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Comparison of intravenous ibuprofen and intravenous ketorolac effectivity for non-specific acute musculoskeletal pain

Rizaldy Taslim Pinzon[*], Tifany Edfa Susanto

Department of Neurology, Faculty of Medicine, Duta Wacana Christian University, Wahidin Sudirohusodo street number 5-25, Yogyakarta 55224, Indonesia

ABSTRACT

Acute musculoskeletal pain is an illness of muscle, bone, joint, and muscle tissue that is caused by an injury or inflammation. Ibuprofen and Ketorolac are Non-Steroid Anti-Inflammatory Drugs or NSAID that are usually used for non-specific acute musculoskeletal pain. The purpose of the study is to compare the pain relief of non-specific acute musculoskeletal pain between intravenous Ibuprofen and intravenous Ketorolac therapy. This study uses a quasi-experimental, non-randomized, non-equivalent, active comparator, open-label study. The total sample for this study is 60 subjects, divided into two groups (n-30), subjects are required by using purposive sampling. Pain measured by Numeric Pain Scale. The mean baseline of the pain intensity were 63.33 ± 8.841 for the Ibuprofen group and 59.33 ± 12.847 for the Ketorolac group. There was not any differences between both of group (p = 0.107) after the medication were given all measurement shows significant differences between two groups (p = <0.05) that Ibuprofen group shows better results. Intravenous Ibuprofen has better effectivity rather than intravenous Ketorolac as a treatment of non-specific acute musculoskeletal pain.

[*]Corresponding Author

Name: Rizaldy Taslim Pinzon
Phone: +62-81294638229
Email: drpinzon17@gmail.com

INTRODUCTION

Musculoskeletal pain is the type of pain that often occurs, There are 20%-30% of people in the world who experience musculoskeletal pain and there are more than 150 diagnoses of muscle, joint, and connective tissue such as tendon and ligament that are associated with pain (WHO, 2021).

Patients with musculoskeletal pain have clinical features such as decreased activity, stiffness, weakness, pain on movement, and decreasing range of motion which is not associated with joint (Arendt-Nielsen *et al.*, 2011).

Musculoskeletal pain therapy in general is NSAIDs (non-steroidal anti-inflammatory drugs), anticonvulsants, opioids, opioid analgesics or nonopioids (Schug and Arshad, 2017).

The therapy should work quickly so that NSAIDs with a fast onset of action such as Ketorolac and Ibuprofen are often the choice.

NPS or Numeric Pain Scale is an instrument to assess pain intensity. NPS was chosen because it has been tested for reliability and validity and describes the pain felt by the patient. NPS could also be used for repeated measurements.

The purpose of this study was to compare the effectiveness of pain reduction between intravenous administration of Ibuprofen and Ketorolac.

MATERIALS AND METHODS

This study used a quasi-experimental method with non-randomized, non-equivalent, active comparison, and open-label study. This study consisted of 60 samples conducted by the purposive sampling method. The samples were divided into two groups, namely the Ibuprofen and Ketorolac therapy groups (n = 30). Therapy is given intravenously at a dose of 800 mg for Ibuprofen and 30 mg for Ketorolac.

This research is registered in the research register of the Ministry of Health's clinic with the title *Comparison of Intravenous Ibuprofen and Ketorolac for Acute Musculoskeletal Pain from Various Etiologies.* This research has received ethical eligibility from the Health Research Ethics Committee of the Faculty of Medicine, Duta Wacana Christian University (ethical eligibility Number: 1146 / C.16 / FK / 2020)

RESULTS AND DISCUSSION

In the study, 60 subjects were divided into two groups (n = 30) with more male subjects than women. The mean age in the Ibuprofen group was 58.50 ± 10.487 and the Ketorolac group 52.9 ± 18.626. The mean initial pain intensity in the Ibuprofen therapy group was 63.33 ± 8.841 and in the Ketorolac group $59.33 \pm 12,847$ (Table 1).
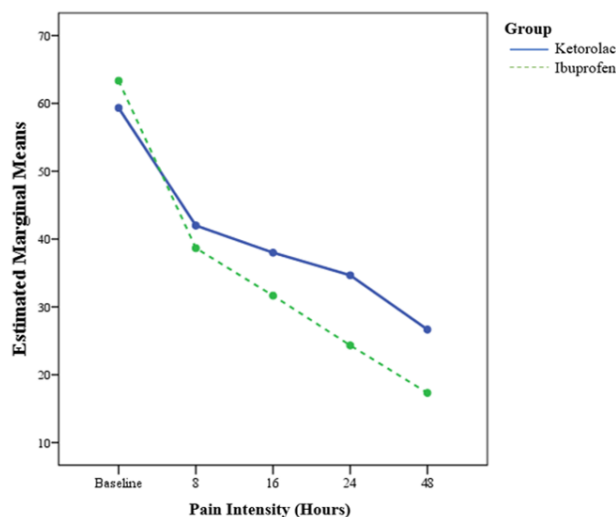

