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High-Volume Infiltration Analgesia in Major Lumbar Spine Surgery. A Randomized, Placebo-Controlled, Double-Blind Trial

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Abstract

Background: High-volume local infiltration analgesia is effective in knee arthroplasty, but the analgesic efficacy of systematic infiltration with high-volume local anesthetic in major lumbar spine surgery in L_3 to S_1 has not been clarified. We conducted a trial to evaluate the analgesic efficacy of intraoperative Local Infiltration Analgesia (LIA) administration and postoperatively via injections through intraoperatively placed wound catheters.

Methods: In a randomized, double-blind, placebo-controlled trial in 48 patients undergoing major lumbar spine fusion surgery, 70 mL saline (n=24) or ropivacaine 0.5% with adrenaline (n=24) was infiltrated using a systematic technique to all tissue incised, handled or instrumented during surgery and with repeated injections at 6, 12 and 24 h postoperatively with 10, 10 and 20 mL. Twenty-two patients in each group were used for analysis. Allocation was determined by using a computer generated random sequence concealed in consecutively numbered sealed envelopes, which were opened on the morning of surgery. For postoperative analgesia 2 multi-hole catheters were placed under the fascia of the m. erector spinae and subcutaneously in accordance with the randomization. The primary end-point was postoperative pain at rest, during leg elevation and walking for 48 hours postoperatively. Secondary end-point was the amount of administered opioid in the same period.

Results: VAS pain scores were only significantly lower at 3 hours postoperatively in the ropivacaine group with straight leg elevation (p=0.0169) and at 7 hours in the ropivacaine group during walking (p=0.0133). At 25 hours postoperatively, there was a slightly significant reduction in pain scores from repeated injection of ropivacaine vs. saline in the catheters both during elevated straight leg test (p=0.0495) and during walking (p=0.0192). Rescue opioid requirements (24 h) were about 30 % lower in the ropivacaine group (p<0.05). No local anesthetic side effects were observed.

Conclusion: Intraoperative high-volume wound infiltration with ropivacaine in major lumbar spine fusion surgery may only have a small analgesic effect in early postoperative pain management and after local anesthetic administration through multiholed wound catheters 24 hours postoperatively.

Keywords: High-volume local infiltration analgesia; lumbar spine surgery; postoperative pain treatment; multi-hole catheters

Key Points

Intraoperative high-volume local infiltration analgesia with ropivacaine may only have a moderate analgesic effect in early postoperative pain treatment after spine surgery.

Postoperative injection of local anesthetic through multiholed wound catheters may have a moderate analgesic effect after spine surgery.

Further studies should examine the concentration vs. volume relationship, duration and type of local anesthetic administration (intermittent vs. continuous) and type of catheter before final recommendations.

Introduction

Major lumbar spine surgery usually causes severe pain, which challenges effective pain management, a prerequisite for early recovery and rehabilitation [1]. So far continuous epidural analgesia has been a common used method, as this technique is superior to intravenous analgesia regarding pain quality, incidence of side effects, and pulmonary, cardiac, and gastrointestinal dysfunction [1-3]. Since surgical pain originates from the surgical wound a rational approach to perioperative pain treatment would be the use of local anesthetics at the site of surgery. Local infiltration analgesia (LIA) is a well-known, simple, safe, and low-cost technique for postoperative analgesia [4]. A systematic review on single administration of local infiltration analgesia with relatively small volumes in different types of lumbar spine surgery concluded that there were only minor and transient analgesic effects [5]. A renewed interest in the concept comes from the recent observations from Kerr and Kohan in Australia where high-volume, low concentration, multi-local infiltration analgesia has been administered in hip and knee replacement and with subsequent intermittent administration through a wound catheter [6-8]. So far, only one study has examined the effect of local anesthetic infiltration analgesia after major spine surgery followed by continuous wound infusion through a multiholed 16-gauge catheter placed between the muscle fascia and the subcutaneous tissues along the wound [9]. This approach led to reduced pain scores and rescue medication requirements.

