Comparing the effects of pethidine and diclofenac suppository on patients with renal colic in the emergency department

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Abstract
Objective: Renal colic is a common cause of emergency room visits. Due to the spontaneous passage of more than 90% of kidney stones, treatment in the emergency department (ED) is limited to pain control. Analgesics currently used are selected based on physician experiences and various theories from different sources. The aim of this study was to compare the common drugs (pethidine and diclofenac) used for renal colic in Iran.
Methods: In this single-blinded randomized clinical trial, 90 patients with renal colic who referred to the ED of Imam Reza hospital in Kermanshah were randomly assigned to each of 3 treatments including pethidine suppository (50 mg, iv), diclofenac suppository (50 mg), and a combination of pethidine and diclofenac suppository. In this regard, the response to treatment and duration of hospitalization were compared.
Results: The best medicine to relieve pain intensity in patients under 25 years was diclofenac suppository. In patients in the age range of 25-45 years, pethidine and diclofenac were the best choice. Conversely, in patients older than 45 years, pethidine was the best treatment. We could also observe a decrease in the length of hospitalization in patients who received pethidine.
Conclusion: It can be concluded that morphine is more appropriate to control pain and reduce the length of hospitalization in patients with renal colic.

Introduction
Kidney stones are the third common disorders of urinary tract system subsequent to the prostate disease and infections (1). Painful attack is the most common clinical manifestation known as renal colic. This condition is one of the most frequent medical emergencies around the world in which many patients refer to hospital emergency departments on a regular basis (2-4). The pain associated with urinary tract stone is usually described as the worst pain a person experiences in lifetime, which requires effective and immediate control. Pain is caused by the increased pressure in the upper urinary tract or dilatation of the kidney capsule and renal pelvis (pyelum) above the blockage due to obstructing stones. It is usually an acute pain that may be accompanied by nausea, vomiting, and microscopic or macroscopic hematuria (5,6). As 90% of the stones are excreted spontaneously, other treatment in dealing with these patients is the elimination of their pain (7). Opioids as the main and the most powerful medications, by inhibiting the pain receptors in the central nervous system through stimulation of μ, δ, and Sigma (8), can release the pain. However, complications such as inhibition of the respiratory center in the medulla and the activation of the vomiting cause some challenges in the opioid usage (8,9). Nonsteroidal Anti-inflammatory Drugs (NSAIDs) through the inhibition of cyclooxygenase enzyme prevent the production of prostaglandin E2 and relieve the pain (9). They can cause side effects such as
gastrointestinal effects, but the overall complication rate is less than opioids (10,11). Today different methods using a variety of opioids and NSAIDs and other compounds according to the physician’s experience and points of view are used. Some researchers believe that the simultaneous use of opium and NSAIDs are more effective than their separate usage. Thus, this leads to an earlier discharge of patients from the ED (12,13), while a number of studies suggest the use of opium when NSAIDs do not work as the first-line therapy choice (14). In another investigation, NSAIDs alone were not recommended due to the delayed onset (15). Considering the controversies available in the management of these patients and the current compounds used in EDs, we studied the effect of pethidine suppository, diclofenac suppository, and the combination of them for relieving the pain in patients with the presentation of renal colic admitted to the ED. In addition, we assessed the impact of different treatment methods on the length of stay in the ED.

Methods
This study was a single-blinded randomized clinical trial conducted on 90 patients with acute renal colic referred to the ED of Imam Reza hospital in Kermanshah in 2011. Individuals with clinical diagnosis of acute renal colic (flank pain associated with urinary symptoms such as polyuria, dysuria, and hematuria confirmed by ruling out other causes of flank pain, physical exam, and paraclinical examination such as ultrasound) who were between the ages of 18 to 60 years and their pain equal or more than 5 on the pain visual analog scale (VAS) were eligible for inclusion. Those with one of the following conditions were excluded from the study: pregnant women, nursing mothers, patients who received pain relief medication (analgesia) 6 hours prior to admission, those who had renal dysfunction, patients treated with warfarin, patients with bleeding disorders, those with a history of gastrointestinal problems after taking NSAIDs, and those who were addicted to drugs. Therefore 90 patients were divided into 3 groups of 30 and each drug was tested on a group. At the beginning of the study, each patient’s level of pain was recorded. Then patients were randomly assigned to one of the 3 active treatment groups: pethidine 50 mg suppository, diclofenac 50 mg suppository, and a combination of the 2 drugs using permuted block randomization. Pain scores were recorded after arrival and 10 minutes after the first administration of each drug. Pain scores were assessed again, 10 minutes after the second administration of each drug at 30 minutes. Patients with persistent pain received 5 mg of morphine at 40 minutes. In this study, the rate of decrease in pain up to 3 degrees in each time was considered as a response to the treatment.

