Regional Anesthesia and Pain

Intra-synovial, compared to intra-articular morphine provides better pain relief following knee arthroscopy menisectomy

[L'administration intra-synoviale de morphine, comparée à l'administration intra-articulaire, fournit une meilleure analgésie à la suite d'une ménisectomie arthroscopique du genou]

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Purpose: To evaluate the analgesic effect of morphine 1 mg administered into the synovial tissue and the outer third of the meniscus after knee arthroscopy.

Methods: In a prospective, double-blind, randomized study, 60 patients who required elective knee arthroscopy were assigned to two groups: Group A consisted of 30 patients who received a direct injection of morphine 1 mg into either the synovial tissue or the outer third of the meniscus following menisectomy. Group B consisted of 30 patients who received a direct injection of NaCl 0.9% 1 mL into the synovial tissue or the outer third of the meniscus following menisectomy. At the end of the operation Group A received an intra-articular injection of NaCl 0.9% 1 mL and bupivacaine 0.5% 10 mL and Group B received an intra-articular injection of morphine 1 mg and bupivacaine 0.5% 10 mL. Analgesic effect was evaluated by pain intensity (visual analogue scale; VAS) and analgesic requirements (paracetamol) during the first one, three, six, 12, 24, and 48 hr postoperatively.

Results: There was no significant difference between the two groups within the first six hours and after 24 hr following the operation regarding VAS score and analgesic requirements. At 12 and 24 hr following the operation, the VAS score and the analgesic requirements were significantly higher in Group B compared to Group A ($P < 0.01$ and $P < 0.01$, respectively). No patient developed side effects.

Conclusion: We conclude that direct morphine injection into the synovia or the outer third of the meniscus provided better pain relief than intra-articular morphine after knee arthroscopy.

Objectif : Évaluer l'effet analgésique d'une dose de 1 mg de morphine administrée dans le tissu synovial ou dans le tiers externe du ménisque après l'arthroscopie du genou.

Méthode : Il s'agit d'une étude prospective, randomisée et à double insu auprès de 60 patients nécessitant une arthroscopie du genou non urgente et répartis en deux groupes. Les 30 patients du Groupe A reçoivent une injection directe de 1 mg de morphine dans le tissu synovial ou dans le tiers externe du ménisque après la ménisectomie. Les 30 patients du Groupe B reçoivent, après la ménisectomie, une injection directe de 1 mL de NaCl à 0,9 % dans le tissu synovial ou dans le tiers externe du ménisque. À la fin de l'opération, les patients du Groupe A ont une injection intra-articulaire de 1 mL de NaCl à 0,9 % et 10 mL de bupivacaine à 0,5 % tandis que ceux du Groupe B ont une injection intra-articulaire de 1 mg de morphine et 10 mL de bupivacaine à 0,5 %. L'effet analgésique est évalué par l'intensité de la douleur, avec une échelle visuelle analogique (EVA), et par les besoins d'analgésiques (paracétamol) à une, trois, six, 12, 24 et 48 h après l'opération.

Résultats : Aucune différence intergroupe significative n'a été notée pendant les six premières heures et après 24 h à la suite de l'opération quant aux scores de l'EVA et aux besoins d'analgésiques. À 12 et 24 h suivant l'opération, les scores de l'EVA et les demandes d'analgésie sont significativement plus élevés chez les patients du Groupe B comparé au Groupe A ($P < 0,01$ et $P < 0,01$, respectivement). Aucun patient n'a connu d'effets secondaires.

Conclusion : Après l'arthroscopie du genou, on note une meilleure analgésie avec l'injection directe de morphine dans la synoviale ou le tiers externe du ménisque, comparativement à l'administration intra-articulaire.

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ARTHROSCOPIC partial meniscectomy is a common procedure that is frequently associated with postoperative pain. Various studies have reported on pain reduction following intra-articular injection with analgesics or opioids.¹ The rationale for intra-articular morphine injection is the evidence of synovial opioid receptor activation in the presence of inflammation.² Yet, there is no evidence of an opioid meniscal receptor, since the meniscus is a fibrocartilage, which has blood and lymphatic vessels, and is innervated only in its outer third. Most studies have demonstrated a prolonged analgesic effect as late as eight to 12 hr following intra-articular administration of morphine.^{3,4}

However, many reports also showed increased pain scores after 12 hr.^{5,6} Thus, it is reasonable to perform the nerve block as close as possible to the pain receptors, which enables local tissue-binding to opioid receptors, enhancing the analgesic effect. To the best of our knowledge, there is no report on the direct injection of analgesics or opioids within the synovia or outer third of the meniscus following knee arthroscopy in the English medical literature. The aim of this study was to evaluate the analgesic effect of the direct injection of morphine 1 mg into either the synovium or the meniscus after arthroscopy.

