

Efficacy of Double Drug Impregnated Autologous Coagulum Patch versus Single Drug Impregnated Autologous Coagulum Patch in Postoperative Pain Management after Spinal Surgery

Abstract

Background: Postoperative pain and cerebrospinal fluid (CSF) leak are common known complications of spinal surgery, both having a synergistic effect on each other. Thus, both need to be dealt simultaneously. Double drug impregnated autologous coagulum patch (DDIAC) is a novel method which reduced both incidences of postoperative CSF leaks as well as pain. **Methodology:** Twenty-seven patients undergoing lumbar disc surgery without instrumentation were included and randomized into DDIAC and single drug impregnated autologous coagulum patch (SDIAC) group. The patients were assessed postoperatively with visual analog scale (VAS). **Results:** There were 21 males and 6 females in the study. Seventeen (63%) patients got randomized for DDIAC patch application and other 10 (37%) patients entered the control arm group (SDIAC) patch use. Preoperative VAS was 5 in both the groups. The average postoperative VAS was 3.01 in DDIAC arm and 4.29 in control arm. The average analgesic shot required in the DDIAC group was 0.41 in 24 h and SDIAC group was 4.1 in 24 h. In DDIAC group, none of these patients had CSF leak from the surgical wound till discharge from the hospital. In the SDIAC group, one (10%, $n = 10$) patient had CSF leak. **Conclusions:** DDIAC patch was effective in controlling pain in the postoperative period; however, few patients may require analgesic shots for pain management. SDIAC patch may control some pain in the immediate postoperative period; however, this was not sufficient for a longer postoperative period.

Keywords: Cerebrospinal fluid leak, double drug impregnated autologous coagulum patch, postoperative pain, single drug impregnated autologous coagulum patch

Background

Postoperative pain and cerebrospinal fluid (CSF) leaks are two important problems following any spinal surgery. Postoperative CSF leak following spinal surgery is as high as 5% of all spinal surgery,^[1-3] whereas postoperative pain is also a major factor in all spinal surgery, which leads to increase in discomfort preventing early ambulation as well as physiotherapy. Both of these issues lead the patient to remain confined to the bed for prolonged period. This starts a vicious circle of aggravation of CSF leak because of dorsal-dependent wound position as a result of spine bed rest. Second, more CSF leak leads to more pain and discomfort.

There has been a very little study done to assess the CSF leak following lumbar spine surgery.^[4,5] Similarly, there are few studies available in literature regarding pain

management following spinal surgery.^[6-10] However, there is no study available in literature, linking this complex relationship of CSF leak with pain management to date.

This study was designed by taking into account of both these above facts. In this study, an innovative method was used, i.e., double drug impregnated autologous coagulum patch (DDIAC) preparation, in which patient's own (autologous) clot was used to provide compact fibrin network over the dura to prevent CSF leak from dura, and a patch of drug-soaked oxidized gelatin sponge containing two drugs such as ropivacaine (Naropin) is a longer-acting local anesthetic acts directly on the neurons and tramadol hydrochloride is an opioid analgesic agent, which also acts both locally as well as at spinal cord level.

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The rationale of using fibrin sealant for dural repair is available in some previous study,^[5] whereas there are enough literature evidences available of using epidural drugs for postoperative pain management.^[8,11,12]

As this involves only autologous clot and serum, this was less costly, easily available, and there were fewer chances of developing transfusion-related diseases such as HIV and hepatitis. DDIAC is a novel method which reduced both incidences such as postoperative CSF leaks as well as pain. Further, this breaks the vicious circle of aggravation of CSF leak following postoperative pain state in patients.

Objectives of the study

- The efficacy of DDIAC in pain management in the postoperative period after lumbar disc surgery
- The efficacy of DDIAC in preventing CSF leaks in postoperative period after lumbar disc surgery
- To know the relationships of pain management and CSF leak following lumbar spine surgery.