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Because this previous trial did not discuss the application technique of LIA in detail, we conducted this randomized, placebo-controlled and double-blind trial in major lumbar spine surgery to clarify the relative importance of intraoperative administration of LIA and postoperatively via injections of local anesthetics through intraoperatively placed wound catheters.

Materials and Methods

The Regional Ethics Committee (Copenhagen, Denmark, Reg.no H-D-2007-0111) and the Danish Data Protection Agency (Copenhagen, Denmark) approved the study. Furthermore, it was registered with ClinicalTrials.gov under the US National Library of Medicine (Code NCT00771459). Forty-eight consecutive patients scheduled for major lumbar spine surgery were included from November 2008 to May 2009. Patients received infiltration with 70 ml ropivacaine 0.5% with adrenaline (5 μg/ml) or 70 ml 0.9% saline according to randomization. Allocation of patients to receive infiltration with ropivacaine or saline was determined by randomization, using a computer generated random sequence concealed in consecutively numbered opaque sealed envelopes, which were opened on the morning of surgery. To ensure complete blinding of the patients to the surgeon and to the investigator recording postoperative pain data, the randomization was not revealed until completion of the entire study, and the medicine used for each individual patient was prepared by one investigator not otherwise involved in patient data collection. Additional bolus injections with ropivacaine or saline were administered postoperatively in two 15 cm multi-holed catheters (Baxter Inc., Amaro, Italy) placed beneath the erector spinae muscle and the subcutaneous tissues of the wound.

Inclusion criteria were

Consecutive patients scheduled for elective major lumbar spine surgery, able to understand and speak Danish, able to give informed oral and written consent to participate. Exclusion criteria were treatment with morphine (>100 mg daily) or equivalents, steroids, history of stroke or any neurological or psychiatric disease potentially influencing pain perception (e.g. depression, diabetic neuropathy etc.) or allergies to any of the drugs administered. Inclusion and data registration were performed by one of two investigators; anesthetic procedures were performed by one of two anesthesiologists and 3 surgeons operated on all patients.

Procedures

During the surgical procedure, all patients received general anesthesia using propofol (2 mg/kg) and remifentanil (1 μg/kg/min) for induction of anesthesia with mivacurium (0.15 mg/kg) used to facilitate tracheal intubation. For the maintenance of anesthesia, additional continuous infusion of propofol (3-5 mg/kg/h) and remifentanil (0.3-0.5 μg/kg/min) was used. Normothermia was maintained with warmed forced air. Operation was performed in the prone position. At the end of the surgery 20 μg of sufentanil was administered to all patients. Patients received a standard midline incision with the lumbar fascia dissected in a subperiosteal manner and advanced from the tip of the spinous process lateral to the tip of the transverse processes. Depending on the levels to be fused the superior and inferior segments were sequentially stripped. Self-retaining retractors were placed on the paravertebral musculature. Subsequently, 60 mL of the project medicine was injected using a systematic technique ensuring uniform delivery of the local anesthetic to all tissue incised, handled or instrumented during the procedure. The rest of the project medicine (10 mL) was infiltrated into the subcutaneous tissues. Before wound closure the two 15 cm multi-holed catheters were placed under direct vision in cranial caudal direction below erector spina in the middle lumbar fascia close to the lamina in the incision right side and the other parallel to the first between the posterior lumbar fascia and subcutaneous tissue in the left side of the incision. In all patients a drain was placed beneath the fascia of the musculus erector spina and removed 24 hours postoperatively after reinjection in the catheters.

Postoperatively, patients were transferred to the postanesthesia care unit (PACU) and then to a specialized lumbar spine surgery unit. All patients received celecoxib 400 mg/day, acetaminophen 4 g/day, gabapentin 900 mg/day initiated preoperatively on the morning of surgery. Apart from administration of additional sufentanil or morphine in the PACU until the VAS was ≤ 3, oral oxycodone 5 mg or i.v. morphine 2.5-5 mg was administered on request if the VAS was ≥ 5 at rest at the surgical ward. Six and 12 hours postoperatively an injection of 10 ml ropivacaine 0.5% or 0.9% saline was administered through the catheters and 24 hours postoperatively 20 ml of ropivacaine 0.5% or 0.9% saline was administered through the catheters in accordance with the randomization, whereupon the catheters were removed.

