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Original Contribution

Comparison of intravenous lidocaine/ketorolac combination to either analgesic alone for suspected renal colic pain in the ED☆

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ABSTRACT

Study objective: To compare analgesic efficacy and safety of intravenous lidocaine and ketorolac combination to each analgesic alone for ED patients with suspected renal colic.
Methods: We conducted a randomized, double-blind trial comparing analgesic efficacy of a combination of intravenous lidocaine (1.5 mg/kg) and ketorolac (30 mg), to ketorolac (30 mg), and to lidocaine (1.5 mg/kg) in patients aged 18–64 presenting to the ED with suspected renal colic. Primary outcome included difference in pain scores between the groups at 30 min. Secondary outcomes included a comparative reduction in pain scores in each group from baseline to 30 and 60 min as well as rates of adverse events and need for rescue analgesia at 30 and 60 min.
Results: We enrolled 150 subjects (50 per group). The difference in mean pain scores at 30 min between Lidocaine and Lidocaine/Ketorolac groups was −2.89 (95% CI: −4.39 to −1.39); between Ketorolac and Lidocaine/Ketorolac group was −0.92 (95% CI: −2.44 to 0.61); and between Ketorolac and Lidocaine was −1.98 (95% CI: −3.69 to −0.27). A comparative percentage of subjects in each group required rescue analgesia at 30 and 60 min. No clinically concerning changes in vital signs were observed. No serious adverse events occurred in either group. Commonly reported adverse effects were dizziness, nausea, and headache.
Conclusion: The administration of intravenous lidocaine/ketorolac combination to ED patients with suspected renal colic results in better analgesia in comparison to lidocaine alone but provides no analgesic advantages over ketorolac alone.
Clinicaltrials.gov Registration: NCT02902770.

1. Introduction

1.1. Background

Renal colic is an extremely painful condition that affects approximately 12% of the population and causes 1.2 million people to seek care in various health care facilities each year [1]. It accounts for 1% of all Emergency Department (ED) visits and 1% of all hospital admissions. In 50% of people with a history of kidney stones, recurrence rates approach nearly 50% after 10 years [2]. The pain of renal colic is multifactorial and is related to the obstruction of urinary flow with a subsequent increase in intra-renal and intra-ureteral pressure and prostaglandins-mediated ureteral spasm [1,2]. The provision of timely and effective analgesia for patients presenting to the ED with renal colic origin is of utmost importance for ED clinicians.

1.2. Importance

The literature regarding analgesic modalities, their combinations and routes of administrations for patients with pain related to renal colic is expanding. Non-steroidal anti-inflammatory drugs (NSAID's) such as ketorolac and opioids such as morphine constitute the primary mode of treatment for renal colic either alone or in combinations [3-7]. Despite their synergism and analgesic superiority when administered

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together [6,22], both classes of these medications possess a set of unfavorable side effects that limit their use [8,9]. Disadvantages to ketorolac use include a lack of titratability, severe nausea and epigastric pain, contraindications to use in patients with renal insufficiency, congestive heart failure, and acute peptic ulcer disease [8]. Opioid administration in the ED can lead to development of nausea and vomiting, hypotension and occasional pruritus, and in some cases, respiratory depression and lethargy [9].

There is limited data supporting the use of intravenous (IV) lidocaine, either alone or in combination with morphine for patients with renal colic, which demonstrated good analgesic efficacy and an acceptable safety profile [10-14]. However, there are no trials that have directly evaluated the role of an intravenous combination of lidocaine and ketorolac as a viable analgesic option in patients who are unable to tolerate or have serious contraindications to opioids.

2. Goals of this investigation

We hypothesized that the combination of IV lidocaine and ketorolac will provide superior analgesia to either lidocaine or ketorolac alone in patients presenting to the ED with presumed renal colic pain.

3. Materials and methods

3.1. Study design and setting

We conducted a randomized, double-blind trial assessing and comparing the analgesic efficacy of the combination of IV lidocaine and ketorolac to each analgesic alone for the treatment of pain clinically suspicious for renal colic in the ED.

We conducted this study at a 711-bed urban community teaching hospital with an annual ED census of >120,000 visits. Patient screening, enrollment, and data collection were performed by study investigators. The Maimonides Medical Center Institutional Review Board approved the trial and registered with clinicaltrials.gov (NCT02902770). We report this trial in accordance with the Consolidated Standards of Reporting Trials Group [15].

