Regional Anesthesia and Pain Medicine 24(3): 202–207, 1999

Percutaneous Epidural Neuroplasty: Prospective Evaluation of 0.9% NaCl Versus 10% NaCl With or Without Hyaluronidase

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Background and Objectives. Percutaneous epidural neuroplasty (epidural neurolysis, lysis of epidural adhesions) is an interventional pain management technique that has emerged over approximately the last 10 years as part of a multidisciplinary approach to treating radiculopathy with low back pain. In addition to local anesthetic and corticosteroid, hypertonic saline (10% NaCl) and hyaluronidase are used for the technique. The objective of this study was to determine if hypertonic saline or hyaluronidase influenced treatment outcomes. *Methods.* Eighty-three subjects with radiculopathy plus low back pain were assigned to one of four epidural neuroplasty treatment groups: (a) hypertonic saline plus hyaluronidase, (b) hypertonic saline, (b) isotonic saline (0.9% NaCl), or (d) isotonic saline plus hyaluronidase. Subjects in all treatment groups received epidural corticosteroid and local anesthetic. *Results.* Twenty-four subjects did not complete the study. Most of the other 59 subjects receiving any of the four treatments as part of their pain management obtained significant relief immediately after treatment. Visual analog scale (VAS) scores for the area of maximal pain (VAS_{max}; back or leg) were reduced in 25% or more of subjects in all treatment groups at all post-treatment follow-up times (1, 3, 6, 9, and 12 months). A smaller fraction of subjects treated with hypertonic saline or hyaluronidase and hypertonic saline required more additional treatments than did subjects receiving the other treatments. *Conclusions.* Percutaneous epidural neuroplasty, as part of an overall pain management strategy, reduces pain (sometimes for over one year) in 25% or more of subjects with radiculopathy plus low back pain refractory to conventional therapies. The use of hypertonic saline may reduce the number of patients that require additional treatments. *Reg Anesth Pain Med 1999: 24: 202–207.*
Key words: low back pain, radiculopathy, epidural, local anesthetic, corticosteroid, hyaluronidase, hypertonic saline.

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Accepted for publication October 22, 1998.

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0146-521X/99/2403-0004$5.00/0

Percutaneous epidural neuroplasty (epidural neurolysis, lysis of epidural adhesions) is an interventional pain management technique that has emerged over approximately the last 10 years (1). At our institution, patients are considered to be candidates for neuroplasty if they have radiculopathy and back pain, if conservative treatment has been ineffective, and after appropriate diagnostic evaluation (physical examination, diagnostic and prognostic procedures) (2). Our development and acceptance of the procedure were based on (a) in-

creased understanding of structural changes in the epidural and intervertebral spaces that can contribute to radicular and low back pain; (b) better definition of what structures in and around the epidural space may be involved in the generation of pain; (c) data regarding the nature and location of pain that is perceived when different pathologic structures in and adjacent to the epidural space are stimulated; (d) improvements in techniques for reliably and safely accessing the epidural space via the percutaneous route; (e) recognition of epidurography as a diagnostic and therapeutic aid; (f) establishment of a clear rationale for the procedure and medications used to accomplish epidural neurolysis; (g) demonstrated patient improvement, and (h) acceptance of the technique by physicians qualified to judge its merits (3–11).

The following pathologic changes may be present in neural and/or other tissues within the bony vertebral canal and/or intervertebral spaces of patients with radiculopathy and with chronic back pain: (a) inflammation; (b) edema; (c) fibrosis; (d) venous congestion; (e) mechanical pressure on the posterior longitudinal ligament, annulus fibrosis, and spinal nerve; (f) reduced or absent nutrient delivery to the spinal nerve or nerve root; and (g) central sensitization (4,12). The goals for neuroplasty are to break down fibrous adhesions that may prevent free movement of structures in the intervertebral foramen and in the bony vertebral canal, to remove any barriers (scar) that prevent application of medication to structures believed to be the source of pain, and to apply medication to the structures (e.g., local anesthetics, corticosteroids). It is important to emphasize that the neuroplasty procedure is lesion specific and involves epidurographic diagnosis, neurolysis, and injection of saline with or without hyaluronidase, and corticosteroid and local anesthetic.

In a retrospective study, we found that hyaluronidase reduced the neuroplasty treatment failure rate from 18 to 6% (12). The purpose of this double-blind, prospective study was to determine if hyaluronidase and/or hypertonic saline improves treatment outcome when used along with corticosteroid, local anesthetic, and fluid lysis of epidural scarring.

