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Comparison of intramuscular injection of ketorolac and conventional treatment in the field of cost-effectiveness, length of stay and pain relief in patients admitted to the emergency department with renal colic

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ABSTRACT

Background: Pain resulting from the stone passage is one of the most severe and intractable pain experiences. The aim of our study is evaluating the effect of intra-muscular ketorolac on pain reduction; reduce the length of stay and cost of patients with renal colic.

Methods: This was a randomized clinical trial study which held in an academic emergency department (ED). Based on defined criteria, 222 patients with renal colic were randomized in two groups: half of them received a single intramuscular injection of 30 mg ketorolac, and other 111 patients got conventional treatment (hydration, morphine sulfate). Demographic characteristics, pain score after 30 minutes, the length of stay in ED, complications as well as hospital costs were recorded for both groups.

Result: The baseline characteristics and pain score were similar in the two groups ($p>0.05$). Ketorolac was significantly ($p<0.001$) more effective than conventional treatment in reducing pain score. Those treated with ketorolac left the ED significantly earlier than those treated with conventional treatment (65.54; 95%CI, 59.7-71.5 vs. 193.1; 95%CI, 172.8-215.2 minutes, $p<0.001$). Drug adverse effects (nausea, dizziness, and drowsiness) and cost of ketorolac group were significantly lower than the control group (43310 Tomans (110$) (95% CI, 42590-44030) vs. 150410 Tomans (350$) (95% CI, 240100-70940). ($p<0.001$).

Conclusion: This study showed that intramuscular ketorolac as a single agent for renal colic is cost-effective and promotes earlier discharge of renal colic patients from the ED.

Keywords: renal colic, ketorolac, pain, emergency department

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INTRODUCTION

About 1.2 million people suffer from colic pain annually, one percent of whom are hospitalized.[1,2] About 12% of the population will experience urinary system stones in their entire life, with about 50% recurrence.[3] The ratio of renal colic in women and men is one third.[1]

Renal colic has always been under investigation due to its widespread prevalence which causes absence from work, disability, and high costs for the government.[4-6] The primary principle of renal colic treatment is to relieve the pain and mostly, the first actions in emergency department (ED) are related to relieving the pain and temporary pain removal.[7,8] Since most urinary tract stones are removed without surgery, pain relieving is one of the most important treatment priorities.[9,10] In the frontline of treatment, two groups of drugs are used: narcotics (like morphine and meperidine) and the non-steroidal anti-inflammatory drugs (NSAIDs).[11] Although narcotics are the most common and suitable pain-killers, finding an alternative is a priority in treating renal colic, primarily, due to the probability of drug dependency or abuse, respiratory system depression,[12] legal obstacles, and official bureaucracies needed when using these drugs. Therefore, a higher tendency toward NSAIDs is observed recently. Apart from direct pain-killing, anti-inflammatory, and anti-edema effects, these drugs have indirect effects on relieving the pain by lowering the release of pain-making materials and chemical intermediates in making anti-pain impulses.[13] This study aimed to compare the intramuscular injection of ketorolac, and conventional treatment in field of cost-effectiveness, length of stay and pain relief in patients admitted to emergency department with renal colic.

MATERIAL AND METHODS

Design and ethical issues

In a randomized controlled clinical trial study, 222 patients referring to ED of Firoozgar Teaching Hospital entered the study after getting their or their parents' informed consent. Since no consensus exists for treating the kidney stone patients today and physicians use various drugs like opioid injections, NSAIDs, and even oral medications and suppository, using each of these methods is ethical. Finally, the study was approved by the Ethical Committee of Iran University of Medical Sciences. This project was registered with a code IRCT201611272745N2.

All information was taken from the volunteers in an anonymous manner. Researchers were obliged to describe to the subjects the administrative process, objectives of the study, benefits, characteristics and period of the study as far as related to him/her. The researchers had to respond to the subject's questions persuasively and compensate for any probable damages.

Inclusion and exclusion criteria

Patients who had cardiovascular or pulmonary diseases, bleeding tendency, history of recent gastrointestinal bleeding and pregnant were excluded from the study. Also, patients presented with fever, renal transplanted, single-kidney and high suspicion of acute abdomen were excluded too. Totally 18 patients were excluded.

Randomization and intervention

Total of 222 patients with probable diagnosis of renal colic was studied. They were randomly classified into two 111-member groups based on the rightmost computer code assigned: one group received intramuscular ketorolac (deltoid muscle), and the other got the conventional treatment in the ED (normal saline serum, intravenous morphine sulfate (0.05 mg/kg), and 1 gram intravenous paracetamol). The drugs were prepared by the pharmacist who responsible for labeling the drugs (A, B).

In the intervention group, a ketorolac syringe (30 mg) was injected in the Deltoid muscle without taking the peripheral venous. In the ketorolac group, six patients (5.4%) swapped to the conventional treatment group due to non-responsiveness; however, they were analyzed in the group due to the type of the intention treat analysis. In fact, in case the intervention group patients didn't respond to the injected ketorolac, they were treated by conventional method.

