Efficacy of Ultrasound-Guided Caudal Epidural Calcitonin for Patients with Failed Back Surgery Syndrome

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Abstract

Context: Pain resulting from failed back surgery syndrome (FBSS) is generally resistant to physiotherapy and pharmacological treatment. Objective: The aim of this study is to evaluate the effect of adding calcitonin to local anesthetic and steroids during ultrasound-guided caudal epidural injection for patients suffering from FBSS. Patients and Methods: Fifty-six patients were randomly allocated into two equal groups. All patients underwent ultrasound-guided caudal epidural injection. Group A received 40 mg (1 mL) methylprednisolone +9 mL lidocaine 0.5% + 1500 iu hyaluronidase in 10 mL normal saline, whereas Group B received 40 mg (1 mL) methylprednisolone +9 mL of 0.5% lidocaine + 1500 iu hyaluronidase in 5 mL normal saline + 50 iu calcitonin in 5 mL normal saline. Results: A statistically significant decrease in visual analog scale, Oswestry Disability Index, and analgesic consumption was recorded in Group B as compared to Group A at 1, 2, and 3 months interval. No side effects were reported in Group A, whereas patients belong to Group B experienced nausea (2 cases), and diuresis for 24 h was detected in two cases. Conclusion: The addition of calcitonin to epidural steroid and local anesthetic injection resulted in better Oswestry disability scale, diminished pain intensity, and less analgesic consumption.

Keywords: Calcitonin, caudal epidural, failed back surgery syndrome

INTRODUCTION

Failed back surgery syndrome (FBSS) is a clinical syndrome encountered after a patient has had one or more surgical procedures aimed at correcting their lumbosacral disease. The patients present with recurrent or persistent back and/or lower extremities pain even after successful (technically, anatomically) lumbosacral spine surgeries. The FBSS is a frequent complication of lumbosacral spine surgery with incidence ranges from 5% to 10% of cases.

Patients suffering from FBSS are presented with chronic debilitating pain with the resultant psychological and social side effects. Many factors are implicated (e.g., local tissue fibrosis or psychosocial factor), but the exact etiology of this pain still unclear.

FBSS patients generally suffer many associated problems, including operations of the lumbosacral area, sleeping problems, depression, family problems (sometimes leading to divorce), economic problems, high-dose opioid use/dependence, and the low probability that further surgery will result in pain relief.

Pain resulting from FBSS is generally resistant to physiotherapy and pharmacological treatment. Treatment options usually include a variety of physical, psychological, medical, and surgical interventions, but no well-known guidelines are confirmed and a significant number of patients are left complaining of pain and disability.

Although the addition of steroid to local anesthetic resulted in prolonged duration of analgesia, repeated injections of steroid have its drawbacks. Hence, the presence of the other medications added to the steroid to minimize the need for repetition of the block seems to be crucial.

Calcitonin is a polypeptide hormone released from the thyroid gland. Calcitonin-induced analgesia might be attributed to its...
effects on prostaglandin and thromboxane synthesis, calcium influx, the cholinergic and serotoninergic systems, B-endorphin release, and direct action on central nervous system receptors.\(^7\)

The study aimed to assess the effect of adding calcitonin to local anesthetic and steroids during ultrasound-guided caudal epidural injection for patients suffering from FBSS. We hypothesized that calcitonin may add clinical value to the analgesic and anti-inflammatory effect of local anesthetic and steroids.

Improvement in pain intensity as evaluated using visual analog score represents the primary outcome, while the secondary outcomes include functional outcome of the patients using Oswestry Disability Index (ODI), complications as infection, sensory or motor deficit, or sphincter dysfunction.

**Patients and Methods**

**Patients**

After getting clearance from our medical institution (R.19.02.474), this prospective randomized, double-blind controlled study was carried out on 56 patients referred to our pain clinic. Written informed consent, including full description of the technique, drugs, and side effects, was obtained from all participants. The included patients had a history of chronic low back pain with or without leg pain of grade ≥6 on a visual analog scale (VAS) for at least 3 months after surgery. Patients were between the age group of 18 and 65 years, of either sex and of the ASA Physical Status I–III. Exclusion criteria included:

1. Patient refusal
2. Bleeding or coagulation disorders
3. Infection at the site of needle entry
4. Uncooperative patient and difficult communication after the procedure
5. Previous chronic opioid use
6. Patients with a history of allergy to any one of the used drugs.

**Randomization**

Patients were randomly allocated into two groups of 28 patients each according to computer-generated randomization program, using closed envelopes identifying the group of the allocation at the time of the first visit to our pain clinic by a nurse who did not participate in the follow-up of patients. Each patient was assigned as (A) or (B) according to his or her group followed by a number from 1 to 56 according to his or her order. A senior resident blinded to the randomization was responsible for patient follow-up and dosage of postprocedure analgesics.

