

Research Article

Analgesic Efficacy of Morphine Versus Concurrent Use of Ketorolac and Acetaminophen In Mandibular Bone Surgery

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ABSTRACT

Background: Pain, a major issue in medical treatment, is one of the major concerns for both the clinician and the patient. Postoperative acute pain management during the initial hours is very important and can prevent side effects. Analgesics (acetaminophen, opioids) and non-steroidal anti-inflammatory drugs are used as medications for pain control.

Objective: This study was performed to compare the analgesic efficacy of morphine versus the concurrent use of ketorolac and intravenous acetaminophen after mandibular bone surgery.

Materials and Methods: In this prospective, single-centered, randomized, double-blind clinical trial study, a total of 60 patients referred to Imam Reza Hospital in 2015 for mandibular bone surgery were randomized post-surgery into two groups: In group 1, acetaminophen (1 g in 100 cc normal saline solution) and ketorolac (30 mg in 100 cc normal saline solution) were infused every 6 hours. In group 2, morphine sulfate (0.1 mg/kg in 100 cc normal saline solution) was infused every 4 hours. The pain level was recorded on the visual analogue scale (VAS) at 1, 2, 4, 6, 12, and 24 hours after surgery.

Results: Significant differences were found between the two groups in most hours. The mean pain level according to the VAS in group 1 and group 2 were 6.87 ± 2.43 vs. 7.20 ± 2.06 ($p = 0.560$) for the 1st hour post operation, 5.80 ± 2.76 vs. 4.03 ± 2.25 ($p = 0.008$) for the 2nd hour post operation, 5.03 ± 3.01 vs. 3.10 ± 2.11 ($p = 0.005$) for the 4th hour post operation, 3.37 ± 3.03 vs. 1.77 ± 1.92 ($p = 0.017$) for the 6th hour post operation, 2.10 ± 2.44 vs. 0.73 ± 1.28 ($p = 0.008$) for the 12th hour post operation and 1.30 ± 1.91 vs. 0.60 ± 1.28 ($p = 0.101$) for the 24th hour post operation. No significant difference was observed in the 1st and 24th hour post-operation. Nausea was seen in the groups as one of the side effects with no significant difference.

Conclusion: Morphine showed better efficiency in pain control than the concurrent use of ketorolac and intravenous acetaminophen.

Key-words: Ketorolac, Acetaminophen, Morphine, Pain, Postoperative, Mandibular Bone Surgery.

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INTRODUCTION

The fear of inadequate pain control after surgery is one of the biggest concerns of the patients. Acute pain occurs after painful stimuli like trauma or surgery, especially in the absence of proper treatment. This stimulus often causes systemic responses with potential side effects that compromise clinical results (1, 2). Insufficient pain control can result in complications like delayed wound healing, infection, long period of hospitalization, and peripheral and central sensitization that can lead to persistent post-operative pain (3-5). So In all surgical procedures, the post-operative pain management is an important part of post-operative care (6, 7).

In recent years, significant progress has been made in understanding the pain process and the development of analgesic agents and the associated techniques. However, in most of the cases, the pain control after surgery has not been successful (5, 8).

According to a previous report (9), 93% of patients undergoing oral and maxillofacial operations experience postoperative pain, and almost 34% of these patients experience severe pain.

Nowadays, surgeons commonly use potent opioids, especially morphine, as a drug of choice for post-operative pain control (5, 10, 11). These opioids have prolonged analgesic effect and offer reduced costs for patients. However, they are also associated with complications, such as reduced consciousness level, respiratory depression, nausea and vomiting, constipation, itching, prolonged period of hospitalization, inadequate pain control, and tendency to overdose.

Recent studies have shown that non-steroidal anti-inflammatory drugs (NSAIDs) and acetaminophen compounds are effective alternatives of opioids for pain control and improve patient compliance. Acetaminophen has been reported to have a proper suppressive effect on peripheral and central pain systems despite its low anti-inflammatory and anti-fever effects (2, 8, 12, 13).

Previous studies have mostly investigated the efficacy of traditional non-selective NSAIDs, including diclofenac, ibuprofen and ketorolac, for cox_2 inhibition.