Figure 1: Graph of Decreased Pain Intensity Between Two Groups

There was no significant difference between the initial pain intensity of the two groups (p = 0.107) with the mean pain intensity of the Ibuprofen group $63.33 \pm 8,841$ and the Ketorolac group $59.33 \pm 12,847$. The pain intensity after giving therapy in the two groups showed a significant difference (p = <0.005) with the mean pain intensity in the Ibuprofen group and the Ketorolac group, respec-

tively, after 8 hours 38.67 ± 10.417 and 42.00 ± 8052, after 16 hours 31.67 ± 11.769 and 38.00 ± 7.144, 24 hours 24.33 ± 13.047 and 34.67 ± 7.303, and after 48 hours 17.33 ± 13.880 and $26.67 \pm 7,581$ (Table 2). There was a significant difference in reduction of pain intensity between the two groups within hours (Figure 1).

Rescue medication was administered to 40 study subjects, namely the Ibuprofen group 23 (76.7%) subjects and 17 (56.7%) Ketorolac subjects (Table 3).

Adverse events in this study occurred in the Ketorolac therapy group with a total of 11 (36.7%) subjects and no adverse events in the Ibuprofen therapy group (Table 4).

The basic characteristics of this study indicated that men experienced more acute musculoskeletal pain than women, but this difference did not have a significant effect on pain intensity and therapy effectiveness (p = 0.794). The mean age of the patients in the two groups did not have a significant difference, namely 58.50 in the Ibuprofen group and 52.9 in the Ketorolac group (Shanechi *et al.*, 2018). Comedication in the form of vitamins and steroids was significant in the Ibuprofen group, and this comedication could have a better effect on reducing pain intensity in the Ibuprofen group.

Vitamins including vitamins C, D, and B complex are known to have a role in pain improvement (Pierik, 2015; Gazoni *et al.*, 2016; Carr and McCall, 2017). Steroids have functions as an anti-inflammatory agent that can inhibit the synthesis of nerve mediators such as PGE2 (Helde-Frankling and Björkhem-Bergman, 2017).

In this study, five measurements of the Numeric Pain Scale (NPS) were taken, the first measurement taken before giving therapy and the fourth measurement after therapy. The mean of the pain intensity on the Ibuprofen group before giving the therapy was $63.33 \pm 8,841$ and the Ketorolac group $59.33 \pm 12,847$, and there was no significant difference in pain intensity in the two groups (p = 0.107). The final measurement after 48 hours, Ibuprofen group showed $17.33 \pm 13,880$ and the Ketorolac group was $26.67 \pm 7,581$, and the amount of reduction in pain intensity in the Ibuprofen group was $46.00 \pm 16,316$, and the Ketorolac group was $32.67 \pm 10,148$. The mean pain intensity and the mean reduction in pain intensity in the two groups showed a significant difference (p = 0.006, p = 0.001). The results obtained indicate that Ibuprofen has better effectiveness in reducing acute musculoskeletal pain compared to Ketorolac.

Table 1: Baseline Characteristics Between Two Groups

Baseline Characteristics		Ibuprofen Groups (n=30)	%	Ketorolac Groups (n = 30)	%	P-value
Gender	Male	18	60	16	53.3	0.794
	Women	12	40	14	46.7	
Age	Mean ± SD	58.50 ± 10.487		52.9 ± 18.626		0.297
Location of Pain	Back	14	46.7	18	60.0	0.438
	Knee	7	23.3	4	13.3	0.505
	Neck	9	30.0	5	16.0	0.360
Initial pain intensity	Mean ± SD	63.33± 8.841		59.33± 12.847		0.107
Comorbid disease	Yes	20	66.7	12	40.0	0.070
	Not	10	33.3	18	60.0	
Comedication	Yes	21	70.0	10	33.3	0.010
	Not	9	30.0	20	66.7	
Types of comedication	Antihypertensive agents	13	43.4	5	16.7	0.049
	Anti Diabetic agent	1	3.3	4	13.3	0.350
	Anti Platelet Agent	13	43.3	2	6.7	0.003
	Proton pump inhibitor/H2 blocker	17	56.7	4	13.3	0.001
	Vitamin	16	53.3	0	0	<0.001
	Steroid	7	23.3	0	0	0.016

