

Postoperative analgesia in total hip arthroplasty

A randomized double-blinded, placebo-controlled study on peroperative and postoperative ropivacaine, ketorolac, and adrenaline wound infiltration

Lasse Juel Andersen¹, Thomas Poulsen¹, Bo Krogh² and Tommy Nielsen²

Departments of ¹Orthopaedic Surgery and ²Anaesthesiology, Odense University Hospital, Middelfart, Denmark
Correspondence LJA: Lasse_Juel@dadlnet.dk
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Background Comfort and lack of pain are important for optimal mobilization after hip replacement. We investigated the efficacy of double wound infiltration.

Patients and methods 40 consecutive patients undergoing total hip replacement were randomized into two groups in this double-blinded study. They received wound infiltration at the end of surgery and through an intraarticular catheter 24 h postoperatively. The catheter was placed at the end of surgery. One group received solutions of ropivacaine, ketorolac, and adrenaline. Patients in the control group were injected with saline instead. The observation period was 6 weeks.

Results The patients who received the analgesic solution had less pain up to 2 weeks postoperatively. They reached an earlier and lower pain minimum during the first days postoperatively, had lower use of analgesia up to day 4 postoperatively, and were more satisfied. Use of analgesic solution resulted in less joint stiffness and better function 1 week postoperatively.

Interpretation Operative and postoperative wound infiltration with multimodal drugs reduces pain and the requirement for analgesics after hip replacement, leading to faster postoperative mobilization.

The often intense pain after total hip replacement (THR) is thought to prolong mobilization and hospitalization (Strassels et al. 2002, Skinner 2004). Because of the side effects of opioid drugs, which include nausea, vomiting, respiratory depression, reduced gut motility, and urinary retention, it would

be of value to find alternative postoperative analgesia. Wound infiltration with multimodal analgesia has been a controversial issue for many years (Dahl et al. 1994). Different modes of peroperative and postoperative local anesthetic instillation have been described in a variety of surgical procedures (Mauerhan et al. 1997, Oakley et al. 1998, Horn et al. 1999, Fredman et al. 2000, Savoie et al. 2000, Lavand'homme et al. 2004, Busch et al. 2006). Few studies have described per- and postoperative wound infiltration for knee arthroplasty (DeWeese et al. 2001, Reilly et al. 2005, Vendittoli et al. 2006). Only one study has described the method for use in THR (Bianconi et al. 2003). Fischer et al. (2005) recently concluded that postoperative wound infusion with local anesthetic may have potential usefulness in THR, but more documentation is needed.

Since postoperative pain is at its most severe on the first and second day (Strassels et al. 2002), we investigated peroperative and postoperative wound infiltration in a prospective randomized double-blinded study. The injected solution consisted of a long-acting local anesthetic (ropivacaine), a non-steroidal anti-inflammatory drug (ketorolac), and a vasoconstrictor (adrenaline).

Methods

The size of the study population was determined by an expected difference of 40% in analgesic

consumption (MERIDIF). Thus, we enrolled 40 patients who were scheduled for THR and able to understand written and spoken information, and who gave their informed consent to take part in this prospective, randomized double-blinded study. To reduce possible bias, patients were included only if they were scheduled for an uncemented THR because of primary osteoarthritis. Patients were excluded if they were more than 80 years old or made habitual use of opioids, had inflammatory joint disease, or had previous fracture of the affected hip, or alternatively, if spinal anesthesia was contraindicated or not technically possible.

The study was approved by the Ethics Review Board of Southern Denmark

47 patients matched the inclusion criteria. During the consecutive inclusion period, 7 patients were excluded due to exclusion criteria. Furthermore, 3 patients who were included in the study were excluded retrospectively due to application of exclusion criteria (one had no pain release by oxycodone, one failed to undergo spinal anesthetic, and 1 had habitual use of opioids). We ended up with 19 patients in the study group and 18 patients in the control group.

The patient groups were similar regarding age, social recordings, and also preoperative pain, stiffness and function of the affected hip. There was a predominance of males in the treatment group (Table 1). All patients received spinal anesthesia with a 27-G pencil spinal needle using 15–20 mg of plain bupivacaine.

Minimally invasive surgery (MIS) by a direct posterior approach was attempted (with an incision of less than 10 cm). The patients were treated with study medicine twice, first at the end of surgery and then on the following morning before mobilization.

