Intra-articular morphine and clonidine produce comparable analgesia but the combination is not more effective

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Summary
Both intra-articular morphine and clonidine produce analgesia. This study was designed to compare the analgesic effects of the two drugs, used separately and in combination. We studied 90 patients undergoing arthroscopy of the knee under general anaesthesia. Patients were allocated randomly to receive 20 ml of intra-articular isotonic saline solution containing morphine 2 mg, clonidine 150 μg or both. Pain was assessed on a visual analogue scale after operation and time for rescue medication was measured. There was no difference in VAS scores between the three groups and the time for rescue analgesic was comparable. We conclude that intra-articular morphine and clonidine have comparable analgesic effects in the doses used. The combination of both drugs did not seem to increase analgesia. (Br. J. Anaesth. 1997; 79: 660–661).

Key words
Analgesia, postoperative. Analgesics opioid, morphine. Sympathetic nervous system, clonidine. Analgesic techniques, regional, i.a.

Since the first clinical studies which demonstrated that intra-articular administration of morphine could provide analgesia, related to a peripheral mechanism of action,¹ this technique has become popular and is used commonly to provide analgesia after arthroscopic knee surgery. Morphine has also been combined with bupivacaine to augment analgesia.² More recently, clonidine has been shown to provide analgesia when administered into the knee joint after arthroscopy.³ As subcutaneous administration of clonidine was not effective in producing analgesia, a local mechanism of action was hypothesized.³ Morphine and clonidine have synergistic analgesic effects when given intrathecally but not i.v.,⁴ but the effect of the combination is not known when administered intra-articularly. Therefore, this double-blind, prospective, randomized study was conducted to compare the analgesic effects of morphine and clonidine when used alone and in combination.

Methods and results
After obtaining informed consent and Ethics Committee approval, we studied 90 ASA I–II patients undergoing knee arthroscopy. Surgery was performed under general anaesthesia using propofol 2 mg kg⁻¹ and alfentanil 10 μg kg⁻¹ for induction, and isoflurane and 50% nitrous oxide in oxygen for maintenance. Patients were allocated randomly in one of three groups according to the analgesic regimen. All received 20 ml of intra-articular isotonic saline solution before tourniquet release containing morphine 2 mg (group M), clonidine 150 μg (group C) or both (group M+C). Pain was assessed after operation using a visual analogue scale (VAS) at 1, 2, 3, 6 and 24 h after intra-articular injection. Patients received propacetamol 2 g i.v. when they complained of pain (VAS > 4). Patients were also monitored for arterial pressure, heart rate and sedation, and side effects (nausea, vomiting or pruritus) were also noted.

Data were analysed using the Mann–Whitney U test for patient data. Median and ranks of VAS scores were compared using Kruskall–Wallis analysis. The number of patients not given propacetamol was compared using the Kaplan–Meyer method and a log-rank test.

The three groups were comparable in age (group C, 36 (range 19–69) yr; group M, 36 (18–72) yr; group M+C, 36 (20–70) yr), weight (group C, 73 (SD 10) kg; group M, 72 (10) kg; group M+C, 67 (11) kg) and height (group C, 173 (8) cm; group M, 172 (8) cm; group M+C, 171 (9) cm). Group C included 20 men and 10 women, group M, 23 men and seven women and group M+C 19 men and 11 women (ns). Mean durations of surgery were 37 (18) min, 35 (20) min and 30 (13) min in groups C, M and M+C, respectively. VAS scores were comparable in the three groups (fig. 1) but the scores decreased significantly over time. Seventeen patients in the morphine and clonidine groups and 16 in the morphine–clonidine combination group did not receive propacetamol (ns). The number of patients who did not require additional analgesia in the post-operative period was comparable in the three groups. Arterial pressure and heart rate did not change significantly.

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Intra-articular morphine and clonidine

significantly. No patient complained of sedation or other side effects.

Comment

We have found that intra-articular morphine 2 mg was equivalent to clonidine 150 μg in terms of postoperative analgesia. In all groups, mean VAS scores were low and rescue medication was limited. The hypothesis that a more painful surgical procedure could have elicited a difference between the two study drugs nevertheless cannot be excluded. For this type of procedure (knee arthroscopy) both drugs appeared to provide effective analgesia in the majority of patients although some patients may have experienced a more painful postoperative course despite intra-articular injection.

We did not compare morphine and clonidine with placebo; this comparison has been performed in previous studies and both drugs were demonstrated to be superior to placebo. A local analgesic action of morphine is thought to be mediated by axonal endogenous opioid receptors while inhibition of noradrenaline release could explain the analgesic action of intra-articular clonidine. The lack of side effects commonly noticed after i.v., extradural or parenteral administration of drugs confirms that a local action probably accounts for most of the analgesic effect.

When combined, the two drugs were not more effective than each given separately. One possible explanation for the lack of additive effect is that morphine and clonidine induced complete pain relief during the first hours after operation and that no additional effect was required or measurable. Nevertheless, 50% of patients received pro-pacetamol at some time during the study, implying that analgesia could be potentially improved. We conclude that small doses of morphine or clonidine provided comparable analgesia after intra-articular administration, but that the combination of these doses of the two drugs would not be useful.

References