Methods

Sixty consecutive patients undergoing elective day-case knee arthroscopic partial, subtotal, or total meniscectomy by the same surgeon (K.M.) were included in the study. Patients with chronic pain or with known hypersensitivity to morphine were excluded.

The study was a double-blind, parallel-group comparison of synovial and meniscal direct injection of either morphine 1 mg (1 mL) or NaCl 0.9% 1 mL.

Using a numbered list, patients were randomly assigned to one of two groups:

Group A comprised 30 patients who received an injection of morphine 1 mg (1 mL) either into the synovial tissue or the outer third of the meniscus following meniscectomy; Group B comprised 30 patients who received an injection of 1 mL 0.9% NaCl into either the synovial tissue or the meniscus following meniscectomy. This randomized study was approved by the Institutional Ethics Committee. All patients gave written informed consent before having the operation.

The anesthetic procedure in both groups included lidocaine 1% 15 mL (Xylocaine, Astra) followed by bupivacaine 0.5% 10 mL for local anesthesia. A tourniquet was not used. At the end of the surgical procedure, a lumbar puncture needle (size: 20G × 9 cm) was inserted endoscopically in the synovial tissue and the outer third of the

meniscus, followed by fluid aspiration. Then the morphine 1 mg (1 mL) in Group A and saline 0.9% (1 mL) in Group B were injected into the meniscus or synovial tissue. In both groups the lumbar needle was not flushed. Thus, the true morphine dose was 0.9 mg. The precise needle location was verified by mild resistance to the injection; if such resistance was absent, the needle was relocated endoscopically. Thereafter, patients in Group A received an intra-articular injection of NaCl 0.9% 1 mL and bupivacaine 0.5% 10 mL and patients in Group B received an intra-articular injection of morphine 1 mg and bupivacaine 0.5% 10 mL.

The patients were evaluated by two of the authors (K.M. and R.V.) postoperatively for pain intensity visual analogue scale (VAS) and analgesic requirements (paracetamol) during the first one, three, six, 12, 24, and 48 hr, at rest and during 20° knee flexion.

Patient evaluations

Patients were evaluated in the hospital at one, three, six, 24 and 48 hr after the operation. Patient evaluation at 12 hr after the operation was performed in the patient's home.

Pain intensity was recorded using a VAS (0=no pain 10=severe pain). Patients were allowed paracetamol 500–1000 mg for pain relief, as needed. There was no criteria for pain treatment and each patient decided by himself when and how much analgesic to use. However, the patient was limited to use no more than 1000 mg in three hours.

Data for pain intensity (VAS), and analgesic requirements were analyzed using Kruskal-Wallis test and Dunn's procedure for post-hoc evaluation. *P* values of less than 0.05 were considered statistically significant.

Power analysis was calculated using the mean and the SD in both groups. We decided that a reduction of 50% of pain would be a clinically acceptable difference

TABLE I Demographic data

	Group A	Group B
Number of patients	30	30
Mean age in yr (SD)	34 (15)	33 (14)
Sex		
Male	18	19
Female	12	11
Mean weight in kg (SD)	70 (19)	68 (17)
Mean duration of operation in min (SD)	38 (0.5)	36 (0.5)
Surgical procedure		
Total meniscectomy	2	3
Partial meniscectomy	21	20
Subtotal meniscectomy	7	7

TABLE II Visual analogue scale at one, three, six, 12, 24, and 48 hr postoperatively

Groups	0 hr	1 hr	3 hr	6 hr	12 hr	24 hr	48 hr
A							
Rest	0.5	1.1 (0.1)	1.3 (0.3)	1.3 (0.4)	0.8 (0.2)	0.1 (0.1)	1.1 (0.8)
Flexion	0.6	1.4 (0.2)	1.6 (0.4)	1.7 (0.5)	1.3 (0.2)	0.2 (0.1)	1.2 (0.6)
B							
Rest	0.5	1.3 (0.2)	1.5 (0.2)	2 (0.7)	2.5 (0.2)	0.6 (0.1)	1 (1.6)
Flexion	0.7	1.4 (0.2)	1.8 (0.3)	2.2 (0.6)	3.4 (0.2)	0.9 (0.2)	1 (1.5)
P value							
Rest	N.S.	N.S.	N.S.	N.S.	<0.001	<0.01	N.S.
Flexion	N.S.	N.S.	N.S.	N.S.	<0.001	<0.01	N.S.

