Diclofenac premedication but not intra-articular ropivacaine alleviates pain following day-case knee arthroscopy

Pekka Rautoma MD PhD,
Ulla Santanen MD,
Risto Avela MD,
Harri Luurila MD PhD,
Vesa Perhoniemi MD PhD,
Olli Erkola MD PhD

Purpose: To compare the postoperative analgesic effects of 50 mg diclofenac *po* before surgery and intra-articular ropivacaine injected after diagnostic day-case knee arthroscopy performed under spinal anesthesia.

Methods: In a randomized, double-blind investigation, 200 ASA physical status 1-2 outpatients, age 18-60 yr, received either 50 mg diclofenac *po* or placebo one hour before operation (100 patients per group), and intra-articular injections of either 20 ml of ropivacaine 0.5% or 20 ml of saline 0.9% (50 patients in each premedication groups). Patients received 50 mg diclofenac *po prn* and, if needed, 0.1 $mg \cdot kg^{-1}$ oxycodone *im* for postoperative pain relief. Patients were discharged home with a supply of 50 mg diclofenac tablets and were given a sheet of paper with knee pain VAS scales and a questionnaire of analgesics taken. Patients rated their VAS scores eight hours after surgery and in the morning and at the end of the first and the second postoperative days, respectively.

Results: The only statistically significant difference was found when the diclofenac groups were combined and compared with the combined placebo premedication groups. The VAS scores of knee pain at eight hours after the operation were 19 ± 22 in the two diclofenac premedication groups and 32 ± 28 in the two placebo groups ($P=0.001$).

Conclusions: Diclofenac premedication *po* reduced the VAS scores at eight hours postoperatively while intra-articular ropivacaine did not.

Objectif : Comparer les effets analgésiques postopératoires de 50 mg de diclofénac *po*, administrés avant l'opération, à la ropivacaïne intra-articulaire, donnée après l'arthroscopie diagnostique sous rachianesthésie.

Méthode : Lors d'une étude randomisée et en double aveugle, 200 patients d'état physique ASA I-II, âgés de 18-60 ans, ont reçu 50 mg de diclofénac *po* ou un placebo une heure avant l'opération (100 patients par groupe), et une injection intra-articulaire de 20 ml de ropivacaïne 0,5 % ou 20 ml de solution salée 0,9 % (50 patients dans chaque groupe de prémédication). Les patients ont reçu 50 mg de diclofénac *po prn* et, si nécessaire, 0,1 $mg \cdot kg^{-1}$ d'oxycodone *im* pour soulager la douleur postopératoire. À leur départ, ils ont reçu des comprimés de 50 mg de diclofénac, un questionnaire concernant la prise d'analgésiques et une feuille de papier où inscrire le niveau de douleur au genou selon l'EVA. Les patients ont estimé leurs scores à l'EVA huit heures après l'opération et au début et à la fin du premier et du deuxième jours postopératoires, respectivement.

Résultats : La seule différence statistique significative a été trouvée en combinant les groupes de diclofénac et en les comparant aux groupes combinés de prémédication placebo. Les scores postopératoires de l'EVA ont été de 19 ± 22 dans les deux groupes qui ont reçu une prémédication de diclofénac et de 32 ± 28 dans les groupes qui ont reçu le placebo ($P=0,001$).

Conclusion : La prémédication au diclofénac *po* a réduit les scores postopératoires de l'EVA à huit heures, mais non pas la ropivacaïne intra-articulaire.

From the Department of Anesthesia, Helsinki City Hospital, Helsinki, Finland.
Address correspondence to: Pekka Rautoma MD PhD, Department of Anesthesia, Maria Hospital, Lapinlahdenkatu 16, 00180 Helsinki, Finland. Fax: +358-9-31063378; E-mail: rautoma@dlc.fi
Accepted for publication November 26, 1999

INTRA-ARTICULAR bupivacaine has been shown in some studies to provide postoperative analgesia after knee arthroscopy,[1–8] but others have failed to demonstrate such an effect.[8–11] These investigations have been performed in healthy patients under general, spinal (subarachnoidal), epidural or local anesthesia. Some authors have used intraoperative opioids, some have used premedication, and the amount of bupivacaine administered has been different between the studies. Therefore, the results of these studies cannot be directly compared. Also, it is unclear how much postoperative analgesia is provided by diclofenac premedication.

Ropivacaine has similar pharmacodynamic and pharmacokinetic properties to bupivacaine but is less prone to elicit central nervous system or circulatory adverse effects.[12–15] The present study was designed to examine the postoperative analgesic effect of intra-articular ropivacaine injected after diagnostic day-case knee arthroscopy performed under spinal anesthesia. We also investigated the effect of 50 mg diclofenac given *po* one hour before the arthroscopy.

