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Comparison of the Analgesic Effects of Intravenous Dexketoprofen, Ibuprofen and Fentanyl in Patients Suffering from Renal Colic Pain in the Emergency Department

Murat Özdemir[1], Gülşen Çığşar[2], Murat Bağcıoğlu[3], Handan Çiftçi[4], Elnare Günal[5]

[1]Uşak Training and Research Hospital, Clinic of Emergency Medicine, Uşak, Turkey
[2]University of Health Sciences Turkey, Ankara Dışkapı Yıldırım Beyazıt Training and Research Hospital, Clinic of Emergency Medicine, Ankara, Turkey
[3]Kafkas University Health, Research and Application Center, Department of Urology, Kars, Turkey
[4]Kafkas University Health, Research and Application Center, Department of Emergency Medicine, Kars, Turkey
[5]Rize Training and Research Hospital, Clinic of Emergency Medicine, Rize, Turkey

Abstract

Aim: Renal colic is a urological emergency usually caused by urolithiasis and manifested by severe pain. Emergency treatment's main purpose is to effectively relieve pain and urinary obstruction without impaired renal function. We measured the efficacy and safety of intravenous ibuprofen on renal colic pain.

Materials and Methods: Two-hundred thirty-five patients who were admitted to the emergency department between 01.01.2016-30.06.2017 and were suspected of renal colic that scored at least 2 points on the visual analog scale (VAS) or FLACC scale were included in the study after obtaining detailed consent. One hundred-fifty four patients whose diagnoses were confirmed radiologically, included in the study as Group A (dexketoprofen) (n=35), Group B (ibuprofen 400 mg) (n=37), Group C (ibuprofen 800 mg) (n=44), and Group D (fentanyl) (n=38). VAS and FLACC scales were re-evaluated on the 20th, 40th, and 60th minutes after drug administration.

Results: 64.9% of the patients were male and 35.1% were female, and the mean age was 42.31 (±15.46). It was observed that all 4 of the medications given to patients who applied to the emergency department with flank pain provided effective analgesia, but the drugs could not establish a statistically significant advantage over each other.

Conclusion: Intravenous administration of ibuprofen is considered as an effective and safe alternative in the treatment of renal colic pain in the emergency department.

Keywords: Analgesia, dexketoprofen, fentanyl, ibuprofen, renal colic

Introduction

Renal colic is a common urological emergency characterized by severe pain, usually associated with urolithiasis, diagnosed, and treated in emergency departments. Each year, more than 1 million patients in the United States present to emergency services due to renal colic (1,2). The cause of pain is usually the presence of an acutely obstructing stone in the urinary tract. Due to this obstruction, dilatation of the ureter and stretching and spasm of the ureteral smooth muscle cells are observed (3). The prevalence of kidney stones worldwide is estimated to be 5-15% in the general population (4).

Pain management is the first-line treatment of renal colic. In 80% of the patients, the stones pass spontaneously, and no additional treatment is needed (5,6). Non-steroidal anti-inflammatory drugs (NSAIDs) and opioid analgesics are widely used all over the world for treating renal colic pain (2). However, opioid analgesics may have side effects such as nausea, vomiting, dizziness, respiratory depression as well as addictive effects (3,4). Therefore, physicians

Corresponding Author: Murat Özdemir MD, Uşak Training and Research Hospital, Clinic of Emergency Medicine, Uşak, Turkey
Phone: +90 535 379 67 26 **E-mail:** doktoraiki@gmail.com **ORCID ID:** orcid.org/0000-0002-8732-5072

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around the world are turning to equally effective and rapid, but safer alternatives for treating renal colic pain. An ideal pain reliever should have a high safety profile and the ability to stop pain quickly and effectively without significant interaction with other pharmacological agents (7). In the literature, there are many studies stating that NSAIDs are effective, fast, and safe for treating renal colic pain (8-11).

We investigate the superiorities and advantages of ibuprofen (400 mg and 800 mg doses), an NSAID used in oral form for many years, by intravenous (IV) administration and compare it with another NSAID, dexketoprofen, and an opioid analgesic, fentanyl, in terms of analgesic efficacy and rate.

