

# A Randomized Trial of IV Ibuprofen and Morphine Combination Therapy in Patients Presenting with Renal Colic

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## Introduction

Renal stones (or “calculi”) are a relatively common condition requiring analgesia in the emergency department. Paired parenteral administration of opioids with non-steroidal anti-inflammatory drugs (NSAIDs) offers the advantage of rapid analgesic effect while minimizing the necessary opioid dose and limiting adverse drug effects.

## Methods

This study is a three-armed double-blinded prospective trial using IV morphine with one of the following agents: IV ibuprofen, IV ketorolac or placebo in patients 18-55 years old presenting with symptoms of renal colic. All patients included had a history of kidney stones, radiographic evidence of kidney stones, or hydronephrosis. Verbal assessment of pain was performed between 0 and 120 min after drug administration. This study was approved by the institutional review board at Maricopa Integrated Health System and the University of Arizona.

### Exclusion Criteria:

- Hemodynamic instability
- Inability to reliably self-report or communicate pain intensity and pain relief
- Current therapy with warfarin, lithium, or combination ACE inhibitor + furosemide
- Inability to consent
- Hepatic, renal or cardiac failure
- NSAID or opioid allergy
- Analgesic therapy within 6 hours of presentation
- History of congenital bleeding diathesis or platelet dysfunction
- Unsuitability for the study in the opinion of the investigator

### Study Timeline:

- One of the three randomized agents were infused over five (5) minutes
- All patients had rescue analgesia with IV morphine 4 mg available
- Pain score and vital signs were measured at the time of drug administration (t=0 min), 15 minutes, 30 minutes, 60 minutes, and 120 minutes
- Incidence of known side effects and of treatment failure, i.e. need for rescue analgesia, was recorded

