Comparing the efficacy of intravenous ketorolac versus intravenous ibuprofen in relieving renal colic pain; a randomized clinical trial

Seyed Hossein Shaker*, Seyed Ahmad Borghei*

Emergency Medicine Department, Iran University of Medical Science, Tehran, Iran

ARTICLE INFO

Article Type: Original

Article History:
Received: 7 June 2018
Accepted: 11 July 2018
ePublished: 29 July 2018

Keywords:
Ketorolac
Ibuprofen
Renal colic
Renal stone

ABSTRACT

Introduction: Various therapies have been used to relieve or improve the urinary colic pain, but many of these treatments have been limited due to side effects associated with the drugs. In this regard, opioid drugs and nonsteroidal anti-inflammatory drugs (NSAIDs) have a higher priority than other treatments.

Objectives: The aim of the present study was to compare the level of pain relief from renal stones after the administration of two types of NSAIDs, including intravenous ibuprofen versus intravenous ketorolac.

Patients and Methods: In this clinical trial (identifier: IRCT20180108038276N1), 70 patients with renal colic pain were randomly treated with intravenous ketorolac (30 mg, n = 35) or with intravenous ibuprofen (800 mg, n = 35). The patient’s pain severity was assessed by the visual analogue scaling (VAS) method before and 20 and also 60 minutes after interventions.

Results: Although pain severity considerably reduced within 60 minutes of prescribing ibuprofen and ketorolac, the trend of the change in pin score was not different between the two groups (P = 0.734). We found no significant difference in appearance of some side effects including nausea and vomiting, requiring use of ondansetron, need to prescribe additional analgesics. However epigastric pain and need to administrating H2 blockers were not revealed in the group receiving ketorolac, but these complications were found in 25.7% of the patients received ibuprofen indicating a significant difference (P = 0.002).

Conclusion: A single dose administration of both intravenous ketorolac and ibuprofen is associated with significant improvement in renal colic pain within one hour after administration. However, due to the lower incidence of gastrointestinal complications in the administration of ketorolac compared to ibuprofen, the use of ketorolac in treatment and relief of renal colic pains is preferable.

Implication for health policy/practice/research/medical education:
In this clinical trial, on 70 patients with renal colic pain which were randomly treated with intravenous ketorolac (30 mg, n = 35) or with intravenous ibuprofen (800 mg, n = 35), we found that single dose administration of both intravenous ketorolac and ibuprofen is associated with significant improvement in renal colic pain within one hour after administration. However, due to the lower incidence of gastrointestinal complications in the administration of ketorolac compared to ibuprofen, the use of ketorolac in treatment and relief of renal colic pains is preferable.

Please cite this paper as: Shaker SH, Borghei SA. Comparing the efficacy of intravenous ketorolac versus intravenous ibuprofen in relieving renal colic pain; a randomized clinical trial. J Nephropharmacol. 2018;7(2):122-125.

Introduction
Renal stone disease or urolithiasis is a very common disease in different centuries (1). The renal colic is characterized by forming an acute pain with a colic nature in the flanks due to stones formation in the renal tubules, especially the urethra. Classical renal colic manifestations include the pain of the flank to the groin area with hematuria (in about 85% of cases) with nausea and vomiting. Renal colic pain is often described as the most severe pain experienced by an individual (2-4). As a result, the use of analgesics such as nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids, or by combining with other drugs, such as antispasmodics plays an important role in the treatment of renal colic pains. Recently, the use of alpha-blockers (with decreasing transit time for urinary tract stones), nifedipine, intravenous lidocaine, and neuronal...
block have also led to a decrease in renal pain (5,6).
Narcotics have been used to control colic pain for many
years (7,8). Although narcotics such as morphine, codeine
and meperidine have been very useful for improving renal
colic pain, these drugs have little effect on the underlying
cause of these pains, such as prostaglandins. The benefits
of using opioids include low-cost, high effectiveness,
and the desirable likelihood of titration. However, most
physicians do not tend to use these drugs because of side
effects such as nausea and vomiting, sedation, shivering,
light stomach, narcotic dependence, disturbances,
respiratory depression, and hypotension (8).