Data collection and analysis

The primary end-point was to compare postoperative pain, which was assessed using a Visual Analogue Scale from 0-10 cm, with 0 indicating no pain and 10 indicating worst pain, at rest, with the leg straight and 45° elevated and during walking. Pain scores were assessed postoperatively at hour 1, 2, 3, 4, 6,7, 24, 25, 36 and 48. Pain scores at hour 7 and 25 were 1 hour after the bolus injection in the catheters. Throughout the 48-hour study period, the amount of administered opioids was registered.

From previous data it was known that approximately 25% of the patients undergoing major lumbar spine surgery had a VAS score greater than 60 at rest. A clinical improvement of the pain scores in the LIA group should include a 30% reduction of pain scores to be considered significant. Subsequently, a power analysis showed that a sample size of 21 patients per group was sufficient to have an 80% power at the 95% significance level. A sample size of 48 patients was obtained to overcome any potential dropouts. Demographic data are presented as medians and interquartile range, and rescue morphine consumption was assessed using the Mann-Whitney U test. The statistical analyses were done using linear mixed models as described in detail in the literature [10-12]. The repeated measurements were analysed with linear mixed models using the statistical software R (R Core Team (2013). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL http://www.R-project.org/) and the package nlme (Jose Pinheiro, Douglas Bates, Saikat DebRoy, Deepayan Sarkar and the R Development Core Team (2013). nlme: Linear and Nonlinear Mixed Effects Models. R package version 3.1-109). Exact p values were reported.

Results

Forty-eight patients' participated, but 4 patients were excluded due to protocol violation. In one patient in each group the data collection were incomplete. One patient in the Ropivacaine group accidentally disconnected the catheters, and one patient in the placebo group declined to participate in the postoperative period (Figure 1). Patient characteristics are presented in Table 1.

No significant interactions between treatment groups and time were observed with patients at rest (Figure 2).

