

# A Comparative Study of the Effect of Intravenous Morphine and Ketorolac on Pain Control in Patients with Renal Colic

Seyed Mehdi Pourafzali<sup>1</sup>, Abdolrahim Sanei<sup>1</sup>, Ali Abdolrazaghnejad<sup>2</sup>, Elahe Poursadra<sup>3</sup>

<sup>1</sup>Department of Emergency Medicine, School of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran, <sup>2</sup>Department of Emergency Medicine, Khatam-Al-Anbia Hospital, Clinical Immunology Research Center, Zahedan University of Medical Sciences, Zahedan, Iran, <sup>3</sup>Community Health Research Center, Isfahan (Khorasgan) Branch, Islamic Azad University, Isfahan, Iran

## Abstract

**Background:** The present study aimed at comparing the effect of ketorolac and morphine on the pain control in patients with renal colic.

**Materials and Methods:** The present clinical trial was performed on 272 patients with renal colic that were divided into two groups. Patients in the first and second groups intravenously received morphine at a dose of 1.0 mg/kg and ketorolac at a dose of 30 mg, respectively. Then, systolic blood pressure, diastolic blood pressure, heart rate, respiration rate (RR), and oxygen saturation percentage (SpO<sub>2</sub>) as well as patients' pain scores before and 5, 15, 30, 60, and 90 min after the intervention were recorded and evaluated.

**Results:** The results of this study revealed that the mean pain scores of patients before and after the intervention were not significantly different between the two groups ( $P > 0.05$ ). However, patients' pain significantly relieved over time in both groups (reduce: Morphine group = 9.4 and ketorolac group = 9.09;  $P < 0.001$ ). In addition, nausea, dizziness, and a decreased SpO<sub>2</sub> in the morphine group were 5.1%, 2.9%, and 1.5%, respectively, and in the ketorolac group only dizziness was 2.2% ( $P > 0.05$ ).

**Conclusion:** According to the results of this study, the efficacy of ketorolac in reducing patients' pain was not significantly different from that of morphine. Therefore, considering that the occurrence of complications in the ketorolac group was lower than that of the morphine group, it can be stated that ketorolac is a safer and more reliable drug than morphine in relieving pain in patients with renal colic.

**Keywords:** Ketorolac, morphine, renal colic

**Address for correspondence:** Prof. Elahe Poursadra, Community Health Research Center, Islamic Azad University, Isfahan Branch (Khorasgan), Isfahan, Iran.

E-mail: [e.poursadra@gmail.com](mailto:e.poursadra@gmail.com)

**Submitted:** 03-Sep-2021; **Revised:** 22-Oct-2021; **Accepted:** 23-Oct-2021; **Published:** 25-Feb-2023

## INTRODUCTION

Renal colic is a complex of sudden severe pain, nausea, and occasional vomiting and requires prompt and appropriate diagnosis and treatment.<sup>[1]</sup> The risk of developing kidney stones during life is 8%–15%.<sup>[2]</sup> Pain caused by stone passage, as one of the most severe and excruciating types of pain, is one of the most significant problems of patients. The mentioned patients have a 1%–10% chance of developing renal colic pain due to stone passage.<sup>[1,3]</sup>

The treatment of this disease is to relieve pain, facilitate the passage of stones, and maintain kidney function.<sup>[4]</sup> According to most researchers, the first step in relieving pain in these patients is the use of opioid analgesics. Opioids and more commonly morphine due to its easier access in the hospital system are widely used drugs to reduce pain. Morphine reduces the patients' discomfort by acting on the central nerve receptor; however, it does not affect the cause of the pain and requires repetition. In addition, its dependence as

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

**For reprints contact:** [WKHLRPMedknow\\_reprints@wolterskluwer.com](mailto:WKHLRPMedknow_reprints@wolterskluwer.com)

**How to cite this article:** Pourafzali SM, Sanei A, Abdolrazaghnejad A, Poursadra E. A comparative study of the effect of intravenous morphine and ketorolac on pain control in patients with renal colic. *Adv Biomed Res* 2023;12:45.

