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Optimizing the dose of local infiltration analgesia and gabapentin for total knee arthroplasty, a randomized single blind trial in 128 patients☆

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ABSTRACT

Background and purpose: Effective analgesia is essential for postoperative recovery and rehabilitation in TKA. The challenge of analgesic regimes is to obtain adequate pain relief and maximum muscle control to mobilize and rehabilitate patients early. However, the optimal dose and best composition are not known. We hypothesized that there would be no differences in reported postoperative pain on the day of the TKA surgery as well as the first day after surgery when different combinations of ropivacain for LIA and gabapentin are given.

Methods: This prospective randomized trial examined 128 TKA patients treated with LIA and gabapentin in four groups. Group A: 300-mg ropivacain/600-300-300-mg gabapentin. Group B: 150-mg ropivacain/600-300-300-mg gabapentin. Group C: 300-mg ropivacain/300-100-100-mg gabapentin. Group D: 150-mg ropivacain/300-100-100-mg gabapentin.
Primary endpoint was pain (NRS) at multiple moments. Secondary endpoints were number of adverse effects, length of hospital stay (LOS), the amount of consumption of pain medication, and wound leakage. Generalized estimating equation (GEE) was used to detect differences between the four groups regarding the course of pain.

Results: No differences regarding adverse effects, LOS, and wound leakage were found. GEE revealed a significant difference in course of pain between group A and B, with group B experiencing higher NRS scores postoperatively than group A ($p = 0.021$). No differences between the other groups were found.

Interpretation: The results of the current study suggest that LIA with 300-mg (150 ml) ropivacain might be more effective than 150-mg (75 ml) ropivacain. Alteration in dose of gabapentin appears not to have influence on the course of pain.

1. Introduction

1.1. Purpose and hypothesis

Total knee arthroplasty (TKA) is associated with moderate to severe postoperative pain [1,2]. Almost all pain after surgery arises as a result of tissue damage at the surgical site and hinders early mobilization and rehabilitation [3,4]. The challenge of an-

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algesic regimes is to obtain adequate pain relief and maximum muscle control to enable the patient to mobilize and rehabilitate early without troublesome side effects [1]. Local Infiltration Analgesia (LIA) is widely thought to be effective and is based on infiltration of local anesthetics in the tissues around the surgical field to achieve satisfactory pain control with little side effects. LIA is frequently applied as part of a multimodal pain strategy due to its simplicity and apparent safety in multiple types of surgery [4,5]. Infiltration of a local anesthetic has been reported to be effective in TKA; however, the optimal dose and best composition in perioperative consummated pain medication are not known [3,5]. In addition to LIA, gabapentin is often used as part of the multimodal pain protocol in TKA. Gabapentin has several possible side effects, such as postoperative nausea and vomiting (PONV) [6–12].

The goal of this prospective randomized clinical trial was to optimize both the dose of local anesthetic for infiltration during surgery and gabapentin as part of our multimodal pain strategy in TKA. We hypothesized there would be no differences in reported postoperative pain on the day of the TKA-surgery as well as the first day after surgery when different combinations of ropivacain for LIA and gabapentin are given.

1.2. Material and methods

In this prospective, randomized, single blind trial, we consecutively included patients with osteoarthritis of the knee, who were scheduled for primary TKA between September 2013 and May 2015 in Reinier de Graaf Hospital (Delft, The Netherlands). The operations were performed by six orthopedic surgeons. Patients were American Society of Anestesiologists (ASA) I–III, were willing to participate, and were not participating in another study. Excluded were patients who were mentally ill, patients with moderate or severe cardiac or pulmonary disease, patients with known allergies against used medication, patients with a body mass index (BMI) >40, alcohol or drugs abusers, chronic opioids users, and patients diagnosed with rheumatoid arthritis. The study was approved by the local Medical Ethics Committee (NL40222.098.12, METC 12-049) and registered in EudraCT (2012-001432-62). Written informed consent was obtained from all included patients.

Patients were randomized into four groups with different doses of locally applied infiltration analgesic and different doses of oral gabapentin before and after surgery (Table 1). Randomization was performed by the hospital pharmacy prior to the study, using stratified blocks of 16 patients. The infiltration consisted of ropivacain and adrenalin in a ratio of 99:1. Both the orthopedic surgeon and patient were blinded for the dose of ropivacain/epinephrine administered during local infiltration. However, gabapentin dosage could not be given fully double blinded. After opening of the package the dosage could be deduced from the appearance and color of dosage form: white capsules (100 mg), yellow capsules (300 mg), or white tablets (600 mg). Every patient received one of these dosage forms according to randomization and dosing time.

All patients were admitted at the day of surgery. At admission, participants received 400-mg celecoxib, one gram of paracetamol and 600 mg or 300 mg of gabapentin according to their randomization. During surgery infiltration of 150 or 300-mg ropivacain was performed by the 'moving needle technique' described by Kerr & Kohan [4,13]. All patients received spinal anesthesia with a low dose of bupivacain (six to nine milligrams). Propofol was administered for sedation with a level of sedation target of one to two. No tourniquet was used during surgery and no drains were used postoperatively. All patients received 1000-mg tranexamic acid intravenously before surgery. The postoperative protocol for pain medication was standardized and consisted of paracetamol and celecoxib in addition to gabapentin. Rescue medication consisted of celecoxib 200 mg after the first night and/or oxynorm 10 mg if necessary, which could be repeated every four hours. Postoperative physiotherapy was performed two times daily, starting four to six hours after surgery, focusing on regaining function, motion, and gait. All patients received the same regimen. The discharge criteria for the patient were functional: the ability to walk 50 m with crutches, to climb stairs if necessary, to get dressed and go to the restroom independently. In addition, adequate pain relieve had to be achieved by oral pain medication before discharge. Numeric Rating Scale (NRS) had to be three or less in rest and five or less during mobilization. Wound leakage had to be minimal.

Primary endpoint of this study was pain, measured with NRS for pain, at multiple moments: one, four and eight hours after operation and in the morning and afternoon at the first day after surgery. Four hours after surgery we expected the influence of LIA to be the greatest [2,14]. Secondary endpoints were number of adverse effects, length of hospital stay (LOS) measured by number of nights, the amount of postoperative consumption of (rescue) pain medication, and wound leakage.

Trained nurses and physiotherapists, who were blinded for the group in which the patient was randomized, scored the NRS for pain and the amount of postoperative consumption of pain medication. Also wound leakage was scored daily by using a five point scale (from no leakage to severe leakage) as well as the intensity and frequency of nausea and vomiting, dizziness, and sedation

Table 1
The four randomized groups.

Group	Ropivacain	Gabapentin pre/8 h/post
A	300 mg[a]	600/300/300 mg
B	150 mg[b]	600/300/300 mg
C	300 mg	300/100/100 mg
D	150 mg	300/100/100 mg

[a] Infiltration with 150 ml ropivacain/epinephrine (2 mg/ml ropivacain / 1,5 ml epinephrine 1 mg/ml).
[b] Infiltration with 75 ml ropivacain/epinephrine (2 mg/ml ropivacain / 1,5 ml epinephrine 1 mg/ml) + 75 ml NaCl 0,9%.

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