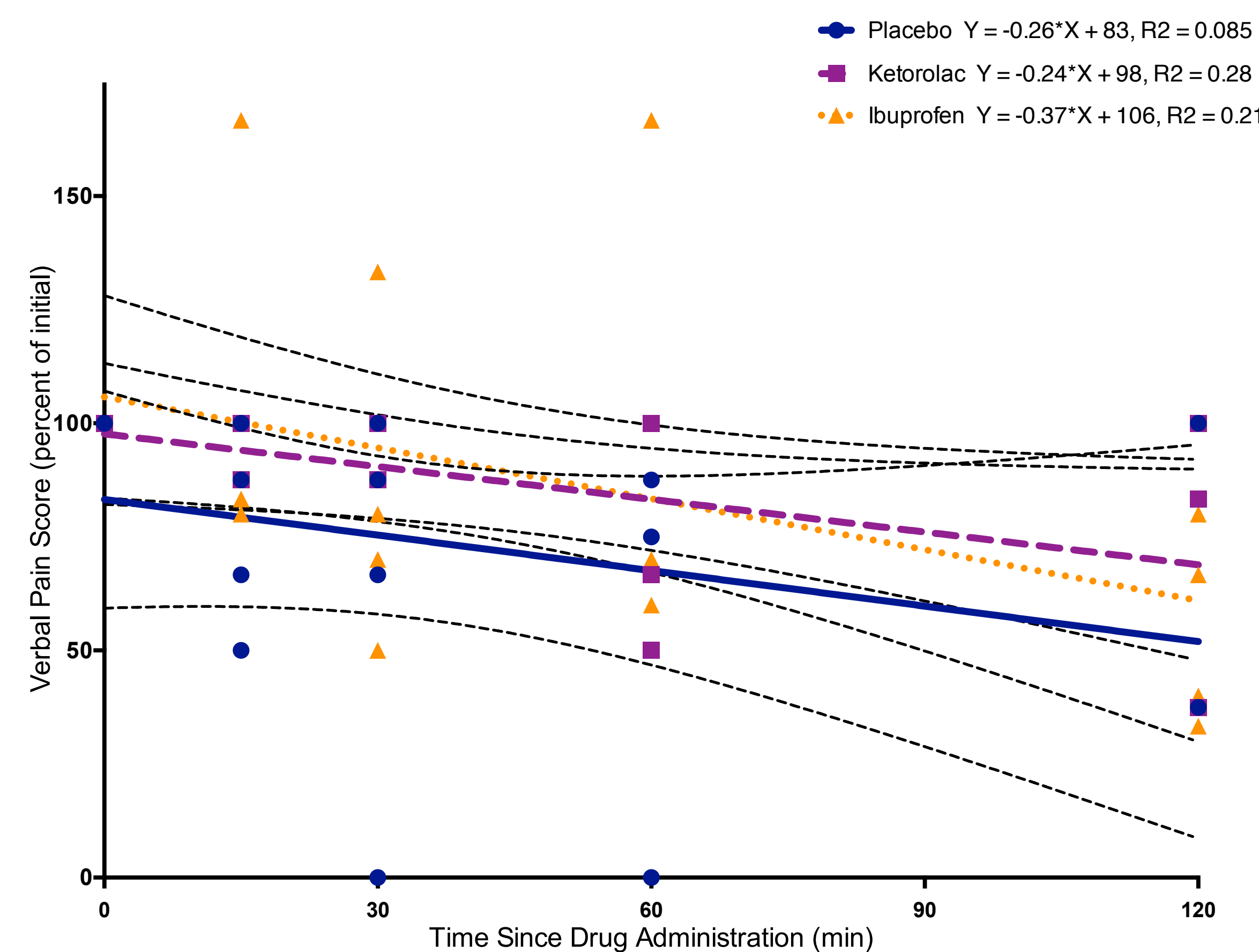


FIGURE 1: Reported pain over time as a percentage of baseline pain score.

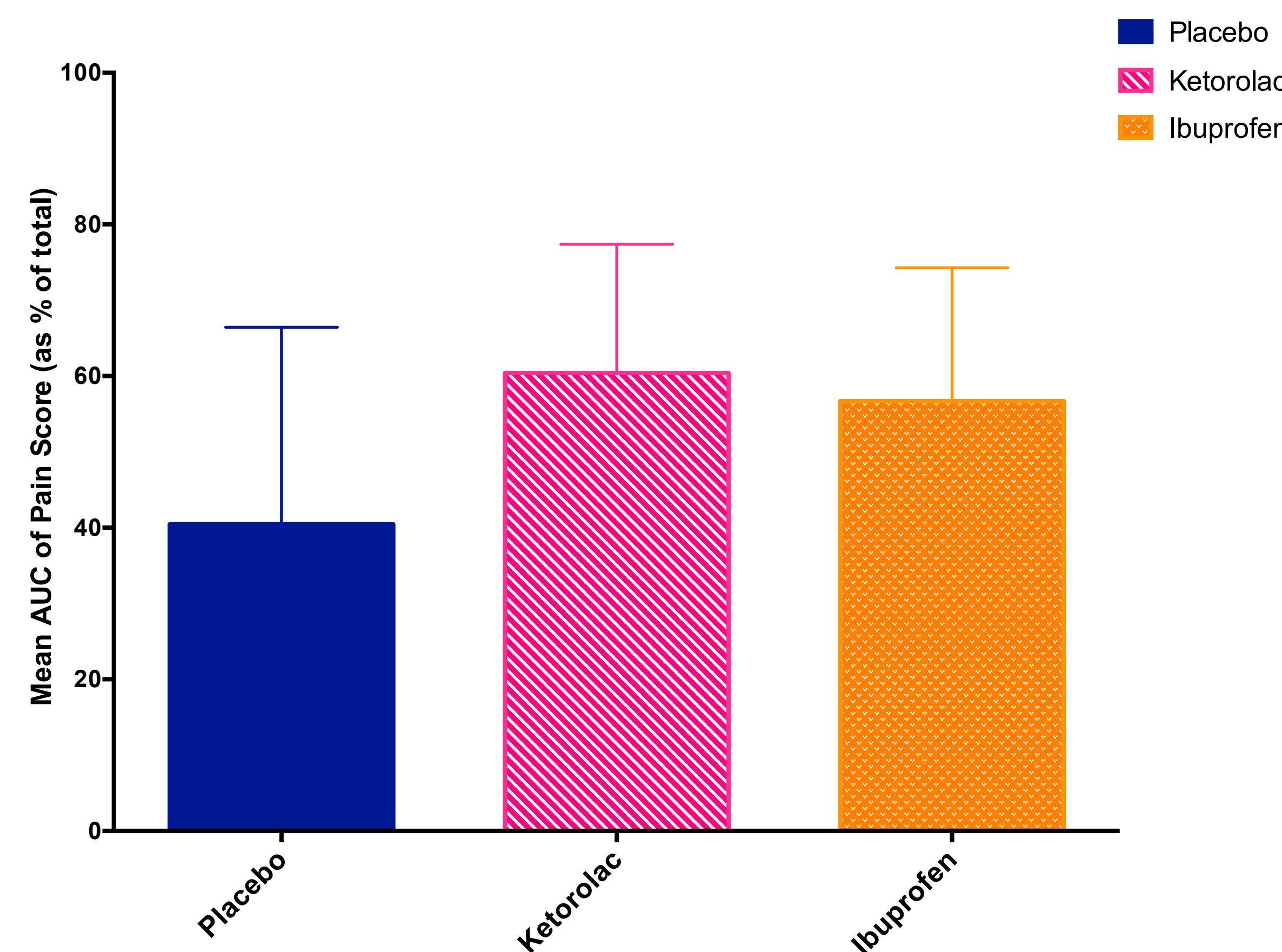
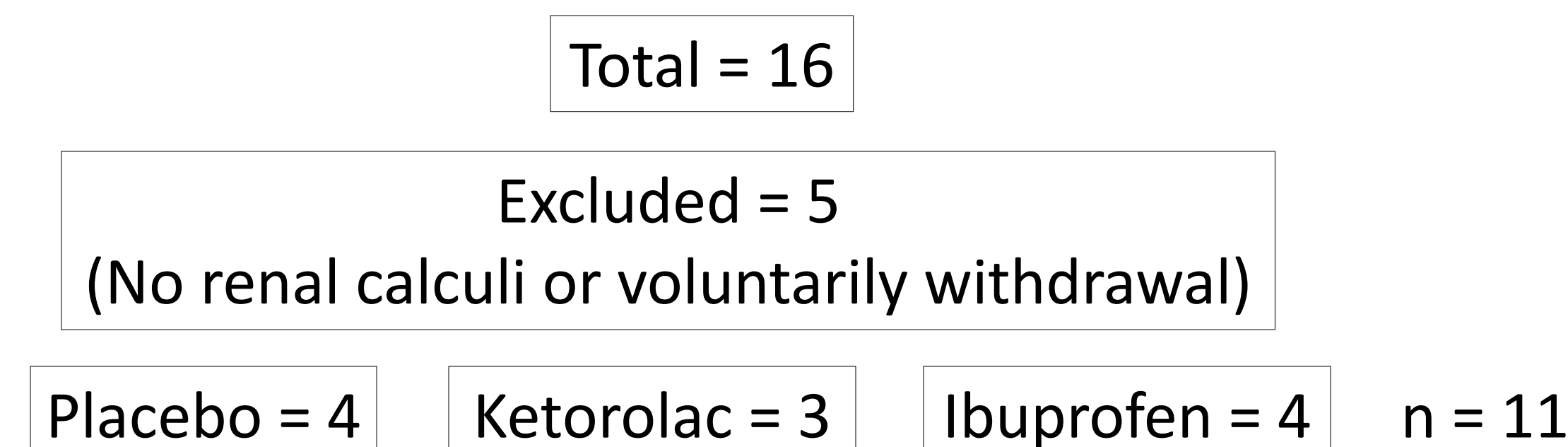


