PICO Search Assignment Worksheet Name__Lisette Romo_____

Brief description of patient problem/setting (summarize the case very briefly)

A 22-year-old female with a past medical history of prediabetes, anxiety, and obesity presented to the emergency department with 2 days of progressively worsening abdominal pain. She reports that the pain is in the left upper quadrant and radiates to the left lower quadrant. She reports that initially she had mild discomfort while outdoors at the park, which was tolerable. However, she states that the pain progressively worsened, became constant, and is now 10/10 in severity. She had multiple episodes of vomiting, and states that she is unable to tolerate oral intake because she vomits every time she tries to eat or drink anything; she has not had a bowel movement in the past 2 days either. On physical exam, the patient appeared visibly uncomfortable, leaning towards the affected side of pain, and was unable to find a comfortable position; the abdomen was soft, non-distended, with tenderness to palpation of the epigastric region, LUQ, and LLQ. CVA tenderness was not assessed due to the severity of her pain. Imaging demonstrated a 3mm kidney stone causing a hydronephrosis in the left kidney, and urology was consulted. For pain control, the patient received IV Morphine. This raised the clinical question of the most effective pain management strategy for acute renal colic, specifically whether IV ketorolac provides similar or better pain relief with fewer adverse effects compared with IV opioids.

Search Question: In adults presenting to the emergency department with acute renal colic, does IV ketorolac compared to IV opioids provide equivalent or superior pain relief with fewer adverse effects?

Question Type: What type of question is this?

□ **Treatment** □ Diagnosis □ Prognosis □ Screening □ Prevalence □ Harms

Assuming that the highest level of evidence to answer your question will be meta-analysis or systematic review, what other types of study might you include if these are not available (or if there is a much more current study of another type)?
Please explain your choices.

Meta-analyses and systematic reviews offer the highest level of clinical evidence; if either were not available, then I would also include randomized controlled trials, cohort studies, retrospective studies, and clinical practice guidelines. Randomized controlled trials are helpful since they can directly compare treatments, including IV ketorolac versus IV opioids for pain management in patients who have renal colic. These studies would be relevant for my patient's case since she was suffering from intense abdominal pain from a kidney stone, leading to hydronephrosis, and required treatment in the ED. Cohort and retrospective studies can also be helpful as well in assessing any outcomes like pain relief, any additional medications, potential side effects, and ED length of stay. Lastly, clinical practice guidelines may also be helpful since they do provide evidence-based recommendations on first-line medications for nephrolithiasis.

PICO search terms:

P (Population)	I (Intervention)	C (Comparison)	O (Outcome)
Adults with acute renal colic	IV Ketorolac	IV opioids	Pain relief
Adults with nephrolithiasis	IM Ketorolac	Morphine	Need for rescue analgesics
Adults presenting to the emergency department with kidney stones	NSAIDs	Hydromorphone	Adverse side effects
Adults with severe flank/ abdominal pain from nephrolithiasis	Non-opioid pain medication	Narcotics for pain management	Symptomatic improvement
Adults with hydronephrosis secondary to kidney stones		Opioid medications	

Search tools and strategy used:

Please indicate what databases/tools you used, provide a list of the terms you searched together in each tool, and how many articles were returned using those terms and filters.

Database	Search Terms Used	Number of Results	Filters/Limiters Applied	Notes/Observations
PubMed	("acute renal colic" OR nephrolithiasis OR ureteral stone) AND pain management	487	English language, adults, the last 10 years	A broad initial search was used to identify high-level evidence regarding pain management for nephrolithiasis and renal colic. Results included a variety of systematic reviews, meta-analyses,

				RCTs, and comparative studies evaluating analgesic options.

Google Scholar	"acute renal colic" OR nephrolithiasis OR ureteral stone pain management ketorolac morphine NSAIDs opioids randomized trial meta-analysis	320	English language, adults, published within the last 10 years, sorted by relevance	Google Scholar returned a broader range of studies than PubMed, including RCTs, systematic reviews, meta-analyses, and other sources of evidence, such as clinical reviews and guideline articles. Search results included studies comparing pain control medications.
CINAHL	("acute renal colic" OR nephrolithiasis OR ureteral stone) AND pain management	55	English language, adults, published within the last 10 years, peer-reviewed	A broader search produced more results and included randomized controlled trials, systematic reviews, meta-analyses, and clinical reviews on pain management options for nephrolithiasis.

Results found:

Identify at least 3 articles (or other appropriate reputable sources) that answer your specific question with the highest available level of evidence.

