Original Article

Efficacy of local wound infiltration analgesia with ropivacaine and dexmedetomidine in tubercular spine surgery – A pilot randomised double-blind controlled trial

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ABSTRACT

Background and Aims: Regional analgesic techniques are difficult to use in tubercular spine patients due to distorted spinal anatomy and presence of infection. This study was conducted with the aim to evaluate analgesic efficacy of local wound infiltration before wound closure in tubercular spine patients. **Methods:** This pilot randomised double-blind controlled study was conducted in 32 American Society of Anesthesiologists I-III patients, age ≥15 years, undergoing elective surgery for spinal tuberculosis. All the patients received general anaesthesia using standard technique and intravenous morphine for intraoperative analgesia. They received wound infiltration with either normal saline (group C) or local infiltration analgesia with 0.375% ropivacaine 3 mg/kg, adrenaline 5 μg/mL and dexmedetomidine 1 μg/kg in a total volume of 0.8 mL/kg (group LIA) before wound closure. Patient-controlled analgesia using intravenous morphine provided postoperative analgesia. The primary objective was to study 24-h morphine consumption, whereas the secondary objectives included pain scores, complications and patient satisfaction. Repeated measures analysis of variance, Chi-square test and Mann–Whitney *U* test were used for statistical analysis. **Results:** Morphine requirement was lower in group LIA (6.7 ± 2.7 mg) than in group C (27.7 ± 7.9 mg); $P < 0.001$. Group LIA also had lower pain scores ($P < 0.001$), longer time to rescue analgesic ($P < 0.001$), better patient satisfaction to pain relief ($P = 0.001$) and lower incidence of postoperative nausea and vomiting than group C. **Conclusion:** Wound infiltration with ropivacaine, adrenaline and dexmedetomidine before wound closure provided good postoperative analgesia with lower morphine requirement.

Key words: Dexmedetomidine, postoperative analgesia, ropivacaine, spinal tuberculosis, wound infiltration

INTRODUCTION

Tuberculosis (TB) of spine, a common spine pathology in India, may require surgical decompression with or without instrumentation. Most of the spine surgeries are very painful and require good postoperative analgesia. It is recommended to use a multimodal analgesic regimen using systemic opioids or nonsteroidal anti-inflammatory drugs; along with regional anaesthesia techniques, if feasible.[1] Various regional techniques, for example, lumbar epidural, caudal epidural or intrathecal, have been used after spinal surgery.[2,3] However, all these regional anaesthetic techniques are difficult to use in tubercular spine patients due to distorted spinal anatomy and presence of infection.

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Nowadays, wound infiltration has become an important component of multimodal analgesia. It contributes to lower opioid consumption and faster patient recovery.[4] The literature does not mention any study that has assessed the efficacy of local wound infiltration for postoperative pain relief in patients undergoing TB spine surgery. In fact, an extensive search of literature could not reveal any publication that has studied pain scores and any postoperative analgesic technique exclusively in TB spine patients. It was hypothesised that a combination of ropivacaine, adrenaline and dexmedetomidine, when used for local wound infiltration, would provide a good analgesic effect and reduce opioid consumption in patients undergoing TB spine surgery.

Hence, the present pilot study was planned to evaluate the analgesic efficacy of single-shot local wound infiltration analgesia using ropivacaine with adrenaline and dexmedetomidine before wound closure in patients undergoing major surgical procedures for management of TB spine, that is, decompression with or without spine stabilisation surgery.

METHODS

This randomised double-blind pilot study was conducted in 32 patients undergoing tubercular spine surgery. The patients were recruited from December 2013 to March 2015. The study was conducted after approval from Institutional Ethics Committee – Human Research and registration of clinical trial. Written informed consent was obtained from all the patients.

The study included American Society of Anesthesiologists (ASA) I/II/III patients, age 15 years and above, undergoing elective surgical decompression with or without instrumented stabilisation for TB of spine.

Patients on chronic antiemetics or pain medications, those having known local anaesthetic (LA) allergy, renal or hepatic insufficiency, or pregnancy were excluded from the study. Patients who were unable to understand numerical rating scale (NRS) for pain assessment and function of patient-controlled analgesia (PCA) pump were not studied.