All patients were followed up by phone within 48 hours of treatment and the certainty of renal colic diagnosis was confirmed using sonography and laboratory tests. After editing and entering to the software, data were analyzed using chi-square analysis and marginal models. The descriptive statistics was used to illustrate the basic features of variables.

Results
In this study 90 patients were evaluated; 66.7% were male. The mean age was 34.50 ± 10.97, 32.20 ± 8.19, and 41.47 ± 11.46 in pethidine suppository, diclofenac suppository, and pethidine-diclofenac groups respectively that were not statistically different. To investigate the relationship between pain intensity with age and medication used, longitudinal analysis and marginal models were used. For this purpose, the age variable was divided into 4 categories: less than 25 years, 25-35 years, 35-45 years, and more than 45 years. As shown in Table 1, there was a significant relationship between pain intensity with time (P = 0.00) and the interaction of the drug and age (P = 0.008). We could also observe a significant relationship for drug interaction with age and time (P = 0.00). The mean of pain intensity in patients aged less than 25 years at the time of 2 and 3 had a greater reduction compared to other age groups. This means that at the beginning of the study, patients under 25 years of age had the highest level of pain while over time a rapid increase occurred in reducing their pain.

The most suitable medication to reduce pain was diclofenac suppository in patients less than 25 years. On the other hand, pethidine was appropriate for the age range of 25-35 and the combination therapy was suitable for 35-45 age groups and in patients over 45 years (Figures 1 and 2 & Table 2). There was a significant relationship between the duration of hospitalization and medication intake. Duration of hospitalization for those who received pethidine suppository was the least and for those who received diclofenac suppository it was the most. Also, the minimum duration of hospitalization was related to the group which received pethidine supposition.

Table 1. Relationship between pain intensity and type of treatment received

<table>
<thead>
<tr>
<th>Variable</th>
<th>F</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug</td>
<td>0.05</td>
<td>0.954</td>
</tr>
<tr>
<td>Age</td>
<td>3.38</td>
<td>0.022</td>
</tr>
<tr>
<td>Time</td>
<td>418.71</td>
<td>0.000</td>
</tr>
<tr>
<td>Drug*age</td>
<td>3.13</td>
<td>0.008</td>
</tr>
<tr>
<td>Drug<em>age</em>time</td>
<td>12</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Table 2. Relationship between duration of hospitalization and type of treatment received

<table>
<thead>
<tr>
<th>Variable</th>
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<th>P value</th>
</tr>
</thead>
<tbody>
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<td>0.000</td>
</tr>
<tr>
<td>Age</td>
<td>1.54</td>
<td>0.217</td>
</tr>
<tr>
<td>Drug*age</td>
<td>9.03</td>
<td>0.000</td>
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</table>
In this study, all 3 treatments were significantly effective in relieving the pain of kidney stones. But given the variable age as an influential factor, the rate of pain relief showed different changes in various ages. The most suitable medication to reduce pain was diclofenac suppository in patients less than 25 years, pethidine in 25-35 and 35-45 age groups, and pethidine-diclofenac in patients over 45 years. There was also a significant difference in the duration of hospitalization of patients in the 3 groups, and pethidine devoted less time for hospitalization. In a study comparing morphine, ketorolac, and their combination on patients with renal colic, no significant differences were found in relieving the pain between groups that received morphine or ketorolac alone, but their combination in relieving acute renal colic was more effective than either drug alone (14). However, considering age as the mediator variable, we conclude that pethidine was the best treatment for 25-45 age groups. But pethidine-diclofenac was the best medicine for pain relief in patients over 45 years of age. In previous studies in order to compare the effects of common pain management in the treatment of acute renal colic, diclofenac suppository (50 mg) was an appropriate option for pain relief (7). As well, it was considered the ideal treatment for the age group less than 25 years in the present study. Regarding opioids used in the treatment of renal colic, several studies have been conducted to compare the efficacy and safety of morphine and pethidine on renal colic pain relief in the ED. According to the results, no significant differences were found between pethidine and morphine for the pain control, but due to more complications of pethidine, morphine was recommended (16). Also some surveys have been carried out to select NSAIDs. In a study that was conducted to compare diclofenac and ketorolac, the safety and efficacy of the 2 drugs were similar and there was no significant difference between them (3).

Conclusion
It can be concluded that the use of morphine can better control pain and reduce the length of hospitalization in patients with renal colic admitted to the ED.

Acknowledgments
We would like to declare our sincere appreciation to all ED personnel of Imam Reza hospital in Kermanshah for their cooperation in this study.

Ethical issues
The research was approved by the Ethics Committee of Kermanshah University of Medical Sciences and researchers were committed to Helsinki Declaration throughout the study. Patients were included in the study after obtaining written consent.

Authors’ contributions
All authors had standard writing criteria based on the recommendations of the International Committee of the Medical Journal Publishers (ICJME).

References