Assessment and measurement

The severity of pain was measured by a numerical scale on hospitalization (before any drugs prescription), 30 minutes after taking the drugs (prescribed by the physician) and on release from the hospital (discharge time). The pain assessment was performed by one of our researcher who did not know about the groups of intervention. All data, including demographic and clinical ones, regarding renal colic history, and medicinal side effects after the injection were gathered by a pre-prepared checklist and analyzed by the SPSS analysis.

The sample size was calculated by Altman's nomogram. Regarding relieving the pain as the main objective, a 0.7 standardized difference was obtained. Considering the power of 80% for the study, a sample size of 200 was obtained for the two groups.

Statistical analysis

All quantitative variables of the study were investigated by the Kolmogorov–Smirnov test regarding normal distribution. In case a normal distribution is followed, parametric tests like t-test, and in case no normal distribution exists, non-parametric tests were used to compare the two groups. Mean, standard deviation and confidence interval of 95% are reported when describing the data, and the Chi-square test is applied to compare the qualitative variables and the determination of the difference between ratios. A significance level of tests was considered $P<0.05$. The analysis was performed using the IBM SPSS 21 statistical package (SPSS Inc., Chicago, IL, USA).

RESULTS

Description of patients

From among 222 patients, 174 were men (78.4%; 73-83.8, CI 95%). The mean age was 34.75 years old (95% CI, 33.37-36.22). The mean severity of pain was 9.18 on admission in ED (95% CI, 9.06-9.31). The pain score was reduced to 5.36 (95% CI, 5.08-5.64) 30 minutes after prescription of the drug. When discharging from the hospital, the pain score was measured again and was 2.39 (95% VI, 1.93-2.97). Sixty undesirable side effects were observed for both groups (27%, 95% CI, 21.2-32.9). The most common side effects included nausea and dizziness. The average length of ED stay (from entering the triage room to discharging from the ED) was 129.32 minutes (95% CI, 115.99-143.98).

Description of each group separately

In ketorolac group, there were 84 men (75.7%, 95%CI, 66.7-82.9) and 27 women (24.3%, 17.1-33.3). In the traditional treatment group, there were 90 men (81.1%, 95% CI, 73.9-88.3) and 21 women (18.9, 95% CI, 11.7-26.1). It was observed that there

is no significant difference between the two groups regarding gender distribution (p=0.328). The mean age of the patients was not significantly different between the two groups (p=0.698). So, the mean age of the patients was 35.02 years old (95% CI, 32.9-37.21) in the ketorolac group and 34.48 years old (95% CI, 32.79-36.26) in the traditional treatment group.

On admission, the average pain score was not significantly different between the two groups (p=0.386), so that in the ketorolac group, the average pain score was 9.13 (95% CI, 8.97-9.28) and in the conventional treatment group was 9.24 (95% CI, 9.05-9.42). The average pain score for the patients 30 minutes after prescribing the drug was significantly different between the two groups (p<0.001), so that in the ketorolac group the pain reduction was significantly higher (4.62; 95% CI, 4.3-4.96 in ketorolac group vs. 6.1; 95%CI, 5.68-6.51 in traditional group). The average pain score in the patients when discharged from the ED was not significantly different between the two groups (p=0.221). In fact, at the discharging time, the average pain score was similar between the groups, 2.7 (955 CI, 1.84-3.9) in the ketorolac group and 2.08 (95% CI, 1.84-2.29) in the conventional treatment group.

The average time of ED stay was significantly different for the two groups (p<0.001), which mean the ketorolac group patients remained in the ED for a significantly shorter time. The length of stay in ED was 65.54 minutes (95% CI, 59.72-71.56) and 193.1 minutes for the conventional treatment group (95% CI, 172.89-215.24).

In the ketorolac group, 18 patients (16.2%, 9-23.4) had one or more side effect of the drug, while the number was 42 (37.8%, 29.7-45.9) for the conventional treatment group. The side effects included nausea, dizziness, and drowsiness. No other side effects were observed. In the analysis made by Chi^2 test, it was shown that there is a significant difference between the two groups regarding side effects. However, these side effects were significantly lower in the ketorolac group (p<0.001)

Costs analysis

The patients charged lower costs in the ketorolac group than the traditional treatment group. In another treatment group, in addition to the visiting cost (which both groups had to pay), the costs included serum injection, intravenous injection, laboratory test, and ultrasound costs; moreover, they had to pay the costs of more than one drug (morphine, paracetamol, etc.). In our study, the average costs of the ketorolac group were 43310 Tomans (110$) (95% CI, 42590-44030), and in the conventional treatment group, the whole cost was 150410 Tomans (350$) (95% CI, 240100-70940). The t-test showed that the difference was significant (p<0.001). The difference in costs resulted from the costs of the laboratory (about 12 to 25 $), sonography (25-50 $), intravenous injections (4-6 $) and drugs (0.5-1.5 $).

