

The effect of intra-articular neostigmine, tramadol, tenoxicam and bupivacaine on postoperative pain

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Abstract

Objective: The present study, investigates the analgesic effects and complications of intra-articular neostigmine, tramadol, tenoxicam and bupivacaine on postoperative pain in patients undergoing day case knee arthroscopy. **Subjects:** Group 1 received 0.5 mg neostigmine, Group 2 received 100 mg tramadol, Group 3 received 20 mg tenoxicam, Group 4 received 20 ml 0.5% bupivacaine (control) in 20 ml normal saline intra-articularly at the end of the surgery. All patients had the same anaesthetic technique. Patients were observed in the recovery room with respect to pain scores, haemodynamic changes and postoperative analgesia at 1, 2 and 4 h postoperatively. Analgesic therapy in the recovery room was managed with 25 mg bolus doses of meperidine when the patients had visual analogue scale (VAS) scores higher than three points. The patients were discharged from hospital with a prescription for diclofenac 75 mg to be used as required. They were asked to complete their pain measures at 24 h and record their analgesic consumption. **Results:** There were no significant differences among the study groups regarding pain scores, haemodynamic changes, the first analgesic requirement time and complications. All patients in our study had adequate postoperative analgesia without any severe complication. **Conclusion:** Intra-articular administration of neostigmine, tramadol, tenoxicam or bupivacaine is a simple and effective postoperative analgesic technique after outpatient arthroscopic knee procedures.

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Keywords: Postoperative analgesia; Arthroscopy; Neostigmine; Bupivacaine

1. Introduction

Arthroscopic surgery of the knee is a common day case procedure. The recent growth in day surgery has presented new challenges in the field of postoperative pain management. Difficulties in adapting common methods of acute postoperative pain management in hospitalized patients to outpatients has resulted in inadequate treatment of pain following day surgery. The search continues for an ideal analgesic technique that is site specific, long-lasting, easily administered and has a high therapeutic safety index [1].

Satisfactory analgesia after arthroscopic knee surgery can be provided with intra-articular bupivacaine, but relief may last for only a few hours [2]. Non steroidal antiinflammatory drugs have been documented to be effective in the treatment of postoperative pain [3,4].

Spinal or epidural administration of the acetylcholine esterase-inhibitor neostigmine results in a dose-dependant analgesia. This central delivery of neostigmine is limited by dose-related side effects such as nausea, vomiting and pruritis caused by cephalad spread of neostigmine in the cerebrospinal fluid [5].

Tramadol not only interacts with opioid μ receptors, but also inhibits the withdrawal of noradrenaline and serotonin in the central nervous system [6].

This study was designed to compare the analgesic effects and complications of intra-articular neostigmine, tramadol, tenoxicam or bupivacaine on postoperative pain in day case knee arthroscopy.

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2. Material and method

After Faculty Ethics Committee approval and informed patient consent were obtained, 40 patients, classified as ASA I or II and scheduled for arthroscopic knee surgery were enrolled in this study. Exclusion criteria included age younger than 18 years or older than 60 years, use of analgesic within the last 24 h before the operation, relevant drug allergy, need for surgical debridement or synovectomy for postoperative intra-articular drainage.

No patients had premedication before the anaesthesia. Anaesthesia was induced with 0.1 mg fentanyl, 2 mg vecuronium, 5–7 mg/kg thiopental and 100 mg succinylcholine. For maintenance of the anaesthesia, 50% nitrous oxide in oxygen and 1–2% inspired sevoflurane were used. Additional opioid (0.1 mg fentanyl) was only given just before starting the operation.

Patients were prospectively studied and assigned in a randomized double-blinded manner to one of four treatment groups to evaluate postoperative analgesia.

Group 1 received 0.5 mg neostigmine, Group 2 received 100 mg tramadol, Group 3 received 20 mg tenoxicam, Group 4 received 20 ml 0.5% bupivacaine (control) intra-articularly. The study solutions were injected into the knee joint at the end of the surgery in 20 ml normal saline 10 min before tourniquet release.

The study patients were introduced to the visual analogue scale (VAS) before anaesthesia. For the VAS, the 100 mm scale included 0 as an indication of 'no pain at all' and 100 as an indication of 'the worst possible pain'. The test was performed at rest by a single interviewer, who was not aware of the study medication given.

