

Comparison of Intravenous Lidocaine/Ketorolac Combination to Either Analgesic Alone for Suspected Renal Colic Pain in the ED

BACKGROUND:

- Renal colic is credited for 1% of all emergency department visits and 1% of all hospital admissions.
- NSAIDs and/or opioids are the primary treatment modalities for renal colic pain, but their use can result in adverse effects.
- No trials have studied the use of intravenous lidocaine and ketorolac combination as a therapy option for patients presenting with renal colic pain.

OBJECTIVE:

- To determine the efficacy and safety of the combination of IV lidocaine and ketorolac compared to lidocaine and ketorolac alone in the treatment of presumed renal colic in patients presenting to the emergency department.

METHODS:

- **Design:** Single-center, randomized, double-blinded parallel trial
- **Duration:** 60 minutes
- **Inclusion criteria:** 18-64 year old patients who presented to the ED with acute flank pain, abdominal pain, or back pain with or without hematuria that the ED physician assumed was due to renal colic and needed to be treated with IV analgesia.
- **Exclusion criteria:** age >64 years, documented or suspected pregnancy, breastfeeding, allergy to ketorolac or lidocaine, contraindications to NSAID's or lidocaine, known renal or hepatic dysfunction, use of NSAID's and/or opioids within 4 hours before presentation, history of bleeding diathesis, history of peptic ulcer disease or gastrointestinal hemorrhage, history of cardiac arrhythmia, severe coronary artery disease, seizures, presence of any peritoneal sign, altered mental status, current use of warfarin or novel oral anticoagulants, HR <50 or >150, and weight >100 kg.
- 150 patients (50 patients per group) received one of the three following options:
 - Single dose of IV lidocaine at 1.5 mg/kg mixed in 100 ml normal saline bag and administered over 15 minutes and a placebo of normal saline as an intravenous push dose
 - Single intravenous push dose of ketorolac 30 mg and a placebo of 100 ml normal saline bag administered over 15 minutes
 - Single intravenous push dose of ketorolac 30 mg and a single dose of IV lidocaine at 1.5 mg/kg mixed in 100 ml normal saline bag over 15 minutes
- **Primary outcome measure:** Difference in pain scores at 30 minutes and 60 minutes between the three groups
- **Secondary outcome measures:** Comparative reduction in pain scores from baseline to 30 minutes and 60 minutes within each group; the need for rescue analgesic at 30 minutes and 60 minutes; rates of adverse effects
- 50 patients per group were needed to detect at least a 1.3 point difference from baseline in the 30 minute pain assessment score to achieve a power of 80%.
- Data handling method used in the study was intent-to-treat.

RESULTS:

- All patients completed the study (50 in each group)
- **Primary outcome measure:**

Difference in Mean Pain Scores		
Time	Group	Difference (95% CI)
30 minutes	Ketorolac – Lidocaine	-1.98 (-3.69 to -0.27)
	Lidocaine – Combination	-2.89 (-4.39 to -1.39)
	Ketorolac – Combination	-0.92 (-2.44 to 0.61)

60 minutes	Ketorolac – Lidocaine	-2.37 (-3.93 to -0.81)
	Lidocaine – Combination	-2.79 (-4.11 to -1.47)
	Ketorolac – Combination	-0.42 (-1.70 to 0.86)

- At 30 minutes, the difference in mean pain scores favored the combination group over lidocaine group and the ketorolac group over the lidocaine group.
- At 60 minutes, the difference in mean pain scores of both the combination group and the ketorolac group were statistically significant when compared to the lidocaine group.
- The difference in mean pain scores between the combination group and the ketorolac group was not statistically significant at both 30 and 60 minutes.
- **Secondary outcome measures:**
 - At 30 minutes, the combination group had improved from 8.40 mean pain score at baseline to 3.14 (difference = 5.26, CI: 4.52-6.00), the ketorolac group improved from 7.94 mean pain score at baseline to 3.88 (difference = 4.06, CI: 3.23-4.89), and the lidocaine group improved from 8.36 mean pain score at baseline to 5.52 (difference = 2.84, CI: 2.23-3.44).
 - There was no statistically significant difference between the three groups and their use of rescue morphine analgesia at both 30 minutes and 60 minutes.
 - No clinically significant adverse effects were reported. The most common adverse effects were dizziness, nausea, and headache. The lidocaine group had the largest percentage of patients reporting adverse effects.
- **Author's conclusion:** The combination group and the ketorolac group had superior efficacy when compared to the lidocaine group, but there were no clinically important differences between the combination group and the ketorolac group in regard to mean pain scores.

STRENGTHS:

- Double-blinded, randomized
- No dropouts
- Inclusion and exclusion criteria were appropriate
- Groups were similar in terms of chief complaints, final diagnoses, and baseline patient characteristics.

LIMITATIONS:

- Single-center study
- Underrepresentation of patients who come to the ED after 8PM and before 8AM
- Short-study, which did not allow for pain recurrence beyond 60 minutes to be studied or the rates of adverse effects to be measured past 60 minutes
- Unable to assess variance in safety of the 3 groups due to small sample size
- Relatively small percentage of subjects with a diagnosis of renal colic after review
- Some differences in baseline pain scores between the combination group and the ketorolac group

CONCLUSION:

- There is a significant difference in renal colic pain relief when comparing the lidocaine/ketorolac combination to lidocaine alone, but the study did not find a significant difference when comparing the combination to ketorolac alone.
- Larger and longer studies may be needed to confirm any difference in side effects.
- Future research with a larger sample size and extended duration is needed to determine if there is any difference between the combination group and the ketorolac alone group or if they truly are equivalent in efficacy.

Reference: Motov S, Fassassi C, Drapkin J, Butt M, Hossain R, Likourezos A, et al. Comparison of intravenous lidocaine/ketorolac combination to either analgesic alone for suspected renal colic pain in the ED. *Am J Emerg Med.* 2020; 38(2): 165-172.