

# Effect on Postoperative Analgesia of Ketoprofen added to Lidocaine during Intravenous Regional Anaesthesia

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## Abstract

**Aim:** Intravenous regional anaesthesia (IVRA) is a safe, effective technique for surgery on the upper extremities, but it provides no postoperative analgesia. The aim of this study was to evaluate the analgesic efficacy of small dose of ketoprofen with IVRA induced by lidocaine.

**Methods:** Forty eight patients undergoing ambulatory hand surgery were randomly assigned to one of three groups: They received 40 mL of 0.5% lidocaine and either 1 mL of isotonic saline (group Control, n = 16) or 50 mg Ketoprofen (group K50, n = 16) or 100 mg Ketoprofen (group K100, n = 16). Visual analogue scale was recorded for 2 h postoperatively. Postoperative pain was treated with morphine in post anaesthesia care unit (PACU) and oral acetaminophen at home.

**Keywords:** Intravenous regional block ; Lidocaine ; Ketoprofen.

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**Results:** The sensory recovery time was longer in the group K100 compared to control group ( $p < 0.01$ ). There was a statistically significant lower VAS in group K100 compared to control group, but not between group K50 and control group or group K50 and group K100. The K100 group needed significantly less morphine in the PACU when compared with control group or K50 group. Postoperative analgesic consumption (acetaminophen) was statistically lower during the first 24 h in group K100 compared to others groups.

**Conclusion:** The addition of 100 mg ketoprofen but not 50 mg to lidocaine for IVRA in patients undergoing hand surgery improves postoperative analgesia during the first postoperative day.

## Introduction

Intravenous regional anaesthesia (IVRA) is a safe and effective way to provide anaesthesia for hand surgery [1]. One the limitation of this technique compared to peripheral nerve is limited by the rapid offset of analgesia. Various analgesics including opioids and alpha2-agonists drugs have been administered with the local anaesthetic in IVRA, but only nonsteroidal anti-inflammatory drugs (NSAID) have shown benefits [2–4]. Multiple studies have investigated various NSAIDs as the sole adjunct to IVRA. The agents investigated were ketorolac [5,6] tenoxicam [7,8] and aspirin [9]. Ketorolac 20mg added to lidocaine provides effective postoperative analgesia after ambulatory hand surgery [10]. Ketoprofen is a NSAID commonly used in its parenteral form to provide peri-operative analgesia but it has never been added to lidocaine for IVRA. It is a widely used analgesic in many countries and has a good safety and efficacy record [11,12]. The usual recommended parenteral dose was 100 mg. We hypothesized that the addition of small dose of ketoprofen to lidocaine for use in IVRA might improve postoperative analgesia.

## Patients and methods

Informed consent was obtained from each patient and the study was approved by the local ethics committee. Forty eight patients, ASA physical status I, undergoing ambulatory surgery of the hand were studied prospectively in this trial. Standard monitors including continuous electrocardiography, noninvasive blood pressure measurement, and pulse oximetry were used. An intravenous catheter (20 gauge) was inserted into a distal vein on the dorsum of the hand of the operative extremity for injection of local anaesthetic solution. An additional intravenous catheter was placed in the contralateral upper extremity for crystalloid infusion.

A double-cuffed tourniquet was placed on the upper operative arm. The affected extremity was exsanguinated by elevating it and wrapping it with an Esmarch bandage. The proximal cuff was inflated to 250 mmHg and the Esmarch bandage was removed. IVRA was established in all patients using 40 mL of a solution of lidocaine 0,5%. The patients were randomly assigned to one of the following three double-blind groups.

- 1) K50-IVRA group received 50 mg of ketoprofen in 1 mL added to the lidocaine after inflation of the tourniquet;
- 2) K100-IVRA group received 100 mg of ketoprofen in 1 mL added to the lidocaine after inflation of the tourniquet;
- 3) control group received 1 mL of isotonic saline added to the lidocaine after inflation of the tourniquet.

After surgery, an anesthesiologist unaware of study-group assignment assessed the patients' pain levels 30 min, 60min, 90 min and 120 min after tourniquet deflation. Pain was assessed using a visual analogue pain scale (VAS), with 0 representing no pain and 10 representing the worst imaginable pain. Intravenous boluses of 2 mg morphine were provided in the postanesthesia care unit (PACU) whenever the visual analogue pain scale exceeded 3. The total number of morphine doses was noted.