DISCUSSION

In the present study, 222 patients were included, among whom 111 patients were randomized to the deltoid muscle injected ketorolac and the others as the control group (normal saline, intravenous morphine, intravenous paracetamol). The two groups had no significant differences when entering the study regarding basic characteristics like gender, age, and pain severity. The studies made in the same direction, like Oosterlinck and Cordell studies which measured the pain scores after ketorolac injection, affirmed its effectiveness in the treatment of renal colic.[14,15] In the study by Oosterlinck et al., a comparison was made between the intramuscular injection of 10 mg ketorolac and injection of 90 mg ketorolac and 100 mg pethidine (meperidine) in 121 renal colic patients. An hour after injection, the pain score was observed in all groups. Injection with 90 mg ketorolac caused the maximum decrease in the pain score. The difference in pain relief was significant between this group and the group that received 10 mg ketorolac.[14] Cordell et al. showed in their study that the intravenous injection of ketorolac, individually or in combination with meperidine is more effective than the injection of meperidine individually. In only 30 minutes, 75% of ketorolac and 74% of ketorolac and meperidine (combinational) groups showed a 50% decrease in the pain score. However, pain relief was 23% in the group who used meperidine alone in the same period. Therefore, intravenous injection of ketorolac, alone or in combination with meperidine, is superior to the intravenous injection of meperidine alone in the moderate severity renal colic patients.[15] Safdar et al. showed in a double-blind clinical trial study that a combination of morphine and ketorolac performs superior in pain relief than using each one individually. It reduces the need for additional analgesic drugs.[16] In another double-blind clinical trial study, the effectiveness of ketorolac and meperidine in relieving the pain of renal colic was investigated. Total 76 patients received 30 mg intramuscular ketorolac, and 78 patients received 100 mg intramuscular meperidine. The pain score was measured by VRS and VAS before injection and 15 minutes after injection. According to the VRS, 88% of patients in both groups experienced a reduction in pain an hour after drug prescription, 56% of patients in the ketorolac group and 74% of patients

in the meperidine group received an additional dose of analgesic. Side effects in the ketorolac group (28%) lower than the meperidine group (51%).[17] In our study, the average pain score had a significant difference between the two groups 30 minutes after prescribing the drug (p<0.001), which mean more pain relieve was observed in the intramuscular-injected ketorolac group.

In the present study, the length of ED stays significantly different between the two groups (p<0.001). So, intramuscular-injected ketorolac group remained in the ED for a shorter time than the other group. Also, 16.2% experienced side effects of the drug in the ketorolac group, but the conventional treatment group incurred 37.8% side effects (p<0.001).

In our study, the costs were significantly lower in the ketorolac group. Cost differences included the costs of laboratory tests, ultrasound, intravenous injections, and drugs. Few studies have been made regarding renal colic treatment costs and their cost-effectiveness. In one study, the costs charged to the renal colic patients admitted to the ED along with its effective factors were investigated between 2007 and 2009. In this retrospective study, 574 patient diagnosed with renal colic entered the study. The average ED cost for these patients was 55.77 Euros. The highest cost is related to the radiological tests (40.5% of all costs) followed by treatment costs (19.7% of all costs). Size and position of the stone and the hospitalization period were independent variables which affected the total costs. The bigger and more distal the stone, the higher the costs were charged.[18] Approaching the patients with standard clinical pathways is one of the activities for lowering the costs. In this way, the treatments will be more effective as well. In our study, laboratory tests and ultrasound were the major factors of high costs. It seemed that these para-clinic measures were not emergent or urgent. In a retrospective study in Sao Paolo, Brazil, 136 renal colic patients were investigated regarding treatment and diagnosis costs. According to the type of treatment used, the patients were classified into two groups: The first group took drugs according to the score of their pain in the WHO Standard Ladder, which included three stages. For the patients with mild pain, simple analgesic and NSAIDs were prescribed. For moderate pain, NSAIDs and weak opioid drugs were used. And in case the pain was severe, a strong, rather than weak, opioid was prescribed. The other group received other treatments not recommended by WHO guidelines. The interesting point was that the costs of renal colic treatment is variable and fluctuates between 42.44 BRD and 1936.98 BRD. However, no significant difference was observed regarding costs between the two groups (p=0.49) with 57% of all costs were related to the diagnostic tests. Also, comorbidities had no effects on the demanded tests and total costs. The length of ED stays had a strong and significant relation with total costs (p<0.001). However, in this study, the relationship between hospital costs, the ED stay, and type of analgesic used was not investigated. The authors stated that the effective treatment and higher caring quality lowered the length of ED stay and the costs.[19]

CONCLUSIONS AND RECOMMENDATIONS

Considering the effectiveness of ketorolac in pain killing, reduction of nausea and vomiting, and reduction of side effects and costs of treatment, it can be used for renal colic patients instead of opioid drugs. Since the study was performed in a single center, a multi-center, comprehensive study based on the cost-effectiveness of ketorolac could be helpful.

CONFLICT OF INTEREST

Author declares there is no conflict of interest regarding all aspect of the study.

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