FIGURE 2: Mean AUC of pain score in each treatment group.

## Results



The ibuprofen group demonstrated consistent improvement in pain on VAS over the course of 120 min of study, with 100% of the patients in that arm demonstrating decreasing pain scores. One adverse drug event was reported in the placebo arm (nausea).

## Data Analysis

- ANOVA demonstrated no significant difference in AUC of pain assessed in any of the three treatment arms ( $p > 0.3$ ). Further analysis with 2-way ANOVA showed no significant interaction between time after drug administration, drug administered, and pain score ( $p > 0.5$ ).
- 100% of the patients in the ibuprofen arm reported decreased pain after 120 minutes as compared to 66% in the ketorolac arm and 75% in the placebo arm. ANOVA demonstrated no significant difference at  $t = 120$  minutes ( $p > 0.7$ )
- There was a statistically insignificant trend toward increased opioid use in the ibuprofen group, with 50% of those participants receiving rescue morphine.

## Discussion

- All treatment groups demonstrated improvement in median pain scores (corrected for pain at presentation) over the 120 minute observation period.
- A statistically insignificant trend toward improved pain control in the ibuprofen group was observed, with 100% of the patients in the ibuprofen arm reporting improved pain from baseline at the termination of the study.
- An increased need for rescue analgesia was observed in the ibuprofen group, with 50% ( $n = 2$ ) of the participants in that group utilizing rescue morphine, versus 0% in the other treatment groups. Possible explanations for this phenomenon include delayed onset of action versus ketorolac, less analgesic efficacy as compared to ketorolac, or a type I error.
- A major limitation of this study is inadequate sample size to draw significant conclusions.

## Conclusion

These preliminary findings and historical success with combination IV NSAID + opioid therapy indicate that IV ibuprofen has potential as an analgesic for renal colic. Further study is required to elucidate what role this novel drug will play in the treatment of renal colic.

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