The NSAIDs have been used alone or in combination
with opioids for the treatment of renal pains for a long
time (7). The analgesic effects of these drugs were due to
inhibiting the synthesis of prostaglandins. As a general
result, NSAIDs inhibit vasodilatation of the renal arteries
and increase vascular permeability, resulting in diuresis
and increased pressure on the urethra. NSAIDs also
reduce the edema, inflammation and hyperactivity of the
ureter muscle (9). The effects of NSAIDs on pain relief in
acute renal colic have been similar to opioids. The only
limitation of NSAIDs compared to opioids is the delay in
initiating their analgesic effects with intravenous opioids.

Objectives
The aim of this study was to evaluate the effects of the two
types of NSAIDs including intravenous ibuprofen and
intravenous ketorolac in patients with renal colic.

Patients and Methods
Study population
In this study, all patients who were referred to one of the
educational hospitals of Iran University of Medical Sciences
due to renal colic with any age and gender were included.
Patients with cardiovascular disease, blood pressure crisis,
or diabetes were excluded from the study. Written consent
was obtained from patients prior to entering the study.
The purpose of the research project was explained for the
participants. In this study, the patient’s pain severity was
first measured by visual analogue scaling (VAS) score.
Then, the patients were randomly assigned to two groups
(using the random number table) receiving intravenous
ibuprofen (800 mg) or intravenous ketorolac (30 mg).
After 20 and 60 minutes, patients were again asked for
pain severity with the same criteria before receiving the
drug. All information such as demographic and clinical
information such as renal colic history as well as drug
history were collected through interviews from patients
and recorded in the checklist. The study endpoint was
to assess and compare the pain severity before and after
study therapeutic protocols in each patient’s subgroups.

Ethical issues
Human rights were respected in accordance with the
Helsinki Declaration 1975, as revised in 1983. The ethical
committee of Iran University of Medical Sciences (Ethical
No. IR.IUMS.FMD.REC.1396.9411307007) approved the
study. The informed consent was taken from the patients
as well as from parents and first relatives. The study was
also registered in the Iranian Registry of Clinical Trials
ir/trial/28954). Additionally, this paper was extracted
from the residential thesis of Seyed Ahmad Borghaei with
number 2812 in Iran University of Medical Sciences.

Statistical analysis
For statistical analysis, results were presented as mean ±
standard deviation (SD) for quantitative variables and were
summarized by absolute frequencies and percentages for
categorical variables. Normality of the data was analyzed
using the Kolmogorov-Smirnoff test. Categorical variables
were compared using chi-square test or Fisher’s exact test
when more than 20% of the cells with expected count
of less than 5 were observed. The quantitative variables
were also compared with t test or Mann-Whitney U test.
For the statistical analysis, the statistical software SPSS
version 16.0 for Windows (SPSS Inc., Chicago, IL) was
used. P values of 0.05 or less were considered statistically
significant.

Results
In this study, 35 patients with renal colic pain were treated
with intravenous ketorolac (30 mg) and 35 patients
received intravenous ibuprofen (800 mg). The two
groups were matched in terms of average age, gender
distribution, and history of renal colic pain (Table 1). As
shown in Table 1, there was no difference in pain severity
between the groups before intervention and 20 and also
60 minutes after medication. According to the repeated
measure ANOVA test, although pain severity considerably
reduced within 60 minutes of prescribing ibuprofen
and ketorolac, the trend of the change in pain score was
not different between the groups (P=0.734) (Figure 1).
Regarding drug-related side effects (Figure 2), we found
no significant difference of various side effects including
nausea and vomiting, requiring use of ondansetron and
need to prescribe additional analgesics. While epigastric
pain and need to administrating of H2 blockers were
not revealed in the group receiving ketorolac, these

Table 1. Baseline characteristics of study population

<table>
<thead>
<tr>
<th>Item</th>
<th>Ketorolac group (n = 35)</th>
<th>Ibuprofen group (n = 35)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, year</td>
<td>36.51 ± 11.64</td>
<td>38.29 ± 11.71</td>
<td>0.528</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td>0.324</td>
</tr>
<tr>
<td>Male</td>
<td>31 (88.6%)</td>
<td>28 (80.0%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>4 (11.4%)</td>
<td>7 (20.0%)</td>
<td></td>
</tr>
<tr>
<td>History of renal stone</td>
<td>18 (51.4%)</td>
<td>22 (62.9%)</td>
<td>0.334</td>
</tr>
</tbody>
</table>

Intravenous ketorolac versus ibuprofen
http://www.jnephrapharmacology.com Journal of Nephropharmacology, Volume 7, Number 2, July 2018 123
complications were found in 25.7% of the patients received ibuprofen indicating a significant difference ($P = 0.002$).

