The Effect of Nerve-Root Injections on the Need for Operative Treatment of Lumbar Radicular Pain

A PROSPECTIVE, RANDOMIZED, CONTROLLED, DOUBLE-BLIND STUDY*

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Abstract

Background: **The purpose of the present study was to determine the effectiveness of selective nerve-root injections in obviating the need for an operation in patients with lumbar radicular pain who were otherwise considered to be operative candidates. Although selective nerve-root injections are used widely, we are not aware of any prospective, randomized, controlled, double-blind studies demonstrating their efficacy.**

Methods: **Fifty-five patients who were referred to four spine surgeons because of lumbar radicular pain and who had radiographic confirmation of nerve-root compression were prospectively randomized into the study. All of the patients had to have requested operative intervention and had to be considered operative candidates by the treating surgeon. They then were randomized and referred to a radiologist who performed a selective nerve-root injection with either bupivacaine alone or bupivacaine with betamethasone. The treating physicians and the patients were blinded to the medication. The patients were allowed to choose to receive as many as four injections. The treatment was considered to have failed if the patient proceeded to have the operation, which he or she could opt to do at any point in the study.**

Results: **Twenty-nine of the fifty-five patients, all of whom had initially requested operative treatment, decided not to have the operation during the follow-up period (range, thirteen to twenty-eight months) after the nerve-root injections. Of the twenty-seven patients who had received bupivacaine alone, nine elected not to have the operation. Of the twenty-eight patients who had received bupivacaine and betamethasone, twenty decided not to have the operation. The difference in the operative rates between the two groups was highly significant ($p < 0.004$).**

Conclusions: **Our data demonstrate that selective nerve-root injections of corticosteroids are significantly more effective than those of bupivacaine alone in obviating the need for a decompression for up to thirteen to twenty-eight months following the injections in operative candidates. This finding suggests that patients who have lumbar radicular pain at one or two levels should be considered for treatment with selective nerve-root injections of corticosteroids prior to being considered for operative intervention.**

Since Macnab[10] described the technique of selective nerve-root injection twenty-nine years ago, numerous investigators have reported on its value in treating patients with radicular pain[9,12-14]. However, there has not been, as far as we know, a single prospective, randomized, double-blind, controlled study evaluating its efficacy for the treatment of lumbar radicular pain.

Most authorities agree that the initial treatment of acute radicular pain in the low back should be bed rest, anti-inflammatory medication, and physical therapy[7,10,14]. However, many patients who have been so treated have persistent pain and seek further intervention. An epidural injection of steroids is a popular treatment method, despite the fact that the short and long-term results of such therapy remain controversial[3,5,7,14]. An alternative method for delivering steroids to inflamed nerve tissue is the use of selective nerve-root injection, which is the term given to the procedure developed by Krempen and Smith[9] twenty-six years ago. Under fluoroscopic guidance, the needle is placed next to the presumed affected nerve root, resulting in a precise and concentrated delivery of the drug to the immediate vicinity of that nerve. While nerve-root injections have been demonstrated to diminish lumbar radicular pain in a number of nonrandomized studies[9,12-14], one could ask whether some of the results might not have been attained with analgesic treatment alone. A more important question is whether these injections can obviate the need for an operation in

*No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article. Funds were received in total or partial support of the research or clinical study presented in this article. The funding sources were the Barnes-Jewish Christian Health System's Innovations in Health Care Grant and Washington University School of Medicine.

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patients who would otherwise be operative candidates. Although it is effective, operative treatment of lumbar radicular pain is associated with both morbidity and mortality. In addition, the overall cost of operative treatment of lumbar radicular pain, including the cost of the operation and lost wages, is exceedingly high. Because of the relatively low cost and morbidity associated with the injections compared with those associated with an operative procedure, injections are likely to be cost-effective if they allow even a small percentage of patients with lumbar radiculopathy to avoid operative intervention.

The purpose of the present study was to critically examine the efficacy of selective nerve-root injections of corticosteroids in a prospective, randomized, controlled, double-blind manner to determine if they could obviate the need for operative intervention in patients with lumbar radiculopathy who otherwise would be operative candidates. The null hypothesis was that there is no significant difference between patients treated with bupivacaine alone and those treated with bupivacaine and steroids with respect to the eventual operative rate.