Methodology

Patient's selection

We screened all patients admitted to the department of neurosurgery with lumbar spine disorder and planned for surgery. After studying the symptomatology, clinical details, and the radiological investigations, we selected the target patients as per the following parameters. Moreover, proper consent for the study and its publication has been taken. However, no institutional clearance was applied.

Inclusion criteria

- Adult patients with single level or double level lumbar disc disease with radiculopathy as predominant symptom and undergoing surgery
- Disc surgery without instrumentation
- Patient wanting to give consent and cooperative for pain assessment with visual analog scale (VAS) score both before and after surgery.

Exclusion criteria

- Patients with back ache as a predominate symptom before surgery
- Patients of lumbar disc disease with cauda equina syndrome, bladder bowel involvement, diabetic neuropathy, morbid obesity, and other associated comorbid conditions, where early postoperative ambulation is delayed
- History of known hypersensitivity to any of the drug in the study.

Visual analog scale

This is a subjective assessment of pain by the patients themselves using a standardized VAS color-coded chart paper. It is scored from 1 to 10, VAS 1 being no pain at all to VAS 10 meaning severe pain feeling. As per international

standards followed worldwide, those with pain score <3 (VAS <5) are said to be within comfort zone and do not require any pain killing medications.

Study design

After the selection of a target patient, randomization was done. All the patients after surgery were monitored for pain with VAS analyzer grading at 2 hourly intervals until sleep for next 24 h. No VAS was recorded when in sleep. Those patients with VAS score above 5 were given short-acting dose of analgesia as per the protocol based on patients' demand. Standard postoperative wound management was carried out and the status CSF leak monitored until patient got discharged from the hospital.

Study arm

The following procedures executed when the patients belonging to study arm are operated.

- After the laminectomy surgery was over and just before the wound closure, the (DDIAC) patch (see later) applied over the dura and the wound closed in standard manner
- Postoperatively, the pain score is noted using the VAS pain score analysis and those with VAS score above 5 was noted and given further dose of injectable analgesia based on demand
- Standard postoperative wound management was carried out and the status CSF leak monitored.

Drugs patch preparation procedure (double drug impregnated autologous coagulum patch patch)

Double drug impregnated autologous coagulum patch preparation

- Oxidized gelatin sponge (Curaspon® Or Gelfoam®) of size equal to operative dural wound, thoroughly soaked with two drugs
 - a. Five milliliters of 2% ropivacaine (Naropin®)
 - b. One milliliter of 100 mg tramadol hydrochloride without preservative (injection Tramadol®)
- Five milliliters of autologous fresh venous blood
 - a. By mixing above two and allowing the fresh blood to form a compact coagulum, the DDIAC is made.

Rationale

Autologous coagulum patch

The oxidized gelatin sponge gives base for clot formation, and the coagulum forms a compact fibrin and thrombin network to seal minor CSF leak. The drug-soaked oxidized gelatin sponge contains the drug for slow delivery to painful spinal roots.

Two drugs

- Ropivacaine (Naropin) is a longer-acting local anesthetic acts directly on the neurons
- Tramadol hydrochloride is an opioid analgesic agent.

Control arm

During the surgery, the existing standard protocol management for laminectomy surgery was applied. In the control group, single drug impregnated autologous coagulum (SDIAC) patch, where only 5 ml of 2% ropivacaine (Naropin) was used instead of two drugs, rest of the procedure for making the patch remaining same as in case of DDIAC. These include a standard surgical method of wound closure and the perioperative pain management using injectable analgesics. After surgery when the patient is reversed (weaned off) from the effect of anesthesia, the postoperative pain control is usually achieved up to approximately 1–2 h by the intraoperative analgesic medications given during surgery. Most patients after this period usually need some form of injectable analgesia as pain management protocol. We used injectable analgesics during this period using the VAS pain score analysis, in patients belonging to the control group as well. All the patients after surgery were assessed with VAS grading and those with VAS score above 5 was noted and given further dose of analgesia. Standard postoperative wound management was carried out, and the status CSF leak monitored until the patient is discharged from the hospital.

