

Epidural Steroid Administration for Acute Inflammatory Radiculopathies

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Objectives

Investigate the administration of epidural steroids in the treatment of acute inflammatory radiculopathies.

INTRODUCTION

Injection into various parts of the peridural space has been advocated for the management of sciatica since 1930⁽¹⁾, but with the findings of Mixter and Barr⁽²⁾ in 1934, linking the signs and symptoms of sciatica with a herniated nucleus pulposus, surgery has continued to be the definitive therapy for this problem. However, over the years except in patients with a rapidly progressive neural deficit, surgery has provided disappointing therapeutic results, so efforts to find a non-surgical therapeutic approach have continued. From a theoretical point of view, two approaches to the problem of non-surgical therapy have been developed, one aiming to remove the etiologic mechanism and the other aiming to modify the response to that mechanism.

CHEMONUCLEOLYSIS

The approach which attempts to remove the disc without surgery was first described by Lyman Smith⁽³⁾, who in 1963 reported a procedure which he termed "chemonucleolysis", in which chymopapain was injected percutaneously into the involved disc. By depolymerizing the cementing protein of the chondromucoid complex, chymopapain was said to reduce the molecular size and viscosity of the nucleus pulposus, resulting in chemical decompression. While Smith was able to provide complete relief in slightly over 80% of his patients⁽⁴⁾, not all reports indicated similar success rates⁽⁵⁾. Though chemonucleolysis appeared to be a simple procedure in expert hands, it was a painful one that required the administration of a general anesthetic, and for the first 12-36 hours following the injection, there was a significant incidence of severe lumbar muscle spasm. Most importantly, there was a 1-2% incidence of anaphylaxis associated with this procedure⁽⁶⁾.

EPIDURAL AND INTRATHECAL STEROIDS

The other approach to non-surgical therapy seeks not to treat the etiologic mechanism itself but rather the radiculopathy which results. This was the approach of Lievre and his associates⁽⁷⁾, who in 1953 reported on the beneficial effect of hydrocortisone injected into the epidural space in 20 patients. Subsequently others began to try this technique in selected cases. Cappio⁽⁸⁾ reviewed the early literature abroad and reported that good results were obtained in 67% of the first 80 of these cases, and later in this country Goebert and his co-workers at the Cleveland Clinic treated 113 patients with painful radiculopathies with hydrocortisone and procaine injected caudally and obtained good results in 72% of the patients⁽⁹⁾.

After first determining its safety in laboratory animals⁽¹⁰⁾, the Cleveland Clinic group then went on to record an improved success rate following the injection of 40 mg of methylprednisolone and 40 mg of procaine intrathecally⁽¹¹⁾ and reported no complications following the injection of steroids with procaine into either the extradural or intradural compartments.

In spite of the simplicity of this therapeutic approach to the management of discogenic pain and its freedom from side effects and complications, the present author, like many others, was initially skeptical of its efficacy. Therefore in 1968 we initiated a preliminary study to evaluate the efficacy of methylprednisolone as a therapeutic modality for discogenic pain and to compare the result obtained when the drug was injected epidurally with the result obtained when the drug was injected intrathecally, with both injections consisting of methylprednisolone alone (without local anesthetic) and both injections being made as close to the level of the lesion as possible. The data obtained in that study indicated that methylprednisolone is an effective therapeutic modality in the management of discogenic pain in about 80% of the patients so treated, and that the success rate is almost identical regardless of whether the drug is injected intrathecally or epidurally, as long as the injection is made as close to the level of the disc as possible⁽¹²⁾

Following publication of this study in 1972, we have continued to obtain a high degree of success using this therapeutic regimen. Unfortunately, most of the patients with sciatica are referred first to surgeons, so there has been little data available indicating the success rate of epidural and/or intrathecal steroids as a primary course of therapy, since most surgeons consider it a "last resort" in the management of discogenic pain in patients in whom laminectomy, with or without fusion, has failed to provide relief. As a result, much of the published data has been obtained in a mixture of patients consisting of a few who refused surgery and many who had failed to obtain relief following surgery.

Therefore, in the mid 1970's we undertook a study of 30 patients with discogenic pain in whom only intrathecal and/or epidural Depo-Medrol was utilized as the primary form of therapy⁽¹³⁾. This study indicated three important findings: First, that of the 30 patients receiving only epidural and/or intrathecal Depo-Medrol, 29 obtained complete and apparently permanent relief. The one patient who did not obtain relief underwent surgery and no disc was found. Second, in the majority of the cases (14 out of 30), one injection of Depo-Medrol was insufficient. Thirteen required two injections and 3 required three. And finally, contrary to the report of Abram, if one route of injection fails to provide relief, the other route of injection may provide success. Such was the case in 8 of the 30 patients in that particular study.

MECHANISM OF ACTION OF EPIDURAL/INTRATHECAL STEROIDS

When mixter and Barr first demonstrated the relationship between disc protrusion and radicular pain⁽²⁾, they believed that the signs and symptoms of sciatica were due to the mechanical compression of the nerve root by the protruded disc; and this mechanical explanation of sciatica is what prompted surgeons to consider laminectomy to be curative. However, the results of surgery failed to support this hypothesis.

