original article

Interaoperative use of epidural methylprednisolone or bupivacaine for postsurgical lumbar discectomy pain relief: A randomized, placebo-controlled trial

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BACKGROUND: Many patients with lumbar disc surgery experience postoperative back and radicular pain, delaying hospital discharge and resumption of normal activity. Some surgeons have used intraoperative epidural corticosteroids and local anesthetics to decrease pain following surgery for a herniated lumbar disc. Controversies still exist regarding the benefits of these drugs. The present study was meant to compare the effects of the intraoperative administration of epidural methylprednisolone and bupivacaine with that of normal saline (placebo) in lumbar disc surgery for postoperative pain control.

PATIENTS AND METHODS: One hundred fifty patients with single level herniated nucleus pulposus (L4-L5 or L5-S1), which was refractory to 6 weeks of conservative management, were divided randomly in three groups. A standard hemipartial lamimectomy and discectomy was performed on all patients. At the end of the surgery, before the closure of fascia, 40 mg methylprednisolone with 3 mL normal saline for group 1, 2 mL bupivacaine 5% with 2 mL normal saline for group 2 and 4 mL normal saline for group 3 were instilled onto the epidural and exposed nerve root. Postoperative back and radicular pain intensity was assessed by a visual analogue scale (VAS) before and at 24, 48, 72, and 96 hours after surgery.

RESULTS: There was no significant difference in back and radicular pain intensity between the three groups.

CONCLUSION: Intraoperative administration of epidural methylprednisolone or bupivacaine does not relieve postoperative back and radicular pain.

Low back and radicular pain, which are common presentations in clinical practice, are frequently caused by disc herniation.[1,2] Lumbar discectomy for herniated nucleus pulposus is one of the most common operations performed on the spine.[3,4] The aim of this therapy is to relieve the pain, but discectomy is painful for many patients.[4] Although clinical and basic knowledge of pain transmission and modulation has grown drastically, most postoperative pains are treated inadequately.[5-8] Postoperative pain delays mobilization and physical therapy, prolongs hospitalization and alters the patient perspective on recovery.[4] Poor pain control has been directly associated with increased complications, including deep venous thrombosis, pulmonary embolism, decreased pulmonary function, infection, myocardial ischemia and postoperative chronic pain.[5] Some clinicians rely on postoperative analgesics, but others use alternative methods, including intraoperative local anesthetics and/or corticosteroids.[9] Current opinion about the efficacy of epidural methylprednisolone and bupivacaine for postoperative pain relief is equivocal. We compared the effect of intraoperative administration of epidural methylprednisolone and bupivacaine with that of normal saline (placebo) in lumbar disc surgery for postoperative pain control.

PATIENTS AND METHODS

One hundred fifty patients (age range, 30 to 50 years) scheduled for surgery because of symptomatic lumbar disc herniation agreed to participate in this randomized, double-blind, clinical trial with placebo control. The study was approved by the ethics committee.

All patients had a clinical presentation and a physical examination consistent with an acute-onset single level (L4-L5 or L5-S1) unilateral herniated nucleus pulposus that was refractory to 6 weeks of conservative management consisting of analgesic and nonsteroidal antiinflammatory drugs. The diagnosis of each patient was confirmed by lumbar magnetic resonance imaging. Patients having motor deficits, spinal or lateral stenosis or previous intervertebral disc surgery were excluded. Patients were randomly assigned by a computer program to one of the three groups with a defined sample size.

All patients were premedicated with diazepam (0.1mg / kg). Anesthesia was induced with 2-3 μg/kg of fentanyl and 3-4 mg/kg sodium thiopental. Orotracheal intubation was facilitated with the administration of intravenous 0.3-0.4 mg/kg of atracurium. Anesthesia was maintained with halothane and 50% nitrogen oxide and 50% oxygen.

A standard surgical procedure consisting of open discectomy and hemipartial laminectomy with unilateral exploration was performed on all patients as follows: skin incision was performed between the L3 and S1 spinous processes. After the incision of the paramedian fascia, the paravertebral muscles were retracted. After identification of the level, hemipartial laminectomy, flavectomy, and discectomy were performed. Before closure of the fascia and subcutaneous tissues, and after hemostasis, 40 mg methyprednisolone with 3 mL of normal saline for group 1, 2 mL of bupivacaine 0.5% with 2 mL of normal saline for group 2, and 4 mL of normal saline for group 3 were flushed into the epidural space and nerve roots. The fascia and subcutaneous tissue were closed after drug administration and the skin was sutured.