All patients received general anaesthesia at the time of surgery. In the preoperative room, they were explained and instructed about the pain assessment using NRS (0–10; 0: no pain, 10: worst imaginable pain) and the use of PCA device. All patients received intravenous (IV) PCA using morphine for postoperative pain relief. The patients were randomly divided into two groups of 16 each, using computer-generated random number table and sealed envelope technique. In group C (control), patients received wound infiltration with 0.8 mL/kg of normal saline before wound closure. Group LIA (local infiltration analgesia) patients received wound infiltration with 0.375% ropivacaine 3 mg/kg with adrenaline 5 μg/mL and dexmedetomidine 1 μg/kg in a total volume of 0.8 mL/kg. The person preparing these study solutions was different from the person monitoring the patient and providing analgesia in the postoperative period. The patient and the observer were blinded to the group allocation.

All patients were premedicated with oral alprazolam 0.25–0.50 mg 2 h prior to surgery. The anaesthetic technique remained the same in both the groups using propofol, vecuronium, oxygen, nitrous oxide and isoflurane. Morphine 0.1 mg/kg was administered at the time of induction for analgesia. Morphine 1 mg was repeated if heart rate (HR) and/or blood pressure increased to 20% above baseline values, despite adequate depth of anaesthesia. The monitoring included electrocardiogram, HR, noninvasive blood pressure and pulse oximetry. Inj. atropine IV was administered to treat bradycardia, defined as HR <50 beats/min. Hypotension, defined as systolic blood pressure less than 90 mmHg, was treated with IV fluids; blood transfusion, if indicated; and mephentermine IV, as and when required. The patients received ondansetron 4 mg IV and diclofenac 1 mg/kg by slow IV infusion or tramadol 1 mg/kg IV, if diclofenac was contraindicated, at the time of wound closure. Neuromuscular blockade was reversed using neostigmine 0.05 mg/kg and atropine 0.02 mg/kg at the end of surgery. The time of adequate recovery from anaesthesia was considered as T0.

The surgeons infiltrated bilateral paraspinal muscles after fascial closure and then the skin all along the wound with the study solution. They were not aware of the group allocation of the patient.

In the postoperative period, HR, blood pressure, oxygen saturation, pain scores using NRS and level of sedation using Ramsay's sedation score[5] were monitored and recorded every 30 min for initial 2 h, then at 4, 8 and 24 h. Time to first analgesic request was noted and analgesia was provided whenever NRS pain score was more than 3 or the patient

demanded pain relief. Morphine 1 mg IV was given every 5 min until NRS pain score decreased to 3 or less. At this point, morphine PCA was provided to the patient. Episodes of nausea and vomiting were recorded and managed with dexamethasone. Any other complaints were also noted and managed accordingly. Patients in both the groups were asked about their satisfaction with pain control at 24 h, graded as good/average/poor.

The primary outcome measure was cumulative IV morphine consumption over 24 h, whereas secondary outcome measures included NRS pain scores, nausea/vomiting, pruritus, bradycardia/hypotension and patient satisfaction with pain relief.

This study was conducted as a pilot study as an extensive search of literature did not reveal any research work that has studied postoperative analgesic consumption and pain scores in patients undergoing surgery for management of TB spine. Sixteen patients in each group were included in the study.

On the basis of the observed estimates of morphine usage in both groups, a *post hoc* power analysis was done. This showed that the power of the study was more than 90% and a sample of 10 cases was required in each group to study the observed difference in morphine use at alpha = 5% and power = 90%.

Statistical analysis was performed using SPSS version 20.0. Two-factor repeated measures analysis of variance was used for comparison of postoperative haemodynamic parameters, pain scores and sedation scores. ASA grading, intraoperative additional morphine requirement, postoperative complications and satisfaction with pain control were analysed by Pearson's Chi-square test. Morphine consumption and time to first analgesic request were studied by Mann–Whitney *U* test. A value of $P < 0.05$ was considered statistically significant.

RESULTS

A total of 42 patients were assessed to study 16 patients in each group. The CONSORT diagram for the study is shown in Figure 1.

The demographic profile and other patient characteristics including baseline haemodynamic parameters, durations of surgery and anaesthesia, and surgical parameters are shown in Table 1.