Results

This study was started on July 24, 2011, after procuring the relevant medicines, pain assessment card (VAS), and other surgical consumables. The first case was recruited on July 24, 2011, after the patient fulfilled the selection criteria and randomization procedure.

Based on the inclusion criteria, we could recruit only 27 patients who gave consent for the procedure. Hence, we recruited 27 patients to be analyzed statistically. There were 21 male and six female patients in total group. The minimum age was 27 years and the maximum age was 78 years (mean age 45.19 years). Table 1 shows the diagnosis profile of these patients.

Of the total 27 patients, 13 (48.1%) patients had bilateral symptoms, 8 (29.6%) patients had right-sided symptoms, and 6 (22.2%) patients had left-sided symptoms.

We randomized the patients with the help of a computer-generated randomization table. Of the total of 27 patients recruited, as per the randomization procedure, 17 (63%) patients got randomized for the DDIAC patch application and other ten (37%) patients entered the control arm group SDIAC patch, where only 5 ml of 2% ropivacaine (Naropin) was used instead of two drugs.

All patients were operated by senior surgeons with over 10-year experience. The surgery consists of single or two level laminectomy with discectomy and laminectomy with b/l foraminotomy distribution in each group is given in Table 2.

Table 1: Diagnosis profile of patients

Diagnosis	Frequency (%)
L4/L5 PIVD with radiculopathy	8 (29.6)
L4/L5 PIVD with LCS	10 (37.0)
L5/S1 PIVD with radiculopathy	5 (18.5)
L5/S1 PIVD with LCS	2 (7.4)
L4/5 and L5/S1 PIVD with radiculopathy	1 (3.7)
L4/5 and L5/S1 PIVD with LCS	1 (3.7)
Total	27 (100.0)

LCS – Lumbar canal stenosis; PIVD – Prolapsed intervertebral disk

Table 2: Surgery performed in individual group

Surgery performed	DDIAC group	SDIAC group
Single level laminectomy with discectomy	14	9
Two level laminectomy with discectomy	1	1
Laminectomy with bilateral foraminotomy	2	Nil

DDIAC – Double drug impregnated autologous coagulum; SDIAC – Single drug impregnated autologous coagulum

In the DDIAC arm, we got 17 (63%) patients, among these the average preoperative VAS score was five, and similarly, the average preoperative VAS in the other groups was also five.

The average postoperative VAS in the DDIAC arm was found to be 3.01, whereas the average postoperative VAS in the SDIAC patch was 4.29. This is not very different statistically. The average analgesic shot required in the DDIAC group was 0.41 in 24 h, whereas the average analgesic shot required relieving the pain as per demand in the SDIAC group was 4.1 in 24 h. To infer this, SDIAC group required a 6 hourly schedule of analgesic shots. The peak hour of highest VAS in the DDIAC group in the immediate postoperative period was in 10th h and 20th h postoperatively. However, only a few of these required analgesic administration, whereas, the highest VAS in the SDIAC group in the immediate postoperative period was in 4th h, 10th h, 20th h, and 24th h postoperatively. Hence, there are two peaks of pain period in DDIAC group and there were four peaks in the SDIAC group.

Of the 17 patients recruited so far, none of these patients had CSF leak from the surgical wound till discharge from the hospital. Only one (5.9%, $n = 17$) patient had delayed wound healing not related to the patch found. Similarly, in the SDIAC group, 1 (10%, $n = 10$) patient had CSF leak and subsequent delayed wound healing due to intraoperative dural tear occurred due to surgery.