3.2. Selection of participants

We included adult patients aged 18–64 who presented to the ED with acute flank pain, abdominal pain, or back pain with or without hematuria suspected to be due to renal colic by the treating ED physician and who warranted IV analgesia. Furthermore, because the study's primary focus was pain relief, the diagnostic work up of selected patients was left to the discretion of the treating ED physician with respect to ordering laboratory testing and imaging studies (bedside ED or radiology ultrasonography (US), non-contrast computerized tomography (CT) scan of the abdomen/pelvis, both CT and US, or no imaging at all). We excluded patients with: 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 h 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.

Screening and enrollment of patients occurred between November 2016 and October 2018, Monday through Friday, 8 AM to 8 PM, when an ED pharmacist was available for blinded medication preparation. Study investigators approached all potentially qualifying participants. All participants provided written informed consent and Health Insurance Portability and Accountability Act authorization. For non-English speakers, a language-appropriate consent form was used and non-investigator, hospital-employed, trained interpreter assisted in the acquisition of informed consent.

3.3. Intervention

The on-duty ED pharmacist prepared medications in identical syringes and intravenous bags according to a predetermined randomization list generated via SPSS (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp) by the research manager. Participants were allocated to three groups according to the predetermined randomization list: Group 1 received a single dose of IV lidocaine at 1.5 mg/kg mixed in 100 ml normal saline bag and administered over 15 min and a corresponding placebo of normal saline as an intravenous push dose (IVP); Group 2 received a single IVP dose of ketorolac 30 mg and a corresponding placebo of 100 ml normal saline bag administered over 15 min; Group 3 received a single IVP 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 min. The choice of 30 mg of IV ketorolac was based on widely accepted and evidence-based regimen used in multiple prior ED studies [16-18] despite the recent trend towards the utilization of smaller (analgesic ceiling dosing) doses in the ED [19].

The research manager and statistician, who were independent of data collection, conducted the programming of the randomization list, confirmation of written consent acquisition, and statistical analyses. ED pharmacy investigators maintained the randomization list, prepared the medication, and delivered it to the nurse caring for the study participant in a blinded manner.

The preparing pharmacist, research manager, and statistician were the only people with knowledge of the study arm to which the participant was randomized; providers, participants, and the data collecting research team were blinded to the medication received. Study investigators included three treating physicians, who assisted in screening and supervision of the research fellow, and research assistants, who enrolled patients and recorded pain scores on a standard 0 to 10 numeric rating scale (NRS), vital signs, and adverse effects at baseline 15, 30, and 60 min. For subjects still requiring pain medication at 30 min post study drug administration, investigators offered IV morphine at 0.1 mg/kg as a rescue analgesic.

3.4. Outcomes measures

The primary outcome included a difference in pain scores between three groups at 30 min with recorded difference up to 60 min. Secondary outcomes included a comparative reduction in pain scores in each group from baseline to 30 and 60 min, rates of adverse events, and need for rescue analgesia at 30 and 60 min.

3.5. Primary data analysis

Research staff recorded all data on data sheets (separate from clinical data), entered them into Microsoft Excel (Microsoft, Redmond, WA), and then imported the data into SPSS 24.0 and SAS software (SAS, version 9.4; SAS Institute, Inc., Cary, NC) for statistical analyses. Data were described in terms of mean (SD) or 95% confidence limits for continuous variables, and frequency (percentage) for categorical variables. Data analyses of the pain data were based on the principle of intention to treat.

We utilized two sets of analyses. In one, we used paired *t*-tests between different time points to examine whether there were changes over time in each group. In the second, we did a multilevel analysis in order to look at whether the different groups showed different rates of improvement over time. To allow for non-linear (or possibly non-monotonic) effects of time, time was treated as a categorical variable.

The main hypothesis was that the combination of IV lidocaine and ketorolac will provide superior pain relief by demonstrating a greater change (difference) in pain score between baseline and every

subsequent time point with the primary comparison pain assessment between baseline and 30 min. In accordance with Bijur [20] and Holdgate et al. [21], we assumed a minimal clinically significant difference of 1.3 points between the 3 groups at the 30-minute pain assessment and an SD of 3.0. A power analysis determined that a sample of 50 subjects per group provided at least 80% power to detect a minimal clinically significant difference of at least 1.3 points at 30 min with alpha = 0.05.

4. Results

We enrolled 150 subjects (50 in each group) in our study. The patient flow diagram is illustrated in Fig. 1. Subjects' demographic characteristics and baseline vital signs are presented in Table 1. Mean ages were 39, 42, and 44 years old in each group with 54%, 56% and 56% of men in each group respectively. Baseline numerical rating scale (NRS) pain scores were equivalently high in all three study groups. In addition, all three groups were relatively similar with respect to chief complaints (predominantly flank and abdominal pain) and final diagnoses (predominantly renal colic) (Table 2).