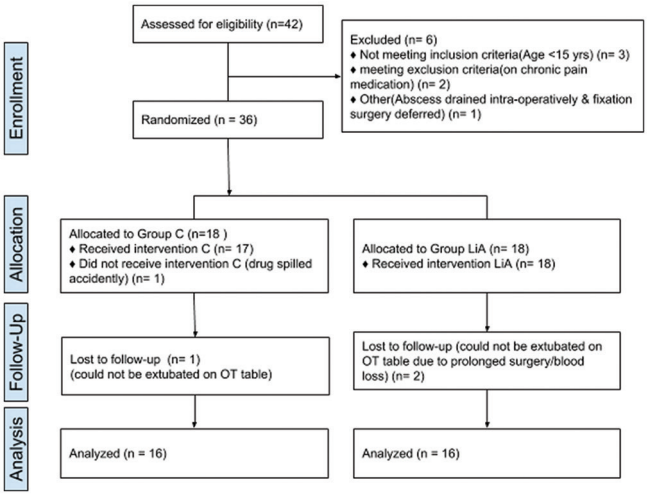

Figure 1: CONSORT diagram

Table 1: Demographic profile and other patient characteristics

	Group C (*n*=16)	Group LIA (*n*=16)
Age (years)	28.4±12.8	40.7±18.8
Weight (kg)	48.5±8.8	48.0±7.3
Sex (M:F)	5:11	5:11
ASA I:II:III	7:6:3	5:5:6
Baseline heart rate (beats/min)	92.9±12.4	83.3±24.6
Baseline systolic blood pressure (mmHg)	115.8±8.1	116.4±12.1
Baseline diastolic blood pressure (mmHg)	73.3±9.9	76.7±12.7
Baseline mean arterial pressure (mmHg)	89.0±8.7	90.5±10.8
Duration of surgery (min)	191.6±44.7	177.5±35.6
Duration of anaesthesia (min)	233.4±47.4	217.5±36.0
Spine level involved (lumbar:thoracic)	10:6	5:11
Neurological deficit (paraparesis:paraplegia:no deficit)	7:4:5	8:4:4
Surgery - decompression (with fixation:without fixation)	9:7	11:5

LIA – Local infiltration analgesia, ASA – American Society of Anesthesiologists, SD – Standard deviation. Values are mean±SD or ratio

During intraoperative period, there was no significant difference in HR ($P = 0.050$) and systolic blood pressure ($P = 0.885$) in the two groups. Postoperatively, systolic blood pressure was comparable in both groups at all time points ($P = 0.094$) [Figure 2]. However, HR values were significantly lower in group LIA when compared with control group at most of the time points ($P = 0.004$) [Figure 3]. Arterial oxygen saturation was maintained above 95% throughout the postoperative period in both the groups.

The patients in both the groups required additional morphine intraoperatively in the range of 0–3 mg ($P = 0.067$). The efficacy of postoperative analgesia in the two groups was compared using NRS pain scores, time to first analgesic request (TFR) and morphine requirements in the postoperative period.

The morphine requirement was lower and TFR was longer in group LIA [Table 2]. The pain scores at all time points were also significantly lower in group LIA than in group C ($P < 0.001$) [Figure 4].

More patients in group LIA were satisfied with their pain relief when compared with group C patients ($P = 0.001$). Thirteen patients in group LIA rated their score as 'good' against only four patients in group C. There were seven patients in group C who rated their satisfaction as 'poor' against none in group LIA.