Patients were observed in the recovery room with respect to haemodynamic changes and postoperative analgesia at 1, 2 and 4 h postoperatively. An observer blinded to the patient's group assignment obtained haemodynamic data (systolic and diastolic blood pressure, heart rate), VAS scores and also recorded the time at which the patient first requested pain medication. Analgesic therapy in the recovery room was managed with 25 mg bolus doses of meperidine when the patients had VAS scores above three points. The presence of nausea, vomiting, hypotension, bradycardia and sedation were also recorded for each patient in the recovery room. Patients satisfaction about the analgesic drugs was measured using a 0–4 grade scale, 0, bad; 1, mild; 2, good; 3, very good; 4, excellent.

Patients were discharged from the hospital with a prescription for diclofenac 75 mg to be used as required and they were asked to complete their pain measures at the 24 h and record their analgesic consumption. Each patient was interviewed by telephone at 24 h postoperatively.

2.1. Statistical analysis

Kruskal–Wallis test was used to compare haemodynamic changes, pain scores and the time to first analgesic requirement. A χ^2 analysis was used for comparison of categorized data such as hypotension and bradycardia. Results are shown as mean \pm S.E.M. A *P*-value of <0.05 was considered to be statistically significant.

3. Results

As shown in Table 1, there were no significant differences among the study groups regarding demographic data including age, gender and the duration of anaesthesia and surgery. The VAS scores at 1, 2, 4 and 24 h postoperatively for the four groups are shown in Fig. 1. There were no statistical differences among the groups regarding postoperative VAS scores at all times. The time to first analgesic requirement was the shortest in the tenoxicam group (6.77 ± 4.91 , 7.40 ± 5.91 , 4.30 ± 4.9 , 7.0 ± 5.49 , respectively). This difference was not statistically significant. The total analgesic consumption during the first 24 h period was similar among the groups (1.77 ± 1.48 , 1.80 ± 0.63 , 2.20 ± 2.0 , 1.60 ± 0.69 , respectively). No significant differences were found when we assessed haemodynamic changes 1, 2, 4 h postoperatively ($P > 0.05$) (Figs. 2–4).

When we assessed postoperative complications, the highest incidence of nausea was observed in the tramadol group. Hypotension was only noted in the tramadol group. We did not record any bradycardia. Sedation was observed in two patients in the neostigmine group, in one patient in the tenoxicam group and in one patient in the bupivacaine group.

When patient satisfaction about the analgesic methods used was compared, no significant differences were found among the groups ($P > 0.05$).

4. Discussion

Knee arthroscopy is one of the most common day case procedures and many studies focused on intra-articular local anaesthetics and opioids have been done to investigate the optimal postoperative analgesia for this procedure [1,2,7–9].

Optimal postoperative pain control for ambulatory surgery should provide complete analgesia of long duration with minimal side effects, facilitate recovery and preferably should have a local site of action [10].

We assessed the effectiveness of intra-articular solutions of neostigmine, tramadol and tenoxicam compared with bupivacaine and we also compared our results with the other investigations. In the present study, we

Table 1
Demographic data

	Neostigmine	Tramadol	Tenoxicam	Bupivacaine
Age (years)	43.50 ± 12	39.50 ± 14.93	41.9 ± 11.11	43.00 ± 12.44
Gender (M/F)	4/6	5/5	3/7	2/8
The duration of surgery	50.00 ± 20.27	45.00 ± 16.32	43.50 ± 10.28	53.00 ± 14.56
The duration of anaesthesia	64.60 ± 19.44	70.00 ± 15.45	54.50 ± 7.97	66.00 ± 16.29

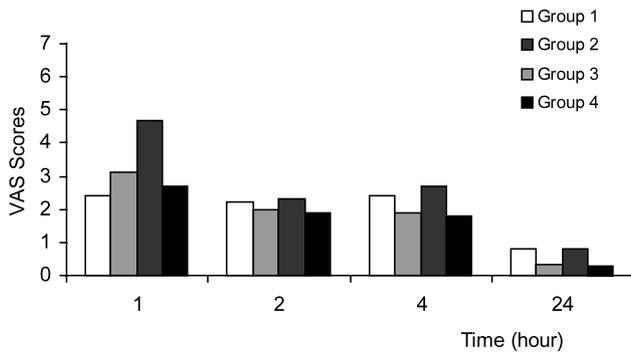


Fig. 1. The changes of VAS scores.

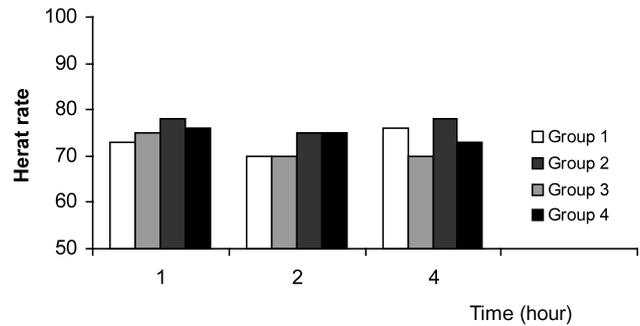


Fig. 4. The changes of heart rate.