More recently Olsson⁽¹⁴⁾ experimentally produced cervical disc protrusion in dogs and

found that the size of the disc and the amount of compression were less important in the production of symptomatology than the accompanying inflammation. The etiologic role of inflammation in sciatica is supported by the observation during lumbar laminectomy under local anesthesia that inflamed spinal nerves adjacent to a prolapsed disc are very sensitive to minor manipulations, whereas uninflamed nerves can be manipulated with very little discomfort⁽¹⁵⁾. Inflammation of nerve roots in patients with low back pain has been demonstrated myelographically⁽¹⁶⁾ and visually at the time of surgery⁽¹⁷⁾ and has been confirmed on histological examinations of biopsy specimens taken from nerve roots during surgery⁽¹⁸⁻²⁰⁾. Indeed, improvement in clinical symptoms has been shown to coincide with the resolution or diminution of nerve root edema in the presence of persistent herniated intervertebral disc⁽¹⁶⁾.

A landmark study in establishing the premise that inflammation is a key in radiculopathy was the work of McCarron who injected autologous nucleus pulposus material into the epidural space of dogs⁽²¹⁾. Those animals that receive an epidural injection of nuclear material daily for five days showed biochemical and histological evidence of intense inflammation on gross inspection and microscopic analysis of the spinal cord, dural sac, and nerve roots as compared with control animals that had only saline injection, indicating that a very small amount of nuclear material can cause a marked inflammatory response. The clinical correlate may be that the leak of a small amount of nuclear material that cannot be detected by routine laboratory studies obtained in the patient's evaluation for radiculopathy does cause significant symptoms. In other words, in spite of the fact that x-rays studies indicate "a mildly bulging disc unlikely to be causing the patient's symptoms", in reality, the patient has a clinically significant, chemical radiculopathy. Saal and his co-workers⁽²²⁾ have crystalized our understanding that inflammation of the nerve roots is the pathological process in patients with radiculopathy by identifying phospholipase A-2 (PLA-2) as the offending substance. PLA-2, which is present in a high concentration in nuclea material is an enzyme that liberates arachidonic acid from cell membranes. A toxic spill of PLA-2 can occur when either leakage or herniation occurs, and provokes and intense inflammatory reaction in the surrounding neural tissue that causes the symptoms of radicular pain⁽²³⁾. Saal and his co-workers reported that the concentration of PLA-2 was 20 to 100,000 times that of normal tissue when samples were obtained from patients at the time of disc surgery. Steroid, then, can prevent the action of PLA-2 on cell membranes (that of releasing arachidonic acid), which further generates substances such as prostglandins that are operative in the inflammatory cascade.

Thus it would appear that a disc degeneration is at first an anatomical event with an associated loss of elasticity of the annular fibers and the creation of fissures within the annulus as it dries with age and is subjected to deforming pressures⁽²²⁾. These changes allow variable amounts of nuclear material to leak out when poorly distributed pressures are applied to the spinal segment. The exact interaction of many biochemical and enzymatic substances involved (proteoglycan, PLA-2, arachidonic acid products, interleukines, etc.) is not clearly defined, but the reality is that inflammation causes pathology that escapes identification with the routine and customary laboratory studies of the patient with low back pain.

The concept that "sciatica" is the result of an inflammatory process of the involved nerve

root(s), gives a rational basis to the use of corticosteroids in the vicinity of the inflamed nerve root(s) to counteract the inflammation. As already pointed out, our own studies, which simply applied this information clinically by treating discogenic pain with intrathecal and epidural steroids supports the "inflammatory hypothesis"^(12,13). Furthermore, understanding that the acute phase of discogenic pain is inflammatory provides insight into the positive relationship between the time of treatment in relation to the onset of symptoms: The earlier epidural steroids are injected, the greater the possibility of success, since the entire process is inflammatory. With the passage of time, the process of healing begins with resultant intra- and extra-neural fibrosis, which causes fixation of the nerve roots within the intervertebral foramina, neural ischemia, and progressively diminishing responsiveness to antiinflammatory agents. Many studies demonstrate the relationship of success to the time of treatment with steroids: Brown, for example, treated 56 consecutive patients with 80 mg of Depo-Medrol and experienced a 100% success rate when the epidural steroids were injected in less than three months and a 20% success rate when utilized thereafter⁽²⁴⁾. Though our success rate was similar with both approaches, because of the increasing concerns of anesthesiologists about the litigious state of medicine, intrathecal steroid injections gave way to epidural injections in spite of the fact that there have been no complications reported in the literature following intrathecal steroid injections, provided (1) reasonable dosages were administered; (2) the number of injections was reasonable; and (3) the patient was free of central nervous system disease, i.e., multiple sclerosis.