1. **Comparison of Acetaminophen, Ketamine, or Ketorolac Versus Morphine in the Treatment of Acute Renal Colic: A Network Meta-Analysis.**
   https://pubmed.ncbi.nlm.nih.gov/37679264/

   Alghamdi YA, Morya RE, Bahathiq DM, et al. Comparison of Acetaminophen, Ketamine, or Ketorolac Versus Morphine in the Treatment of Acute Renal Colic: A Network Meta-Analysis. The American Journal of Emergency Medicine. 2023;73:187-196. doi:10.1016/j.ajem.2023.08.029.

Abstract

Background: Renal colic is a disease in which a calculus obstructs the urinary tract, resulting in severe pain do ureteric peristaltic movements. Other symptoms, such as hematuria, nausea, and vomiting, may accompany the pain. This network meta-analysis aimed to compare the efficacy and safety of different analgesic agents for the treatment of acute renal colic.

Objectives: To compare the efficacy and safety of intravenous acetaminophen, ketamine, ketorolac, and morphine for the treatment of acute renal colic by evaluating pain scores at 15, 30, and 60 minutes, adverse events, and the need for rescue therapy.

Methods: Medline, Embase, and CENTRAL databases were searched. Randomized controlled trials (RCTs) that compared different analgesic agents, either alone or in combination, were included. For the management of acute renal colic, analgesic agents were selected based on the current standard medical practice. The medications included intravenous acetaminophen, ketamine, ketorolac, and morphine. This study sought to evaluate the pain score on the visual analog scale (VAS) at 15, 30, and 60 min; adverse events; and the utilization of rescue therapy. The efficacy of different analgesic agents was explored through a frequentist network meta-analysis using the Netmeta statistical package in R software. All treatments were ranked using the Netrank function, yielding P-scores.

Results: Twelve RCTs were deemed eligible. As per the P-scores, acetaminophen was the most effective in reducing pain score at 15 min (P-score = 0.74). Ketorolac was the most effective in reducing the pain score at 30 and 60 min (P-score = 0.84) (P-score = 0.99), whereas morphine was the least effective (P-score = 0.07). Moreover, morphine was correlated with the highest odds of adverse events after treatment (P-score = 0.89). Morphine was the most frequently required rescue therapy in cases of suboptimal pain relief (P-score = 0.96).

Conclusions: This network meta-analysis demonstrated that ketorolac and acetaminophen were the most effective analgesic agents according to the pain score. Morphine showed the highest adverse event profile and the highest rate at which rescue therapy was required for the management of acute renal colic.

Keywords: Acetaminophen; Acute renal colic; Ketamine; Ketorolac; Morphine.

Why I chose this article:

I decided to choose this article since it directly relates to the patient case scenario, who presented with severe pain from nephrolithiasis, causing hydronephrosis. She required pain control and received opioid medication, morphine, due to the severity of her symptoms and inability to tolerate oral intake. This article was very helpful since it compared commonly used medications for acute renal colic, including ketorolac, morphine, etc. The article also provided a high level of evidence since it was a network meta-analysis of randomized controlled trials. The results demonstrated that ketorolac was more effective for pain relief, specifically at 30 and 60 minutes, with a lot less side effects in comparison to morphine. While Morphine was found to have the highest rate of rescue medication use, in other words, patients need more treatment for pain control. The patient in the case scenario experienced significant pain, nausea, and vomiting, so it is crucial to determine what medication would provide the best pain relief.

Key Points:

i. 12 RCTs were included in this network meta-analysis

ii. Ketorolac provided effective pain relief and reduced pain at 30 and 60 minutes.

iii. Morphine was the least effective medication for pain relief and was associated with the highest rates of adverse effects.

iv. This study supports ketorolac as an effective first-line option for acute renal colic pain in the emergency department.

2. **Comparison of the Efficacy of Nonsteroidal Anti-Inflammatory Drugs and Opioids in the Treatment of Acute Renal Colic: A Systematic Review and Meta-Analysis**
https://pmc.ncbi.nlm.nih.gov/articles/PMC8828916/

Leng XY, Liu CN, Wang SC, et al. Comparison of the Efficacy of Nonsteroidal Anti-Inflammatory Drugs and Opioids in the Treatment of Acute Renal Colic: A Systematic Review and Meta-Analysis. Frontiers in Pharmacology. 2021;12:728908. doi:10.3389/fphar.2021.728908

Abstract

Background: Although multiple randomized controlled trials (RCTs) and systematic review and meta-analysis were performed to investigate the efficiency and safety of nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids in the treatment of acute renal colic, the therapeutic regimen of renal colic is still controversial. Therefore, the aim of this study was to derive a more concise comparison of the

effectiveness and safety between NSAIDs and opioids in the treatment for patients with acute renal colic by a systematic review and meta-analysis.