The solutions given at the operation were injected in equal proportions for the whole length of the wound, subcapsular and muscles and subcuticular tissues. A multi-holed epidural catheter was placed at the end of surgery, with the catheter tip in the joint and then penetrating the capsule, and running parallel under the entire wound over the fascia. The catheter penetrated the skin near the end of the cicatrice, and was connected to a bacterial filter. It was retracted during infusion on the second day and then removed. Wound drainage was not used.

Table 1. Patient characteristics for the treatment and control groups

	Group	
	Treatment (n = 19)	Control (n = 18)
Age (years) ^a	62	64
Male/Female	16/3	10/8
Working	12	8
Living with partner	17	17
Preoperative Hb ^b (mmol/L) ^a	9.7	8.9
(range)	(8.1–10.6)	(7.4–10)
Intraoperative bleeding (mL) ^a	425	400
(range)	(200–1300)	(200–1500)
Preoperative pain level		
WOMAC, pain ^a	39 (5–75)	39 (13–66)
WOMAC, stiffness ^a	49 (4–96)	53 (4–80)
WOMAC, function ^a	44 (19–91)	48 (13–78)

^a Median. ^b Hb: hemoglobin.

Patients were randomized with a computer-generated sequence and each patient was assigned to the treatment group or the control group by opening a sealed envelope.

Patients in the treatment group were injected with 151.5 mL of saline solution containing 300 mg ropivacaine, 30 mg ketorolac, and 0.5 mg adrenaline by the end of surgery. The next morning, they received 21.5 mL of saline solution containing 150 mg ropivacaine, 30 mg ketorolac, and 0.5 mg adrenalin, through the multi-hole epidural catheter. The control group received pure saline solution as the study medicine in the same amounts.

During the first 8 h after surgery, pain assessments were made by using a visual analog scale (VAS) at rest and on attempting to raise the leg. In addition, pain, stiffness, and physical function were determined using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (Bellamy et al. 1988). We collected all 3 parts preoperatively, and after 1, 2, 4, and 6 weeks. Postoperatively, WOMAC score for pain was registered on a daily basis.

EuroQol (EQ-5D) is considered to be a valid scoring system for outcome of THA (Brooks 1996, Soderman 2000). EuroQol registrations were done preoperatively and 6 weeks postoperatively.

The consumption of patient-controlled analgesics was measured 2, 4, and 8 h postoperatively, and daily thereafter until the patients left the hospital. The patients were treated with the rescue

medicine Oxycodon. During the first 8 h, they received Oxycodon intravenously if VAS was > 30 mm. Generally, the patients self-administered 5 mg Oxycodon orally. The surgeon could prescribe Oxycodon (10 mg) orally at a ward round if the patient had had a severe requirement for analgesia. The amount of intravenous Oxycodon was multiplied by a factor of 2 to calculate the total amount delivered (intravenous Oxycodon is considered to be twice as potent as that orally administered). All patients received 1 g Paracetamol 4 times a day.

Patients were asked on a daily basis about adverse events, particularly dizziness, nausea, and vomiting—and also about satisfaction concerning pain treatment. Patients were registered as being able to be discharged when they were able to walk 50 meters with two crutches, and to get in and out of bed by themselves.

Statistics

The results were analyzed using the non-parametric Mann-Whitney U test, Fisher's exact test, or Chi-squared test. A p-value of < 0.05 was considered to be statistically significant.

Results

We found a statistically significant difference in postoperative pain intensity in the treatment group vs. the control group, starting at 4 h and continuing up to 2 weeks after operation. The VAS score was lower in the treatment group at 4 and 8 h postoperatively, at rest and in relation to leg raising at 8 h (Table 2). The treatment group had significantly lower WOMAC pain scores from day 1 until day 4, and 1 and 2 weeks postoperatively. No significant differences in WOMAC pain scores were observed 4 and 6 weeks after the operation. Furthermore, the treatment group reached their pain minimum significantly earlier during the first 4 days postoperatively, and had a significantly lower pain minimum (Figure).

The treatment group had significantly less joint stiffness (WOMAC joint stiffness subscale) and better physical function (WOMAC physical function subscale) 1 week postoperatively. No significant differences were observed at 2, 4, and 6 weeks. According to the WOMAC physical function score

there was an overall reduction from approximately 45 to 8, preoperatively until 6 weeks after the operation.

The median amount of rescue medication administered was significantly lower in the treatment group than in the control group from 8 h to 96 h postoperatively (Table 2).