Materials and methods

The project was institutionally approved, and written informed consent was obtained from each patient before operation. Two hundred outpatients (ASA physical status 1-2, aged 18-60 yr) undergoing spinal anesthesia for elective knee arthroscopy were studied. The surgical procedures included arthroscopy for diagnostic purposes or partial or total meniscectomy not requiring intra-articular drainage postoperatively. Exclusion criteria were bilateral arthroscopy, acute traumatic injury to the knee, known cruciate ligament tear, the use of oral narcotics or constant use of non-steroidal antiinflammatory drugs, history of allergy to any study medication, patient refusal, contraindication for spinal anesthesia, and body mass index not within normal limits (not between 15-28).

Before operation, each patient was instructed in the use of a 100-mm visual analogue scale (VAS) with 0 labelled "no pain" and 100 "the worst pain imaginable". The preoperative knee pain was recorded on the ward before premedication. Thereafter, pain scores were recorded at eight hours after surgery and in the morning and at the end of the first and the second postoperative days, respectively. All of the pain scores were recorded with the appropriate knee on movement (at 90 flexion when possible). Patients were given a sheet of paper with VAS scales and a questionnaire of analgesics taken. They were asked to rate their pain intensity on the VAS scale at the above fixed times. All of the knee pain VAS scores were rated by the patient, not by the authors or the nurses. Patients also were asked if they had postoperative nausea, vomiting or difficulty in voiding urine. We provided a stamped, addressed envelope in which the patients could return the completed data sheets.

In a double-blind, randomized investigation, 200 patients received either 50 mg diclofenac (Voltaren®, Novartis Ltd) or a placebo pill (Placebo®, Leiras, Finland) one hour before spinal anesthesia. The person who administered the premedication had nothing further to do with the patient. There were 100 patients in each premedication groups. All patients received spinal anesthesia with 1.5-2.5 ml hyperbaric 0.5% bupivacaine through a #27 gauge spinal needle with a 22 gauge introducer. We did not use local anesthesia to the skin. If the patient was very afraid of the skin puncture, nervous or unhappy and requested premedication, a bolus dose of 0.5 mg alfentanil was given as a rescue premedication. The number of patients receiving alfentanil was recorded. Routine monitoring was used. In addition, patients were randomized to receive, in a double-blind fashion, intra-articular injection of either 20 ml ropivacaine 0.5% (Naropin®, Astra Ltd) or 20 ml saline 0.9% through the arthroscope at the end of knee arthroscopy, ten minutes before release of the tourniquet. Fifty patients in each premedication (diclofenac or placebo) group received ropivacaine, and the remaining 50 patients in each premedication group received saline 0.9% intra-articularly.

When needed, patients received 50 mg diclofenac *po* for postoperative pain relief. If this did not give enough help, patients also received 0.1 $mg \cdot kg^{-1}$ oxycodone *im.* Patients were discharged home with a supply of 50 mg diclofenac tablets to be taken *prn* to a maximum of four tablets per 24 hr. The postoperative need for analgesics was recorded in the recovery room, at the ward and at home.

Statistical analysis

All randomizations were computer-generated. Data are expressed as mean ± standard deviation (SD). In the figures, mean ± standard error of the mean (SEM) is used. Analysis of variance (ANOVA) was used to analyze the data followed by Scheffe´s F-test. The VAS pain scores were analyzed by a 3-way ANOVA (2x2x5) with (1) type of premedication (diclofenac or placebo) and (2) type of intra-articular injection (ropivacaine or NaCl) as the between-group factors and (3) time (pm operation day, am 1. postoperative day, pm 1. postoperative day, am 2. postoperative day, pm 2. postoperative day) as the within groups factor. The chi square test was used to test the difference in the proportion of patients requesting postoperative diclofenac tablets or oxycodone. A P value $\leq$ 0.05 was considered statistically significant.

TABLE I Patient characteristics. There were no statistically significant differences among the groups with regard to age, height, weight or gender. Values are mean ± SD.

Group	*Sex m/f*	*Age (yr)*	*Height (cm)*	*Weight (kg)*
diclofenac-ropivacaine	16/23	41.3 ± 10.9	171 ± 10	72.7 ± 12.9
diclofenac-saline	19/24	41.8 ± 12.1	171 ± 9	73.6 ± 11.9
placebo-ropivacaine	21/15	38.9 ± 12.4	173 ± 9	75.1 ± 11.6
placebo-saline	19/18	43.8 ± 11.5	173 ± 10	72.5 ± 11.9

TABLE II The number of patients receiving additional premedication (alfentanil) and postoperative pain medicines (diclofenac or oxycodone) during the first eight postoperative hours, and the number of patients who suffered from postoperative nausea and vomiting (PONV) or difficulties in voiding urine postoperatively. There were no statistically significant differences between the groups.