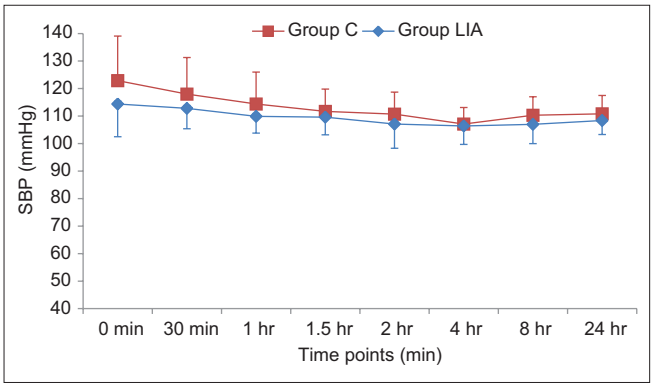

Figure 2: Trends of systolic blood pressure in postoperative period

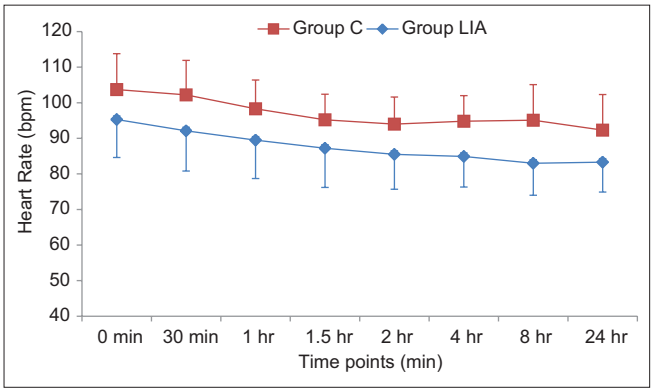

Figure 3: Trends of heart rate in postoperative period

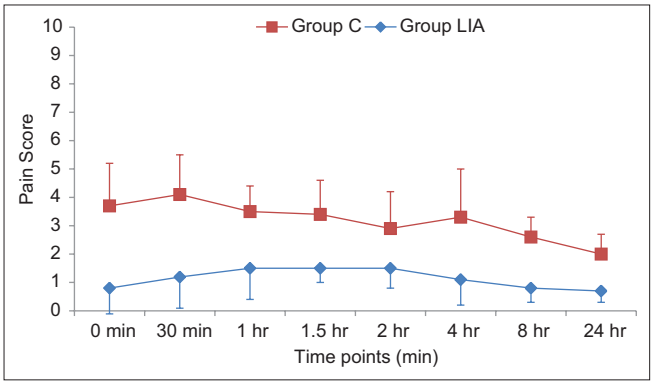

Figure 4: Pain scores in postoperative period

The difference in sedation scores between group C and group LIA was statistically significant at 0 min, 30 min, 1.5 h and 8 h ($P < 0.001$). These were higher in group LIA at 0 min, 30 min and 8 h and in group C at 1.5 h. The scores at other time points were comparable.

Thirteen patients in group C complained of nausea of which 12 vomited. On the other hand, only three patients in group LIA complained of nausea of which two vomited. This difference in the incidence of nausea and vomiting in the two groups was statistically significant ($P < 0.001$). However, the incidence of postoperative pruritus was comparable in both the groups ($P = 0.101$).

DISCUSSION

The results of this study demonstrated that local wound infiltration with ropivacaine, adrenaline and dexmedetomidine resulted in lower 24 h morphine consumption, NRS pain scores and nausea/vomiting, with better patient satisfaction.

TB of spine is one of the most common spine pathologies in India, constituting 40%–50% of osteoarticular TB.[6] Tubercular spine with neurological complications may require surgical decompression with or without instrumentation, whereas spinal deformities require kyphotic deformity correction which entails anterior decompression, posterior column shortening, instrumented stabilisation and anterior and posterior bone grafting.[7]

Wound infiltration is a simple method of providing postoperative analgesia that can be easily administered by the surgeons just prior to closure of the wound. By improving postoperative analgesia, it contributes to lower opioid consumption and faster patient recovery.[4] In orthopaedic surgery, it has been used with good results in hip and knee arthroplasty,[8,9] shoulder surgery[10] and lumbar spine surgery.[11,12] However, we could not find any evidence in literature of use of local wound infiltration technique in patients undergoing tubercular spine surgery.

Table 2: Postoperative analgesic requirement

Parameters	Group C (*n*=16)	Group LIA (*n*=16)	*P*
Time to first analgesic request (min)	7.8±2.8	169.1±161.1	<0.001
Initial morphine bolus (mg)	2.8±0.7	1.7±0.6	<0.001
PCA morphine (mg)	24.9±7.7	5.0±2.4	<0.001
Total morphine (mg)	27.7±7.9	6.7±2.7	<0.001

LIA – Local infiltration analgesia, PCA – Patient-controlled analgesia, SD – Standard deviation. Values are mean±SD

Bianconi *et al.* used local wound infiltration with 0.5% ropivacaine 40 mL followed by continuous infusion of 0.2% ropivacaine 5 mL/h for 55 h after spine fusion surgery and reported lower pain scores and rescue analgesic requirements.[11] A systematic review and meta-analysis was performed to find out the effect of intramuscular LA infiltration before wound closure after lumbar spine surgery.[12] It demonstrated a longer time to the initial analgesic demand and a lower postoperative opioid requirement. A reduction in pain scores was seen at 1 h but not at 12 or 24 h. The authors suggested a need for further research on choice and strength of LA agents to be used for infiltration.