The difference in mean pain scores at 30 min between Lidocaine and Lidocaine/Ketorolac groups was −2.89 (95% CI: −4.39 to −1.39) favoring the combination group; between Ketorolac and Lidocaine/Ketorolac groups was −0.92 (95% CI: −2.44 to 0.61); and between Ketorolac and Lidocaine groups was −1.98 (95% CI: −3.69 to −0.27) favoring Ketorolac group. Furthermore, at 60 min both Lidocaine/Ketorolac and Ketorolac groups had statistically significant difference in mean pain scores in comparison to the Lidocaine group (Table 3). However, the difference between Lidocaine/Ketorolac group and Ketorolac group with respect to mean pain score was not statistically significant at 30- and 60-minutes post-analgesic administration.

Table 1
Baseline patient characteristics.

Characteristics	Group		
	Lidocaine	Ketorolac	Combination
Age, mean (SD)	39.34 (10.95)	42.34 (10.47)	43.92 (10.36)
Male sex, frequency (%)	27 (54)	28 (56)	28 (56)
Pain, mean (SD)	8.36 (1.65)	7.94 (1.67)	8.4 (1.67)
Blood pressure, mm Hg			
Systolic	125.82 (17.64)	131.84 (19.65)	132.92 (18.56)
Diastolic	76.22 (13.53)	82.10 (13.26)	80.68 (11.60)
Pulse rate, beats/min	76.72 (13.53)	77.12 (13.89)	73.44 (10.29)
Respiratory rate, beats/min	18.16 (3.34)	18.70 (3.33)	18.90 (3.55)
Oxygen saturation	98.96 (1.24)	98.44 (1.50)	98.14 (2.04)