Group	*n*	*Alfentanil (n)*	*oxycodone 0.1 mg·kg^{-1} im (n)*	*diclofenac 50 mg po (n)*	*diclofenac 100 mg po (n)*	*PONV (n)*	*Difficulties in voiding urine (n)*
diclofenac-ropivacaine	39	7	1	22	5	4	2
diclofenac-saline	43	11	3	26	6	4	7
placebo-ropivacaine	36	18	1	21	4	5	2
placebo-saline	37	10	0	20	4	9	3

TABLE III The knee pain VAS scores in the four study groups at different time points. There were no statistically significant differences between the groups. Values are mean ± SD.

Group	*VAS preoperatively*	*VAS 8 hr postoperatively*	*VAS 1. Postoperative day 08 am*	*VAS 1. Postoperative day 08 pm*	*VAS 2. Postoperative day 08 am*	*VAS 2. Postoperative day 08 pm*
diclofenac-ropivacaine	17.2 ± 24.2	20.0 ± 24.8	9.1 ± 14.9	8.3 ± 13.6	4.1 ± 8.7	5.0 ± 14.0
diclofenac-saline	15.7 ± 12.5	18.5 ± 18.4	10.3 ± 17.4	10.4 ± 17.6	7.1 ± 14.8	8.6 ± 17.4
placebo-ropivacaine	19.0 ± 19.5	27.0 ± 28.4	14.8 ± 19.0	14.9 ± 21.4	9.7 ± 16.7	9.0 ± 17.3
placebo-saline	17.5 ± 16.6	36.1 ± 27.3	13.8 ± 19.6	10.6 ± 14.4	6.4 ± 9.2	4.7 ± 7.1

Results

Patient characteristics are presented in Table I.

Four patients were excluded from the study because they received midazolam for sedation, and two patients because of general anesthesia. One patient was excluded because of postoperative drainage, and one patient because of chest pain. The questionnaires were returned by 80.7% of the remaining patients (37 patients did not return the questionnaires). There wee 8, 6, 12 and 11 patients in the diclofenac-ropivacaine, diclofenac-saline, placebo-ropivacaine and placebo-saline groups who did not return the questionnaires. Therefore, only 155 patients were available for analysis.

The number of patients who received 0.5 mg alfentanil *iv* for sedation is presented in Table II. The surgery time was 35 ± 10 (15-55) min. Patients stayed 1.5 ± 0.5 hr in the recovery room where no patient needed diclofenac or oxycodone. The number of patients who received diclofenac or oxycodone during the first eight postoperative hours is also presented in Table II.

There were no differences in the VAS scores of preoperative knee pain among the groups (Table III). The postoperative knee pain VAS scores did not differ between ropivacaine- and NaCl-treated patients at any time (Table III, Figure 1). However, when two of the four groups were combined, the VAS scores of knee pain were lowest in the two diclofenac premedication groups (with or without intra-articular ropivacaine) at eight hours after the operation (Table III, Figure 2) (P=0.001).

The number of patients who suffered from PONV or difficulties in voiding urine is presented in Table II. The discharge time home after the end of the operation was 7.3 ± 1.5 (4.3-10.3) hr (P : NS).

Discussion

This study failed to demonstrate a decrease in postoperative VAS scores at eight hours and later postoperatively when 20 ml of ropivacaine 0.5% was injected intra-articularly after day-case diagnostic knee arthroscopy performed under spinal anesthesia. Our

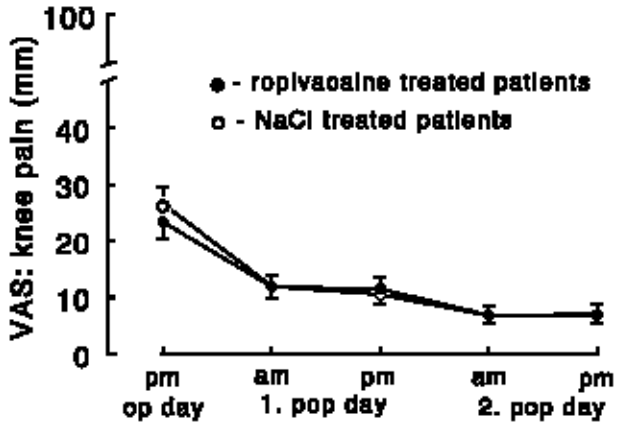

FIGURE 1 Visual analogue scale (VAS) of knee pain against time. There were no differences among the groups. Data are mean ± SEM.

