to the inflamed nerve tissue is the use of a technique developed at Texas Tech Health Sciences Pain Center, published in 1989 (10).

Epidural lysis of adhesions (LOA), also known as epidural neuroplasty, is a minimally invasive technique for the treatment of axial spine or radicular pain when ESI or 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 anesthetic, steroids, and other fluids are administered (11).

Regardless of whether the epidural scar tissue was created by a surgical procedure or is a non-surgical phenomenon, a common premise for treating FBSS and painful radiculopathy (disc hernia, disc protrusion, 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 in multiple studies, and is still being debated. Kuslich *et al*. were the first to describe 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). A few years later, the study by Ross *et al*. showed that nerve roots exiting the spinal canal in the lateral recess were 3.2 times more likely to produce radicular pain if surrounded by scar tissue (13).

Another proposed mechanism of action for epidural LOA is the washout of inflammatory cytokines from the affected area. Upon systematic literature analysis, Rabinovitch *et al*. concluded that there was a relationship between the amount of volume injected and the magnitude of pain relief. The mechanisms they propose include increasing the total amount of volume to ensure broad lavage of the epidural space, suppression of ectopic discharge from injured nerves, and enhancing blood flow to ischemic nerve roots (14).

We hypothesized 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 to assess the role of hyaluronidase when added to fluoroscopically guided steroid and local anesthetic epidural injection.

METHODS

Subjects

After approval of the Investigational Review Board, informed consent was obtained from patients participating in the study. There were 54 patients, some with previous back surgery who were compared to the others who had not undergone spine surgery but had radicular low back pain with 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, and minimum visual analog scale (VAS) pain score of 6/10.

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

Methods

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

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

In each group, the cutaneous entry site was infiltrated with 2% lidocaine and the lysis procedure 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, 10 mL of radiopaque contrast material (Omnipaque 300 Mg iodine /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 anterolateral area of filling defect and confirmed by 5 mL of radiopaque contrast material. Then 10 mL of normal saline was injected through the catheter followed by 10 mL of normal saline containing 1500 IU hyaluronidase. At the end, another volume of 10 mL saline with local anesthetic ropivacaine (3 mL of 0.75% Ropivacaina Molteni, Italy) and 8 mg dexamethasone was slowly injected. After the synchronous withdrawal of the needle and the catheter, local skin was covered with a piece of aseptic compress. In addition, patients were asked to lie in bed on the treated/dependent side for at least half hour before turning on back.

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

Evaluation

All patients were evaluated for demographic data (age, gender, Oswestry Disability Index (ODI), VAS), duration of pain in months/years, segmental level of surgery, medical and surgical history, physical examination, and radiographic examinations (magnetic resonance imaging, MRI).

Follow-up and outcome

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

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

The effects of the procedures were evaluated by measuring the VAS, level of LOA efficacy, and level of satisfaction with pain control before the procedure, in the 4th and 12th week of the procedure. Each patient underwent standard physical examination and was asked to complete a 100-mm VAS questionnaire in which 0 mm represented no pain and 100 mm represented 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 12th week was evaluated using the modified Macnab evaluation standard, as follows:

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

In the 4th and 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 in the quality of daily life after the epidurolysis experience.

The use of pharmacotherapy was recorded during the time before the procedure and evaluated during the follow-up at the 4th and 12th week. By proper instructions, the patients were allowed to slightly modify the core pain therapy.

The level of pharmacotherapy use was assessed as none, basic (NSAID), mild (tramadol <200 mg/day or oxycodone <20 mg/day), neuropathic (mild therapy plus pregabalin <150 mg/day), moderate (tramadol >300 mg/day, oxycodone >20 mg/day, pregabalin >150 mg/day), heavy (transdermal fentanyl, buprenorphine, morphine) based upon dosage, frequency and schedule.

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

Statistics

The SPSS 18.0 statistical program for Windows was used on 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 the repeated measures ANOVA. Between-group comparison was done by using ANOVA. Global impression of pharmacotherapy use was analyzed using nonparametric Friedman test for within-subject effect and χ^2-test. The p value of less than 0.05 was considered statistically significant.

RESULTS

Fifty-four patients were included in the study, of which 33 FBSS and 21 radiculopathy. Patient characteristics were similar in the two groups regarding demographic data (age, sex), duration of pain, Oswestry Disability Index (ODI) scores, segmental level of spine disease, and average time from the last surgery (Table 1).

Table 1.
General characteristics of patients

	FBSS group (N=33 patients)	**Radiculopathy group (N=20 patients)**
Age	52.5±1.8	53.7±2.9
Gender (male/female)	11/22	7/13
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%)	20 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	5/33 (15.2%)	
Discectomy	11/33 (33.3%)	
Level of spine disease		
L2/L3/L4	1	3
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; FBSS – failed back surgery syndrome; VAS – visual analog scale; ODI – Oswestry Disability Index score; ESI – epidural steroid injections; LOA – lysis of adhesions

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

All patients completed treatment with a success rate of 92.6% of epidural anterior tube indwelling. Varying degrees of adhesions 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 volume was given at the detected level of epidural obstruction. The total volume injected in all patients was 45 mL, i.e. 15 mL of radiopaque contrast material and 30 mL of normal saline with 1500 IU hyaluronidase, 22.5 mg of ropivacaine and 8 mg of dexamethasone.

