Increased flexion and reduced hospital stay with continuous intraarticular morphine and ropivacaine after primary total knee replacement

Open intervention study of efficacy and safety in 154 patients

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Background **A single injection of bupivacaine after wound closure reduces the need for analgesics and increases flexion after total knee replacement (TKR). We have therefore studied the effect of continuous injection of morphine and ropivacaine after TKR on range of movement and length of hospital stay.**

Patients and methods **In an open intervention study, we assigned 154 consecutive patients who had primary unilateral TKR for osteoarthrosis. The intervention was continuous intraarticular injection of morphine 20 mg/mL, 0.5 mL plus ropivacaine 2 mg/mL, 100 mL; bolus 20 mL and 2 mL/hour from 24 to 72 hours postoperatively. Group 1 (10 women and 8 men) received standard postoperative analgesics and group 2 (11 women and 7 men) also received continuous intraarticular morphine and ropivacaine as described above. Group 3 (14 women and 4 men) received double this dose (4 mL/hour) from 24 to 72 hours postoperatively. To assess the safety of the intraarticular treatment, an additional group of 100 consecutive patients was followed (group 4).**

Results **At discharge, flexion was 70° (60–100) in group 1, 100° (70–115) in group 2 and 110° (90-130) in group 3. Hospital stay was reduced from 9 (7–11)days in group 1, to 7 (5–10) days in groups 2 and 3. Number of days elapsed until the patient was walking with crutches was reduced from 5 (3–8) to 4 (3–6) and 3 (3–9), respectively. In the intervention groups, the need for analgesics was reduced during the hospital stay. Deep infection was registered in 1 patient.**

Interpretation **Continuous intraarticular morphine and ropivacaine reduce pain and enhance rehabilitation after total knee replacement. Before advocating this as a standard procedure, further large-scale randomized studies will be needed to assess the safety of this regimen.**

Single-dose intraarticular injection of morphine and bupivacaine after arthroscopic knee surgery manages pain effectively (Rasmussen et al. 1998). Badner (1996) noted that a single injection of bupivacaine after wound closure reduced the need for analgesics and increased flexion after total knee replacement (TKR). In contrast, Ritter et al. (1999) reported no or contrary effect after injection of morphine and/or bupivacaine. Pain after TKR may impair the early mobilization and physiotherapy, and subsequently prolong the hospital stay. The objective of this trial was to enhance recovery after TKR by improving postoperative analgesia with continuous intraarticular injection of an anesthetic.

Patients and methods

All patients who underwent primary unilateral TKR for degenerative osteoarthrosis and who gave informed consent were candidates for inclusion in the study. We planned to investigate 154 consecutive patients, all of whom were to be recruited in Copenhagen at Hamlet Private Hospital between April 1999 and May 2001. Altogether 161 patients

Demographic data in patients undergoing primary total knee arthroplasty who were given intraarticular morphine and ropivacaine (M+R), or nothing (control)

Characteristics	Group 1 Control	Group 2 M+R 2 mL/h	Group 3 M+R 4 mL/h	Group 4 M+R 4 mL/h
Sex (M/F)	8/10	7/11	4/14	39/61
Age (years), median and range	65 (48–79)	65 (51–87)	70 (68–83)	62 (40–87)
Osteoarthritis	18	18	18	100
ASA group I/II	11/7	12/6	13/5	61/39
Operation time (min), median and range	75 (50–85)	75 (60–75)	75 (60–75)	75 (55–80)

were admitted, where two patients had bilateral TKR, two had revision and one patient had TKR secondary to a fracture. Participants attended clinical visits preoperatively and at 3-month follow-up. Patient demographics were similar in the different groups (Table).

The arthroplasty was performed under spinal and epidural anesthesia at level L2-3 with spinal marcaine and epidural ropivacaine and sufentanil, and with a tourniquet. Midline incision and parapatellar medial approach was used. We used the Biomet AGC cemented knee arthroplasty with resurfacing of the patella. Following the completion of the procedure, an epidural catheter was placed intraarticularly from superior-medially and a drain superior-laterally. All patients received peroral morphine (10 mg) on demand, rofecoxib (25 mg × 1), acetaminophen (1 g × 4), and epidural infusion of ropivacaine 2 mg/mL with sufentanil 1 μg/mL and adrenaline 5 μg/mL, 4 mL/h for 72 h. The drains were removed the day after surgery and 1 hour before initiating the intraarticular treatment.