Access this article online	
Quick Response Code: 	Website: <a href="http://www.advbiores.net">www.advbiores.net</a>
	DOI: 10.4103/abr.abr_278_21

well as nausea, vomiting, constipation, drowsiness in higher doses, respiratory depression, and hypotension have caused physicians to avoid its prescription as much as possible.<sup>[5]</sup> To this end, attention has recently been drawn to the use of nonsteroidal anti-inflammatory drugs (NSAIDs) to reduce the pain of acute renal colic. Although these drugs are less effective in the first 10 min, they have the same effect as opioids within 20–30 min.<sup>[6]</sup> The analgesic effects of NSAIDs are due to the inhibition of prostaglandins, which in turn reduce vasodilation, increase their permeability, have diuretic effects on kidneys, and increase the pressure of pelvic and the urinary system.<sup>[6]</sup> They also reduce swelling, inflammation, and contractile activity of the ureteral muscles. Although the gastrointestinal and renal effects of NSAIDs have limited their use, their injectable generation such as ketorolac has minimized this complication, and researchers have focused on the use of this drug in controlling and reducing pain. However, limited studies have compared this drug with other nonsteroidal and opioid drugs.<sup>[7–12]</sup>

For instance, some previous studies reported that pain relief in groups receiving morphine and ketorolac alone was not significantly different from each other.<sup>[7,13]</sup> In contrast, NSAIDs, as compared with opioids, have been reported to reduce pain more and have fewer complications regarding renal colic.<sup>[14]</sup> Other studies have suggested that the combined administration of ketorolac and morphine may be more effective in reducing the duration of pain and inducing analgesia than either alone; however, it seems that the administration of the combined drugs will increase the risk of complications.<sup>[15,16]</sup>

Therefore, considering the significance of the issue, the severe pain in patients with renal colic, and the importance of selecting the best treatment to relieve pain with the least complications, a comparative study of the effect of ketorolac and morphine on pain control in patients with renal colic was performed.

## MATERIALS AND METHODS

The present study was a double-blind clinical trial. The study population included all patients with a high clinical suspicion of kidney stones and renal colic that referred to the emergency departments (EDs) of Shahrekord Medical Sciences Hospitals from May 2019 to May 2020. From the mentioned population, 272 patients (136 patients in each group) were selected by the simple random sampling technique considering the sample size formula for between-group comparisons, the confidence interval of 95%, the test power of 80%, the error level of 0.4, and the standard deviation of pain scores in the two groups receiving morphine and ketorolac<sup>[7]</sup> to be equal to 1.02 and 0.88, respectively.

Inclusion criteria included the age range of 16–65 years, the definitive diagnosis of renal colic (with renal colic symptoms and the presence of stones confirmed by CT), the weight of 50–100 kg (for the effectiveness of the dose of 30 mg ketorolac), the pain intensity of equal to or more than 7, the nondrug addiction, and the patients' consent to participate

in the study. The patients were not included in the study in case of having a history of morphine or ketorolac allergy, pregnancy or suspected pregnancy, breastfeeding, a history of taking painkillers over the last 4 h, having traumatic eye or head injuries, having one kidney or a kidney transplant, having cerebral hemorrhage or the possibility of its occurrence, having mental disorders, having fibromyalgia, having vascular and brain lesions, having coagulation disorders, using angiotensin-converting enzyme inhibitor or anticoagulants, or the past medical history such as pulmonary diseases, a history of kidney failure (creatinine of 1.08 and above), a history of cardiovascular disease, kidney failure, a history of digestive diseases, and a history of diabetes mellitus. Moreover, they were also excluded from the study in case of a change in the patients' level of consciousness or the occurrence of severe complications. In this study, no patient was encountered with the mentioned cases and the study sample did not decrease.

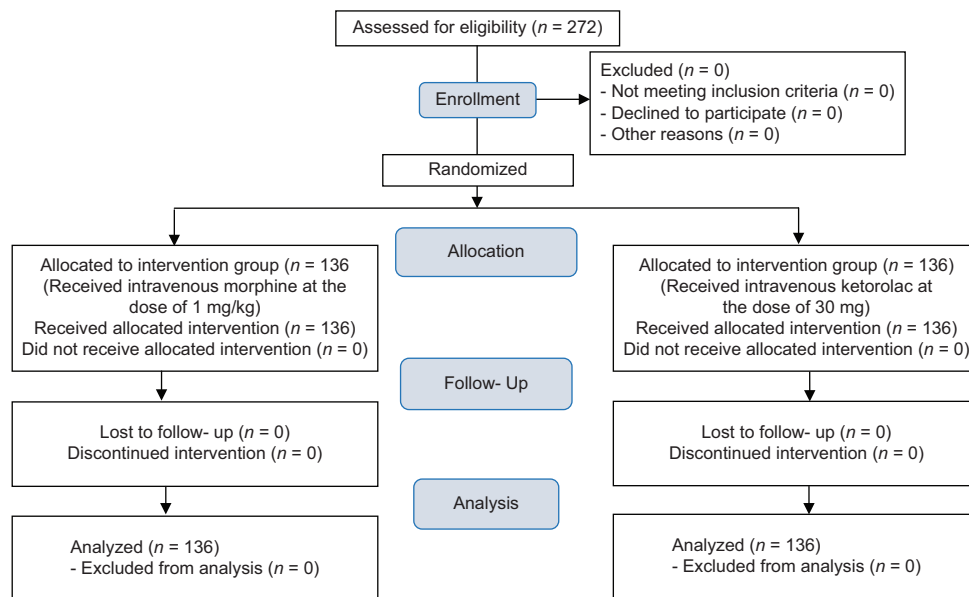
After obtaining the code of ethics from the Ethics Committee of Shahrekord University of Medical Sciences (IR.SKUMS.REC.1398.143) and obtaining a clinical trial code (IRCT20200825048515N40) and getting the eligible patients' consent to participate in the study, patients were first divided into two groups of 136 according to the table of random numbers [Figure 1]. At the beginning of the study, patients' baseline characteristics such as age, sex, height, weight, body mass index (BMI), and their underlying disease history were recorded.