Data are given as mean $\pm$ SD; N.S.=no significant difference between groups.

TABLE III Analgesic requirements (paracetamol 500 mg) during the first 48 hr postoperatively

Groups	0–6 hr	6–12 hr	12–24 hr	24–48 hr
A median	0	2	1	1
(range)	(0–3)	(0–9)	(0–5)	(0–5)
B median	0	4	3	1
(range)	(0–5)	(0–8)	(0–5)	(0–7)
P value	N.S.	$P < 0.01$	$P < 0.01$	N.S.

between the two groups.

Results

There were no significant differences between the two groups in the demographic data with regard to sex, age, weight, duration of surgery, or surgical procedure (Table I).

The VAS scores were not different between groups at one, three and six hours postoperatively. Only two patients in Group A had a pain score over 2. The majority of patients in Group A and B had pain scores less than 2 throughout the first six hours (Table II).

At 12 and 24 hr following the operation, the VAS scores were significantly lower in Group A than in Group B ($P < 0.001$ and $P < 0.01$, respectively).

There was a significant difference in rescue analgesic requirements between the two groups throughout the six to 24 hr following the operation ($P < 0.01$). Seven patients in Group A required supplemental analgesia within the six to 12 hr period, while in Group B, 13 patients used analgesia in the same time period (Table III). However, in the first six hours and after 24 hr, there was no significant difference between the two groups. One patient in Group A and two in Group B were allowed to take another analgesic in order to provide more adequate pain relief.

In both groups there was a correlation between post-

operative pain and analgesic requirements. There was no significant difference between postoperative pain and analgesic requirements of patients relative to injection location (meniscus or synovial tissue) in either group.

Based on the results, it was calculated that the power to detect a 50% reduction in pain at 12 and 24 hr after the operation and consumption of rescue analgesics between six and 24 hr was above 80% ($\alpha = 0.05$). However, based on pain scores up to six hours or at 48 hr, the power to detect a 50% reduction of pain or consumption of rescue analgesics was insufficient (less than 50%).

No patient developed significant postoperative side effects, nausea, or vomiting, which required medication.

Discussion

Postoperative pain is considered the main cause of morbidity after knee arthroscopy. Various studies report reduction of both postoperative pain and analgesic drug consumption after systemic administration of non-steroidal anti-inflammatory drugs (NSAID), intra-articular steroids, NSAID, and opioids.¹ The latter, reportedly, have the longest analgesic effect, lasting as long as eight to 12 hr following the intra-articular administration of morphine.^{3,4}

It is known that opioid receptors are present on peripheral nerves.⁷ Two mechanisms are responsible for the analgesic effect of locally administered opioids.^{3,4} First, disruption of the perineurium at the end of the peripheral nerve, allows easier access of opioids to the neuronal receptors. Second, in the presence of inflammation, the inactive opioid receptors become active and local tissue binding to opioids increases. Direct injection into the inflamed tissue of either the meniscus or the synovia may increase the period of tissue-binding to opioids, creating a longer and stronger effect. Whitford *et al.* found that after keeping the tourniquet inflated for ten minutes, opioids had a superior analgesic effect, probably because of increased tissue-binding.⁸

In the current study, direct opioid injection into the inflamed tissue of both the synovium and the outer third of the meniscus was evaluated in terms of the duration of analgesic effect. In Group A, direct injection of morphine 1 mg into the synovia or the outer third of the meniscus significantly reduced pain scores at 12 hr and 24 hr postoperatively. Although the difference in pain scores between patients in Group A and Group B was statistically significant, absolute pain scores were quite low. The clinical benefit of intra-synovial injection was confirmed by reduced requirements for additional analgesia *po*.

Another variable that may affect the analgesic efficacy of intra-articular morphine is dosage.^{2,9-12} High doses of morphine may be associated with central nervous system side effects. Intra-synovial injection of morphine may decrease dose requirements, providing pain relief and diminishing side effects. In the present study, the dose of morphine was 1 mg, rendering the incidence of side effects negligible.

We conclude that direct injection of morphine into the synovial tissue or the outer third of the meniscus provides better pain relief than intra-articular morphine. We hypothesize that the presence of meniscal opioid receptors at the outer part of the meniscus, in addition to the known opioid receptor in synovial tissue, may explain our findings.

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