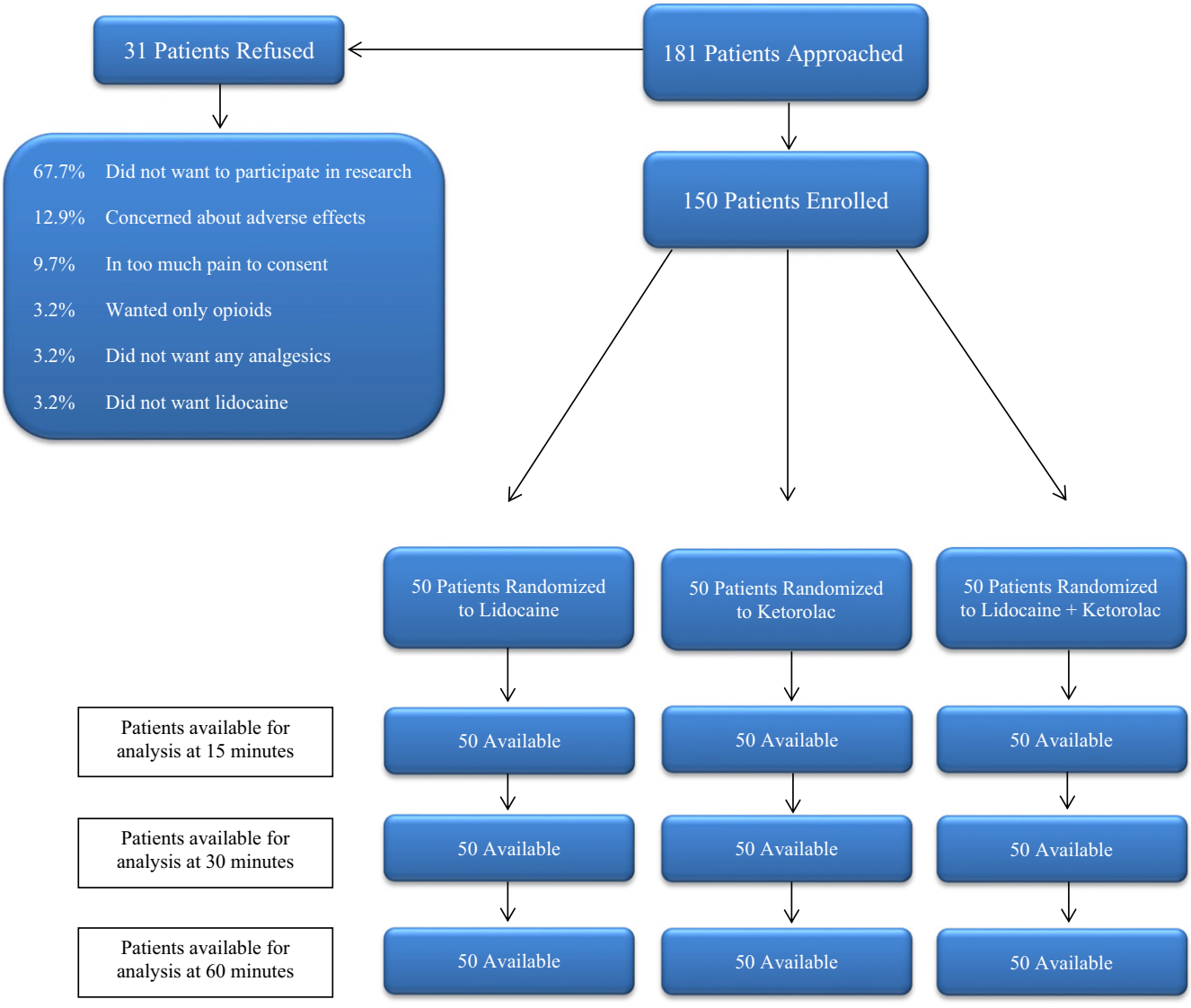

Fig. 1. Patient flow diagram.

Table 2
Chief complaints and diagnoses at discharge.

Group	Chief complaint					
	Flank pain	Abdominal pain	Back pain	Urinary frequency/burning	Groin pain	Bloody urine
Lidocaine	39 (78.0)[a]	9 (18.0)	1 (2.0)	1 (2.0)	–	–
Ketorolac	38 (76.0)	8 (16.0)	1 (2.0)	1 (2.0)	1 (2.0)	1 (2.0)
Combination	36 (72.0)	12 (24.0)	1 (2.0)	–	1 (2.0)	–
Total	113 (75.33)	29 (19.33)	3 (2.0)	2 (1.33)	2 (1.33)	1 (0.67)

Group	Diagnosis						
	Renal colic	Flank pain	UTI	Abdominal pain	Pyelonephritis	Back pain	Ovarian cyst
Lidocaine	29 (58.0)	5 (10.0)	1 (2.0)	6 (12.0)	2 (1.33)	4 (8.0)	3 (6.0)
Ketorolac	28 (56.0)	12 (24.0)	3 (6.0)	3 (6.0)	3 (6.0)	1 (2.0)	–
Combination	33 (66.0)	6 (12.0)	2 (4.0)	5 (10.0)	–	2 (4.0)	2 (4.0)
Total	90 (60.0)	23 (15.33)	6 (4.0)	14 (9.3)	5 (3.33)	7 (4.67)	5 (3.33)

[a] Frequency (percentage of group).

Additionally, at the 30 min mark, subjects randomized to a combination of 1.5 mg/kg IV lidocaine and 30 mg IV ketorolac improved from 8.40 to 3.14 (difference = 5.26, CI: 4.52 to 6.00). The 30 mg IV ketorolac group improved from 7.94 to 3.88 (difference = 4.06, CI: 3.23 to 4.89), and the group receiving IV lidocaine at 1.5 mg/kg improved from a mean pain score via NRS at baseline of 8.36 to a mean score of 5.52 (difference = 2.84, CI: 2.23 to 3.44). Reductions in pain scores from baseline to 30 min in each group were clinically important (>1.3 points) and statistically significant (95% CI does not include 0 for all groups). However, both lidocaine/ketorolac and ketorolac groups had larger changes in pain score than the lidocaine group at 30 min post-administration (Table 4). Furthermore, there were no clinically important differences between mean NRS pain scores at all time points between lidocaine/ketorolac and ketorolac alone (Table 4).

All groups showed a reduction in mean NRS pain scores relative to baseline at all subsequent time points (15 to 60 min). However, as shown in Fig. 2, the box plots at each time point underscore the analgesic superiority of lidocaine/ketorolac and ketorolac groups in comparison to the lidocaine group at 15, 30 and 60 min.

Similarly, the spaghetti plots comparing three groups with respect to initial and individual pain scores (5 and greater) over the study time periods (15–60 min) demonstrated a greater change in pain score in the lidocaine/ketorolac and ketorolac groups than in the lidocaine group (Appendix 1).

The multilevel model (Table 5) demonstrated a significant pain decrease between each time point and each subsequent time point for all three groups, and the analgesic superiority of the lidocaine/ketorolac group and the ketorolac group over the lidocaine group at 15, 30 and 60 min. Most importantly, the combination group had faster improvement in pain scores than either of the other groups between the baseline and each subsequent time point.