The frequency of nausea, vomiting, and dizziness was unaffected by the treatment modality throughout the study period. The patients were discharged from hospital after median 2.6 days (treatment group) and 2.8 days (control group) ($p > 0.05$) (Table 2).

There was a trend toward greater patient satisfaction concerning the analgesia in the treatment group, and the difference was statistically significant 8 h postoperatively, on day 1, on day 3, and in weeks 1, 2, and 4 postoperatively (Table 3).

EuroQol life quality assessments were similar in both groups preoperatively and 6 weeks after operation. There was a significant improvement in both groups preoperatively to postoperatively (data not shown).

We did not see any adverse effects of the treatment, including systemic toxicity from Ropivacaine or prosthesis infections.

Discussion

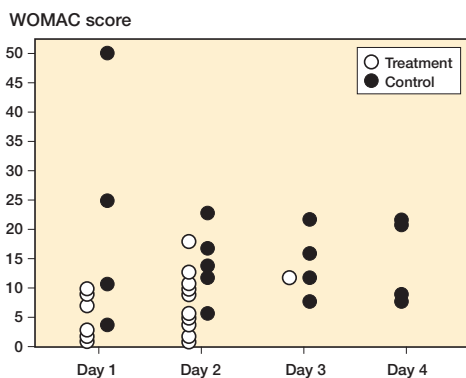
The use of a multimodal joint cocktail was inspired by Drs Kerr and Kohan in Sydney. They have used this method successfully in over 2,000 patients (personal communication). Ropivacaine is a long-acting local anaesthetic. The benefit of using Ketorolac is pain relief and inhibition of the inflammatory process. Ketorolac is approved for intraarticular use, with a well-documented positive effect on postoperative pain—described in a review article by Rømsing et al. (2000). The reason for adding adrenaline to the joint cocktail is to slow down the uptake of the drugs and thereby reduce potentially toxic blood concentrations, and to prolong the effects of the drugs in the wound.

NSAIDs have a beneficial effect on tendon healing in rats (Forslund et al. 2003). In addition, NSAIDs have a positive effect on soft-tissue healing and prevention of heterotopic ossification (Dahners and Mullis 2004). Despite the fact that there

Table 2. Results concerning pain and stay in hospital

	Group		n (T/C) ^a	P-value
	Treatment	Control		
VAS 4 h, rest ^b	0 (0–55)	11 (0–100)	19/18	0.04
VAS 8 h, rest ^b	7 (0–57)	34 (0–91)	19/18	0.02
VAS 8 h, leg raise ^b	22 (0–70)	60 (30–90)	8/11	0.002
WOMAC, pain on day 1	20 (1–39)	49 (4–86)	19/18	< 0.001
Day 2	6 (1–26)	25 (6–65)	19/18	< 0.001
Day 3	5 (1–15)	16 (5–64)	14/16	0.002
Day 4	5 (0–16)	13 (5–69)	9/14	0.003
WOMAC, pain 1 week postop.	11 (0–30)	18 (10–50)	19/18	0.001
2 weeks postop.	5 (2–66)	13 (2–44)	19/17	0.01
4 weeks postop.	4 (0–51)	8 (0–30)	19/17	0.1
6 weeks postop.	2 (0–50)	7 (0–13)	19/17	0.07
WOMAC, stiffness 1 week postop.	24 (4–67)	35 (13–67)	19/17	0.04
2 weeks postop.	11 (0–47)	15 (8–53)	19/17	0.06
4 weeks postop.	10 (0–35)	12 (2–58)	19/17	0.3
6 weeks postop.	7 (1–46)	10 (3–35)	19/17	0.2
WOMAC function 1 week postop.	26 (9–51)	39 (14–71)	19/17	0.02
2 weeks postop.	16 (3–46)	24 (5–39)	19/17	0.2
4 weeks postop.	13 (2–42)	14 (1–38)	19/17	0.3
6 weeks postop.	6 (0–40)	10 (1–21)	19/17	0.3
Oxycodon consumption (mg)				
Day 1	20 (0–60)	53 (5–135)	19/18	< 0.001
Day 2	15 (0–75)	28 (5–100)	19/18	0.01
Day 3	10 (0–70)	20 (0–105)	15/16	0.02
Day 4	10 (0–30)	20 (0–120)	9/15	0.01
Discharged per day, n				
at day 1	1	0	1/0	c
at day 2	11	7	12/7	c
at day 3	4	6	16/13	c
at day 4	1	5	17/18	c
at day 5	1	0	18/18	c
at day 6	1	0	19/18	c

^a n: numbers of registrations in the two groups.
^b Postoperative VAS pain score.
 VAS, WOMAC and Oxycodon consumption: Values are median (range).
^c p > 0.05, when analyzing distribution of patients fulfilling the criteria of discharge from days 1 to 6.



