Original Research

Does Venous Ketorolac Have An Effect On Pain Control After Upper Limb Orthopedic Surgery? A Double-Blind, Randomized Clinical Trial Study

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Abstract:

Background:

Postoperative pain is an unpleasant experience causing physiological disorders in all body systems. Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most widely used medications to control postoperative pain. Therefore, this study was conducted to evaluate the prophylactic effect of venous ketorolac in pain control after upper limb surgery in patients referred to Shahid Mohammadi Hospital in Bandar Abbas in 2020.

Methods:

In this double-blind randomized clinical trial study, 60 patients with anesthesia class I and II underwent upper limb orthopedic surgery. Patients were randomly divided into intravenous ketorolac and control groups. Systolic and diastolic blood pressure, mean arterial pressure, and heart rate before surgery, 1, 10, and 20 minutes after surgery were recorded. The pain was measured before, 6, 12, and 24 hours after surgery. Postoperative medication use was recorded in both groups. Data analysis was performed using SPSS software version 21 and descriptive and inferential statistical tests.

Results:

Ketorolac and control groups were similar in terms of gender, age, BMI, and ASA. Repeated measures analysis showed that the intragroup trend of systolic and diastolic blood pressure was significant in ketorolac and control groups ($P = 0.019$). At recovery and 6 and 12 hours after surgery, the pain was significantly lower in patients in the ketorolac group than in the control group ($P<0.05$); Also, the intragroup pain trend was significant in ketorolac and control groups ($P<0.05$). Mean pain in the ketorolac group decreased more than control ($P<0.001$)

Conclusion:

The results of the present study showed that venous ketorolac is more effective in controlling pain intensity than the control group. It seems that in orthopedic surgeries, upper limb ketorolac has a good effect on controlling postoperative pain.

Keywords: Ketorolac, Pain, Orthopedics, Upper Limb.

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Introduction

The use of techniques and drugs that have the least side effects and the most effective in terms of analgesia has always been the desire of researchers in this field (1). The results of studies have shown that orthopedic surgeries are often significantly associated with severe and prolonged postoperative pain and analgesia (2-3). Pain control is especially important in orthopedic patients. Undesirable pain control in patients can be associated with delayed movement and limited joint movements (4-6). Therefore, various drugs and methods have been used to reduce pain and, consequently, increase patient satisfaction and accelerate recovery after surgery (7-8). Drugs and NSAIDs are among the most widely used classes of drugs for pain control in the emergency room (9). Ketorolac is one of the most common analgesics used in the nonsteroidal anti-inflammatory group (10). This group has anti-inflammatory, antipyretic, and analgesic effects by inhibiting prostaglandin production through competitive blockade of cyclooxygenase enzyme (11). Ketorolac is a non-steroidal anti-inflammatory drug with analgesic properties; it inhibits both the enzymes lipoxygenase and cyclooxygenase. (12). Ketorolac is administered intravenously for moderate to severe pain at a dose of 30 mg and reaches its peak serum concentration within one to three minutes in intravenous form (11). Due to the need to control pain in orthopedic patients of the upper limb and also the lack of sufficient studies in this field, researchers decided to investigate the effects of this drug on pain control in orthopedic surgery of the upper limb.

Method

Study design:

The present study is a double-blind randomized clinical trial that was performed over two months from September 2020 to November 2020 in patients aged 18 to 70 years who had been referred to Shahid Mohammadi Hospital in Bandar Abbas for upper limb orthopedic surgery.

Ethical considerations:

Before entering the patients in this study, the research process was explained and informed consent was obtained from them. Throughout the study, researchers adhered to the principles of the Helsinki Declaration and the confidentiality of patient information. All costs of the project were covered by the researchers and no additional costs were incurred by the patients. This study has been approved by the ethics committee of Hormozgan University of Medical Sciences under the ethical code IR.HUMS.REC.1399.290.