CONTROVERSIAL ASPECTS OF EPIDURAL STEROIDS

Other investigators have been unable to reduplicate our high success rates. Carron has challenged the credibility of our reports; but we are convinced that the success rate will depend, to a large degree, upon the accuracy of the diagnosis. If the patient has truly and only discogenic pain, then the chances of success are great. Our studies have also been criticized for not providing concurrent controls and/or randomization, and this is true. However, Dilke and his co-workers⁽²⁵⁾ the first three months, and only 20% when treated later. Ryan & Taylor⁽²⁷⁾ tried to make an even more precise correlation between the time of treatment and success therefrom, finding in their study of 108 patients the following results: Patients who were treated within the first two weeks of symptoms achieved a 77% success rate, from 2-4 weeks a 72% success rate, from 4-6 weeks a 60% success rate, and over 6 weeks a 43% success rate. However, unlike their predecessors, the latter investigators actually injected 40 mg of methylprednisolone intrathecally, followed by 40 mg epidurally. Nonetheless, these two investigators felt that their data and the obvious relationship between time of treatment and incidence of success provided clinical support for the theory that epidural steroids are effective in disc protrusion with "irritative" [inflammatory] neuropathy, but not "compressive neuropathy". In other words, they felt that the reason for the progressive decrease in success with time was due to the fact that as time progresses, the continued inflammatory response produced progressively increasing intraneural fibrosis and ischemic changes that become irreversible, and that will not be affected by steroids.

Finally, while most anesthesiologists dilute their depo-steroid with local anesthetic (usually up to 10 cc), we do not do so for very definite reasons: First of all, the large volume of the diluted solution causes it to spread and to bathe many normal nerves. We want to deposit the steroid on the inflamed nerve only. Secondly, the solution that does bathe the inflamed nerve is diluted 5-10 fold, so less steroid gets to the targeted nerve root. Thirdly,

the local anesthetic stops the pain, but the pain returns before the steroid has become effective, and this has a definite negative psychological effect. And finally, in reviewing over thirty epidural steroid treatments that resulted in litigation, I encountered four patients who died because of the addition of the local anesthetic. In view of the fact that the local anesthetic added to the steroid has no therapeutic effect, the risk/benefit rate of adding had already reported on a randomized study of 100 consecutive patients with low back pain and radicular pain in the lower extremity, in which 10 ml of normal saline and 80 mg of methylprednisolone were injected epidurally in the study group, while the control group received an injection of 1 ml of sterile saline in the intraspinal ligament in the lumbar area. Of the patients who received Depo-Medrol, 46% reported complete pain relief one week after the injection, compared with 11% of the control group. More recently Cuckler⁽²⁶⁾ and his coworkers have carried out a prospective, randomized, and double-blind study comparing methylprednisolone and saline in patients with radicular pain due to a herniated nucleus pulposus or due to spinal stenosis. They detected no statistically significant difference between the control and experimental groups, whether the pain was due to acute disc herniation or spinal stenosis.

The problem with both of these studies is the fact that only a single dose of steroid was utilized and the success or failure of the technique was based on this one therapeutic intervention. Our studies have shown rather conclusively that two and in many cases three injections are necessary, and that for some reason, in certain patients one route of injection (intrathecal or epidural) succeeds where the other has failed. In view of the simplicity and safety of this technique, with the virtual absence of significant side effects, it would appear that in patients with an acute herniated nucleus pulposus, this form of therapy should be carried out prior to any other. The early use of epidural/intrathecal steroids could markedly reduce the loss of income resulting from prolonged bed rest and traction, and may even save the expense of a CAT scan if the therapy is successful.

As a matter of fact, there is good evidence that the earlier this treatment is initiated the greater will be the chance of success. Brown⁽²⁴⁾ was the first to report that the success rate was related to the duration of symptoms at the time of treatment; noting 100% efficacy in those patients treated within it is unacceptable. And in addition, I feel that our high success rate is a result of the fact that we do not dilute the steroid.

However, there are specific indications for injecting local anesthetic BEFORE injecting Depo-Medrol into the epidural space: First, if a patient is in such pain he cannot cooperate, a few cc's of local anesthetic will allow him/her to do so. Furthermore, in a patient with a previously operated back, such an injection of local anesthetic (prior to the injection of steroid) will verify whether the needle is in the epidural space and whether there is sufficient scarring to prevent the local anesthetic from reaching the nerve roots. Obviously, if interference with the spread of the local anesthetic results from old scarring, it must be anticipated that the spread of the Depo-Medrol will be obstructed as well. And finally, from a medico-legal point of view, the use of such a test-dose will indicate definitively that the needle (and the subsequent injection) is in the epidural space.

CONCLUSIONS

In short, for optimal results with epidural steroids, it is critically important that the

diagnosis be correct, i.e. (that one is dealing with an inflammatory neuropathy), that the treatment is instituted early (while the process is predominantly inflammatory) and that the sequence and timing of the injections are appropriate. The use of the proper steroid is equally important, if not for success, for preventing complications: We have only utilized Depo-Medrol, since Gardner showed this to be the safest agent when used intrathecally, though others have achieved results similar to ours using dexamethasone. Hydrocortisone should never be utilized, as it is irritating to the meninges and can cause grand-mal seizures^(28,29). The beauty of this form of therapy is that if it does not provide the expected relief, other therapeutic modalities can still be carried out. However, if this therapeutic approach were followed routinely in patients having their first acute herniated disc, very few would ever need to undergo a laminectomy and discectomy.

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