**Discussion**

Various therapies have been used to relieve or improve the urinary colic pain, but many of these treatments have been limited due to side effects associated with the drug. In this regard, opioid drugs and NSAIDs have a higher priority than other treatments. However, serious side effects such as hypotension, respiratory depression and gastrointestinal bleeding, as well as increased risk of coronary artery disease, or an increased risk of renal or cardiac failure, have prevented the selection of the best treatment regimen. In this regard, the use of NSAIDs with various forms and doses has been studied in recent years. What we assessed in this study was a comparison of the improvement in pain relief from kidney stones after the administration of two types of these drugs, including intravenous ibuprofen and ketorolac. In the current clinical trial, these drugs were injected in a single dose of 30 and 800 mg, respectively, and the severity of the colic pain at 0, 20 and 60 minutes after injection was evaluated and compared, as well as the adverse effects associated with the administration of drugs were also determined. First, our study found, no significant difference on the effect of the two drugs to reduce renal colic pain. In other words, in both regimens, although the reduction in the severity of pain was evident within 60 minutes of treatment, the superiority of a regimen to the other regimen was not detected. Therefore, regarding the efficacy and therapeutic effectiveness, no difference between the two drugs was seen. Although no difference between the groups in terms of the frequency of nausea and vomiting and the need for administration of ondansetron and also the need for additional doses of opioids was detected, however, the prevalence of epigastric pain and the consequent need for administration of ranitidine in the group treated with ibuprofen was far higher than that of the ketorolac group. In fact, in the ketorolac group, no complication of pain or epigastric discomfort was reported. Therefore, regarding safety, ketorolac is superior to ibuprofen, and in general, the administration of ketorolac will be preferable to improve real colic pain.

Although most of the studies have emphasized the high efficacy and safety of ketorolac versus other NSAIDs. In the study by Larsen et al (10), in patients treated with intravenous ketorolac (30 mg), a median pain score of 9 at intervention time reduced to score 1 about 30 minutes after intervention with no drug-related adverse effects which was perfectly in accordance with our study. In Neighbor and Puntillo's trial (11), there was no difference between the two groups receiving intravenous ketorolac and intravenous ibuprofen in terms of severity of pain during the study period. Likewise, both groups had a significant reduction in pain, which was completely consistent with our study. However, it is imperative that by choosing the best dose of the drugs to be studied, in particular for ketorolac, in addition to increasing the chances of relieving colic pain, the side effects of drugs including nausea and vomiting and the need for supplemental analgesics can be also minimized.

Although ketorolac is effective in reducing colic pain, some side effects should always be taken into account. In various studies, there was an increased risk of exacerbation of ischemic heart disease and the risk of myocardial infarction. In general, the administration of this drug in the following cases should be very cautious; having allergy to ketorolac, peptic ulcer disease, bleeding disorders or coagulation disorders, history of trauma to the brain or cerebrovascular accidents, bleeding during recent surgery, severe renal disease or history of dehydration, history of asthma or severe allergic reaction after taking aspirin or NSAIDS, pregnancy or lactation, as well as history of any ischemic heart disease.

**Conclusion**

In the final conclusion, it can be concluded that single
dose administration of both intravenous ketorolac and ibuprofen is associated with significant improvement in renal colic pain within one hour after administration. However, due to the lower incidence of gastrointestinal complications in the administration of ketorolac compared to ibuprofen, the use of ketorolac in treatment and relief of renal colic pains is preferable.

**Study limitations**
During the research, we encountered some problems such as inconsistencies in implementation and time constraints.

**Authors’ contribution**
SHH and BA designed the study, observed accuracy and validity of the study. BA collected the data and follow the study. SHH and BA supervised the project. SHH and BA wrote the paper. All authors edited and revised the final manuscript and accepted its publication.

**Conflicts of interest**
The authors declared no competing interests.

**Ethical considerations**
Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

**Funding/Support**
The authors declare that there is no source of funding for the research reported.

**References**

**Copyright © 2018 The Author(s); Published by Society of Diabetic Nephropathy Prevention. This is an open-access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.**