With regard to the pain management is concerned, all the patients belonging to both the groups (DDIAC and SDIAC) remained pain free until 24 h postoperatively, due to on-demand analgesic use based on VAS. In the DDIAC group, ten patients (58.8%, $n = 17$) did not require any analgesic shot within 24 h postoperative period and seven (41.2%) patients needed only one shot in the

postoperative period, whereas in the SDIAC group, five patients (50%, $n = 10$) required four analgesic shots, three patients (30%, $n = 10$) required two analgesic shots, and two patients (20%, $n = 10$) required three analgesic shots, within 24 h postoperative period. This is to be noted that all the patients were covered with analgesics only when the VAS exceeded 5 based on patients demand to have a pain-free period after surgery.

There has been no incidence of any side effects both in terms of exaggerated pain and/or infections in any patients.

Discussion

For effective postoperative pain relief, a multimodal therapy is required, which is the use of two or more analgesic agents or techniques in combination. Multimodal analgesia refers to the use of two or more agents throughout the pain pathway. Individual agents given at high enough doses may achieve desirable analgesia, but a multimodal approach maximizes the benefits of each agent while minimizing the adverse events associated with higher doses. The guiding principle is that a balance of agents will provide optimal pain control combinations of opioids and non-opioid analgesics improve the quality of postoperative analgesia, reduce opioid requirements, and reduce associated side effects.

Surgical injury results in acute nociception as well as sensitization of the dorsal horn of the spinal cord, which can lead to hyperalgesia and allodynia. During laminectomy and discectomy, there is trauma to the soft tissues and bony structures, which can result in severe pain at rest as well as during movement. There may be an additional component of neuropathic pain due to nerve root manipulation-related injury. Pharmacokinetic studies have shown that epidural administration produces higher CSF levels and longer elimination half-life than intravenous administration.^[13]

Ropivacaine is a first single long enantiomer-specific compound and long-acting amide local anesthetic, which has a reduced risk of cardiac toxicity, neurotoxicity, and rapid recovery of motor function. Postoperative pain relief is an important function of ropivacaine; it has been used with many adjuvants for lower abdominal surgery which has other side effects. Hence, our concern is of using a drug as an adjuvant with ropivacaine which provides better intraoperative hemodynamic condition as well as prolonged postoperative analgesia with minimal side effect. New amide ropivacaine has minimal cardiovascular and CNS toxicity as well as a lesser property of motor block during regional anesthesia. Tramadol is a centrally acting analgesic which acts on opioid receptors and also appears to modify the transmission of pain impulses by the inhibition of monoamine reuptake.^[14] A few studies have shown that epidural or caudal tramadol can be free from postoperative analgesia side effects combination of ropivacaine and tramadol, as an epidural patch in lumbosacral nerve roots

decompressive surgery and/or fusion for postoperative back and radicular pain relief has yet not been reported.^[15,16]

Cai *et al.*^[11] observe the anesthetic effects of epidural ropivacaine with tramadol during lower limbs surgery. Thirty patients planned for lower limb surgery in their study were evaluated randomly divided into two groups with 15 patients in each group: Group ropivacaine (R) and Group ropivacaine with tramadol (T). In result, the time of sensation block which reached T12 and T10, and the time to the highest plane of analgesia decreased significantly in Group T than that in Group R ($P < 0.05$). The lasting time of analgesia in Group T was longer than that in Group R ($P < 0.05$). There was no significant difference in the potency of analgesia, the degree of sedation and motor block, and the side effects ($P > 0.05$). Thus, they conclude that the epidural ropivacaine with tramadol enhanced the anesthetic effects of ropivacaine.

Conclusions

This study conclusion in 27 odd patients (with a mean age of 45.19 years) with similar disease profile demonstrated that DDIAC patch was effective in controlling pain in the postoperative period; however, few patients may require analgesic shots for pain management. SDIAC patch may control some pain in the immediate postoperative period; however, this was not sufficient for a longer 24 h postoperative period. However, larger studies are required to prove this statistically. There is no incidence of any adverse effects arising out of the study. Both these patches do not affect the wound management in the routine postoperative period.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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