Materials and Methods

The study was planned as a prospective, randomized single-blind study. The study was initiated with the approval of a Kafkas University Faculty of Medicine Hospital Ethics Committee (no: 01, date: 27.01.2016).

Study Population and Sample

Patients over the age of 18 who applied to the emergency department of a university hospital by themselves or via 112 Emergency Ambulance Service between 01.01.2016 and 30.06.2017 with flank pain and diagnosed with renal colic (urolithiasis) by physical examination and radiological imaging who scored 2 or higher on the visual analogue scale (VAS) or FLACC (Face, Legs, Activity, Cry, Consolability) pain scales were included in our study (Table 1, Figure 1) (12,13). Patients whose diagnosis could not be confirmed radiologically, and patients who were diagnosed other than renal colic during the evaluation process were excluded from the study. Patients who applied recurrently due to renal colic were accepted as new admissions, provided that at least 48 h had passed since the previous application.

Data Collection Form

Demographic data and medical history of the patients included in the study were recorded in the data collection form. FLACC and VAS scores were recorded at the 0th min after vital signs were obtained and they were examined. Patients scoring 2 points or more on at least one of both scales were randomized by simple random sampling by drawing one of the 4 previously determined cards (ace of spades for Group A, ace of hearts for Group B, ace of diamonds for Group C, and ace of clubs for Group D) from the deck of cards. According to the cards they drew, they were divided into 4 groups: IV 50 mg dexketoprofen (Group A), IV 400 mg ibuprofen (Group B), IV 800 mg ibuprofen (Group C), and IV 0.75 mcg/kg fentanyl (Group D). The medicines were administered IV as a 20-minute infusion in 100 cc 0.9% NaCl solution. Care was taken to ensure that the liquids given were colorless and odorless and that they were given in the same amount and at the same time. VAS and FLACC scores at 0, 20, 40, and 60 min were recorded for all patients.

Exclusion Criteria

Those who are allergic to fentanyl, NSAIDs, or opiates, have hemodynamic instability, fever ≥38 °C, peritoneal irritation findings on physical examination, pregnant or suspected pregnancy, breastfeeding, known or suspected aortic dissection or aneurysm, using pain medication in the last 24 h, and patients with cardiac, renal or hepatic insufficiency and a history of transplant were excluded from the study. Patients who developed drug-related side effects during infusion and whose treatment could not be completed were excluded from the study.

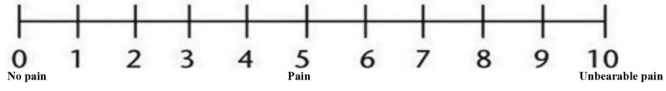

Figure 1. Visual analog scale

Use of the scale: The patient is asked to mark the most suitable place for her on the scale according to the severity of their pain, with 0 being the lowest and 10 being the highest

Table 1. FLACC pain scale

Categories	0	1	2
Face	No particular expression	Occasional grimaces or frown	Frequent to constant quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless, and tense	Kicking or legs drawn up
Activity	Lying quietly, normal position moves easily	Squirming, shifting, back and forth, tense	Arched, rigid or jerking
Cry	No cry (awake or asleep)	Moans or whimper, occasional complaint	Crying steadily, screams, or sobs, and frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging, or being talked to, distractible	Difficult to console or comfort

Use of the scale: The patient is evaluated using five parameters. A score between 0 and 2 is given for each parameter. The patient is given a total score of 0 to 10

Statistical Analysis

Data analysis was done with Statistical Package for the Social Sciences for Windows 22 package program. Whether the distribution of continuous variables was close to normal was investigated by the Kolmogorov-Smirnov Z test. Descriptive statistics were presented as mean±standard deviation or median (minimum-maximum) for continuous variables, and number of cases and (%) for categorical variables. The significance of the difference between the groups in terms of means was evaluated with Student's t-test and one-way ANOVA F, and the significance of the difference in terms of median values was examined using the Mann-Whitney U test. Categorical variables were evaluated using the chi-square test. The effect of independent factors was calculated by linear regression analysis. Results for $p<0.05$ were considered statistically significant.