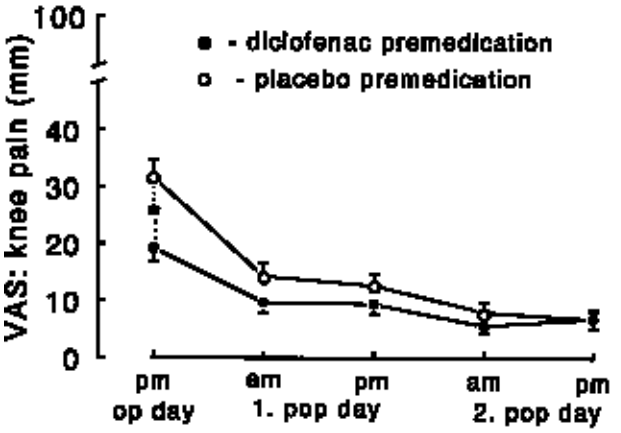

FIGURE 2 Visual analogue scale (VAS) of knee pain against time in the two premedication groups. Group diclofenac was different from group placebo at eight hours after the operation (operation day pm). Data are mean ± SEM.

results are in accordance with those of Heard *et al.* who also used spinal anesthesia in one of the study groups.[1] In their study patients who received spinal anesthesia had lower VAS scores than patients who had received general anesthesia, irrespective of the intra-articular treatment and existed up to 12 hr postoperatively. Therefore, we did not ask the patients to rate their postoperative knee pain before eight hours postoperatively.

Some studies report that protecting the nervous system from the noxious insults of surgery, using regional analgesic techniques, results in blunting of the neuroendocrine response and reduces postoperative pain.[16–19] Raja *et al.* used epidural anesthesia, which may have reduced postoperative pain by attenuating spinal cord hyperexcitability.[20–21] Sørensen *et al.* showed that additional local anesthesia, intra-articular bupivacaine after intra- articular lidocaine, did not improve postoperative analgesia.[11] We think that the lack of effect of intra-articular ropivacaine in the present study was due to the effects of spinal anesthesia. It may also be that the effect of intra-articular ropivacaine 0.5% was too short-acting and, therefore, was masked under the effects of spinal anesthesia. More studies are needed to examine if higher concentrations of ropivacaine under the same circumstances would improve the knee pain VAS scores.

Diclofenac premedication reduced postoperative pain scores eight hours after the operation. This time exceeded the clinical duration of action of the preoperatively given diclofenac. Thus, under these circumstances, a pre-emptive analgesic effect of diclofenac may exist. Postoperative pain may originate from the peripheral fibres at the surgical incision enhanced by central sensitization.[22] Pre-emptive analgesia is based on the assumption that an analgesic drug given before surgical stimulus can prevent sensitization and thus reduce postoperative pain more than the same analgesic drug given postoperatively.[12] However, it may not be possible to study pre-emptive analgesia if the noxious stimuli are already obliterated by central neural axis blockade, i.e. spinal anesthesia. Therefore, this study was not designed to study pre-emptive analgesia itself but we merely wanted to examine if diclofenac premedication is clinically useful. We think that the effect of 50 mg diclofenac given one hour before surgery was due to the well documented peripheral anti-inflammatory effects of diclofenac.

The knee pain VAS scores following arthroscopy were very low in all groups regardless of treatment. However, we think that even the small 13 mm change in the postoperative knee pain VAS score caused by diclofenac premedication is beneficial to the individual patient. Diclofenac tablet is cheap and we think that this treatment is cost-effective and causes minimal trouble and side-effects to the patients.

In summary, intra-articular ropivacaine injected after diagnostic day-case knee arthroscopy performed under bupivacaine spinal anesthesia was of no benefit at eight hours and later postoperatively. On the contrary, diclofenac *po* premedication reduced postoperative pain scores eight hours after the operation. We recommend 50 mg diclofenac *po* be given one hour before surgery for suitable patients when day-case knee arthroscopy is to be performed under spinal anesthesia.

References

1 *Allen GC, St. Amand MA, Lui ACP, Johnson DH, Lindsay P.* Postarthroscopy analgesia with intraarticular bupivacaine/morphine. A randomized clinical trial. Anesthesiology 1993; 79: 475–80.