With respect to the use of rescue morphine analgesia at any time, no statistically significant differences were observed between three groups (Table 6).

There were no clinically concerning changes in vital signs nor clinically significant adverse effects related to the study medications. The most commonly reported adverse effects were dizziness, nausea, and headache with the largest percentage of patients experiencing these adverse effects in the lidocaine group (Table 7).

We carried out additional data analyses of subsets of subjects with radiologically documented ureterolithiasis, obstructive/non-obstructive uropathy, and hydronephrosis via US, CT scan or both in the lidocaine/ketorolac group, lidocaine group, and ketorolac group (Appendix 2). The results again demonstrated analgesics superiority of the lidocaine/ketorolac and ketorolac groups in comparison to the lidocaine group. Similarly, there were no clinically important differences between mean NRS pain scores at all time points between lidocaine/ketorolac group and ketorolac group (Table 8).

5. Limitations

This was a single-center study in which subjects were enrolled as a convenience sample according to availability of members of both the research and pharmacy teams which may have led to selection bias or underrepresentation of patients who may present to the ED late at night. Our stringent exclusion criteria and small sample size of 150 subjects were inadequate to assess variance in safety of the 3 different study medications. The study duration was not designed to compare the rates of pain recurrence (beyond 60 min) and the rates of adverse effects, such gastrointestinal bleeding and renal impairment, specific to ketorolac.

6. Discussion

In the ED setting, NSAID's are one of the most commonly used analgesics for managing renal colic [1,8]. Parenterally administered

Table 3
Difference in mean pain scores between all groups at 15, 30 and 60 min.

Time	Comparison	Difference (95% CI)
Baseline	Ketorolac – lidocaine	−0.20 (−1.15 to 0.74)
	Lidocaine – combination	−0.20 (−1.09 to 0.69)
	Ketorolac – combination	−0.41 (−1.32 to 0.51)
15 min	Ketorolac – lidocaine	−1.60 (−3.19 to −0.01)
	Lidocaine – combination	−2.12 (−3.52 to −0.73)
	Ketorolac – combination	−0.53 (−2.01 to 0.95)
30 min	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 min	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)

Table 4
Pain scores for all groups over time.

Time	Group	Mean (SD)	95% CI
Baseline	Lidocaine	8.36 (1.65)	5–10
	Ketorolac	7.94 (1.67)	5–10
	Combination	8.40 (1.66)	5–10
15 min	Lidocaine	6.34 (2.62)	1–10
	Ketorolac	5.22 (2.74)	0–9
	Combination	4.28 (2.54)	1–9
30 min	Lidocaine	5.52 (3.07)	4–10
	Ketorolac	3.88 (2.92)	0–9
	Combination	3.14 (2.61)	0–7
60 min	Lidocaine	4.48 (3.04)	0–10
	Ketorolac	2.70 (2.96)	0–9
	Combination	2.16 (2.30)	0–7

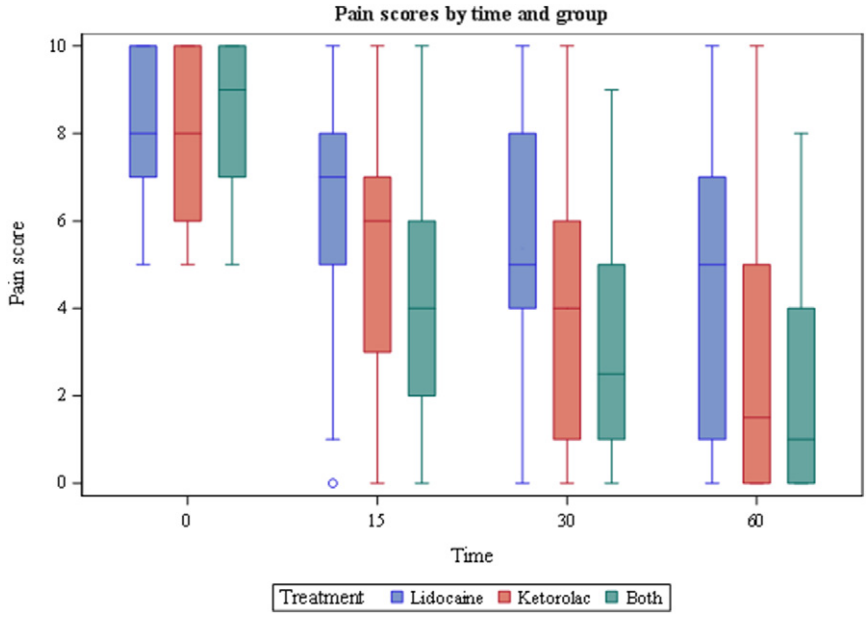

Fig. 2. Box-plots for reported pain NRS comparing groups over time.