Results

The data of 235 patients who presented to the emergency department of a university hospital with flank pain, either by themselves or through the 112 Emergency Ambulance Service, were analyzed for the study. Of these patients, 79 were excluded because the diagnosis of renal colic could not be confirmed radiologically, and 2 of them were excluded because of their missing data. A total of 154 patients, 100 (64.9%) male and 54 (35.1%) female, were included in the study. The ages of the patients ranged from 19 to 74, with a mean age of 40.96±13.68 for men and 44.80±18.19 for women.

62.3% of the patients had a history of renal colic. The most common complaint was flank pain (94.8%), and the most common physical examination findings were costovertebral angle tenderness (CVAT) (87.7%) and abdominal defense (48%). Hematuria was detected in urinalysis in 77.9% of the patients. Other complaints of admission to the emergency department and physical examination findings are given in Table 2.

Table 2. Complaint and anamnestic demographic data

Complaints and findings of physical examination	Number of patients n (%)
History of colic attack	96 (62.3)
Flank pain	146 (94.8)
Nausea	68 (44.2)
Burning sensation during urination	66 (42.9)
Presence of abdominal pain	56 (36.4)
Color changes in urine	41 (26.6)
Vomiting	36 (24.4)
CVAT	135 (87.7)
Hematuria	120 (77.9)

CVAT: Costovertebral angle tenderness

After the patients were diagnosed with renal colic, they were divided into four groups as Group A (dexketoprofen), Group B (ibuprofen 400), Group C (ibuprofen 800), and Group D (fentanyl) according to the given medication. The grouping of the patients according to the treatment given is given in Table 3. The reason for the difference in the number of patients in the four groups is that the groups were randomized before analgesic treatment, but the radiological examination could be performed after treatment.

Medication was started after VAS scoring was performed at the 0th minute. The analgesic efficacy of the given medications was compared by performing the VAS scoring at the 20th, 40th, and 60th minutes. However, there was no statistically significant difference (p=0.368, p=0.368 and p=0.368, respectively) (Figure 2).

Medication was started after FLACC scoring was performed at the 0th minute. The analgesic efficacy of the given medications was compared by performing the FLACC scoring at the 20th, 40th, and 60th minutes. However, there was no statistically significant difference (p=0.368, p=0.368 and p=1.000, respectively) (Figure 3).

No statistically significant difference was found between the medication groups in terms of analgesic efficacy. Notably, in the groups given ibuprofen 400 mg and ibuprofen 800 mg, no

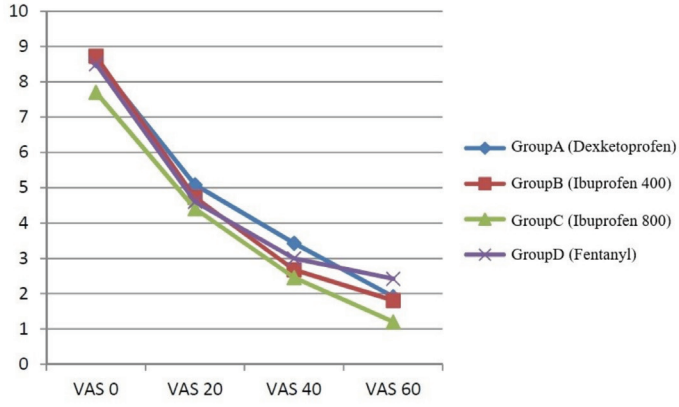

Figure 2. Pain relief efficacy between groups according to the VAS scale

VAS: Visual analog scale

Table 3. Distribution of patients by a given medication

	Medication	Number of patients n (%)
Group A	Dexketoprofen	35 (22.7)
Group B	Ibuprofen 400	37 (24.0)
Group C	Ibuprofen 800	44 (28.6)
Group D	Fentanyl	38 (24.7)
	Total	154 (100)

significant difference could be found in pain relief, although the drug dose was twice as high.

In terms of FLACC scoring, although it was not statistically significant, faster pain relief was found in Groups A and Group C in the first 20 min. In Group D, the pain relief activity at the 20th min was observed to be at the lowest. No similar situation was found for VAS scoring.