Materials and Methods

Inclusion and Exclusion Criteria

The study subjects were selected from patients who were seen at the offices of four spine surgeons (three orthopaedic surgeons and one neurosurgeon) at one institution during a one-year period from December 1996 to December 1997. All patients who were more than twenty-one years old and who had degenerative lumbar radicular pain with a disc herniation or central or foraminal spinal stenosis confirmed by magnetic resonance imaging or computed tomography-myelography were eligible. There were no differences between the experimental and control groups with regard to any of the measured variables, including age, gender, number of levels of disease, diagnosis (herniated nucleus pulposus or stenosis), and number of previous operations. In addition, we included patients who had had a previous operation and demonstrated persistent or new neurological compression. They had to have completed a course of nonoperative management including anti-inflammatory medication, physical therapy, and activity modification for at least six weeks without adequate benefit. An exception to the six-week rule was made only if the patient had intractable pain despite the use of the maximum dosage of anti-inflammatory medication, supplemented with narcotic pain medication, and activity modification. Both the patient and the treating surgeon had to agree that operative treatment was the next indicated step. Prior to the era of the use of nerve-root injections, operations would have been scheduled for all of these patients.

The criteria for exclusion were acute trauma, cauda equina syndrome, a progressive neurological deficit, a motor deficit, a pathological or infectious etiology, a patient who was not an operative candidate, involvement with a Workers' Compensation claim, a history of an adverse reaction to corticosteroids or local anesthetics, lack of a radiographically detectable abnormality, more than two radiographically abnormal and symptomatic levels on either side such that three or more separate injections would be necessary to alleviate the symptoms, and an absence of substantial radicular pain as the presenting symptom.

All patients who met the criteria were offered enrollment in the present study, and a total of fifty-five patients agreed to participate. There were twenty-seven men and twenty-eight women. After signing an informed consent approved by the Human Studies Committee at our institution, the enrolled patients had a thorough initial physical examination by the spine surgeon. Then they filled out a nerve-root-injection questionnaire, and a North American Spine Society low-back-pain outcome questionnaire[6] was administered by a nurse. On the basis of the patient's symptoms, signs, and radiographic findings, the surgeon picked one or, at most, two levels to be injected. The patients were randomly assigned to the experimental or the control group by the study administrator (Y. Y.), a full-time radiology research fellow with no involvement in patient care. They were then referred to our radiology department for a selective nerve-root injection with bupivacaine alone (control group) or bupivacaine with betamethasone (experimental group). One of three radiologists, each experienced in the injection technique, performed all of the injections. Care was taken to try to ensure that all of the injections were performed in as identical a manner as possible. All of the injections were performed according to a strict protocol (described below) and after a contrast radiculogram had been made to ensure that the correct nerve root was being injected. Neither the patient nor the treating spine surgeon knew the group to which the patient had been randomized. Just prior to the procedure, each patient completed a nerve-root-injection questionnaire indicating his or her pain level on a scale of 0 to 100 points (with 100 points indicating the worst pain and 0 points, no pain).

Injections

The patient was placed prone on a fluoroscopic table with c-arm capability to allow adjustment of the angle of the x-ray beam in order to visualize the target area in posteroanterior, oblique, and lateral positions. An entry site that allowed visualization of the lateral edge of the pars interarticularis, transverse process, and articular facets on the side to be injected was selected within a few centimeters lateral to the spine. Usually, the disc space at that level was also profiled. The entry site was marked with indelible ink. Sterile preparation was performed with alcohol followed by Betadine (povidone-iodine) solution. Local superficial anesthesia with 1 percent lidocaine buffered with a small amount of bicarbonate was injected. A 22-gauge, five-inch (thirteen-centimeter) spinal needle with a short bevel, which had its tip bent to allow easier entry into the foramen, was placed, under fluoroscopic control, into the anterosuperior portion of the selected lumbar foramen. Contrast solution was injected, under fluoroscopic control, through a connecting tube to verify that contrast material and subsequent medication were passing about the desired nerve root and also to be sure that the injectant was not flowing intravascularly. The connecting tube then was removed, and the selected injectant was delivered with a single syringe. Radiculogram radiographs for final verification were made for the permanent records, and a report was generated, but the contents of the injectant were not noted in the report.

Prior to the procedure, the results of the randomized selection had been given by the project coordinator to the radiologist. All patients received one milliliter of 0.25 percent bupivacaine, while those who had been selected for treatment with steroids also received one milliliter of betamethasone (six milligrams per milliliter). In either case, the injectant was delivered by means of one syringe. Following the procedure, the needle was removed, the site was cleaned, and Betadine (povidone-iodine) ointment and a bandage were applied. The patient then was taken from the radiology suite, and a form for follow-up measurement of pain and an instruction sheet describing the procedure were given to the patient to take home.

Failure of Treatment

The patient was allowed to choose to receive as many as four injections at any time during the follow-up period. This is consistent with our normal routine for treating patients with corticosteroid injections. If one or more additional injections were requested, the patient received the same medication that he or she had received for the first injection, in a double-blind manner. The injection therapy was not considered to have failed if the patient received two or three

additional injections; however, it was considered to have failed if the patient opted for operative treatment.