Sampling:

The study population was patients undergoing upper limb orthopedic surgery. The sample size was obtained using the above formula and beta, considering X = 0.05 and 1-B = 0.9 in each group of 27 people, with a probability of loss in each group of 30 people was considered. Then, to have an equal chance of being in the intervention group or control group, the samples were randomly assigned to the study groups (30 Patients in each group) using a random number table. Subjects were randomly divided into two groups of intravenous ketorolac and control based on the inclusion and non-exclusion criteria. Sampling was performed to achieve agreement between the two groups in terms of basic characteristics.

Inclusion criteria:

All patients aged 18 to 70 years and class I and ASA II are candidates for upper limb surgery in Shahid Mohammadi Hospital.

Exclusion criteria:

Patients with a history of asthma, gastrointestinal bleeding, allergic rhinitis, renal failure, liver failure, and history of ketorolac allergy

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Intervention:

After signing a written consent to participate in the study, patients were treated equally (30 subjects in each group) using the Block Randomization method based on inclusion and exclusion criteria. All patients underwent careful monitoring including ECG, pulse oximetry, and NIBP cuff after being placed on the operating table. Peripheral intravenous access (IV Line) was established for all of them. Before administration of the drug and induction of anesthesia, the first group received 30 mg of intravenous ketorolac. The patient was given 30 mg of intravenous ketorolac for 10 seconds and 100 ml of normal saline was given as an infusion to homogenize the patient over 30 minutes. In the control group, 10 cc of normal saline was infused over 30 minutes. The person prescribing the drug was unaware of the grouping of patients and was only responsible for prescribing the drug, anesthetizing the patients, and recording the required symptoms in the questionnaire. The recorder of patients' information also did not know the type of medication they received. To provide initial oxygenation (Preoxygenation), patients received 100% oxygen through a face mask of 6 liters per minute for 3 minutes with normal breathing. Then, as a premedication, all patients were prescribed midazolam (0.03 mg/kg) and 2 mcg/kg fentanyl intravenously and general anesthesia by intravenous induction by propofol (2 mg/kg) was established as the main anesthetic and atracurium (0.6 mg/kg) as a neuromuscular relaxant for patients. As soon as induction drugs were prescribed, patients underwent mask ventilation (BMV). After about 3 minutes and ensuring the onset of muscle relaxant effect, direct laryngoscopy was performed in the Sniff position by anesthesia assistants under the direct supervision of professors. Intubation was performed by selecting a tracheal tube size 7.5 for women and 8 for men, and anesthesia was maintained for all patients with propofol at a dose (100 min/mcg/kg). The type of anesthesia and how to do it, the type of medication used, and all conditions related to anesthesia were the same for all patients and the fluid therapy was 6 cc/kg for all patients. This was done by the same person who was unaware of the grouping of patients. He was solely responsible for performing anesthesia and recording vital signs in the questionnaire. After the surgery, the patients were transferred from the operating room to the recovery room and the patients were monitored for at least one hour in the recovery room. Also, the severity of patients' pain, according to VAS criteria, was assessed and recorded in the recovery ward at 6, 12, and 24 hours after surgery by an anesthesia assistant who was unaware of the patient grouping. In the case of VAS> 3, pethidine was injected in the amount of 25 mg intravenously or sometimes one gram of Apotel according to the opinion of the treating physician according to the patient's condition in recovery condition and the total dose and number of analgesic injections were recorded in the form.

Data collection:

To collect information in this study, a researcher-made checklist was used which includes: age, gender, duration of operation, drug use, pain intensity, blood pressure, and heart rate. This checklist was completed separately for each patient and other clinical information was entered in the checklist during surgery and postoperatively. Also, for each patient, an information form or research questionnaire was considered that contains personal information as well as the variables under study.

Data analysis:

Data analysis using SPSS software version 21 and descriptive (mean, percentage, and standard deviation) and inferential statistical tests (repeated measurement, Anova, Kruskal-

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Wallis, and repeated measures analysis of variance) and at a significant level P <0.05 done.