Additional treatment was needed in 9.1% of the patients who received treatment. Mild dizziness was observed after treatment in 1.3% of the patients included in the study, and no treatment was required. No statistically significant difference was found between the treatment given to the patients and the need for additional treatment (p=0.578).

Discussion

Renal colic is a disease frequently seen in emergency departments and is characterized by severe pain. There are many studies in the literature on pain management in patients with renal colic.

In our study, the most common complaint of the patients at the time of admission was flank pain (94.8%), which is consistent with the literature (14,15).

Defense, rebound, and rigidity can be detected in the abdominal examination. Nausea and vomiting occur in about half of the patients. Most patients have CVAT. Hematuria is present in 80% of patients, but it is obvious in only one-third. Upper ureteral stones may cause flank pain, and middle ureteral stones may cause pain that radiates to the lower abdominal quadrants (16). In middle ureter stones, the patient's clinic may be confused with appendicitis on the right and diverticulitis on the left. As the stones approach the bladder, signs of irritative micturition may be seen. Abdominal pain lasting less than 12 h, flank pain or costovertebral angle tenderness, and hematuria (>10 erythrocytes) are the most important findings of acute renal colic (17).

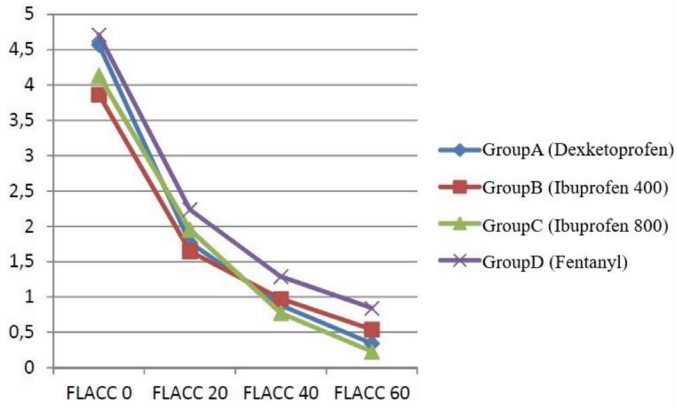

Figure 3. Pain relief efficacy between groups according to the FLACC scale

In the study published by Pathan et al. (18) in 2016, CVAT was found to be positive in 68.1% of the patients. In the study by Duran et al. (15) in 2014, 80.5% of the patients were found to be positive for CVAT. Similarly, our study detected unilateral or bilateral positive CVAT in 87.7% of the patients. In 79.9% of the patients, CVAT was positive unilaterally. The presence of unilateral CVAT positivity in patients who applied to the emergency department with the complaint of flank pain can be evaluated as an examination finding that strengthens the diagnosis of renal colic.

Considering the studies comparing drug efficacy in patients treated with renal colic, Serinken et al. (19) reported that there was no statistically significant difference in the pain relief effectiveness of both drugs in their 2012 study in which they compared the pain relief effects of morphine and acetaminophen on renal colic. In a similar study by Azizkhani et al. (20) in 2014, the analgesic effectiveness of morphine was found to be significantly higher than acetaminophen. Pathan et al. (18) in 2016 compared the pain efficacy of diclofenac, morphine, and acetaminophen on renal colic and concluded that the analgesic efficacy of NSAIDs was significantly higher than morphine. Masoumi et al. (21) reported in 2014 that acetaminophen was more effective in renal colic pain than morphine. Cevik et al. (10) in 2011 compared the effects of IV forms of tenoxicam, lornoxicam, and dexketoprofen on renal colic pain, and no significant difference was found in terms of pain effectiveness in all 3 drug groups. In a systematic review published in 2022 suggested that dexketoprofen has a similar pain relief effect compared to lidocaine and dexmedetomidine but is more potent than acetaminophen (22). Another systematic review and meta-analysis report that there is no significant difference between various NSAIDs, opioids, ketamine, and lidocaine in terms of pain relief (23). In 2018, Cenker et al. (7) compared the pain efficacy of 800 mg IV ibuprofen and 1000 mg IV acetaminophen in renal colic using VAS at the 15th and 30th min and reported that ibuprofen provided significantly more effective analgesia in both groups. A randomized double-blind study compared the analgesic effects of IV ibuprofen and IV tenoxicam in patients with acute musculoskeletal pain due to ankle injury. VAS scores were recorded at 15, 30, 60 and 120 minutes, and in conclusion, both drugs provided equal pain relief (24). In the study by Forouzanfar et al. (1) in 2019, 800 mg IV ibuprofen and 30 mg IV ketorolac were given to patients with renal colic pain, and it was determined that the pain relief effectiveness of ibuprofen was more effective than ketorolac at the 30th and 60th minutes. A randomized double-blind study compared the analgesic effects