Ketorolac is a non-steroidal agent with analgesic and anti-inflammatory effects. It is administered as its tromethamine salt orally, intramuscularly, intravenously and as a topical ophthalmic solution. Clinical studies have indicated that a single-dose of ketorolac has a greater efficacy in controlling moderate to severe post-operative pain compared to morphine, pethidine (meperidine) and pentazocine (2, 13, 14).

Studies have proved that the combination of acetaminophen and NSAIDs has greater analgesic effects than their individual administration (15). Thus, considering the possible side effects of opioids, a combination of intravenous acetaminophen and NSAIDs can be a good treatment alternative for reducing pain.

According to authors, all pain control strategies must be explained to patients undergoing oral and maxillofacial surgery.

The aim of the present study was to compare the effects of morphine and concurrent use of ketorolac and intravenous acetaminophen in treating acute post-operative pain.

MATERIALS AND METHODS

This prospective, single-centered, randomized, double-blind, clinical trial study considered 60 patients who were referred to the Imam Reza Hospital (general governmental hospital affiliated to Tabriz University of medical science, Tabriz, Iran) in 2015 for mandibular bone surgery.

Inclusion and exclusion criteria:

Inclusion criteria: The patients, aged 18 to 50 years, referred to the Oral and Maxillofacial Department of the institution for open mandibular bone surgery with Champy's fixation technique, having no systemic problems or previous surgeries on other organs were included in this study.

Exclusion criteria: The exclusion criteria are as follows: 1) history of drug allergy to acetaminophen, ketorolac or morphine; 2) history of alcohol or drug abuse; 3) mental disorders; 4) surgery of more than 2 hours; 5) consumption of monoamine oxidase inhibitors (MAO) inhibitors; 6) psychopathic patients; 7) surgery on other parts of the head, face or jaws; and 8) patients who need or claim more analgesics.

Protocol:

A day before the surgery, the patients were trained how to explain their pain using the visual analogue scale (VAS).

VAS is a valid scale to evaluate pain severity rating from 0 to 10, where 0 means there is no pain and 10 means most severe pain (3).

All the patients received 8 mg dexamethasone and 1 g cefazoline before the surgery. For better hemostasis, 5 ml of lidocaine (2%), and epinephrine (1/100000) were injected into the site of surgery.

All patients underwent general anesthesia with the same drugs and followed the same protocol. Surgery was done by the same surgeon for all patients.

After surgery, the patients were divided into two groups by simple randomization. The randomization table was prepared by one of the resident doctors blinded to the study.

The first dose of injection was administered 30 minutes after the surgery by one of the nurses who were blinded to the study.

In group 1, acetaminophen (1 g in 100 cc normal saline solution) and ketorolac (30 mg in 100 cc normal saline solution) were infused every 6 hours.

In group 2, morphine sulfate (0.1 mg/kg in 100 cc normal saline solution) was infused every 4 hours.

The patients were examined at 1, 2, 4, 6, 12 and 24 hours after injection of the first dose, and their pain levels were recorded on the VAS scale by another resident doctor who is blind to the study. Variables including age, sex, weight, duration of surgery and side effects (nausea and vomiting, vertigo, headache, dizziness) were also recorded for each patient.

Ethical issue:

This study was approved by the Legal and Ethics Committee of the Tabriz University of Medical Science, and written informed consents were obtained from all the patients. This study was registered at the Iranian registered clinical trial site (ID: IRCT138810173018N1).

Statistical analysis

The obtained data was analyzed by using the SPSS statistical software version 20 (SPSS Inc., Chicago, and IL., USA). Variables of age, sex, weight, duration of surgery were compared between the groups by independent sample t-test and chi-square test. Pain measurements according to VAS were analyzed by repeated measurements test and then t-test. Post-operative side effects were also described by frequency and percentage and were compared by chi-square test. In this study, the P-value was found to be less than 0.05 (P<0.05) and was considered statistically significant.