Postoperative pain scores with elevated straight leg raising from 1 to

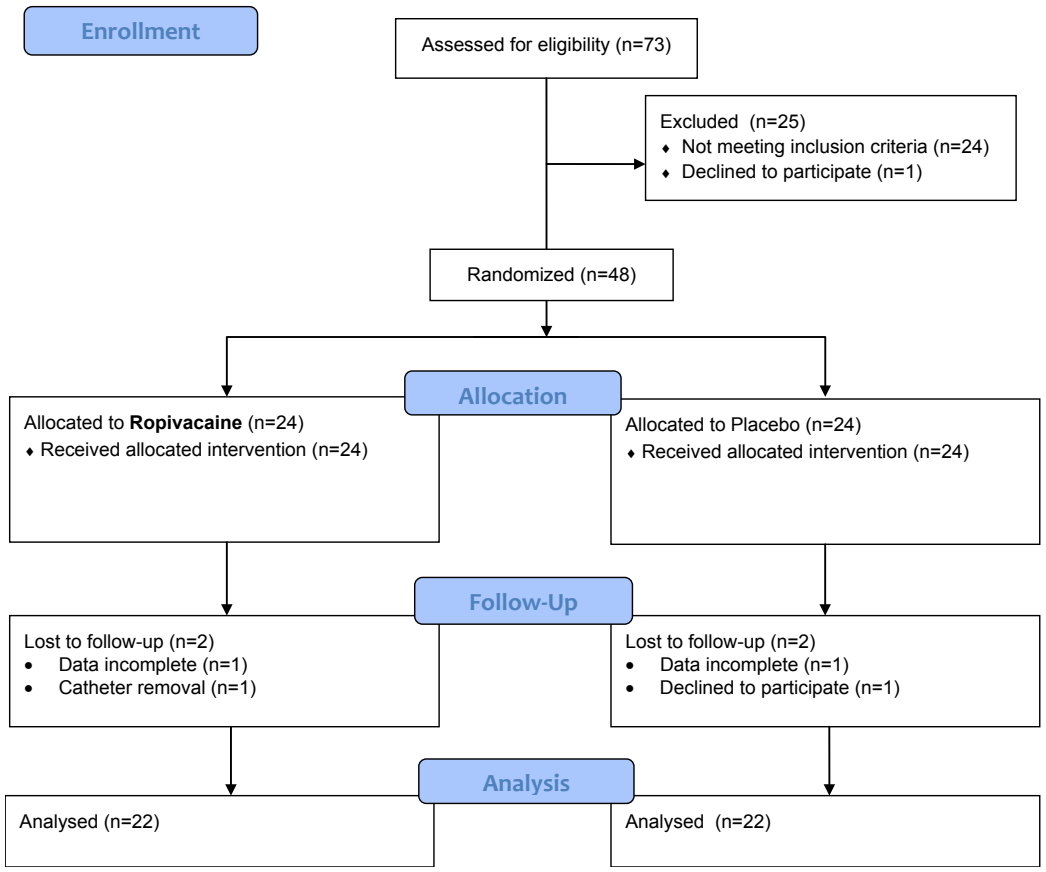

Figure 1: Diagram of the flow through the study of patients undergoing major lumbar spine surgery.

	Ropivacaine (n=22)	Placebo (n=22)
Sex, F/M	19/3	9/13
Weight, kg	78 (68.00-83.50)	88 (77,75-92.75)
BMI, kg/m^2	27 (23.42-30.00)	28 (25.25-30.75)
Age, yrs	58 (50.25-64.00)	55.5 (43.25-59.75)
Height, cm	165 (163.2-172.8)	172.5 (168.5-177.5)
ASAm I/II	10/12	8/14

Values are numbers medians and first and third quartiles.

Table 1: Demographic data from 44 patients.

7 hours were significantly reduced in the ropivacaine group at 3 hours (p=0.0169) and at 25 hours postoperatively, there was a significant reduction in pain scores from injection of ropivacaine vs. saline in the catheters (p=0.0495) (Figure 3). There was no difference in the number of patients being able to walk, but VAS scores during walking were significantly reduced at hour 7 (p=0.0133) and 25 (p=0.0192), one hour after injection in the catheters (Figure 4). All patients were able to walk without assistance 48 h postoperatively.

In the PACU, [median, (interquartile range)] administration of sufentanil was 30 µg (20-60) in the ropivacaine group and 45 µg (30-75) in the placebo group, respectively (p=0.22). However, 6 hours postoperatively the cumulated administration of oxycodone [median, (interquartile range)] was significantly less in the ropivacaine group, 10 mg (5-15) versus 15 mg (10-20), p<0.02. At 6 hours postoperatively i.v. administration of morphine [median, (interquartile range)] was 5 mg (0-10) and 5 mg (5-15) respectively (p=0.45). At 24 hours postoperatively the cumulated administration of oxycodone [median, (interquartile range)] was significantly less in the ropivacaine group, 20 mg (15-30) versus 37.5 mg (20-45), p<0.04. The cumulated administration of i.v. morphine [median, (interquartile range)] 24 hours postoperatively was 10 mg (5-20) and 15 mg (5-25), respectively (p=0.15). 48 hours postoperatively the cumulated administration of oxycodone [median, (interquartile range)] was 30 mg (20-45) and 47.5 mg (25-75) respectively (p=0.08), and the cumulated administration of i.v. morphine [median, (interquartile range)] was 10 mg (5-20) and 20 mg (5-35) respectively (p=0.18).

No clinical signs of wound infection, local anesthetic or systemic toxicity were observed.