Data

The treating surgeon was blinded to the medication throughout the entire period of the study. The orthopaedic nurse conducted a complication survey two weeks after the injection. The first follow-up evaluation by the surgeon was at one to four weeks following the injection. The follow-up questionnaires, including the nerve-root-injection and North American Spine Society questionnaires, were mailed to the patient eight weeks after the injection. One year after the injection, a follow-up evaluation was performed in person or by telephone, and the two questionnaires were administered again by a nurse. Final scores were calculated separately for each section of the North American Spine Society questionnaire. In February 1999, final follow-up telephone calls were made to all of the patients who had not, to our knowledge, had an operation, to make sure that they had not had an operation performed by a different surgeon. The control and experimental groups were compared with use of chi-square tests. The findings before the procedure and the result at one year after the injection were compared with use of a paired t test.

Measurement of Outcome Data with Use of the North American Spine Society Outcome Instrument

The North American Spine Society outcome instrument included questions regarding medical history, expectations, and outcome[6]. The follow-up questionnaire included questions on whether the patient's baseline expectations had been met following treatment.

We compared the baseline and follow-up questionnaires for all of the patients who had avoided an operation. We analyzed these data in two ways. First, we calculated the mean scores at baseline and compared them with the mean scores at the final follow-up evaluation. We then performed a t test to determine if there was a significant difference. In addition, we used the recommendations of the North American Spine Society outcome measurement tool[6], which states that a difference of 1 point in any subsection is significant. We counted the number of individuals in each group for whom the score had increased or decreased by 1 point.

We stratified the data further to compare the baseline with the follow-up data for patients with a diagnosis of stenosis as well as for those with a diagnosis of herniated nucleus pulposus. We assumed that the injections might help the patients with a herniated disc more than those with stenosis.

Results

Comparison of Baseline Data Between Experimental and Control Groups

Twenty-eight patients were injected with bupivacaine and betamethasone, and twenty-seven were injected with bupivacaine only. No differences between the experimental and control groups were detected with regard to any of the measured variables, including age, gender, number of levels of disease, diagnosis (herniated nucleus pulposus or stenosis), and number of previous operations. In addition, no significant differences between the experimental and control groups were found with respect to the baseline North American Spine Society outcome measurements.

Follow-up

A final follow-up evaluation was performed for all fifty-five patients at thirteen to twenty-eight months (mean, twenty-three months) following the first injection. The patients who had opted not to have an operation were followed for a minimum of fifteen months (mean, twenty-three months; range, fifteen to twenty-eight months). As a group, the patients with stenosis who had opted not to have operative treatment had the longest duration of follow-up (range, sixteen to twenty-eight months). The duration of follow-up for patients with a herniated disc ranged from fifteen to twenty-eight months. The patients who had an operation were followed for a mean of twenty-two months (range, thirteen to twenty-eight months).

All of the patients who succeeded in avoiding operative treatment filled out the North American Spine Society low-back-pain outcome questionnaire at a minimum of one year following the injection.

Operative Treatment (Failure of Injection Treatment)

Twenty-six of the fifty-five patients opted to proceed with an operation, and twenty-nine chose not to have one. Of the twenty-seven patients who had received bupivacaine only, eighteen opted for operative intervention whereas nine did not. Of the twenty-eight patients who were treated with bupivacaine and betamethasone, only eight proceeded with an operation while twenty chose not to have one. The difference was highly significant ($p < 0.004$). Stated another way, of the twenty-six patients who opted for operative intervention, eighteen had received bupivacaine alone and eight had received bupivacaine and betamethasone.

Comparison of Baseline and Follow-up Questionnaires for All Patients Who Avoided Operative Treatment

Although there was a trend toward a decrease in the neurological symptoms from the baseline to the final follow-up evaluation in all of the patients who avoided operative treatment, the difference was not significant. When we analyzed the data in the subgroups of patients who had stenosis and those who had herniated nucleus pulposus, we found that the patients with stenosis had a significant decrease in neurological symptoms from the baseline to the final follow-up evaluation ($p < 0.03$). We also found that the patients with stenosis had significant relief of low-back pain between the baseline and final follow-up evaluations ($p < 0.008$) and that the patients with herniated nucleus pulposus had a trend toward relief ($p < 0.07$). The most dramatic improvement was reflected by the patients' responses regarding their treatment expectations, with significant improvement from the baseline to the final follow-up evaluation in both the group that had stenosis ($p < 0.00004$) and the group that had herniated nucleus pulposus ($p < 0.000018$). The job-exertion and job-stress values were unchanged.

