Low-Dose Short-Term Scheduled Ketorolac Reduces Opioid Use and Pain in Orthopaedic Polytrauma Patients: A Randomized Clinical Trial

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INTRODUCTION:

The posttraumatic inflammatory response after orthopaedic injury is a complex process that can lead to posttraumatic pain. A double-blinded, randomized controlled trial was conducted to determine whether scheduled low-dose, short-term ketorolac is associated with reduced length of stay, opioid use, and pain in orthopaedic polytrauma patients.

METHODS:

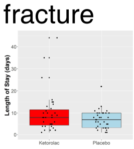
Orthopaedic trauma patients between 18-70 years of age with a New Injury Severity Score (NISS) > 9 and without contraindication to non-steroidal anti-inflammatory drugs (NSAIDs) were recruited from a level I trauma center. Patients were randomized to the ketorolac or placebo group with the ketorolac group receiving 15 mg of intravenous (IV) ketorolac every 6 hours for up to 5 inpatient days and the placebo group receiving 2 mL of IV normal saline in a similar fashion. The main outcome measurements were length of stay (LOS), morphine milligram equivalents (MME), and daily visual analog scale (VAS) scores. Group-level summary statistics were calculated for clinical and demographic variables, and differences between the two groups were evaluated using two-sample t-tests for quantitative measures and Fisher's exact tests for categorical measures, as appropriate. Due to right-skewness, LOS and MME values were log-transformed before analysis and summarized using medians and interquartile ranges for each group. The VAS model was adjusted for baseline levels as a covariate, which differed significantly between groups.

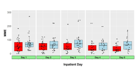
RESULTS:

In total, 70 participants were enrolled, with 35 randomized to the ketorolac group and 35 to the placebo group. Study groups were balanced with respect to age, BMI, and NISS. LOS was not significantly different between groups (p = 0.275). Over the 5-day treatment period, the ketorolac group experienced a 32% reduction in average MME (p = 0.013) and a 12-point reduction in baseline-adjusted mean VAS (p = 0.037) compared to the placebo group.

DISCUSSION AND CONCLUSION:

Scheduled low-dose, short-term IV ketorolac was associated with significantly reduced inpatient opioid use and pain in orthopaedic polytrauma patients with no significant difference in LOS and no apparent short-term adverse effects. The results support the use of scheduled low-dose, short-term IV ketorolac for acute pain control among orthopaedic polytrauma patients. Future studies are needed to delineate lasting clinical effects and potential long-term effects, such as fracture healing.





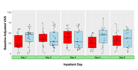


Table 1: Multimodal Analgesia Protocol

Scheduled
Acetaminophen* 1000mg tablet PO q6h for pain
Gabapentin 100mg capsule PO, 3 TID x 7 days then 1 TID
Ketorolac* 15 mg IV q6h (stopped after 4 doses)
As needed Medication (PRN)
Oxycodone Taper: POD#0-1, 5-10 mg q4h; POD#2, 5 mg q4h; POD#3-5, 5mg q6h; POD#6-7, 5mg q8h
Ibuprofen* 400mg tablet, 1 PO q6h PRN for pain, (begins on POD #1 after 4 doses of ketorolac)
Methocarbamol 750mg tablet, 1 q6h PRN for muscle spasms
Morphine IV 2-4 mg q 2h PRN for severe pain
Tramadol 50mg tablet PO, q4h PRN for pain unresponsive to non-opioids

*Non-steroidal anti-inflammatory drug (NSAID), temporarily held during the 5-day treatment period

Table 2. Patient Characteristics

Demographic Variable	Sublevel	Ketorolac (*n* = 35)	Placebo (*n* = 35)
Age (years)		39.5 ± 17.2	40.0 ± 16.2
BMI*		28.2 ± 7.3	29.5 ± 6.4
NISS^		14.0 ± 5.2	15.1 ± 6.4
Surgery Count		1.2 + 0.6	1.4 + 0.7
Surgery Count	1	30 (85.7%)	24 (68.6%)
	2	4 (11.4%)	8 (22.9%)
	3	----	3 (8.6%)
	4	1 (2.9%)	----

*BMI, body mass index
^NISS, New Injury Severity Score

Table 3. Group-Level Summary Statistics of Length of Stay*

Group	Median (IQR**)	*p*-value^
Ketorolac (*n* = 35)	8 (4.5 to 11.5)	0.275
Placebo (*n* = 35)	7 (3 to 10)	

*Length of stay measured in days
**IQR, interquartile range (first quartile – third quartile value)
^*p*-value comes from ANOVA model on log-transformed values of length of stay, correcting for heavy right-skewness

Table 4. Group-Level Summary Statistics of Morphine Milligram Equivalents

Group	Day	*n*	Median	IQR^
Ketorolac	0 (Enrollment)	34	86	38 to 120
	1	34	48.75	19 to 82
	2	31	53	26 to 75
	3	28	38.25	28 to 75
	4	25	30	23 to 60
	5	23	30	18 to 52
Placebo	0 (Enrollment)	35	82.5	49 to 118
	1	34	67.75	48 to 81
	2	29	62	38 to 90
	3	26	72	45 to 99
	4	24	60	28 to 78
	5	20	63.75	32 to 88

^IQR, interquartile range (first quartile – third quartile value)

Table 5. Group-Level Summary Statistics of Visual Analogue Scale Pain Scores

Group	Day	*n*	Mean	SD^
Ketorolac	0 (Enrollment)	33	68.2	24.4
	1	31	42.7	25.6
	2	28	47.4	27.7
	3	25	56.3	26.0
	4	23	43.3	24.0
	5	17	52.6	21.9
Placebo	0 (Enrollment)	35	55.1	27.5
	1	32	52.2	31.3
	2	25	53.9	26.5
	3	24	54.1	27.3
	4	20	59.5	26.9
	5	16	59.2	25.6

^SD, standard deviation