Results

Sixty patients undergoing upper limb surgery in the ketorolac (n = 30) and control (n = 30) groups participated in the study. The results of statistical analysis showed that ketorolac and control groups were similar in terms of gender, age, BMI, ASA (Table 1). The results of the t-test showed that systolic and diastolic blood pressure at ten minutes postoperatively in the ketorolac group was significantly lower than the control group (P=0.040). The results of analysis of variance with repeated measures showed that the intragroup trend of systolic and diastolic blood pressure was significant in ketorolac and control groups (P = 0.019). In the ketorolac group, the systolic and diastolic blood pressure decreased until ten minutes after surgery but after that (Table 2). The results of the t-test showed that there was no significant difference between ketorolac and control groups in terms of MAP and heart rate at baseline, one, ten, and thirty minutes after surgery (P>0.05); However, the intragroup MAP trend and heart rate trend were significant in ketorolac and control groups (P<0.05). Mean MAP and heart rate decreased more in the ketorolac group than in the control group (Table 2). The results of the Kruskal-Wallis test showed that at intervals in recovery and 6 and 12 hours after surgery, pain in patients of the ketorolac group was significantly less than the control group (P<0.05); Also, the intragroup pain trend was significant in ketorolac and control groups (P<0.05). Mean pain in the ketorolac group decreased more than in the control (P<0.001) (Table 3). Comparison of opioid use in the ketorolac group (6.7% of Apotel and 10% of Pethidine) and control group (30% of patients with pethidine) was not significant (P-value = 0.069).

Discussion

Effective management of postoperative pain is now part of the surgical process and not only reduces patient suffering but also mortality and improves rapid and early discharge from the hospital improves the patient's quality of life and reduces costs (13-15). Pain after orthopedic surgery is also considered very severe pain (16). The results of the Kruskal-Wallis test showed that at intervals in recovery and 6 and 12 hours after surgery, pain in patients of the ketorolac group was significantly less than the control group (P <0.05); Also, the intragroup pain trend was significant in ketorolac and control groups (P <0.05). Mean pain in the ketorolac group decreased more than in the control (P <0.001) (Table 3). Various studies have shown the effects of ketorolac compared to other drugs in reducing pain in different patients such as musculoskeletal pain, kidney stone pain, migraine headaches, and surgeries (17-18). In Watcha et al.'s (1992) study comparing acetaminophen and ketorolac in analgesia after Myringotomy, it was observed that ketorolac could significantly reduce patients' pain after surgery, and this amount of pain reduction compared to the Acetaminophen group was significantly better (19). In Bahadori et al.'s (2018) study, which aimed to investigate the effect of prophylactic administration of ketamine or intravenous ketorolac on pain relief after cesarean section under spinal anesthesia, the results showed that ketorolac injection as a premedication in the cesarean section can reduce postoperative pain in mothers (20). El-Tahan et al. (2007) in their study examined the prophylactic administration of ketorolac in pregnant women candidates for cesarean section and showed that the mean pain score in the first 2 hours after surgery was significantly lower in the ketorolac group than in the control group. (21). In a study conducted by Abdoli et al. (2019) to compare the effect of ketorolac and morphine on pain control in patients with spinal cord trauma in the emergency department, the