RESULTS

All patients completed the test, and no one claimed extra analgesics. Of 60 patients, 31 received both acetaminophen and ketorolac (group 1) and 29 patients received morphine sulfate (group 2). Variables of age, sex, weight and duration of surgery were described in Table 1, and no significant difference was observed between them. (p>0.05)

Table 1: Demographic data of the patients (n=60)

Characteristics	Group 1	Group 2
Number of patients	31	29
Age (years)	34.2±14.2	33.4±15.1
Sex		
Male	22(70.9%)	20(68.9%)
Female	9(29%)	9(31%)
Weight (kg)	72.2±11	70.5±12.5
Duration of surgery (hours)	1.3±0.22	1.18±0.16

The pain score was significantly different between the groups except in the first and 24th hour. Pain level was decreased in a time-dependent manner in both the groups. (Table 2)

We had six patients with nausea and vomiting in group 1, and 10 patients in group 2 who experienced more nausea and vomiting but the difference was not significant ($p=0.18$). No other side effects were seen.

Table 2: Comparison of pain scores between the groups.

	Groups	Mean \pm SD	P value
Hour 1	Group 1	6.87 \pm 2.43	0.560
	Group 2	7.20 \pm 2.06	
Hour 2	Group 1	5.80 \pm 2.76	0.008
	Group 2	4.03 \pm 2.25	
Hour 4	Group 1	5.03 \pm 3.01	0.005
	Group 2	3.10 \pm 2.11	
Hour 6	Group 1	3.37 \pm 3.03	0.017
	Group 2	1.77 \pm 1.92	
Hour 12	Group 1	2.10 \pm 2.44	0.008
	Group 2	0.73 \pm 1.28	
Hour 24	Group 1	1.30 \pm 1.91	0.101
	Group 2	0.60 \pm 1.28	

DISCUSSION

In this study, we compared the analgesic efficacy of morphine versus the concurrent use of intravenous acetaminophen and ketorolac in hospitalized patients post surgery. This is the first study to use ketorolac and acetaminophen in combination to evaluate its analgesic effects.

However, the analgesics, such as opioids and acetaminophen and NSAIDs have been previously used for postoperative pain management. Therefore, a combination therapy proves to be more effective than a single therapy (7). The medical routes of administration include oral, intravenous, intramuscular, subcutaneous, rectal, transdermal, intrathecal, and epidural analgesics (5, 11). Although oral medications are successful in pain control, most hospitalized patients with acute pain require intravenous analgesics (16-18).

We observed that the combined administration of intravenous acetaminophen and ketorolac was not as effective as morphine and had less analgesic effects, but an exception was observed in the 1st and 24th hours post-surgery. The pain was found to be significantly lower for most hours in the morphine administered group although it was reduced in both the groups.

Serink et al. (19) conducted a comparative study including 133 patients with renal colic pain and observed higher effectiveness of intravenous paracetamol over morphine. In a recent study by Jalili et al. (20), paracetamol was administered in combination with morphine in limb trauma, and paracetamol was found to be more effective than morphine. Conversely, some studies stated that paracetamol is not a suitable analgesic agent for acute post-operative phase, especially in the first eight hours post-surgery (21, 22). However, in the present study morphine had a better efficacy in acute post-operative pain control.

Fayaz et al. (23) stated that combination of diclofenac and acetaminophen are effective for post operation pain reduction, which is consensus with our study findings.

In a study, Davis et al. (24) stated that using paracetamol significantly controlled post-operative pain, which is parallel to our findings.

In their study, Paulo et al. (25) stated that ketorolac effectively controlled inflammation and postoperative pain, which is also consistent with our findings in the acetaminophen and ketorolac group.

The limitation of our study is the subjective pain statements by the patient. Patients might have knowingly or unknowingly bias their responses based on their beliefs, expectations, or personal goals. This may lead to inaccuracy resulting from distortions in memory of the patients.

In conclusion, control of acute pain in post-operative phase is very important and according to the results of this study Morphine sulfate is a better choice in comparison to the concurrent use of acetaminophen and

ketorolac. However, complete pain control need further evaluation and in-depth studies to find out drug-related adverse effects.

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