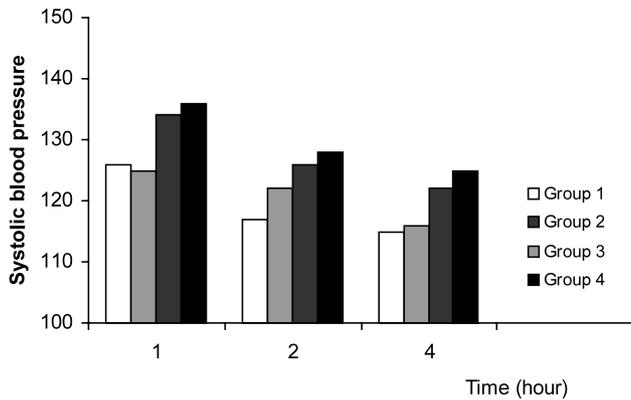


Fig. 2. The changes of systolic blood pressure.

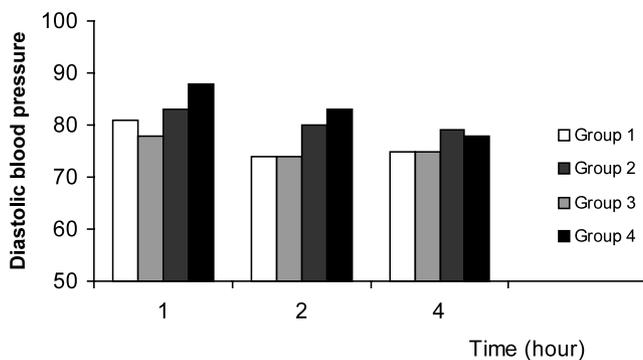


Fig. 3. The changes of diastolic blood pressure.

achieved an effective analgesia in all treatment groups without any severe side effect.

Recently new interest has focused on cholinergic systems that modulate pain perception and transmission. The analgesic effects of neostigmine are more likely to be related to muscarinic than to nicotinic receptor stimulation [5,11].

Lin-Cheng et al. studied different doses of intra-articular neostigmine and morphine in patients undergoing knee arthroscopy and they showed that intra-articular injection of neostigmine produced a moderate but significant analgesic effect [5].

A study of intra-articular non-steroidal anti-inflammatory drugs revealed an analgesic effect equivalent to that of intra-articular local anaesthetic agents and morphine [12]. Elhakim et al. compared tenoxicam 20 mg both intra-articularly and intra-venously with saline [4]. They concluded that intra-articular tenoxicam 20 mg provided better analgesia and decreased the requirements of postoperative analgesic compared with intra-venous tenoxicam 20 mg. In the study which was performed by Colbert et al., intra-articular tenoxicam was found superior to the intra-venous route [3].

Cook et al. compared intra-articular tenoxicam 20 mg with 0.25% bupivacaine and saline. They concluded that there were no differences between pain scores in any of the three groups and less analgesic was used in the first 24 h in the tenoxicam group [12]. Although we reached the highest VAS scores and the most postoperative analgesic consumption in the tenoxicam group, this difference was not significant. We reached adequate analgesia in the tenoxicam group as well as the other groups.

Opiate receptors and endogenous opiates have been demonstrated in brain and spinal cord and also in peripheral nerves and the dorsal root ganglia [1]. Opioids administered intra-articularly produce conflicting data with respect to their analgesic efficacy. Some reports showed intra-articular opioids to be ineffective [13]; others reported a significant positive effect on postoperative analgesia [14].

Antinociceptive effects of opioids have been attributed primarily to an activation of receptors located in the central nervous system. However, animal studies revealed the existence of peripheral opioid binding sites, which appear to become especially active in the presence of inflammation [15]. These first observations were later confirmed in human clinical trials [16].

Haynes et al. observed that the addition of bupivacaine to morphine was of no benefit [9]. Pooni et al. compared intra-articular fentanyl with bupivacaine for postoperative pain relief after knee arthroscopy. The results showed that intra-articular bupivacaine produced superior analgesia in the immediate postoperative period [2]. We observed the lowest VAS scores in the bupivacaine group at all times except at 1 h.

We conclude that the intra-articular administration of neostigmine, tramadol, tenoxicam and bupivacaine after day case arthroscopic knee procedures is a simple, effective, safe and well-tolerated analgesic technique, offering superior postoperative pain control.

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