Nine patients who received bupivacaine only continued with nonoperative treatment. The only significant difference between the baseline and follow-up

outcome data in this subgroup was in their scores on the questions regarding treatment expectations ($p < 0.001$). The patients who had a diagnosis of stenosis and were injected with bupivacaine and betamethasone had significant relief of the low-back pain ($p < 0.049$) and significant improvement in their scores on the questions regarding treatment expectations ($p < 0.002$). The patients who had herniated nucleus pulposus also had a significant difference, between the baseline and follow-up evaluations, in their scores on the questions regarding treatment expectations ($p = 0.001$).

Multiple Injections

Nineteen patients received more than one injection: ten had two injections, six had three injections, and three had four injections. The minimum interval between the injections was six days; the maximum was 10.5 months. Thirteen of the nineteen patients who had multiple injections avoided operative treatment, while six did not. The difference almost reached significance ($p = 0.059$).

Discussion

We found that nerve-root injections were indeed effective in obviating the need for an operation in more than half of the operative candidates. Twenty-nine of the fifty-five patients who had requested operative intervention and who were considered to be operative candidates by their treating spine surgeons avoided an operation. Compared with injection of bupivacaine alone, injection of bupivacaine with the steroids was significantly ($p < 0.004$) more likely to result in the avoidance of an operation. Interestingly, nine of the twenty-seven patients who had received bupivacaine alone still managed to avoid an operation.

We were surprised that so many of our patients who received bupivacaine with steroids avoided an operation. Normally, all of these patients would have been treated operatively. Unfortunately, our data do not give us a good explanation as to why. We propose several possible theories. First, it may be that any new treatment modality that is added to the existing treatment regimen may help to decrease the need for operative intervention; a similar study comparing the results of any new interventional treatment may have yielded similar results. Second, most patients who have sciatica do not have steady, intractable pain but, rather, intermittent, varying degrees of pain. Patients may have intolerable pain for just a few hours during the day or perhaps for just a few days during the week. We found that the patients who proceeded to have an operation had higher baseline scores for back pain and neck pain than did those who avoided an operation, regardless of the treatment group. Treatment with bupivacaine with or without corticosteroids certainly can diminish the pain in the short term. As long as the patient feels that there are alternatives to an operation that can diminish the pain, no matter how transiently, they may feel that they have enough control over the pain to avoid the more aggressive route. This theory is supported by the fact that there was a highly significant improvement in the scores for the questions on "expectations of improvement" by the time of the final follow-up. Third, even asymptomatic individuals can have radiographic evidence of stenosis[2,15], and patients who are symptomatic may improve either spontaneously or with anti-inflammatory medications and physical therapy. As stated previously, these are mere conjectures; we do not really know why so many patients were able to avoid an operation.

In previous studies in which only the degree of pain relief was measured[1,4,8,11], several of our patients who managed to avoid operative intervention would have been considered to have had failure of treatment. Indeed, some of these patients actually had a higher score for leg or back pain on the final follow-up evaluation compared with that on the baseline evaluation. The difference is that no patient had a higher (worse) score for pain in more than one category, and every patient who avoided an operation showed a highly significant improvement in the scores on the expectation questions.

Limitations of the Study

As with any study, the present investigation may have several potential problems. Because of the relatively small number of patients who were randomized, any absence of statistical significance that we found may be suspect. In other words, the absence of statistical significance may be due to a true lack of difference or to an inability to detect small differences because of an insufficient sample size, or to both. On the other hand, if the sample size had been larger, we may have been able to detect a difference between the patients who had herniated nucleus pulposus and those who had spinal stenosis with respect to the outcome measures. It is recognized that patients with herniated nucleus pulposus can fully recover spontaneously. In contrast, stenosis is expected to gradually worsen with time, so the effects of injection treatment may eventually disappear. Our follow-up period of fifteen to twenty-eight months for the patients with stenosis may not be adequate to determine if these patients will avoid an operation in the long term. While it is likely that a patient with herniated nucleus pulposus who avoids operative treatment for fifteen months has a reasonable chance of avoiding operative treatment forever, it is difficult to say the same about a patient who has spinal stenosis. Given the fact that patients who have spinal stenosis tend to be older, postponing the operation until they are even older and perhaps more medically unstable may not be in their best interest. For this reason, we plan to follow these patients during the next few years to determine whether they are able to continue to avoid operative intervention.

As a direct result of the present study, our treatment algorithm for patients who have one or two-level radiculopathy in the lumbar spine without substantial motor or sensory deficits now routinely includes the use of selective nerve-root injections of bupivacaine and corticosteroids. Only if they refuse the injections or fail to improve after a maximum of three or four such injections are they offered operative intervention. Given the highly significant difference between the control and the experimental group in this prospective, randomized, controlled, double-blind study, we recommend that this algorithm be more widely considered.

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