All patients and staff involved in postoperative pain management and data collection were unaware of the group to which patient had been assigned. All patients received the same postoperative pain management: 100 mg of meperidine intramuscularly followed 4 hours later by a second dose. Assessment of pain was performed with a 10-cm visual analogue scale (VAS) (0 cm=no pain, 10 cm=worst pain imaginable). Back pain and radicular pain intensity were assessed the day before surgery. It was also assessed at 24, 48, 72, 96 hours after surgery.

The back and radicular pain intensity of the three groups were compared by the repeat measure method using the model "back or radicular pain = Person + Group + Time (Group) + residual" for statistical analysis with Minitab software (version 13). The results are reported as mean ± standard error (SE). A $P< 0.05$ was considered statistically significant. With a confidence and power level of 95%, using the "compare groups" formula, the maximum sample size, based on a standard deviation of 0.82 for methylprednisolone and 0.70 for bupivacaine and a maximum error of 0.55 for each group, was 50 patients.

RESULTS

The three groups did not differ statistically with regard to age, weight, sex, level of surgical discectomy, and length of the surgery (Table 1). There was no significant difference in the severity of radicular pain between the three groups (P=0.595) at any particular time point (Table 2). However, the main difference between the three groups was related to time of evaluation (P= 0.0001). In other words, the longer the post-surgical time is, the less the severity of radicular pain. There was no significant difference in severity of back pain between the three groups (P=0.948) at any particular time point (Table 3). However, the major difference between the three groups was related to time of evaluation (P=0.0001). In other words, as time passes from surgery, the severity of back pain decreases.

DISCUSSION

The causes of back and radicular pain in patients with lumbar disc herniation are still unclear.[10-13] For many decades sciatica and nerve dysfunction in conjunction

Table 1. The age, sex, operated level, weight and duration of operation for the three groups.

	Mean age (years)	Male	Female	L4-L5	L5-S1	Weight (kg)	Duration of operation (mean)
Bupivacaine	38.16±0.16	20 (40%)	30 (60%)	28 (56%)	22 (44%)	75.1±0.25	70.2±0.48
Methylprednisolone	37.2±0.51	23 (46%)	27 (54%)	26 (52%)	24 (48%)	74.2±0.32	74.1±0.23
Normal saline	38.92 ±0.66	24 (48%)	26 (52%)	29 (58%)	21 (42%)	76.5±0.18	73±0.34
P value	0.144	0.704	0.704	0.828	0.828	0.437	0.418

Values are mean±SD

Table 2. Severity of radicular pain in the three groups at different times.

Time of evaluation	Methylprednisolone	Bupivacaine	Normal saline
Before operation	6.14±0.2	6.28±0.2	6.10±0.19
24 h after operation	2.88±0.22	2.84±0.27	2.76±0.19
48 h after operation	2.56±0.23	2.02±0.18	2.38±0.21
72 h after operation	1.46±0.18	1.34±0.14	1.52±021
96 h after operation	1.04±0.14	1.04±0.11	0.90±0.16
	P =0.595 between three groups		

Values are mean±SD

Table 3. Severity of back pain in the three groups at different times.

Time of evaluation	Methyl prednisolone	Bupivacaine	Normal saline
Before operation	4.14±0.27	4.06±0.31	4.30±0.27
24 h after operation	4.64±0.22	4.88±0.24	4.38±0.21
48 h after operation	3.84±0.17	3.48±0.20	4.08±0.22
72 h after operation	3.22±0.17	3.04±0.16	3.02±0.18
96 h after operation	2.32±0.14	1.04±0.17	2.18±0.14
	P=0.948 between three groups		