Methods

After receiving approval from the Institutional Review Board for the Protection of Human Subjects and after obtaining informed consent, 83 subjects scheduled for lysis of epidural adhesions were enrolled in this prospective study. Enrollment criteria included patient scheduled for epidural neuroplasty, with pain radiating unilaterally distal to the knee and low back pain. Subjects had a presumptive diagnosis of epidural fibrosis based on history, physical examination findings, and presence of a filling defect on an epidurogram in the suspect area (Fig. 1). The pain clinic only accepts patients by physician referral and generally is a tertiary referral center. Therefore, most subjects had received multiple treatments at two or more health care facilities before referral to our clinic.

The technique used for neuroplasty is described in detail elsewhere and is summarized in Table 1 (2). Subjects were randomly assigned to one of four treatment groups (Table 2). They received the neuroplasty treatment with or without hyaluronidase and received either 0.9 or 10% NaCl in addition to bupivacaine and corticosteroid.

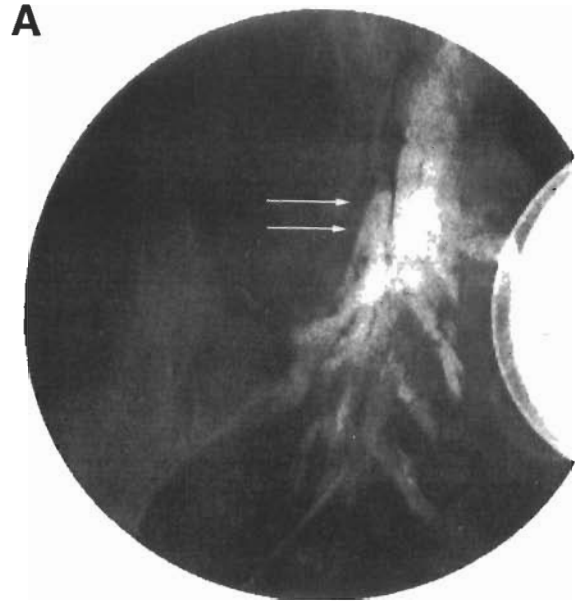
Subjects were asked to complete questionnaires related to their pain just before treatment, after completion of treatment, and at 1, 3, 6, and 12 months after treatment. When possible, questionnaires were completed during scheduled visits; otherwise, information was obtained by mail. All data were collected by personnel not involved in the care of the subjects. The following questionnaires were used: Short Form McGill Pain Questionnaire (SFM) and Visual Analog Scale for back pain (VAS_B) and leg pain (VAS_R, VAS_L; R indicates right, L indicates left).

Subjects were observed and questioned to determine if major side effects occurred. The side effects associated with neuroplasty included unintentional subdural or subarachnoid injections, paralysis, bowel/bladder dysfunction, infection, cardiac arrhythmias and perineal numbness lasting up to 1 month.

Data Analysis

The SFM was scored by adding the values of pain ratings assigned to each of the 15 descriptions on the SFM (0 = none; 1 = mild; 2 = moderate; 3 = severe) (13). Visual analog scale scores were obtained using a horizontal 100-mm line labelled on the left end as 0 = no pain, and on the right as 100 = pain as bad as it can be. Subjects marked on the scale how they rated their pain at present. In addition to recording VAS, pain was ranked (using VAS) as none or mild (VAS = 0–29), moderate (VAS = 30–54), or severe (VAS = 55–100) (14).

Visual analog scale and SFM data was treated in quantal (improved/not improved) fashion (i.e., the follow-up scores were rated as improved if VAS at



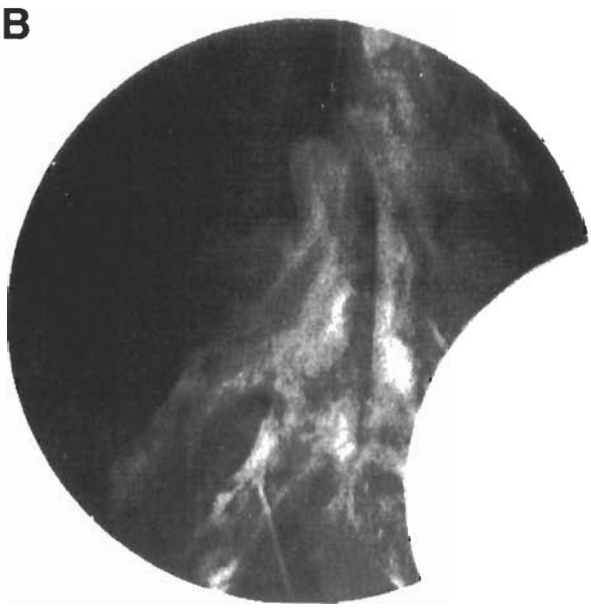


Fig. 1. (A) Epidurogram of patient showing filling defect (arrows) before neurolysis. After neurolysis (B), contrast material flows into the epidural filling defect and through the intervertebral foramen along nerves. This patient has an intrathecal catheter in place and was receiving morphine intrathecally. Following neurolysis, intrathecal infusion requirement was reduced by 50%. Extra vigilance to avoid subdural or intrathecal spread during neurolysis is advised when performing the procedure on patients with intrathecal catheters in place.