Discussion

This randomized, double-blind trial demonstrated an overall small analgesic efficacy of high-volume LIA in major lumbar spine surgery,

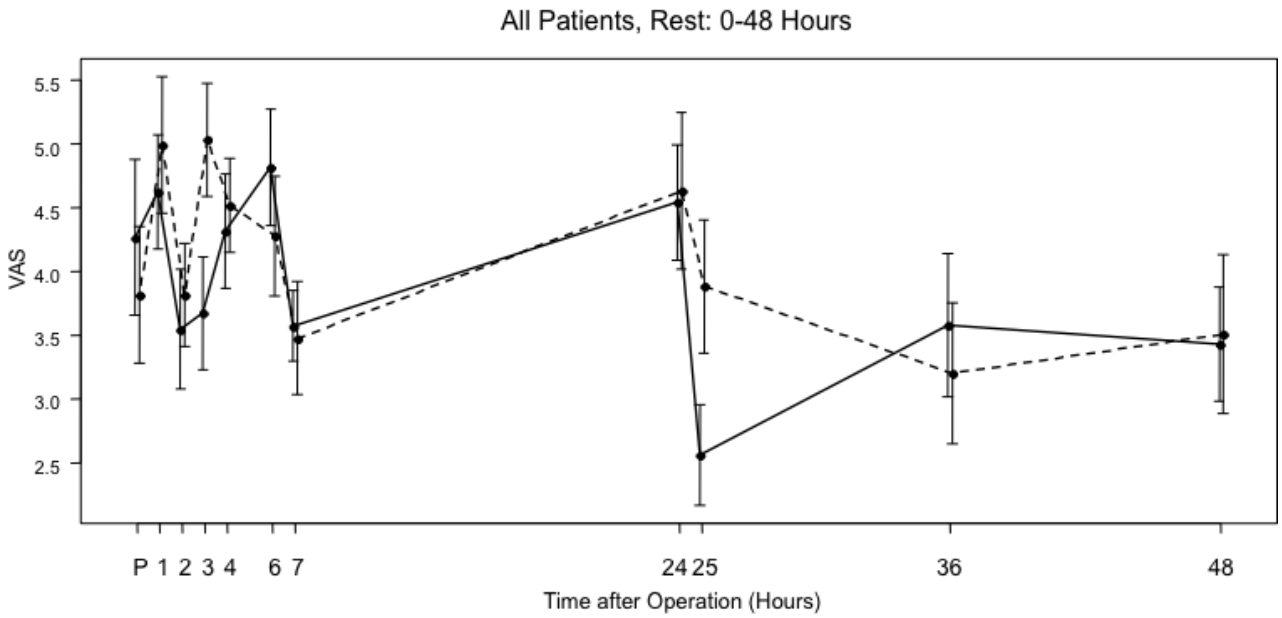

Figure 2: _____ = Ropivacaine group, ------- = Placebo group. Means are reported together with standard errors of the mean. No significant interactions between treatment groups and time were observed. P=preoperative.