Table 2: Comparison of Pain Intensity Between Two Groups

Assessment time	Ibuprofen group	Mean ± SD	Ketorolac group	Mean±SD	P-value
Early		63.33± 8.841		59.33± 12.847	0.107
8 hours after treatment		38.67 ± 10.417		42.00 ± 8.052	0.003
		Δ 24.67±10.080		Δ17.33± 7.849	0.003
16 hours after treatment	30	31.67 ± 11.769	30	38.00 ± 7.144	0.006
		Δ 31.67±12.888		Δ 21.33± 9.371	0.002
24 hours after treatment		24.33 ± 13.047		34.67 ± 7.303	< 0.001
		Δ 39.00± 12.959		Δ 24.67 ± 11.366	< 0.001
48 hours after treatment		17.33 ± 13.880		26.67 ± 7.581	0.006
		Δ 46.00± 16.316		Δ 32.67 ± 10.148	0.001

Table 3: Comparison of Rescue Medication Between Two Groups

Rescue Medication		Ibuprofen Group (N=30)	%	Ketorolac Group (N=30)	%	P-value
Patients receive	Yes	23	76.7	17	56.7	0.171
Rescue Medication	No	7	23.3	12	43.3	
Type of	Oral	18	13.9	6	3.4	0.207
Medication	Injection	5	3.8	11	6.2	

Table 4: Comparison of Adverse Events between Two Groups

Adverse Event		Ibuprofen Group (N=30)	%	Ketorolac Group (N=30)	%	P-value
Patient who	Yes	0	0.0	11	36.7	0.001
Adverse Event	No	30	61.2	19	63.3	

There was no significant difference in giving rescue medication to the two groups (p = 0.171). In the Ibuprofen therapy group, 23 subjects needed rescue medication in the form of pain relief due to pain that arose between the times of giving Ibuprofen therapy. Intravenous ibuprofen 800 mg has a maximum concentration time of 30 to 60 minutes and a maximum concentration time of 0-4 hours depending on the subject's metabolism (Samuel *et al.*, 2017).

In the Ketorolac therapy group, there were 17 subjects who received rescue medication, 30 mg intravenous ketorolac could reach a maximum concentration in 1 to 2 hours, and the effects can last for 6 to 8 hours (Kroll, 2012; Lyon *et al.*, 2019).

Adverse events occurred only in the Ketorolac therapy group. Intravenous ketorolac can be given in a dose of 10 mg to 30 mg with a maximum dose of 1 day in adults is 120 mg. The higher the intravenous ketorolac dose, the greater the chance for adverse events to occur. In this study, Ketorolac was administered every 12 hours as much as 30 mg, thus allowing adverse events to occur (Shanechi *et al.*, 2018). Adverse events that can be identified in this study were disorders of the gastrointestinal tract in the form of pain. Subject experiencing Gastrointestinal pain is given therapeutic treatment in the form of proton pump inhibitors or PPIs. The absence of an adverse event in the Ibuprofen therapy group can be influenced by comedication in the form of PPIs or H2 blockers, which can prevent pain from occurring to gastrointestinal bleeding (Nugent *et al.*, 2018)

The limitation faced by the researcher is that this study uses a non-randomized quasi-experimental method in which the subjects are not randomly divided into each group, this causes a bias in the intensity and reduction of pain felt by the subject due to various pain etiologies. In this study was also conducted with non-blinding, namely, there is no disguise in the administration of therapy so that researchers know the drugs given to the research subjects.

CONCLUSION

Intravenous ibuprofen has better effectiveness in treating non-specific acute musculoskeletal pain than intravenous Ketorolac. Intravenous Ibuprofen has shown superiority in safety that proven in the adverse event, although intravenous ibuprofen group has higher needs of rescue medication.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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