Objective: The aim of this study was to derive a more concise comparison of the effectiveness and safety between NSAIDs and opioids in the treatment for patients with acute renal colic by a systematic review and meta-analysis.

Methods: We searched PubMed, Embase, and Cochrane Central Register of controlled trials for seeking eligible studies. The pooled mean difference (MD) or risk ratio (RR) with 95% confidence interval (CI) was calculated using the random effects model. The primary outcome was assessed according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE).

Results: A total of 18 studies involving 3,121 participants were included in the systematic review and meta-analysis. No significant difference between the NSAID and opioid groups was observed, with changes in the visual analog scale (VAS) at 0–30 min (MD = 0.79, 95% CI: −0.51, 2.10). NSAIDs in the form of intravenous administration (IV) had no better effect on the changes in the VAS at 0–30 min, when compared to opioids (MD = 1.25, 95% Cl: −4.81, 7.3). The NSAIDs group in the form of IV had no better outcome compared to the opioids group, as well as the VAS at 30 min (MD = −1.18, 95% Cl: −3.82, 1.45; MD = −2.3, 95% Cl: −5.02, 0.42, respectively). Moreover, similar results of this outcome were also seen with the VAS at 45 min (MD = −1.36, 95% Cl: −5.24, 2.52). Besides, there was a statistical difference in the incidence of later rescue (RR = 0.76, 95% CI: 0.66, 0.89), drug-related adverse events (RR = 0.44, 95% CI: 0.27, 0.71), and vomiting (RR = 0.68, 95% CI: 0.49, 0.96).

Conclusion: There is no significant difference between the NSAIDs and opioids in the treatment of renal colic in many outcomes (e.g., the VAS over different periods using different injection methods at 30 and 60 min), which has been focused on in this study. However, the patients who were treated using NSAIDs by clinicians can benefit from fewer side effects.

Keywords: acute renal colic, nephrolithiasis, kidney stones, NSAIDs, opioids, ketorolac, morphine.

Why I chose this article:

I chose this article since it is a systematic review and meta-analysis, which provides a high level of evidence by combining results from various studies. This included 18 studies with approximately 3,000 participants, providing more reliable evidence that can be applicable in real-world clinical scenarios. The results demonstrated that both NSAIDs and opioids provided very similar efficacy in managing pain, yet NSAIDs had fewer adverse effects, with less need for a rescue analgesic. This is significant in the patient's case since the clinician was deciding which pain medication would be most appropriate to give the patient; ultimately, it was decided that Morphine would be given instead. However, it should be important to consider any additional side effects that come with opioid administration.

Key Points:

i. A systematic review and meta-analysis including 18 studies with 3,121 participants

ii. NSAIDs and opioids provided similar pain relief

iii. NSAIDs were associated with fewer adverse side effects and less vomiting

iv. Ketorolac is an effective first-line option for symptomatic relief in patients with acute renal colic pain.

3. A Systematic Review and Meta-analysis Comparing the Efficacy of Nonsteroidal Anti-Inflammatory Drugs, Opioids, and Paracetamol in the Treatment of Acute Renal Colic.
https://pubmed.ncbi.nlm.nih.gov/29174580/

Pathan SA, Mitra B, Cameron PA. "A Systematic Review and Meta-analysis Comparing the Efficacy of Nonsteroidal Anti-inflammatory Drugs, Opioids, and Paracetamol in the Treatment of Acute Renal Colic." Eur Urol. 2018;73(4):583-595. doi:10.1016/j.eururo.2017.11.001. PMID: 29174580.

Abstract

Background: Renal colic is a common, acute presentation of urolithiasis that requires immediate pain relief. European Association of Urology guidelines recommend nonsteroidal anti-inflammatory drugs (NSAIDs) as the preferred analgesia. However, the fear of NSAID adverse effects and the uncertainty about superior analgesic effect have maintained the practice of advocating intravenous opioids as the initial analgesia.

Objective: The objective of this systematic review and meta-analysis was to compare the safety and efficacy of NSAIDs with opioids and paracetamol (acetaminophen) for the management of acute renal colic.