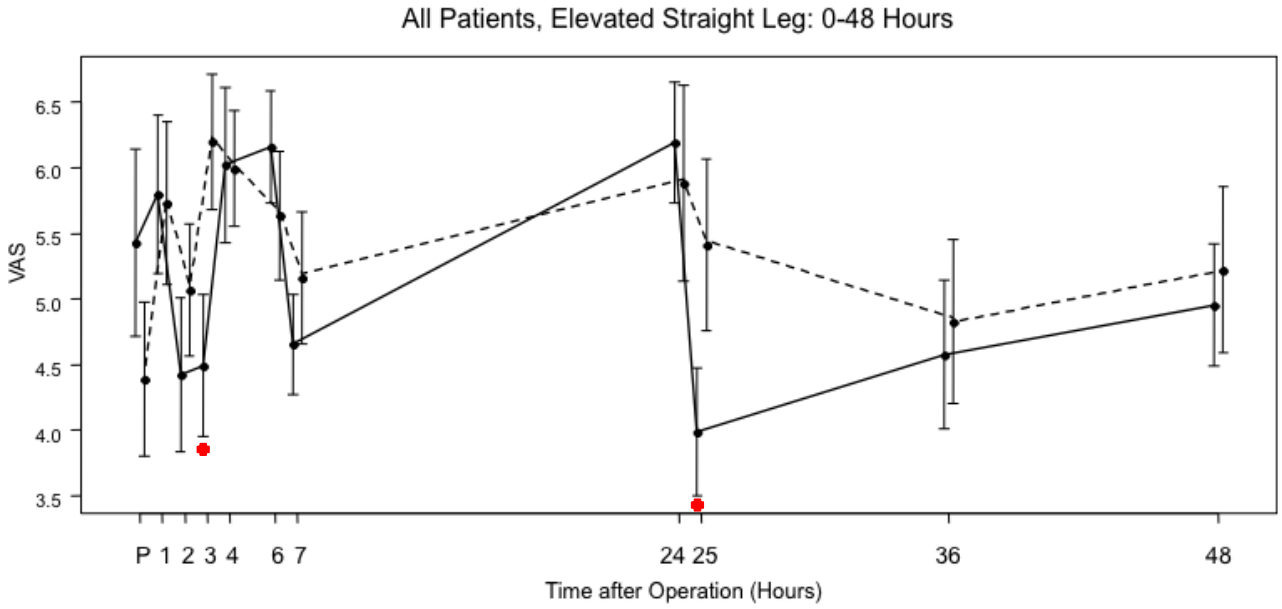

Figure 3: _____ = Ropivacaine group, ------- = Placebo group. = significance. Means are reported together with standard errors of the mean. Significant interactions between treatment groups and time were observed after 3 hours (p = 0.0169) and 25 hours (p=0.0495). P = preoperative.

both during elevated straight leg test in the early postoperative period and after wound catheter local anesthetic injection 6 and 24 hours postoperatively. However, the analgesic effect was not consistent at the different assessments after all injections intraoperatively, at 6, 12 and 24 hours postoperatively. Despite these variable analgesic effects, the need for rescue analgesics was significantly reduced.

The only comparable study was performed in a non-blinded set-up by Bianconi [9] in which the combination of 40 mL of 0.5% ropivacaine bolus infiltration of the paraspinal and superficial layers of the wound, followed by 55 h of continuous infusion of 0.2% ropivacaine through an indwelling multiholed catheter placed between the muscle fascia and the subcutaneous tissue, reduced postoperative pain scores at rest and during passive mobilization as well as rescue analgesia requirements were reduced compared with systemic analgesia. Despite discontinuation of the ropivacaine infusion, pain was still lower at 72 hours after surgery.