Lowest achieved WOMAC pain level from day 1 to day 4, for each patient.

have been some studies suggesting that NSAIDs have an inhibitory effect on bone healing (Aspenberg 2002), we believe that the positive effects of NSAIDs outweigh the disadvantages.

High plasma concentrations of ropivacaine are neurotoxic and cardiotoxic. The toxicity threshold and safe amount of injected ropivacaine has been well defined (Dahl et al. 1994, Knudsen et al. 1997). The dosages of ropivacaine injections selected (300 mg and 150 mg) appeared to be sufficient and distinctly below the safe dosage limit used in well-documented studies. Infiltration with 375 and 400 mg ropivacaine in relation to inguinal hernia repair (Pettersson et al. 1998) and total knee

Table 3. Patient satisfaction at 8 hours, at day 1 and 2, and 6 weeks postoperatively

	8 h postop.		Day 1		Day 2		at 6 weeks	
	Treat.	Control	Treat.	Control	Treat.	Control	Treat.	Control
Very satisfied	16	8	15	6	15	7	13	6
Satisfied	1	5	4	8	4	9	4	10
Not completely satisfied	2	3	0	3	0	2	2	1
Dissatisfied	0	2	0	1	0	0	0	0
Total	19	18	19	18	19	18	19	17
P-value ^a	< 0.05		< 0.05		< 0.1		< 0.1	

^a Chi-squared test

arthroplasty (Busch et al. 2006, Vendittoli et al. 2006), respectively, showed plasma concentrations far below the toxic threshold (0.6 µg/mL)—and without any reported side effects. Accumulation of plasma ropivacaine is to be expected (Fredman et al. 2000), but should not lead to concentrations above the toxic threshold, with an interval of 24 h between instillations.

There was a predominance of males in the group receiving the joint cocktail, but there is no evidence that sex affects pain tolerance after surgical procedures (Unruh 1996, Kelly 1998).

At 8 h postoperatively, the patients had much higher pain levels when performing leg raising than at rest. This illustrates the importance of evaluation of pain on using or challenging the operated area.

Data concerning pain related to leg raising could not be recorded until 8 h postoperatively, because until then most patients were affected by the spinal analgesia. The 5 WOMAC pain score assessments—concerning pain while walking, climbing stairs, lying in bed at night, sitting, and standing—provide useful information about pain related to physical challenges. From day 1, all patients had a mobility that allowed use of the WOMAC pain score.

The effect of the LA infiltration appears to have been prolonged according to the low WOMAC pain scores up to day 4, and to measurements 1 and 2 weeks postoperatively. The same pattern has been seen in other studies (Kopacz et al. 1989, Bianconi et al. 2003).

When determining the “day of lowest pain level” of each patient (see Figure), we considered differences of 9 mm or below to be insignificant, a limit

suggested by Kelly et al. (1998) to be the minimum clinically significant difference when using a visual analog scale. It is very valuable to analyze the pain levels of patients during a longer period instead of a fragmentary period, such as daily. Our results show that use of wound infiltration results in a pain minimum that is achieved earlier and that this pain minimum is lower (when considering the first 4 postoperative days). Both of these observations were statistically significant. This consideration has not been dealt with before.

In addition, initially the treatment group reported less joint stiffness and better physical function, had faster mobilization and discharge, and there was better patient satisfaction. This multimodal effect of optimal initial analgesia is well known (Strassels et al. 2002).

It is noteworthy that WOMAC score for function and EuroQol life quality assessments were clearly improved as early as 6 weeks postoperatively. In addition, these results indicate that the physical function and life quality of patients is close to normal 6 weeks postoperatively.

The earlier references regarding wound infiltration after knee arthroplasty (DeWeese et al. 2001, Reilly et al. 2005, Vendittoli et al. 2006) mainly favor the use of wound infiltration. In spite of the results of Bianconi et al. (2003) and our favorable results concerning wound infiltration after THR, it could be interesting to evaluate the efficacy of local anesthetic wound instillation in other study designs, for instance by continuous or more frequent injections.

Contributions of authors

LJA: collected, compiled and analyzed the data, and wrote the manuscript. TP: performed surgery, designed the study, and edited the manuscript. BK and TN: designed the study and edited the manuscript.

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