Methods: Systematic review and meta-analysis of randomized controlled trials comparing NSAIDs, opioids, and paracetamol for acute renal colic. Databases searched included Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, WHO International Clinical Trials Registry Platform, Google Scholar, and reference lists through December 2016. Two reviewers independently screened studies, assessed risk of bias, and extracted data. A total of 36 RCTs with 4,887 patients were included.

Results: From 468 potentially relevant studies, 36 randomized controlled trials (RCTs) including 4887 patients, published between 1982 and 2016, were included in this systematic review. The treatment effect observed indicated marginal benefit of NSAIDs over opioids in initial pain reduction at 30min (11 RCTs, n=1985, mean difference [MD] -5.58, 95% confidence interval [CI] -10.22 to -0.95; heterogeneity I^2=81%). In the subgroup analyses by the route of administration, NSAIDs required fewer rescue treatments (seven RCTs, n=541, number needed to treat [NNT] 11, 95% CI 6-75) and had lower vomiting rates compared with opioids (five RCTs, n=531, NNT 5, 95% CI 4-8). Comparisons of NSAIDs with paracetamol showed no difference for both drugs at 30min (four RCTs, n=1325, MD -5.67, 95% CI -17.52 to 6.18, p=0.35; I^2=89%). Patients treated with NSAIDs required fewer rescue treatments (two trials, n=1145, risk ratio 0.56, 95% CI 0.42-0.74, p<0.001; I^2=0%).

Conclusion: NSAIDs were equivalent to opioids or paracetamol in the relief of acute renal colic pain at 30min. There was less vomiting and fewer requirements for rescue analgesia with NSAIDs compared with opioids. Patients treated with NSAIDs required less rescue analgesia compared with paracetamol. Despite observed heterogeneity among the included studies and the overall quality of evidence, the findings of a lower need for rescue analgesia and fewer adverse events, in conjunction with the practical advantages of ease of delivery, suggest that NSAIDs should be the preferred analgesic option for patients presenting to the emergency department with renal colic.

Keywords: Analgesia; Emergency department; Nonsteroidal anti-inflammatory drugs; Opioids; Paracetamol; Renal colic; Urolithiasis; Urology.

Why I chose this article:

I chose this article since it provided a strong level of evidence and was very comprehensive in answering my PICO question. This was a study comprised of 36 RCTs with 4,887 patients, which gives a broader view into how NSAIDs, opioids, and paracetamol medications take effect in the setting of nephrolithiasis. I also chose it since it did not just look into pain reduction alone, but also considered other outcomes such as need for rescue analgesic and vomiting side effects, which are very relevant in an emergency department setting. This was important because the patient in the case scenario had severe pain caused by a 3mm kidney stone, causing obstruction and leading to a hydronephrosis. In a patient like this, it is crucial to consider several factors, such as whether it reduces pain, worsens nausea, or requires giving more pain medication later on. Similar to the other two articles, this article also found that NSAIDs provided similar efficacy in pain relief compared to opioids. This article strengthened the overall evidence considering ketorolac as an effective first-line medication in patients with this condition.

Key Points:

i. Systematic review and meta-analysis of 36 randomized controlled trials with 4,887 patients

ii. Pain relief at 30 minutes was similar between NSAIDs, opioids, and paracetamol

iii. NSAIDs showed slightly better early pain reduction compared with opioids

iv. The overall findings support NSAIDs, especially ketorolac, as a strong first option for pain control in renal colic

What is the clinical "bottom line" derived from these articles in answer to your question?

Overall, NSAIDs like Ketorolac should be considered first-line medications in patients dealing with pain from nephrolithiasis, as they give comparable pain relief to opioids with less significant side effects. Across studies, ketorolac demonstrated stronger pain relief by 30 and 60 minutes, with fewer side effects compared to morphine and other opioids. This is crucial information to understand, particularly in emergency medicine patients, because providers often have to make rapid decisions in patients who are in severe pain. In my patient's case, she had severe pain from a 3mm kidney stone,

leading to hydronephrosis, with repeated vomiting and visible discomfort. She received morphine due to the severity of her symptoms. She underwent imaging, confirming a 3 mm kidney stone with hydronephrosis, and continued to vomit during her CT scan, which might have potentially been worsened by opioid administration. Ketorolac might have been a better initial choice since it provides similar pain relief without potentially worsening her nausea and vomiting. The evidence supports using ketorolac first, while reserving opioids for patients with contraindications to NSAIDs, severe refractory pain, or cases where more pain control is needed.