Final analysis of the results in the radiculopathy group was based on 20 instead of 21 patients initially included because one of the participants quit the study.

A significant reduction of pain intensity was observed in both groups after 4 weeks and 12 weeks following treatment. The results showed that both groups attained statistically significant ($p<0.05$) reduction of pain during the follow-up period, and the groups acted equally related to time ($p<0.05$). According to the repeated measure methodology, the tests of within-subject effects showed that there were significant differences in VAS over time ($F=139.94$, $p<0.0001$), confirming that the reduction of pain over time continued to improve within each group, but between-group difference in VAS did not reach statistical significance ($F=0.770$, $p=0.384< 0.05$) (Table 2).

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

	FBSS group (n=33)	**Radiculopathy group** (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**	
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; FBSS – failed back surgery syndrome; LOA – lysis of adhesions; VAS – visual analog scale;

Table 2 shows a decrease in VAS values in the 4th and 12th week after the procedure in comparison to the values before the procedure. As we can see, the decrease of pain was constant over time but more pronounced in the group of radiculopathy (p=0.004).

To test if the pain relief was achieved in short time, the ratios of patients that showed at least 50% reduction in pain in the 4th and 12th week were calculated by group. In the FBSS group, , 9.1% of patients had more than 50% of pain relief at the 4th week after adhesiolysis and 27.3% of patients had more than 50% of pain relief at the 12th week. In the group without surgery, i.e. patients with radicular pain, 10% of patients had more than 50% of pain relief at the 4th week after adhesiolysis and 25% of patients had more than 50% of pain relief at the 12th week (Table 2). In the 4th and 12th week after the procedure, the patients from the FBSS group estimated the improvement in daily functions as being by 24% better against the beginning, and the group of radiculopathy patients expressed 25% satisfaction in achieving better daily living (Table 2).

In the 4th and 12th week after clinical examination, using the modified Macnab questionnaire, each 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 estimated LOA as a procedure with disappointing/poor improvement, but satisfaction was expressed by 39% of FBSS and 45% of radiculopathy patients. Later, in the 12th week, the number of unsatisfied patients did not grow but declined in 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% in the FBSS group and 35% in the radiculopathy group. In conclusion, the radiculopathy group expressed more improvement and satisfaction after LOA procedure with higher evaluation mean score (3.15 points *vs*. 2.88 points; p<0.05) (Table 3).

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

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

LOA – lysis of adhesions; FBSS – failed back surgery syndrome

As illustrated in Table 4, during the follow-up period after treatment we can conclude that the level of drug use over time decreased in both groups (p<0.05). The dynamically changing course of pharmacotherapy use compared to the baseline use is presented in Table 5 and was significant in both groups (p<0.05). Especially the use of drugs for neuropathic pain relief (gabapentin/pregabalin) was reduced significantly in both groups.

Table 4.
Mean rank of drug level with Friedman tests for within-subject effects

	FBSS group (n=33)	**Radiculopathy group (n=20)**
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)

FBSS – failed back surgery syndrome

Table 5.
Drug use during follow-up period compared to pre-treatment therapy

	Pre-treatment		**After 4 weeks**		**After 12 weeks**	
	FBSS Group n=33	**Radiculopathy group n=20**	**FBSS group n=33**	**Radiculopathy group n=20**	**FBSS group n=33**	**Radiculopathy group n=20**
None	0	0	0	1	**6**	3
Basic	3	0	**10**	**5**	**10**	**8**
Mild	16	16	13	12	13	**9**
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; FBSS – failed back surgery syndrome

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, bladder 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 central nervous system. There are many possible etiologies of epidural fibrosis, including an annular tear, hematoma, infection, and surgical trauma (15). MaCarron *et al*. investigated the irritating effect of the 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 root canals, termed sleeves, containing the existing nerve root and dorsal root ganglia susceptible 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 computed tomography or MRI scans. The epidurography technique seems to be the only one appropriate but it is rarely used as routine practice, and that is why percutaneous adhesiolysis is the only suitable method that allows to inject targeted high volume mixture of hyaluronidase and steroids to open these 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 diffusion of the injected substances. The dura, which 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 lead to local dissection of the anatomic structures into the region of adhesions that exist in chronic local inflamed anatomic regions such as the epidural space if extruded disc material or bulged disc is 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 caused 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 responsible for symptomatic improvement in patients with severe nerve root pathology. 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 has intermediate, and betamethasone has the smallest particles. These particles or their aggregates 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 (20). Kennedy *et al*. in their study showed that the effectiveness of dexamethasone was not significantly less than that of particulate steroids (21).

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 (22).