follow-up was 10 points lower than the subject's baseline VAS). Short form McGill Pain Questionnaire was rated as improved if the SFM score at follow-up was 3 points lower than the subject's baseline SFM score.

Visual analog scale scores at discharge and number of patients requiring additional treatments for the different groups were compared using the Fisher's exact test (2-by-2 tables) and the generalized Fisher's exact test (4-by-2 tables). The SMF variable and VAS after discharge were not evaluated statistically because of variable number of subject data available at different follow-up times.

Table 1. Percutaneous Epidural Neuroplasty Technique

In the operating room:
- Place epidural needle.
- Inject iohexol (Omnipaque-240) and visualize spread of contrast medium (epidurogram).
- If filling defect corresponding to area of pain is present, thread Racz Tun-L-Kath (Epimed, Gloversville, NY) catheter into filling defect (scar), while injecting normal saline through the catheter; observe fluoroscopically to visualize washout of contrast and opening of scar.
- Inject additional iohexol to ascertain opening of scar and spread of injectate within the epidural space.
- Inject preservative-free saline with or without hyaluronidase (Wydase, Wyeth-Ayerst Laboratories, Philadelphia, PA).
- Inject 0.25% bupivacaine and triamcinolone.
- Tape catheter in place.

In the postanesthesia care unit:
- Inject 0.9% or 10% saline 30 minutes after steroid/local anesthetic injection.

In clinic area:
- Once on each of the following 2 days, inject 0.25% bupivacaine; 30 minutes later, inject 0.9% or 10% saline.
- After the last treatment, remove the epidural catheter.

Results

Twenty-four of the 83 subjects were removed from the study before the injection series was completed. Reasons for discontinuation included catheter problems that interfered with injections, psychological factors that interfered with patient assessment, or subject withdrawal from the study. Demographics for the remaining 59 subjects in the four treatment groups are shown in Table 3. The average age (50–58 years) and age range for subjects in the four groups was similar. The ratio of

Table 2. Treatment Paradigms

	Group A	Group B	Group C	Group D
Hyaluronidase	X			X
Hypertonic saline	X	X		
Isotonic saline			X	X

A, hypertonic saline + hyaluronidase; B, hypertonic saline; C, normal saline; D, normal saline + hyaluronidase.

Table 3. Subject Demographics

	Groups			
	A	B	C	D
No. of subjects	17	15	17	10
Male	11	9	5	5
Female	6	6	12	5
Age (y)	54 (29–75)	58 (22–79)	53 (31–76)	50 (33–70)
Ethnicity				
Caucasian	76%	93%	70.5%	70%
African-American	0%	0%	6%	0%
Hispanic	24%	7%	23.5	30%

A, hypertonic saline + hyaluronidase; B, hypertonic saline; C, normal saline; D, normal saline + hyaluronidase.

males to females varied from group to group. Some variability was observed among groups with respect to anatomic location (right or left leg, back), at which subjects reported the maximal VAS rating (Table 4). More than 50% of the subjects rated low back pain as most severe, based on VAS score, in all but the 0.9% saline group. Duration of pain ranged from less than 2 years to more than 30 years. Thirty-eight subjects had had back surgery at least once prior to presentation.

The percentage of subjects showing improvement based on decreased VAS_{max} and SFM score at each follow-up is shown in Fig. 2. Between 33 and 100% of the subjects in each group had improvement at each follow-up on at least one of the two pain scores. However, the percentage of subjects with improved scores varied between SFM and VAS_{max}, and among follow-up periods. Percentage of subjects with VAS_{max} improvement did not differ among treatment groups; the percentage was highest on discharge (80–88%), and ranged from 25 to 60% at all other follow-up periods (Fig. 2).

A smaller but nonsignificant fraction of subjects in the hypertonic saline plus hyaluronidase and hypertonic saline groups required more additional treatments than in the other two treatment groups (Fig. 3). On average, the number of days (about 70) following neurolysis before additional treatments were administered did not differ significantly among groups (Fig. 4). Additional treatments included repeat neurolysis, lumbar facet injections, hypogastric plexus blocks, quadratus/psoas muscle injection, spinal cord stimulation, and nerve root injections. No adverse responses were noted.