The patients who were allocated to group 1 (n = 18) had no catheter and no intraarticular treatment. Those in group 2 (n = 18) received continuous intraarticular injection of morphine 20 mg/mL, 0.5 mL plus ropivacaine 2 mg/mL, 100 mL, bolus 20 mL and 2 mL/hour from 24 to 72 h postoperatively. Patients in group 3 (n = 18) and group 4 (n = 100) received continuous intraarticular injection of morphine 20 mg/mL, 0.5 mL plus ropivacaine 2 mg/mL, 100 mL, bolus 20 mL and 4 mL/h from 24 to 72 h postoperatively.

In this study we tested the hypothesis that intraarticular pain treatment after TKR would reduce pain and increase mobilization, and thereby increase range of motion and reduce hospital stay. The primary endpoints were range of motion and number of days until discharge. Additional analyses were done on use of analgesics and improvement in walking with aids. In groups 1, 2 and 3 (3 × 18 patients), use of morphine, rofecoxib and acetaminophen after surgery was registered by a nurse. Assessments by a trained physiotherapist included number of days until walking with a wheeled frame, frame or crutches, and number of days until climbing stairs. A trained physiotherapist or a consultant registered the number of days until 90 degrees of flexion, flexion at discharge and number of days until discharge. Group 4 (100 patients) was used to register any complications. All patients had a clinical follow-up at 3 months after surgery. Two consultants, two physiotherapists and four nurses made the assessments.

The study was approved by the local ethics committee and was in accordance with the Declaration of Helsinki.

Statistics

The sample sizes for groups 1, 2 and 3 were calculated on the basis of range of motion and days until discharge. This was calculated for observations on the interval scale. Type 1 and 2 errors were both set at 5%. The estimated standard deviation in range of motion was set at 12. The smallest difference between the means not to be overlooked was set at 15 degrees. The number of patients in each group was calculated to be 16. Based on 0.85 power to detect a 1-day difference in hospital stay between two groups, with an assumed standard deviation of 1 day, 17 patients in each group would be required. To compensate for nonevaluable patients, we planned to enroll 18 patients in each group. The sample size for group 4 was set at 100 patients receiving intraarticular treatment, to evaluate the

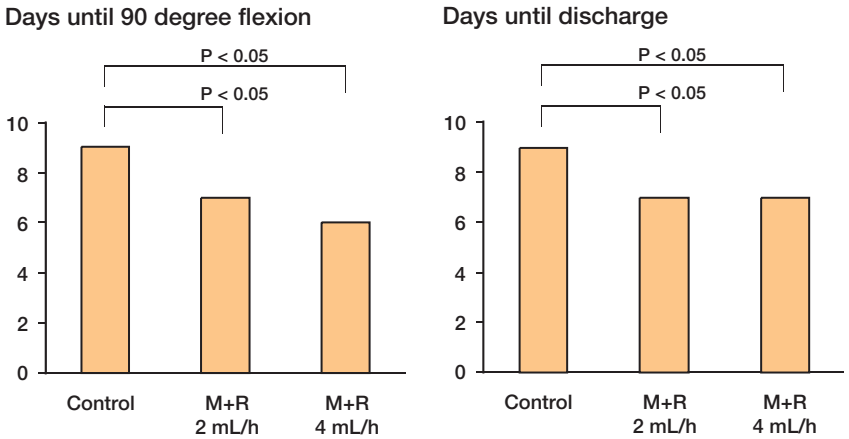

Figure 1. Number of days until 90 degrees of knee flexion and discharge in patients undergoing primary total knee arthroplasty who were given intraarticular morphine and ropivacaine (M+R), or nothing (control).

safety of the treatment and register any complications. The study was designed as an open intervention of 154 patients in 4 consecutive groups. Results are described with median and ranges, and were analyzed using chi-square, Wilcoxon and Mann-Whitney test where appropriate. $P < 0.05$ was considered significant. The statistical program Medstat was used to calculate sample size.