ketorolac provides better analgesia, a better safety profile, lesser amount of rescue analgesia, and faster discharge from the ED in comparison to parenteral opioids [3,4,7]. Furthermore, a combination of IV ketorolac and morphine resulted in better pain relief, smaller analgesic doses, reduced rates of rescue analgesia, and better side effects profile when compared to either medications alone in adult patients presenting to the ED with acute renal colic [6,18]. Similarly (although based on one study), IV lidocaine administered at 1.5 mg/kg over 10 min for patients with renal colic provided better analgesia at 60 min in comparison to morphine (90% vs. 70% of patients) and similar rates of side effects [11]. Additionally, a combination of IV lidocaine and morphine resulted in faster onset of analgesia and less nausea in comparison to morphine alone [12]. However, a recently published systematic review evaluating the role of IV lidocaine in managing pain of renal colic in the ED could not support its widespread use in the ED [14].

We compared the analgesic efficacy and safety of lidocaine/ketorolac combination based on the synergistic mechanism of action towards relieving the ureteral spams and inflammation with enhanced passage of the stone to each analgesic alone with the goal of proving analgesic superiority of this combination. We were able to demonstrate a significant difference in pain relief between the lidocaine/ketorolac combination at all time points and lidocaine alone, but did not identify analgesic superiority in comparison to ketorolac alone. Furthermore, we showed that subjects receiving ketorolac alone had the lowest rates of adverse effects when compared to lidocaine and lidocaine/ketorolac in combination. Lastly, both the lidocaine/ketorolac combination group and the

Table 5
Mixed effect table depicting decrease in pain over time.

Solution for fixed effects							
Effect	Group	Time	Estimate	Standard error	Degrees of freedom	*t* value	Pr > |t|
Intercept			8.4000	0.3585	147	23.43	<0.0001
time		15	−4.1200	0.3248	441	−12.69	<0.0001
time		30	−5.2600	0.3248	441	−16.20	<0.0001
time		60	−6.2400	0.3248	441	−19.21	<0.0001
time		0	0	.	.	.	.
Group	Lidocaine		−0.04000	0.5069	441	−0.08	0.9371
Group	Ketorolac		−0.4600	0.5069	441	−0.91	0.3647
Group	Combination		0	.	.	.	.
Group * time	Lidocaine	15	2.1000	0.4593	441	4.57	<0.0001
Group * time	Lidocaine	30	2.4200	0.4593	441	5.27	<0.0001
Group * time	Lidocaine	60	2.3600	0.4593	441	5.14	<0.0001
Group * time	Lidocaine	0	0	.	.	.	.
Group * time	Ketorolac	15	1.4000	0.4593	441	3.05	0.0024
Group * time	Ketorolac	30	1.2000	0.4593	441	2.61	0.0093
Group * time	Ketorolac	60	1.0000	0.4593	441	2.18	0.0300
Group * time	Ketorolac	0	0	.	.	.	.
Group * time	Combination	15	0	.	.	.	.
Group * time	Combination	30	0	.	.	.	.
Group * time	Combination	60	0	.	.	.	.
Group * time	Combination	0	0	.	.	.	.

Table 6
Rates of rescue morphine.

Time	Group	Frequency (%)
30 min	Lidocaine	7 (14)
	Ketorolac	3 (6)
	Combination	4 (8)
60 min	Lidocaine	7 (14)
	Ketorolac	5 (10)
	Combination	3 (6)
Time	**Comparison**	**Difference (95% CI)**
30 min	Ketorolac vs. lidocaine	0.08 (−0.04 to 0.20)
	Lidocaine vs. combination	0.06 (−0.06 to 0.18)
	Ketorolac vs. combination	0.02 (−0.08 to 0.12)
60 min	Ketorolac vs. lidocaine	0.04 (−0.09 to 0.17)
	Lidocaine vs. combination	0.08 (−0.04 to 0.20)
	Ketorolac vs. combination	0.04 (−0.06 to 0.15)

ketorolac group had >50% change in pain score from the baseline to 60 min with similar rates of rescue analgesia between the groups at 30 and 60 min.

We believe that despite a small sample size, our ability to retain all 150 patients through the entire study period with full set of data with respect to pain scores and side effects, and to conduct a sub-analysis of subjects with documented renal colic, has strengthened the findings of our study that the combination of IV lidocaine and ketorolac possesses analgesic superiority over lidocaine alone but provides no analgesic advantages over ketorolac alone for patients with renal colic (suspected or documented) in the ED.