Sensory recovery time, defined as "Time elapsed after tourniquet deflation up to recovery of pain in all dermatome determined by pinprick test", was recorded. Quantification of analgesic consumption was recorded and included the total amount administered during the first 24 h after surgery. Analgesics administered at home consisted of oral acetaminophen.

Data are expressed as mean as mean  $\pm$  SD. Demographic data, operative and tourniquet times were analyzed using analyse of variance. Sex, type of surgery were analysed with a chi-square

test. VAS scores and analgesic requirements were analysed using the Kruskal-Wallis non-parametric test. P-values < 0.05 were considered as being statistically significant.

## Results

There were no significant differences between the three groups with respect to patient age, sex, tourniquet time, the distribution of surgical procedures or the duration of the operation (Table 1).

Anesthesia was successful in all cases. There was no statistical difference between groups compared for mean arterial blood

**Table 1** Patient demographics and surgical data.

Group	Control (n=16)	K50 (n=16)	K100 (n=16)
Age (yr)	31±10	32±16	34±11
Weight (Kg)	66±8	67±13	67±9
Duration of surgery (min)	63±21	61±24	60±26
Tourniquet time (min)	70±19	68±20	67±22
Sensory recovery time (min)	12±7	16±14	24±18 §
Type of procedures (n)			
- bone	3	6	5
- muscle	13	10	11

Data are presented as mean ±SD § p < 0.01 between groups control and K100  
K50: intravenous regional anesthesia with 50 mg of ketoprofen  
K100: intravenous regional anesthesia with 100 mg of ketoprofen

pressure, heart rate and SpO<sub>2</sub> at any intraoperative or postoperative time. The sensory recovery time was longer in the group K100 compared to control group (p < 0.01). There was a difference between groups in postoperative VAS scores after tourniquet release at 30, 60, 90 and 120 min. Specifically, group K100 had statistically significant lower VAS scores compared to control group, but there were no differences between group K50 and control group or group K50 and group K100 (Fig 1). The K100 group needed significantly less morphine in the PACU when compared with control group or K50 group. Postoperative analgesic consumption (acetaminophen) was statistically lower during the first 24 h in group K100 compared to other groups (Table 2).

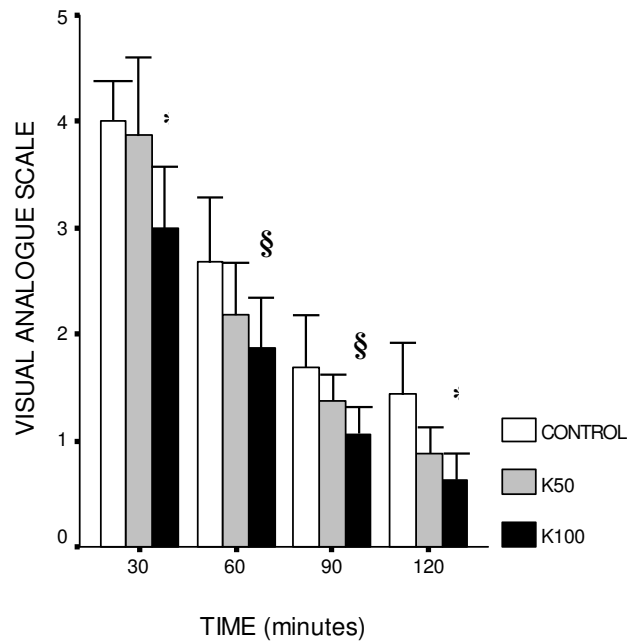
No postoperative complications were observed including wound

**Table 2** Postoperative Analgesic Requirements.

Group	Control (n=16)	K50 (n=16)	K100 (n=16)
Morphine in PACU (mg)	5.4±1.3	4.3±1.7§	3.1±1.1*
24 h total acetaminophen (mg)	2000±683	1625±341§	1542 ± 406*

Values are mean ± SD § p < 0.05 between group control and K50  
\*p < 0.01 between group control and K100

bleeding.



**Figure 1** Visual Analogue Scale scores in the postoperative period. Data are presented as mean ± SD. § p < 0.05 between group control and K100 \*p < 0.01 between group control and K100.