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results showed that due to the better effect and fewer side effects of ketorolac than morphine, It seems that ketorolac can be used as a suitable alternative in controlling pain in patients with spinal trauma referred to the emergency department (22). In the study of Masoumi et al. (2017), the effect of ketorolac was compared to morphine in reducing pain in patients with long bone fractures in the emergency department and the results showed that ketorolac within one hour after injection had a better analgesic effect than morphine; also, fewer side effects. However, the difference between the two groups was not statistically significant (17). Akhavan Akbari in his study compared the effect of ketorolac infusion and intravenous acetaminophen in reducing pain and drug use after surgery in patients undergoing orthopedic surgery of the lower extremities. The results of their study showed that the effect of acetaminophen and ketorolac varied at different hours (12). In the study of Roche et al., the results showed that the prophylactic use of ketorolac was not significantly superior to placebo (23). The reason for this discrepancy in the results of these studies could be related to the difference in the method of administration of ketorolac. In controlling the pain of patients after surgery, the effectiveness of ketorolac is equivalent to the effectiveness of narcotics in low and medium doses, and ketorolac is often referred to as a highly effective analgesic (24), which was also proven in the present study. The results of the t-test showed that systolic and diastolic blood pressure at ten minutes postoperatively in the ketorolac group was significantly lower than the control group (P = 0.0400); The results of analysis of variance with repeated measures showed that the intragroup trend of systolic and diastolic blood pressure was significant in ketorolac and control groups (P = 0.019). In the ketorolac group, the systolic and diastolic blood pressure decreased until ten minutes after surgery but after that (Table 2). The results of Bahadori et al.'s study showed that ketorolac performed better than morphine in controlling systole and diastolic blood pressure (18). In the study of Porfakhr et al. the effects of ketorolac and gabapentin on postoperative analgesia was evaluated in orthognathic surgery. The results of this study showed that ketorolac is more effective in hemodynamic parameters than the control group (25). A similar finding was made in a study by El-Tahan et al. on the cardiovascular protective effect of ketorolac on systolic and diastolic hypertension during cesarean section (21). It seems that the prophylactic use of ketorolac in patients is associated with cardiovascular protective effects.

Conclusion

The results of the present study showed that intravenous ketorolac is more effective in controlling pain intensity than the control group. It seems that in orthopedic surgeries, upper limb ketorolac has a good effect in controlling postoperative pain. It is recommended that further studies be conducted in this field to confirm the findings obtained in this study in a multicenter manner and also to be compared with other drugs such as morphine or pethidine and to measure the effectiveness of these drugs against narcotics.

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Tables

Table 1: Description of demographic variables in ketorolac and control groups

		Control		Ketorolac		P-value
		n	%	n	%	
Sex	Male	27	90	29	96.7	0.61
	Female	3	10	1	3.3	
ASA	I	23	76.7	28	93.3	0.15
	II	7	23.3	2	6.7	
Age		8.04±28.50		7.72±29.50		0.93
BMI		4.57±23.26		3.34±22.95		0.52

Table 2: Comparison of blood pressure at different times in ketorolac and control groups

Variable		Ketorolac		Control		P-value
		Mean	SD	Mean	SD	
	Base	137.63	17.67	139.27	19.69	0.74

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Systolic blood pressure	1 minute	121.9	18.28	124.43	21.44	0.62
	10 minute	120.73	15.04	129.23	16.2	0.04
	30 minute	123.58	16.25	126.44	19.9	0.58
	P-value	0.003		0.019		
Diastolic blood pressure	Base	79	12.4	82.57	17.68	0.37
	1 minute	71.6	11.59	71.43	15.21	0.96
	10 minute	67.73	10.56	74.97	14.99	0.024
	30 minute	73	11.17	72.88	16.78	0.65
	P-value	0.048		0.032		
MAP	Base	92.5	16.84	96.33	14.55	0.18
	1 minute	82.53	14.6	85.4	14.56	0.41
	10 minute	82.47	11.21	88.83	13.5	0.053
	30 minute	85.63	11.2	90.16	15.3	0.19
	P-value	0.067		0.023		
HR	Base	78.97	15.83	84.23	14.28	0.14
	1 minute	77.63	15.26	80.43	14.87	0.37
	10 minute	70.1	13.71	73.43	13.58	0.31
	30 minute	69.08	12.44	68.36	17.57	0.99
	P-value	0.001		0.001		

Table 3: Comparison of pain at different times in ketorolac and control groups

	Ketorolac		Control		P-value
	Mean	SD	Mean	SD	
Pain-based	4.55	1.55	5.17	1.34	0.11
Pain in recovery	3.77	1.61	5.8	1.54	0.001
6 hours after surgery	3.3	1.21	5.5	1.61	0.001
12 hours after surgery	3.7	1.56	4.57	1.41	0.03
24 hours after surgery	2.97	1.3	3.47	1.17	0.135
P-value	0.001		0.001		

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