Our results have several important implications for clinical practice. First, we were able to demonstrate that administration of IV ketorolac as a single agent resulted in great pain relief with minimal rates of adverse effects for short-term analgesia in the ED. Second, the administration of IV lidocaine at 1.5 mg/kg over 15 min as a sole analgesic is inferior to either ketorolac or lidocaine/ketorolac combination with respect to pain relief and rates of adverse effects. This in fact, precludes IV lidocaine form being the first-line analgesic modality for ED patients with renal colic. Lastly, the lidocaine/ketorolac combination provided similar analgesia to ketorolac administered as a single agent but resulted in higher rates of adverse effects.

In conclusion, administration of an IV lidocaine/ketorolac combination to ED patients with suspected or documented renal colic results in better analgesia in comparison to parenteral lidocaine alone but provides no analgesic advantages over parenteral ketorolac alone. The utility of this analgesic combination for ED patients suffering from renal colic requires further investigation with larger and longer lasting studies before it can be recommended for widespread use in the ED.

Table 8
Pain scores for patients with confirmed renal colic over time.

Time	Group	Mean (SD)	95% CI
Baseline	Lidocaine	8.31 (1.75)	5–10
	Ketorolac	8.11 (1.81)	5–10
	Combination	8.52 (1.75)	5–10
15 min	Lidocaine	6.27 (2.84)	1–10
	Ketorolac	4.68 (3.14)	0–10
	Combination	4.15 (2.63)	0–10
30 min	Lidocaine	5.62 (3.19)	0–10
	Ketorolac	3.64 (3.24)	0–10
	Combination	2.73 (2.72)	0–8
60 min	Lidocaine	4.52 (3.02)	0–10
	Ketorolac	2.14 (2.85)	0–10
	Combination	1.73 (2.14)	0–8

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Conflicts of interest

All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. The authors have no independent disclosures or conflicts of interest.

Author contributions

Study concept and design: SM.
Acquisition, analysis, or interpretation of data: All authors.
Statistical analysis: AL, PF.
Drafting of the manuscript: SM, JD.
Critical revision of the manuscript for important intellectual content: SM, JM.
Study supervision: SM, AL, JM.

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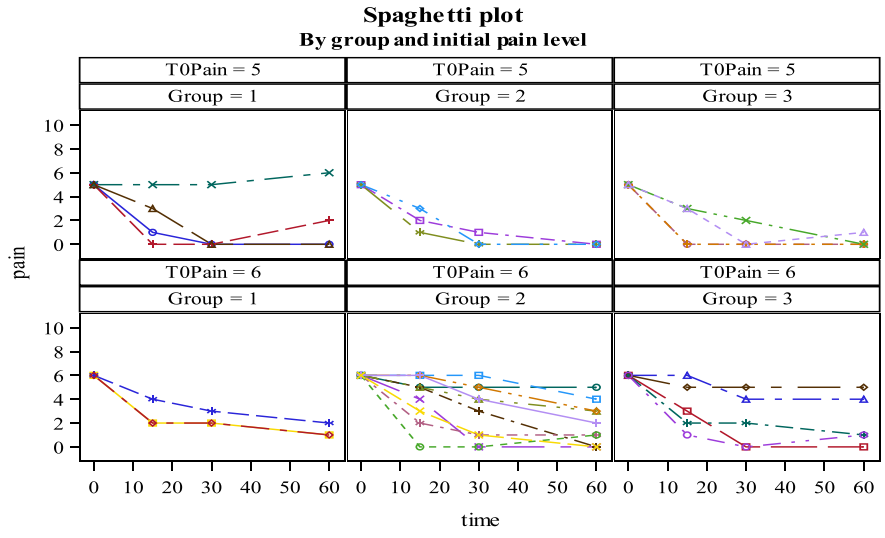
Table 7
Rates of adverse events.