Discussion

The important findings gained from this study are: (a) most subjects receiving any of the four neuroplasty treatment regimens as part of their pain management obtained significant relief immediately after the treatment; (b) maximum VAS scores for either the back or the right or left leg were improved in 25% or more of the subjects in all treatment groups at all follow-up times; and (c)

Table 4. Frequency of Highest VAS Location (VAS_{max})*

			Right Leg	Left Leg	Back	Two Locations
Group A	n=15	Severe	2	2	9	2
	n= 2	Moderate			2	
	n=17					
Group B	n=14	Severe	4	2	8	
	n= 1	Moderate			1	
	n=15					
Group C	n=15	Severe	3	6	6	
	n= 2	Moderate	1		1	
	n=17					
Group D	n= 7	Severe	1	2	3	1
	n= 3	Moderate		1	2	
	n=10					

* VAS_{max} 55–100 = severe; 30–54 = moderate. See reference 14.
A, hypertonic saline + hyaluronidase; B, hypertonic saline; C, normal saline; D, normal saline + hyaluronidase.

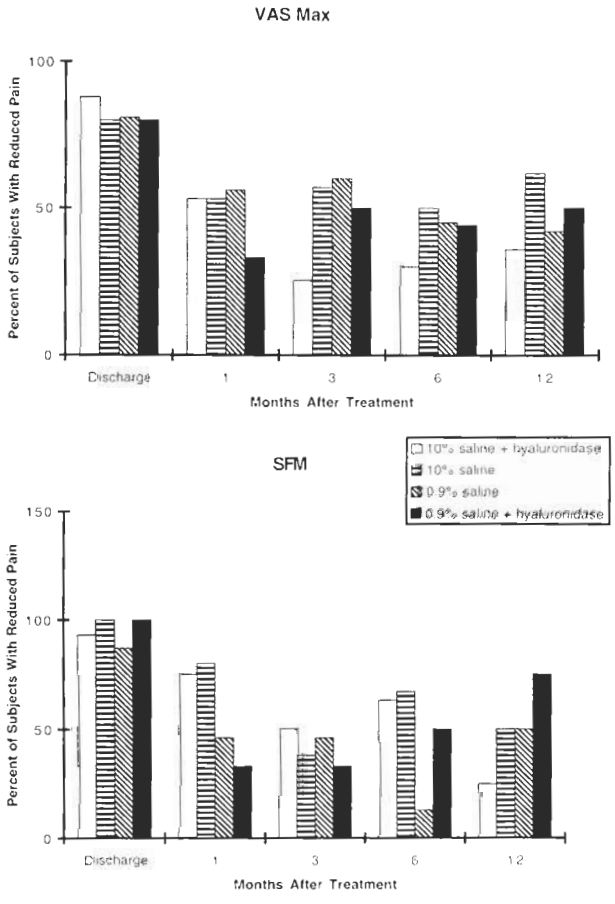


Fig. 2. Percentage of subjects in each treatment group with VAS_{max} and SFM reduction (less pain) at indicated times after percutaneous epidural neuroplasty.

subjects treated with hypertonic saline or hyaluronidase and hypertonic saline were less likely to require other treatments than were subjects given normal saline or normal saline and hyaluronidase.

We cannot discount the possibility that the differences in gender representation and/or location of maximal pain influenced the outcomes of the group comparisons. Half or more of the subjects were male and rated back pain as VAS_{max} in all but the group that received 0.9% saline. In the 0.9% saline group, 12 of the 17 subjects were female, and 10 of the subjects rated leg pain as VAS_{max}. No study has been performed regarding epidural neuroplasty outcomes in patients with radiculopathy vs back pain as the most severe source of pain nor of male vs female responses.

There is no agreement in the literature about how much of a change in score for either of the pain measures we used is necessary to be considered clinically meaningful. Campbell and Patterson (15) concluded that to achieve a meaningful reduction in postoperative pain in 50% of patients, it is necessary to reduce pain intensity as represented by the VAS by between 31 and 48% depending on the initial VAS score. We used criteria based on estimates of detectable change on scales for the pain VAS and SFM questionnaire.

VAS_{max} was taken to be the primary indicator of outcome of neuroplasty because the procedure is lesion specific (i.e., the target is the source of the primary pain complaint, VAS_{max}). In addition, VAS ratings of pain have been demonstrated to be reliable, generalizable, and internally consistent measures of clinical and experimental pain sensation intensity (16). The SFM provides more general information with respect to the overall state of the subject than does the VAS. According to Melzack (13), data obtained with the SFM provide information on the sensory, affective, and overall intensity of pain. Subjects in this study generally had multiple pain complaints in which successful neuroplasty treatment would reduce VAS_{max}, but, because of other pain, may not reduce SFM score.