of IV ibuprofen plus morphine, IV ketorolac plus morphine and morphine alone in patients with acute renal colic. VAS scores were recorded at 15, 30, 60 and 120 minutes, and in conclusion, both ibuprofen plus morphine and ketorolac plus morphine provided similar pain relief but better than morphine alone (4). In a study by Imamoglu et al. (2) in 2017 on 125 patients, the effects of IV fentanyl and nebulized fentanyl on VAS and verbal pain scale (VPS) at 15th and 30th min were compared, and no significant difference was found. In the study by Zamanian et al. (8), published in 2016, on 158 patients, suppository forms of morphine, an opiate analgesic, and indomethacin, an NSAID, were compared in terms of pain relief in renal colic, using VPS at the 20th, 40th, 60th, and 90th minutes. The pain relief effectiveness of morphine at the 20th min was statistically significant, but no significant difference was found at the 40th, 60th, and 90th minutes. In our study, no statistically significant difference was found in terms of VAS scores at the 20th, 40th and 60th minutes in the pain relief activities of the four groups, which is consistent with the literature. Additionally, no statistically significant difference was found between the pain relief activities of the four groups at the 20th, 40th and 60th minutes in terms of FLACC scoring. In our literature search, no study was found in which the FLACC pain scale was used in renal colic.

In our study, no statistically significant results were obtained in terms of the need for additional medication, medication given, gender, CVAT localization, or history of renal colic, which was consistent with the literature. Similar results are also observed in studies in the literature. This shows that the demographic characteristics of the patients do not affect the requirement for additional medication. The fact that there is no statistically significant difference between the pain relievers given in terms of analgesic effectiveness may result in the absence of a significant difference in terms of the need for additional medication.

Study Limitations

Our study had some limitations. Only the patients who presented to the emergency department with flank pain and whose radiological diagnosis of urolithiasis was confirmed were included in the study. Patients whose diagnosis was not confirmed radiologically could also be evaluated in another group, and the analgesic efficacy of medications could be compared. In our study, the patients were followed for 60 min after analgesia was given, and after the 60th minute, the patients were not followed up in terms of pain relief effectiveness. In our study, to minimize the placebo effect, the colour, odor, and volume of the medications were the same. All medications were given as IV infusions over the same period. Administration of different analgesics at different times or in different ways (intramuscular, inhaler, etc.) was not preferred since it would affect the absorption volume and absorption time of the medication. Studies with larger patient samples comparing different opioids and NSAIDs are needed for safe analgesia choices for treating renal colic.

Conclusion

NSAIDs cause fewer side effects than opioid analgesics and do not have addictive effects. It is seen that the pain relief efficacy and speed are the same as opioid analgesics. There are different treatment methods in the literature for treating renal colic pain. It is possible to find studies on the administration of different analgesics at different doses or in different ways. As seen in our study, different analgesics or different doses of the same analgesic do not make a significant difference for treating renal colic pain. Almost all drugs used for treating renal colic provide effective and rapid analgesia. Considering the patient's medical history, the analgesic to be chosen for treating renal colic pain should be the most comfortable treatment with the least side effects.

Ethics

Ethics Committee Approval: The study was approved by the Kafkas University Faculty of Medicine of Local Ethics Committee (no: 01, date: 27.01.2016).

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.Ö., G.Ç., H.Ç., E.G., Concept: G.Ç., M.B., Design: G.Ç., M.B., Data Collection or Processing: M.Ö., G.Ç., H.Ç., E.G., Analysis or Interpretation: M.Ö., G.Ç., M.B., Literature Search: M.Ö., H.Ç., Writing: M.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

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