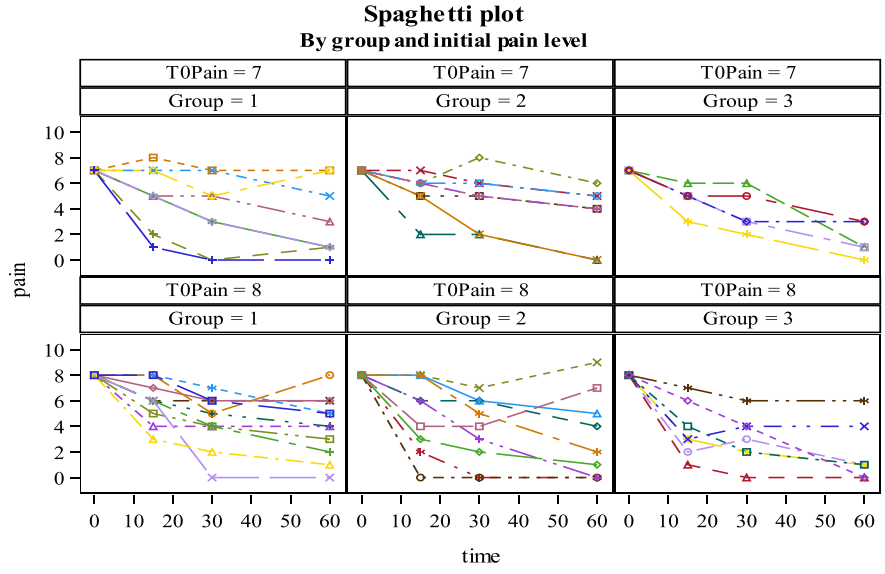
Time	Group	Adverse event								
		None	Dizziness	Nausea/vomiting	Perioral numbness	Periorbital numbness	Change in hearing/tinnitus	Headache	Epigastric pain	Drowsiness
15 min	Lidocaine	32 (64)[a]	6 (12)	5 (10)	2 (4)	–	1 (2)	2 (4)	2 (4)	–
	Ketorolac	43 (86)	–	3 (6)	–	–	–	4 (8)	–	–
	Combination	36 (72)	6 (12)	3 (6)	1 (2)	1 (2)	1 (2)	2 (4)	–	–
30 min	Lidocaine	34 (68)	9 (18)	2 (4)	–	–	1 (2)	2 (4)	2 (4)	–
	Ketorolac	47 (94)	2 (4)	–	–	–	–	–	1 (2)	–
	Combination	41 (82)	5 (10)	1 (2)	1 (2)	–	–	2 (4)	–	–
60 min	Lidocaine	39 (78)	3 (6)	4 (8)	–	–	–	2 (4)	–	2 (4)
	Ketorolac	47 (94)	1 (2)	1 (2)	–	–	–	1 (2)	–	–
	Combination	41 (82)	4 (8)	3 (6)	–	–	–	1 (2)	–	1 (2)

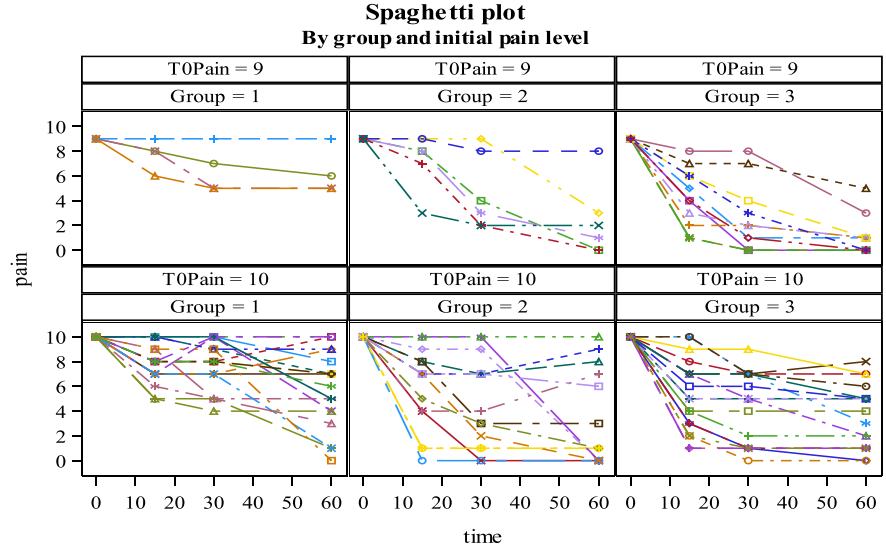
[a] Frequency (percent).

Appendix 1. Change in pain over time by group from baseline pain score (NRS 5 through 10)



*Group 1: Lidocaine, Group 2: Ketorolac, Group 3: Combination





Appendix 2. Diagnostic imaging

Group	CT		Ultrasound		Both CT and ultrasound	
	Total completed	positive Reading	Total completed	Positive reading	Total completed	Number positive
Lidocaine	33	18	13	8	8	3
Ketorolac	33	22	15	9	5	3
Combination	31	19	15	6	7	1

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