Results

All 154 patients completed the study. Flexion at discharge was improved from 70 (60–100)° in the control group to 100 (70–115)° in group 2 and 110 (90–130)° in group 3 ($p = 0.005$), the difference between the two treatment groups receiving different amounts of intraarticular analgesics not being statistically significant. Number of days until 90 degrees of flexion and until discharge was reduced in group 2 compared with the control group ($p = 0.03$ and 0.02) (Figure 1). There was no statistically significant difference between the two treatment groups. Morphine (10 mg) on demand was reduced from 22 (9–36) doses to 2 (0–20) and 2 (0–17) doses, respectively. Rofecoxib (25 mg × 1) was used for 8 (3–10), 5 (4–8) and 4 (2–10) days, respectively. Acetaminophen (1 g × 4) was used for 8 (7–9), 5 (3–6) and 5 (3–10) days, respectively. The use of morphine, rofecoxib and acetaminophen was significantly less in groups 2 and 3 as compared to the control group ($p = 0.001$ and 0.001; 0.005 and 0.005; 0.006 and 0.008). There was no difference between the two treatment groups.

Number of days until walking with a wheeled frame, frame or crutches, and days until using stairs were reduced in group 3 compared with the two other groups ($p = 0.01$ and 0.3; 0.008 and 0.1; 0.009 and 0.03; 0.01 and 0.04), the difference between the control group and group 2 also being significant ($p = 0.02$; 0.01; 0.03; 0.04) (Figure 2). Days until walking with crutches was reduced from 5 (3–8) in group 1 to 4 (3–6) and 3 (3–9) in groups 2 and 3, respectively. No complications, infections or reoperations were registered at 3-month follow-up in groups 1, 2 and 3. In group 4, one patient had a deep infection which was treated by irrigation, synovectomy and antibiotics. Another patient was resubmitted for brisement to increase flexion. Hospital stay, which was reduced from 9 (7–11) days in the control group to 7 (5–10) days in group 2 and 7 (5–9) days in group 3, remained at 7 (4–10) days in group 4.

Discussion

Postoperative intraarticular infusion of morphine and ropivacaine led to a clinically relevant early improvement in motion. The convalescence was improved and hospital stay was shortened. Furthermore, there was a reduced need for crutches and the use of stairs was quickly improved. A pos-

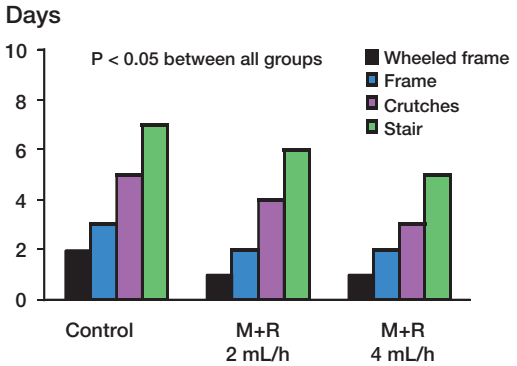

Figure 2. Number of days until walking with a wheeled frame, frame or crutches, and number days until using stairs (median) in patients undergoing primary total knee arthroplasty who were given intraarticular morphine and ropivacaine (M+R), or nothing (control).

sible mechanism and explanation of this effect is the importance of local synovial morphine receptors, thereby allowing a more effective pain treatment, including an inhibition of the inflammatory response. Another explanation may be an inhibition of the neuroendocrine stress response to surgery due to the use of local anesthetic. Also, early mobilization probably enhances convalescence.

The explanation of the fact that our results were so good compared to other studies in TKR (Badner et al. 1996, Ritter et al. 1999) with less or no effect remains unclear, except that we used continuous injection. Equally good results have already been presented after arthroscopic meniscectomy (Rasmussen et al. 1998) and ankle surgery (Rasmussen and Kehlet 2000). The weakness of our study is that it was not randomized and not blinded. The risk of complications with our method has not been established. The risk of infection in the use of continuous injection through a catheter in TKR may be comparable to the use of drains. Drains are an independent risk factor for wound infection, and are associated with an increase in incidence from 5% to 12% (Cobb 1990, Ritter et al. 1994). We removed the drains one day after surgery, and before initiating the intraarticular treatment. Consequently, we may not have increased the risk of infection.

The combined use of continuous intraarticular local anesthetic and morphine is effective in enhancing rehabilitation following total knee replacement. Because of the promising results obtained, more extensive randomized studies should be performed to help establish this postoperative analgesia in TKR.

No competing interests declared.

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