The results of the present study showed that epidural lysis of adhesions using hyaluronidase and steroids in high volume was effective in managing chronic low back and lower extremity pain in patients shown to suffer pain nonresponsive to direct epidural steroid injections and other conservative treatments. The analysis confirmed that adhesiolysis could be an effective method for treating pain conditions that are the consequence of FBSS but was successful even among patients with chronic lumbar radicular pain. This study showed that significant pain relief was achieved in patients suffering the same form of pain but from different source of cause. The study showed that in the 4th week, only 9% of patients in FBSS group and 10% of patients in radiculopathy group had >50% pain relief, but in the 12th week 27% of patients in the FBSS

group and 25% of patients in the radiculopathy group had >50% pain relief. The significant improvement in most patients was achieved in different time. Significant pain relief (>50%) was also associated with significant reduction in drug use early within 12 weeks of the procedure (FBSS, from 2.52 to 1.52; radiculopathy, from 2.48 to 1.48) (<0.001). In both groups, less pain and less painkiller use was associated with improvement in the range of motion, functional status, physical health and mental health. Through analysis of modified Macnab questionnaire, this study also showed that the majority of all patients evaluated the procedure of adhesiolysis as successful (after 12 weeks, 57% of patients in the FBSS group and 75% of patients in radiculopathy group).

The results of the present study are similar to the results of the randomized trial by 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 in those who received either drug alone (23).

A later multi-center randomized, double-blind study by 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 ODI scores. The statistically significant benefit favoring the treatment group was maintained throughout the 12-month follow-up (24).

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 methylprednisolone, or the same mixture with 1500 units of hyaluronidase added. Although significant improvements in pain and function were noted in both groups over 3-month follow-up, only those patients who received hyaluronidase continued to experience benefit at 6 and 12 months 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 researchers found a strong correlation between the volume of epidural injection 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 findings of this study are complementary to positive findings of other studies that examined the safety and efficacy of epidural adhesiolysis (25).

One limitation of our study was the unknown effect of each single treatment component. Based on our findings, we cannot give any recommendation whether full cycle of treatment and parameters used is necessary to achieve these results, or 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 epidurography and the mechanical effect of the navigable catheter have an important effect on the positive outcome.

CONCLUSIONS

Percutaneous LOA with a mixture of hyaluronidase and steroid should be the first-choice treatment option for patients with FBSS and those with chronic lumbosacral radicular pain, which is presented with clinical conditions similar to those in the patients enrolled in our study. It is a simple, safe and effective treatment almost without any adverse reaction.

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S A Ž E T A K

EPIDURALNA ADHEZIOLIZA U LIJEČENJU KRONIČNE KRALJEŽNIČKE BOLI KOD SINDROMA NEUSPJELE OPERACIJE KRALJEŽNICE I KOD LUMBALNE RADIKULARNE BOLI: JEDNOGODIŠNJE ISKUSTVO U OPĆOJ BOLNICI PULA

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Cilj: Cilj ove randomizirane studije bila je procjena izvodivosti i učinkovitosti adheziolize u liječenju kronične kralježničke boli, njezin utjecaj na poboljšanje kvalitete života, odnosno njezin učinak na kroničnu analgetsku terapiju. Epiduralna adhezioliza omogućava postavljanje posebno dizajniranih katetera u ventrolateralni aspekt epiduralnog prostora, tj. u neposrednoj blizini izlazaćeg živčanog korijena i preciznu primjenu steroida, hijaluronidaze i lokalnih anestetika u cilju smanjenja fenomena boli. ***Metoda:*** U studiju su uskljućena 54 bolesnika podijeljena u dvije skupine: bolesnici s kroničnom boli nakon neuspjele kralježničke operacije (FBSS) naspram bolesnika s kroničnom radikularnom boli bez prethodnog kirurškog iskustva. Nakon 4. odnosno 12. tjedna od postupka praćene su promjene u vizualno analognoj ljestvici boli (VAS), u farmakoterapijiskom unosu, u stupnju subjektivnog životnog zadovoljstva bolesnika, kao i procjena ukupnog učinka adheziolize. ***Rezultati:*** Prosječna razina boli (VAS) bila je značajno smanjena u obje skupine i u 4. i u 12. tjednu. Statistički značajno smanjenje izraženo je u skupini radikulopatije (VAS 0 = 7,5 0,87 / VAS 12th = 4,6 1,05) u odnosu na FBSS skupinu (VAS 0 = 7,6 0,85 / VAS 12th = 5,0 1,58) (p <0,001). Poboljšanje, odnosno smanjenje stupnja boli, rezultiralo je značajnim smanjenjem ukupne razine farmakoterapije (p <0,001), a klinička učinkovitost od > 50 % smanjenja inicijalne boli iskazala se u 27 % pacijenata s FBSS i u 25 % bolesnika s kroničnom radikularnom boli. ***Zaključak:*** S obzirom na naš mali uzorak, ostvareni rezultati u kratkoročnom ublažavanju boli ukazuju da epiduralna adhezioliza može biti učinkovita metoda u liječenju bolesnika s kroničnom radikularnom boli kao što je to u bolesnika s FBSS.

Ključne riječi: epiduralna adhezioliza, sindrom neuspjele kralježničke kirurgije, kronična radikularna bol, hijaluronidaza, klinički ishod