2 *McSwiney MM, Joshi GP, Kenny P, McCarroll SM.* Analgesia following arthroscopic knee surgery. A controlled study of intra-articular morphine, bupivacaine or both combined. Anaesth Intensive Care 1993; 21: 201–3.

3 *Kaeding CC, Hill JA, Katz J, Benson L.* Bupivacaine use after knee arthroscopy: pharmacokinetics and pain control study. Arthroscopy 1990; 6: 33–9.

4 *McQuay HJ, Carroll D, Moore RA* Postoperative orthopaedic pain - the effect of opiate premedication and local anaesthetic blocks. Pain 1988; 33: 291–5.

5 *Joshi GP, McCarroll SM, O'Brien TM, Lenane P.* Intraarticular analgesia following knee arthroscopy. Anesth Analg 1993; 76: 333–6.

6 *Morrow BC, Milligan KR, Murthy BVS.* Analgesia following day-case knee arthroscopy-the effect of piroxicam with or without bupivacaine infiltration. Anaesthesia 1995; 50: 461–3.

7 *Chirwa SS, MacLeod BA, Day B.* Intraarticular bupivacaine(Marcaine) after arthroscopic meniscectomy: a randomized double-blind controlled study. Arthroscopy 1989; 5: 33–5.

8 *Heard SO, Edwards WT, Ferrari D, et al.* Analgesic effect of intraarticular bupivacaine or morphine after arthroscopic knee surgery: a randomized prospective, double-blind study. Anesth Analg 1992; 74: 822–6.

9 *Henderson RC, Campion ER, DeMasi RA, Taft TN* Postarthroscopy analgesia with bupivacaine. A prospective, randomized, blinded evaluation. Am J Sports Med 1990; 18: 614–7.

10 *Milligan KA, Mowbray MJ, Mulrooney L, Standen PJ.* Intra-articular bupivacaine for pain relief after arthroscopic surgery of the knee joint in daycase patients. Anaesthesia 1988; 43: 563–4.

11 *Sørensen TS, Sørensen AI, Strange K.* The effect of intra-articular instillation of bupivacaine on postarthroscopic morbidity: a placebo-controlled, double-blind trial. Arthroscopy 1991; 7: 364–7.

12 *Katz JA, Bridenbaugh PO, Knarr DC, Helton SH, Denson DD.* Pharmacodynamics and pharmacokinetics of epidural ropivacaine in humans. Anesth Analg 1990; 70: 16–21.

13 *Concepcion M, Arthur GR, Steele SM, Bader AM, Covino BG.* A new local anesthetic, ropivacaine. Its epidural effects in humans. Anesth Analg 1990; 70: 80–5.

14 *Scott DB, Lee A, Fagan D, Bowler GMR, Bloomfield P, Lundh R.* Acute toxicity of ropivacaine compared with that of bupivacaine. Anesth Analg 1989; 69: 563–9.

15 *Knudsen K, Beckman Suurküla M, Blomberg S, Sjövall J, Edvardsson N.* Central nervous and cardiovascular effects of i.v. infusions of ropivacaine, bupivacaine, and placebo in volunteers. Br J Anaesth 1997; 78: 507–14.

16 *Breslow MJ, Jordan DA, Christopherson R, et al.* Epidural morphine decreases postoperative hypertension by attenuating sympathetic nervous system hyperactivity. JAMA 1989; 26: 3577–81.

17 *Rutberg H, Håkanson E, Anderberg B, Jorfeldt L, Mårtensson J, Schildt B.* Effects of the extradural administration of morphine, or bupivacaine, on the endocrine response to upper abdominal surgery. Br J Anaesth 1984; 56: 233–8.

18 *Tverskoy M, Cozacor C, Ayche M, Bradley EL Jr, Kissin I.* Postoperative pain after inguinal herniorraphy with different types of anesthesia. Anesth Analg 1990; 70: 29–35.

19 *Jebeles JA, Reilly JS, Gutierrez JF, Bradley EL Jr, Kissin I.* The effect of pre-incisional infiltration of tonsils with bupivacaine on the pain following tonsillectomy under general anesthesia. Pain 1991; 47: 305–8.

20 *Raja SN, Dickstein RE, Johnson CA* Comparison of postoperative analgesic effects of intraarticular bupivacaine and morphine following arthroscopic knee surgery. Anesthesiology 1992; 77: 1143–7.

21 *Katz J, Kavanagh BP, Sandler AN, et al.* Preemptive analgesia. Clinical evidence of neuroplasticity contributing to postoperative pain. Anesthesiology 1992; 77: 439–46.

22 *Wall PD.* The prevention of postoperative pain (editorial). Pain 1988; 33: 289–90.