The drugs used for wound infiltration should have good efficacy, long duration of analgesia and low toxicity. Longer duration becomes even more important if single-shot infiltration is planned, as many surgeons do not prefer to leave a catheter in the wound. Addition of adjuvants to LA should produce better results as they are known to improve the quality and duration of various blocks and reduce the supplemental analgesic requirement.[13] Ropivacaine is known to have a lower potential for systemic toxicity than bupivacaine and is an ideal LA agent in situations where large volumes are needed as it is less cardiotoxic and less neurotoxic than bupivacaine.[14] Addition of 5 μg/mL adrenaline to ropivacaine significantly delays systemic absorption, further reducing its peak plasma concentration.[15] Dexmedetomidine, a highly selective alpha-2 adrenoreceptor agonist, is commonly used as an adjuvant to LA agents. It has been shown to improve the quality and prolong the duration of wound infiltration analgesia.[16-18]

In this study, ropivacaine was used in a concentration of 0.375% and volume of 0.8 mL/kg as per the recommended maximum safe dose, that is, 3 mg/kg. Dexmedetomidine has been used as an adjuvant with LA in a dose of 1 μg/kg for wound infiltration by Kang *et al.* in inguinal hernia repair[16] and Singh and Prasad in abdominal hysterectomy[18] with good results. Therefore, it was decided to use dexmedetomidine in the dose of 1 μg/kg for wound infiltration in this study.

In this study, wound was infiltrated only once before closure and no catheter was inserted to provide continuous infiltration. Providing additional analgesia through a catheter is expected to improve pain control and shorten hospital stay. However, a small but potentially important increase in infection rate has been observed in patients receiving infiltrate through a catheter after wound closure.[8] Marques *et al.*, in their systematic review and meta-analyses of short- and long-term effectiveness of LA infiltration in total hip and knee replacement, observed eight cases of deep infection requiring surgical debridement or revision.[8] The overall infection rate was calculated as 0.34%. The authors concluded that providing additional analgesia through a catheter enhances the pain relief, but this benefit of improved analgesia should be weighed against the risk of possible infection.

On within-group comparison in this study, there was no significant difference in pain scores at different time points in group LIA. On the other hand, in group C, pain scores at later time points were lower when compared with scores in early postoperative period. This decrease in pain with time could be explained by pain relief obtained by administration of IV morphine as bolus and through PCA.

Dexmedetomidine administration may be associated with side effects such as hypotension and bradycardia due to decrease in central sympathetic outflow.[19,20] However, no significant haemodynamic effects were observed in our study. Heart rate was lower in group LIA than in group C at most of the time points, but blood pressure in the two groups did not show statistically significant difference. None of the patients in either group developed significant hypotension or bradycardia in the postoperative period. The lower HR in group LIA could be due to haemodynamic effects of dexmedetomidine or could also indicate better pain control in this group.

Sedation scores gradually decreased with time in both the groups; however, no uniform trend was noted. Sedation may be associated with use of dexmedetomidine and opioids. More sedation in immediate postoperative period in group LIA patients could be due to the effect of dexmedetomidine. However, at later time points, effect of morphine administered intravenously could have contributed to sedation.

The lower morphine requirement in group LIA was associated with a lower incidence of opioid related side effects such as postoperative nausea and vomiting. The satisfaction scores in group LIA were also significantly better than in group C, indicating superior analgesic efficacy of wound infiltration.

This study has a limitation. It would have been ideal to follow the patients for at least 48–72 h but in our

study, because of logistic reasons, the patients could be followed for only 24 h in the postoperative period. Thus, the long-term complications and duration of hospital stay could not be studied.

CONCLUSION

Local wound infiltration analgesia using ropivacaine, adrenaline and dexmedetomidine before wound closure provided good postoperative pain relief in terms of lower pain scores and decreased morphine consumption in patients undergoing surgery for TB spine. It resulted in good patient satisfaction and was not associated with haemodynamic instability or any other major complications.

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Conflicts of interest

There are no conflicts of interest.

Presentation

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Clinical Trial Registry

Registered at Clinical Trials Registry of India (CTRI/2014/01/004368).

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