- Group A (control group), \((n = 28)\) will receive 40 mg (1 mL) methylprednisolone plus 9 mL lidocaine 0.5% plus 1500 iu hyaluronidase in 10 mL normal saline and thus, the total volume will be 20 mL injectate
- Group B (study group), \((n = 28)\) will receive 40 mg (1 mL) methylprednisolone plus 9 mL of 0.5% lidocaine plus 1500 iu hyaluronidase in 5 mL normal saline plus 50 iu calcitonin in 5 mL normal saline to reach the same volume of Group A.

**Technique of ultrasound-guided caudal epidural injection**

Standard monitors for measurement of noninvasive blood pressure, electrocardiogram, and pulse oximetry were applied before the procedure. An intravenous cannula was placed for crystalloid infusion. Patients were premeditated with intravenous midazolam 0.05 mg/kg.

The patient was in a prone position. The lumbosacral area was sterilized. The pathway of Touhy needle was anesthetized using 3 mL lidocaine 1%.

Under ultrasound guidance, either linear or curvilinear probe was used according to the body habitus. The transducer was put on the sacrum at the midline in a transverse fashion, under this transverse view, the cornua of the sacrum, the sacrococcygeal ligament, and the sacral hiatus opening could be observed [Figure 1].

And then, the transducer will be changed to long axis to rest between the two cornua of the sacrum. The eighteen gauge Touhy needle; guided by ultrasound was inserted into the caudal epidural space. The advancement of the needle between the two cornua to the sacral hiatus and then into the epidural space was done under real-time imaging [Figure 2]. The epidural space was detected by the loss of resistance technique.

**Collected data**

1. Demographic data: At pre-procedure level
2. VAS\(^8\) It was reported at pre-procedure, and 1, 2, 3 months after the procedures.
3. ODI\(^9\) It was reported at pre-procedure, and 1, 2, 3 months after the procedures.

It is a self-administered questionnaire contains 10 sections, used to assess the degree of limitation of different daily activities. Each item is followed by six statements. The patient then checks the statement which resembles their situation. Each question is scored on a scale of 0–5 with the first statement being zero and indicating the least degree of disability, and the last statement is scored 5 indicating the greatest

**Figure 1:** Short axis view over sacrococcygeal membrane. SCM = sacrococcygeal membrane
The summed scores for all questions are put into as a percentage through using the equation: Total score/50 × 100.

iv. Analgesic consumption (mg/day): At 1, 2, and 3 months after the procedures. Acetaminophen was the available analgesic and given on request with a maximum dose 4 m/day. The total amount was divided by the follow-up period to detect the daily requirement at each follow-up interval.

v. Complications as infection, sensory or motor deficit, or sphincter dysfunction.

Sample size calculation
G power program (version [3.1.9], faculty at the Institute for Experimental Psychology in Dusseldorf, Germany) was used. For the current study, the calculation of sample size was based on the detection of a 2 point difference for the pain score (VAS) with estimated standard deviation (SD) of 2.4. Assuming α error = 0.05 and power (1 – β error) = 0.80, a sample size of 24 patients will be necessary. To compensate for dropouts and deviation from normality, 28 patients will be included in each group.

Statistical analysis
Analysis of data was performed using the Statistical Package for Social Sciences (SPSS), (IBM Crop. Released 2013. IBM Statistics for window, Version 22, IBM Crop., Armonk, NY, USA). First, the Shapiro test was used to test data distribution. Data were presented in the form of mean and SD, median, and range or numbers and percentages. The unpaired t-test will be used to compare between mean values (normally distributed data) of both groups. While, for categorical data (pain score), the Mann–Whitney U-test was used. The Fisher’s exact test was used for comparison of categorical data. Value of P ≤ 0.05 was considered as statistically significant.

RESULTS
A total of 56 patients were recruited in this study [Figure 3]. The two groups of participants did not show statistically significant difference regarding patient characteristics, duration, or site of pain [Table 1]. A statistically significant decrease in VAS, ODI, and analgesic consumption was recorded in Group B compared to Group A at 1, 2, and 3 months interval [Tables 2-4].

A statistically significant decrease in comparison with basal values was noticed in both groups regarding the VAS, the significant decrease compared to basal values continued only for 2 months in Group A and persisted up to 3 months in Group B [Tables 2 and 3].

DISCUSSION
The aim of the current study is to assess the efficacy of adding calcitonin to steroids and local anesthetic during ultrasound-guided caudal epidural injection for patients suffering from FBSS. The study documented diminished pain intensity and improved quality of life after the addition of calcitonin to the caudal epidural injectate for the management of such cases.