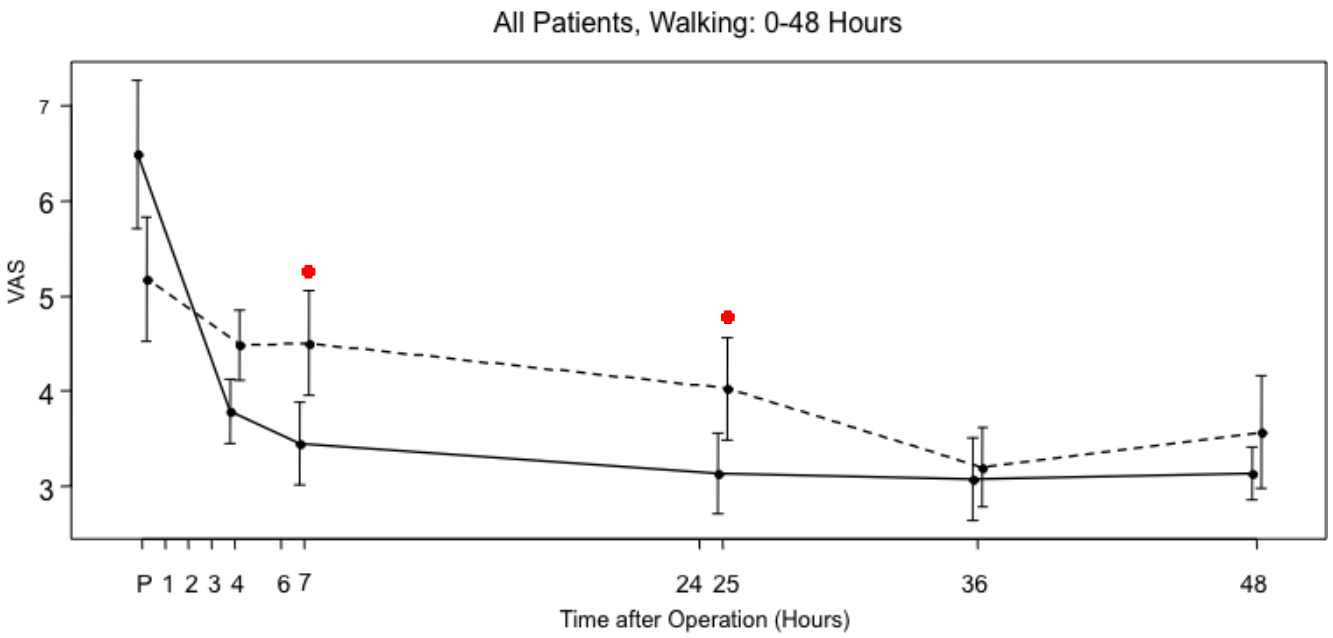

Figure 4: _____ = Ropivacaine group, ------- = Placebo group. = significance. Means are reported together with standard errors of the mean. Significant interactions between treatment groups and time were observed after 7 hours (p=0.0133) and 25 hours (p=0.0192). P=preoperative.

The choice of the postoperative analgesic regime after major lumbar spine surgery may include continuous epidural analgesia [1,2], patient-controlled analgesia (PCA) [13] or intrathecal morphine administration [14]. In contrast, relief of postoperative pain by single-shot LIA with 40 ml bupivacaine 0.25% in the paravertebral muscle after spine fusion surgery did not provide any advantages [15]. Which analgesic technique that is preferred depends on the efficacy, side-effects, cost and needs for expertise. In this context, the LIA technique with an intermittent or maybe a continuous infusion postoperatively fulfills most of these demands [16]. Particularly, the systemic side-effects seen with central neural blockades (e.g. motor blockade, hypotension, nausea and vomiting) may be avoided. Furthermore, additional opioid analgesic requirements may be reduced, with fewer opioid-related side-effects [4,17]. However, the additional analgesic effect of our high-dose Ropivacaine regimen showed only modest analgesic effects.

The present study, with detailed information on the infiltration technique confirms the findings of the Bianconi study [9], although we did not observe the same pronounced efficacy in pain reduction. An explanation hereto could be that the single-shot infiltration was followed by a continuous infusion or the differences in design, our study being double-blind and placebo-controlled. Another explanation could be the effectiveness of our multimodal oral regimen with a COX-2 inhibitor, gabapentin and acetaminophen in lowering overall pain scores.

Despite the promising results regarding the LIA technique [6,7] in total knee arthroplasty (but not hip arthroplasty) [18], the optimal concentration and volume for the local anesthetic administration and the optimal site of placement of the wound catheter remains to be clarified in those operations [19]. These conclusions also apply to spine surgery where only 2 RCT's are available (the present study and the Bianconi study) [9]. Furthermore, more safety data are required if this technique is going to be recommended. Finally, it remains to be clarified whether a multi-hole catheter is preferable compared to a single- or few hole catheter [20].

Conclusions

In conclusion, the results from this randomized, double-blind, placebo-controlled trial in patients undergoing major lumbar spine surgery, confirm that both an intraoperative high-volume LIA technique and top-up injections in wound catheters provides some additional analgesia. However, further studies should examine the concentration vs. volume relationship, duration and type of local anesthetic administration (intermittent vs. continuous) and type of catheter before general recommendations can be made.

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