Values are mean+SD

with lumbar disc herniation were believed to be solely due to mechanical compression of the spinal nerve roots. In contrast to what was thought earlier, spinal nerve roots undergo functional and histological changes after epidural exposure to nucleus pulposus without any mechanical compression. Thus, nerve root pain and dysfunction probably have a more complex pathophysiology, comprising compression and nerve root inflammation.[9,12-22] Inflammation plays a major role in the evolution of symptoms. The nucleus pulposus contains materials that are inflammatory and neuroexcitatory.[15-18,22-25] The nerve root does not become sensitized or begin to transmit pain signals until an inflammatory process is generated. Once inflammation is established, however, the nerve becomes exquisitely sensitive to pressure, producing pain with even gentle pressure.[15,24] A number of chemical modulators interact to foster the inflammatory cascade and to sensitize nerve endings. Phospholipase A2, an inflammatory mediator, is present at a high level in the human intervertebral disc. It may play a role in painful disc pathology. Pain-related neuropeptides such as substance P or vasoactive intestinal peptide may be released, which then leak from the nucleus through the annulus, sensitizing or irritating the adjacent nerve root. Different proinflammatory substances have been proposed as present in the nucleus pulposus such as tumor necrosis factor alpha, interleukin-1, interleukin-6, nitric oxide, platelet-activating factor, prostaglandin E2, leukotrienes, and reactions by histamine-like substances.[22,25]

In addition to various inflammatory mechanisms, immunological reactions have been suggested. The nucleus pulposus, normally confined within the annulus fibrosus, has no contact with the systemic circulation in the adult. This avascular localization could theoretically give the nucleus the status of a foreign body, not recognized by immunocompetent cells. Therefore, nucleus pulposus has been proposed to possess antigenic properties.[22]

Epidural steroids are commonly used in the treatment of back pain and radiculopathy.[24,26] The mechanism of corticosteroid activity is not yet fully understood.[25] Various modes of the action of the corticosteroids include blockade of phospholipase A2 activity and prostaglandin synthesis,[16,19,21,27-29] membrane stabilization,[16,19,27-29] a reversible local anesthetic effect,[19,21,25] prolonged suppression of ongoing neuronal discharge,[21,28] and inhibition of peptide synthesis or suppression of sensitization of dorsal horn neurons.[21] The safety of steroids and preservatives at epidural therapeutic doses has been demonstrated in both clinical and experimental

studies.[29] Methylprednisolone is the least irritating, the most beneficial and the longest acting among corticosteroids.[29]

In a randomized clinical study, Debi et al assessed the effectiveness of epidural methylprednisolone acetate to reduce pain following lumbar disc surgery. They reported significant back pain relief on postoperative days 1, 2, 6 and 14 in the group that received steroids. No difference between the two groups was found 1 year after surgery or when radicular pain was compared.[8] Davis et al showed that intraoperative application of an epidural steroid such as methylprednisolone in a unilateral lumbar discectomy leads to a shorter hospital stay because of less pain and spasm.[30] Lavyne et al reported that epidural corticosteroid administration after microsurgical lumbar discectomy for unilateral disc herniation does not lessen postoperative morbidity or improve functional recovery.[31]

Local anesthetic agents have been widely used in surgical operations to reduce postoperative pain.[9,32] Bupivacaine is a long-acting amide local anesthetic used for analgesia in acute and chronic pain. It has been infused epidurally and intrathecally as a single drug or in combination with other agents.[33] After epidural administration, these drugs need to cross the spinal meninges to reach their site of action.[32] The primary site of action of epidurally administered local anesthetics appears to be the dorsal and ventral spinal root as they exit the spinal column.[5] Epidurally administered local anesthetic drugs block sensory and motor nerve function in a concentration dependent manner so that it is possible to achieve selective sensory blockade without motor block by limiting the concentration of the drug.[5,34] Bupivacaine is a high potency and long duration local anesthetic that can be used safely in the epidural space.[5,35] In a double-blind randomized trial, Milligan et al described 60 patients in whom, based on the VAS score and narocotic use in the first 24 hours after surgery, bupivacaine was beneficial. In another study, bupivacaine was considered to be beneficial because there were significant differences between the groups considering the time of the first postoperative use of narcotic analgesic.[9] An interesting finding is that the combination of corticosteroids and bupivacaine diminished postoperative back pain and opioid usage without complication.[9]

In summary, we report that intraoperative use of epidural methylprednisolone or bupivacaine compared with that of normal saline (placebo) has no beneficial effect on postoperative pain relief during the 96 hours following lumbar disc surgery. According to this study we conclude that the intraoperative use of epidural methylprednisolone and bupivacaine do not have beneficial effects on postoperative pain relief following lumbar discectomy surgery. Therefore, we do not recommend the use of these drugs for postoperative pain control.

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