Persistence of the pain after spinal surgery represents a challenge either for the patient or the pain physician. The suspected etiology varies according to age, pathology, and the interval between the first and the revision surgery.[11]

Resorting to conservative therapy or revision surgery for adequate pain relief in those patients is often unsuccessful.[5]
Calcitonin is a polypeptide hormone released by the thyroid gland and plays a role in calcium homeostasis; it decreases the plasma level of calcium through inhibition of bone reabsorption and helping the renal excretion.[12]
Table 1: Demographic data of the studied groups (n=28)

| Group | Group (A) | Group (B) | P |
|-------|-----------|-----------|---|
| Age (years) | 54±13 | 52±15 | 0.59 |
| Gender (male/female) | 19/9 | 20/8 | 0.77 |
| Duration of pain (days) | 320±27 | 316±46 | 0.69 |
| Site of pain | | | |
| Back pain more than leg pain | 6 | 5 | 0.4 |
| Leg pain mainly | 10 | 13 | |
| Back pain + leg pain | 11 | 10 | |

Data are presented as mean±SD/N. SD=Standard deviation

Table 2: Basal and follow-up values of the visual analog scale of the studied groups (n=28)

| Group (A) | Group (B) | P |
|-----------|-----------|---|
| Basal (before block) | 7 (7-8) | 8 (7-8) | 0.59 |
| 1 month | 5 (3-7) | 4 (3-8) | 0.001* |
| 2 months | 5 (3-7) | 4 (3-8) | 0.001* |
| 3 months | 6 (7-8) | 4 (3-9) | 0.001* |

Data are presented as median (range). *P≤0.05 was considered as statistically significant between the two groups. †P<0.0001 was considered as highly significant in comparison with basal value

Table 3: Basal and follow-up values of the Oswestry Disability Index of the studied groups (n=28)

| Group (A) | Group (B) | P |
|-----------|-----------|---|
| Basal (before block) | 74 (65-84) | 70 (61-82) | 0.7 |
| 1 month | 30 (25-36) | 17 (15-25) | <0.0001* |
| 2 months | 35 (25-40) | 19 (16-28) | <0.0001* |
| 3 months | 48 (34-50) | 21 (16-29) | <0.0001* |

Data are presented as median (range). *P≤0.05 was considered as statistically significant between the two groups

Table 4: Analgesic consumption (mg/day) of the studied groups (n=28)

| Group (A) | Group (B) | P |
|-----------|-----------|---|
| 1 month | 976.5±253.2 | 770.2±245.1 | 0.003* |
| 2 months | 1200.1±854.1 | 758.5±270.3 | 0.01* |
| 3 months | 2602±772.5 | 792.1±210.2 | 0.0001* |

Data are presented as median (range). *P≤0.05 was considered as statistically significant between the two groups. SD=Standard deviation

The exact mechanism of the analgesic effect of calcitonin is not well described, but the rational for its usage depends on its direct analgesic effect through B-endorphine release, other suggested mechanisms include inhibition of synthesis of prostaglandin and thromboxane, reduction of blood supply of bone by decreasing its metabolic activity, and so; increases blood supply to the affected neural tissues. It is suspected to have an effect on the cholinergic and serotoninergic systems. The adverse effects noticed with calcitonin can be explained by increased serotonergic activity, but they are usually mild and self-limiting.

An explanation of these side effects to the patient before the procedure besides the use of antiemetic prophylaxis is quiet sufficient. 5-HT3 antagonists such as ondansetron should be avoided as they may reduce the analgesic efficacy of calcitonin.

In the current study, the side effect reported in the calcitonin group was diuresis in two patients and persists for 24 h only. Two cases suffered from nausea and responded well to antiemetic. Short follow-up duration is a limitation of our study. We recommend more evaluation of the drug over a longer follow-up period and more delineation of the safety of epidural injection of calcitonin in further studies.

**Conclusion**

The findings of the study concluded that during ultrasound-guided caudal epidural injection for the management of FBSS, the addition of calcitonin to steroid and local anesthetics resulted in better Oswestry disability scale, diminished pain intensity and less analgesic consumption.

**Financial support and sponsorship**

Nil.

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The use of steroid with local anesthetic in the control group accounts for extension of the duration of analgesia beyond the local anesthetic effect. It is assumed that steroids exert their effect through relief of inflammatory edema and decreasing the sensitization at the dorsal horn. An additional value of water-soluble enzyme, hyaluronidase was reported when injected with steroid to treat pain resulting from tissue synechiae surrounding the nerve roots as part of failed back surgery. The enzyme increased the duration and improved the efficacy of epidural injections.

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The rapidity and persistence beyond the anticipated pharmacological duration of action characterize the analgesic action of calcitonin. It is used effectively for the management of phantom limb pain and acute pain resulting from vertebral fractures. However, the optimum dose of calcitonin, route of administration, and duration of therapy are not determined yet.

In the current study, the participants received calcitonin in the epidural injectate showed a more significant improvement of VAS and ODI compared to control (steroid) group at the three follow-up intervals.

It was not surprising to find that the analgesics consumption increased about three times during the follow-up period in the steroid group, whereas in the calcitonin group, the analgesic consumption did not increase at all which may account for the significant improvement in ODI in the calcitonin group during the follow-up period compared to the control (steroid) group.

The initial improvement in the control group can be attributed to the local anesthetic that improves the blood supply to compromised neural tissues through the sympathetic blockade and vasodilatation. Furthermore, it inhibits neural sensitization and neurotransmitters release.

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Conflicts of interest
There are no conflicts of interest.

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