It is important to emphasize that subjects for this study represented a subset of difficult-to-care for patients. They generally had long-standing pain that was refractory to commonly used treatment modalities. Thus, pain reduction, even if not permanent, represents progress and is appreciated by the patient. It is also important to stress that neu-

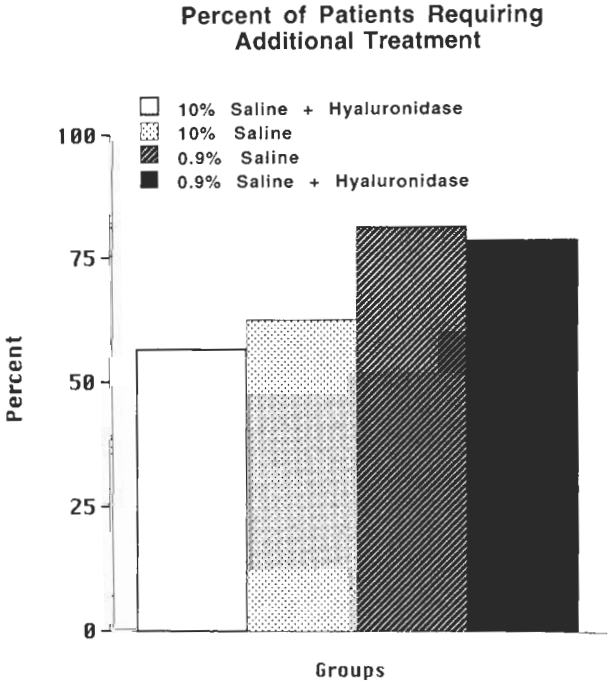


Fig. 3. Percentage of subjects in each treatment group requiring additional treatments during the 1-year follow-up.

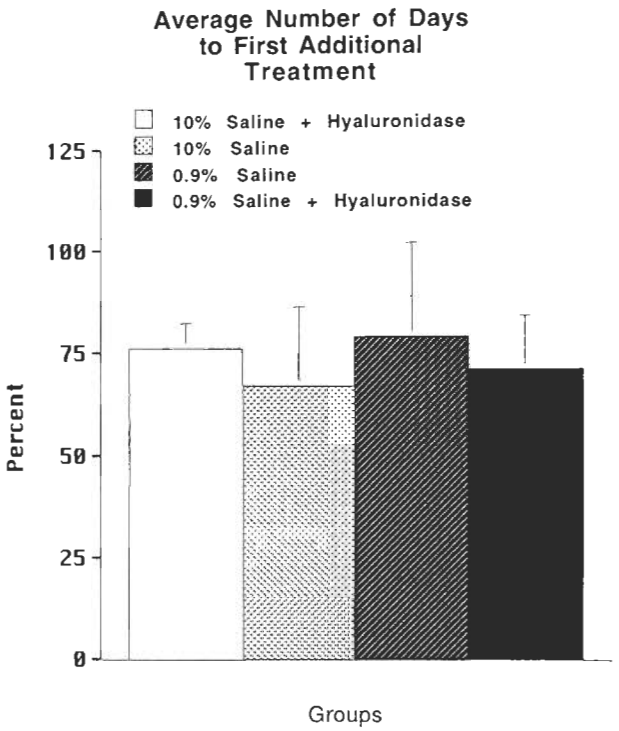


Fig. 4. Average number (with SD) of days before subjects in each group received the first additional treatment after neuroplasty.

roplasty is used as part of an overall pain management strategy and thus other aspects of the strategy likely influenced results of the study.

In conclusion, the results of our study confirm the benefits of percutaneous epidural neuroplasty as part of an overall pain management strategy and the safety of the procedure. Although the results do not show superior outcome when hyaluronidase is used, they do indicate that less subjects given hypertonic saline required additional treatments than did subjects given normal saline.

Acknowledgment

The authors thank Katherine McDaniel, Angela Moore, and Kyle Kenmore for providing expert technical support for this project, and Dani Joyner for her assistance in producing the manuscript. We also would like to thank Dr. Michael Hammer, The Comprehensive Pain Treatment Center, Birmingham, Alabama, for directing our attention to the publication by Drs. Kuslich, Ulstrom, and Michael, and Dr. Nathan Pace, University of Utah Medical School, for his expert statistical assistance.

The majority owners of the company that manufactures the catheters used in this study are the sons of Dr. Gabor B. Racz.

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