## Discussion

Our study demonstrated that the addition of ketoprofen to lidocaine for IVRA improved the quality of postoperative analgesia without side effects.

Among the numerous studies that have investigated NSAID as the sole adjunct to IVRA, the most popular used was ketorolac [5,6,10]. In one study of IVRA with lidocaine 0,5%, ketorolac 60 mg as a component of IVRA was compared with systemic administration of ketorolac in patients following elective hand surgery. In this study, patients with ketorolac in IVRA had less pain during the first postoperative hour, required no supplemental analgesia in the PACU and consumed fewer analgesics during the first postoperative day [5]. In a similar study using a small dose of lysine acetyl salicylate (LAS) added to prilocaine for foot and ankle surgery, Corpataux et al. showed that pain scores were significantly lower in LAS-IVRA group during the first 3 postoperative hours compared with placebo [9]. Hoffman showed that tenoxicam, a long acting NSAID, improved the postoperative pain scores but only during the first 30 min after the release of the tourniquet [8]. In contrast Jones and Pugh observed a significant lower analgesia requirement during the first 24 hours when tenoxicam had been administered [7].

Ketoprofen is a NSAID with a short half-life (two hours) commonly used in its parenteral form to provide postoperative analgesia in many types of surgery [13,14]. The recommended dose usually used systemically is 100mg [11]. By concentrating ketoprofen at the surgical site, we hypothesized that a smaller dose of 50mg can provide optimal postoperative analgesia. It has been shown in systematic review that there is a relationship between the dose of NSAID and its analgesic effect [15].

Steinberg et al. found that 20mg of ketorolac is equally effective as 60mg in IVRA. A linear dose-response relationship was showed between the dose of ketorolac used and the duration of analgesia [10]. For tenoxicam and lysine acetylsalicylate, the dose response studies have not been performed so the ideal dose remains unknown. Kostawana et al. found that ketorolac 30mg was equally efficacious as diclofenac 75mg and ketoprofen 100mg for the treatment of postoperative pain after hip replacement surgery [16]. In our study

the dose of ketoprofen 100mg was more effective than ketoprofen 50 mg. Perhaps larger IVRA ketoprofen doses might have provided more prolonged analgesia than we observed. However, we chose to use a ketoprofen dose of 100mg based on previous studies.

Postoperative pain scores were significantly improved in IVRA ketoprofen 100 mg group compared with the control group. The 24h consumption of supplementary analgesics was significantly reduced in the IVRA ketoprofen 100 mg group compared with the control group. In fact, we considered the use of a systemic administration group to be unnecessary as the local effect of NSAID used as component of IVRA had been demonstrated in previous studies [17], but we cannot totally exclude a systemic effect of ketoprofen. A possible redistribution of residual ketoprofen from the operative arm to the systemic circulation after tourniquet deflation could explain the prolonged postoperative analgesia and less analgesic requirement.

Several studies have demonstrated an enhanced analgesic effect from NSAID when concentrated at a peripheral site compared to the systemic administration of the same drug. Studies suggest a predominantly peripheral site of action [18,19]. NSAIDs inhibit the production of arachidonic acid metabolites such as prostaglandins and thromboxanes that mediate the inflammatory process. Surgical trauma leads to the sensitization of peripheral nociceptors to the analgesic action of allogenic substances. NSAIDs alter peripheral nociceptors by reducing the local concentration of these agents such as bradykinin and histamine and lead to a reduction in postoperative pain.

There is evidence for a clinically relevant peripheral analgesic action of intra-articular NSAID, while results of IVRA with NSAID in postoperative pain were inconclusive [17]. The analgesic effect of NSAID appears to be mediated peripherally and not the result of central redistribution. Many studies suggest that the risk of bleeding varies among NSAIDs. In one tonsillectomy study, ketorolac was associated with a higher incidence of bleeding than ketoprofen [20]. In our work, there was no case of excessive bleeding in the ketoprofen groups during the postoperative period.

To our knowledge, this is the first clinical study using ketoprofen as a component of IVRA. However, interpretation of the data in this study must consider several limitations related to the absence of systemic administration group.

In conclusion the addition of 100 mg of ketoprofen but not 50 mg to lidocaine 0,5% for IVRA improved analgesia in the PACU during the first 2h after operation and diminished the need for analgesia supplements during the first 24 h after operation, without causing excessive bleeding.

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