Patients in the first group received intravenous morphine at the dose of 1 mg/kg while patients in the second group received intravenous ketorolac at the dose of 30 mg.<sup>[7]</sup>

To meet the conditions of blindness, two drugs were previously prepared by an emergency medicine specialist and identified in ready-made packages with codes A and B so that the person prescribing the drug and the person recording patients' clinical and baseline characteristics were not aware of the type of intervention. The drug was also administered by a resident that was blind to the type of the drug selected and the patient groups. Patients' hemodynamic parameters including systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), respiration rate (RR), oxygen saturation percentage (SpO<sub>2</sub>), and patients' pain score (according to VAS criteria ranging from 0 to 10) were recorded at the beginning of the study and 5, 15, 30, 60, and 90 min after the intervention.

It should be mentioned that if the patient's pain score did not decrease within 30 min after the intervention (<3), additional drug (morphine 1 mg/kg) was used. In the mentioned cases, the additional dose of analgesic was recorded as well. Moreover, possible complications such as nausea, vomiting, dizziness, loss of consciousness, decreased oxygen saturation, and hypotension were recorded up to 90 min after intervention.

Finally, the collected data were entered into SPSS software (version 25; SPSS Inc., Chicago, Ill., USA). Data were presented as means ± standard deviation or *n* (%).



**Figure 1:** Consort flowchart of patients

At the level of inferential statistics, according to the result of Kolmogorov–Smirnov test indicating the normal data distribution, Chi-square test was used to compare the frequency distribution of qualitative variables between the two groups. An independent samples *t*-test was used to compare the mean of quantitative variables between the two groups. Moreover, a univariate analysis was used to compare the mean of quantitative variables between the two groups by adjusting for the additional dose of the administered analgesia, age, and sex as confounding variables. Furthermore, the repeated measures analysis was employed to compare the mean changes of quantitative variables over time in each of the two groups. The significance level of  $<0.05$  was considered in all analyses.

## RESULTS

In the present study, out of 136 patients receiving morphine with the mean age of  $36.54 \pm 9.74$  years, 95 (69.9%) and 41 (30.1%) patients were male and female, respectively. Moreover, out of 136 patients receiving ketorolac with the mean age of  $36.95 \pm 9.75$  years, 91 (66.9%) and 45 (33.1%) patients were male and female, respectively. The two groups were similar in terms of baseline characteristics including age, sex, height, weight, BMI, and the past medical history ( $P > 0.05$ ) [Table 1].

In addition, the patients' mean hemodynamic parameters including SBP, DBP, HR, RR, and SpO<sub>2</sub> at the beginning of the study and 5, 15, 30, 60, and 90 min after the intervention were not significantly different between the two groups ( $P > 0.05$ ). Moreover, none of the two interventions caused significant changes in the mentioned parameters ( $P > 0.05$ ) [Table 2].

Furthermore, the mean pain score of patients at the beginning of the study was not significantly different between the two groups ( $P > 0.05$ ). In addition, their mean pain scores were not significantly different between the two groups 5, 15, 30, 60, and

**Table 1: Patients' basic characteristics in the two groups**

Variables	Morphine group (%)	Ketorolac group (%)	P
Sex			
Male	95 (69.9)	91 (66.9)	0.602
Female	41 (30.1)	45 (33.1)	
Age (years)	$36.54 \pm 9.74$	$36.95 \pm 9.75$	0.732
Weight (kg)	$66.61 \pm 10.64$	$70.48 \pm 11.81$	0.146
Height (cm)	$164.39 \pm 8.05$	$168.19 \pm 9.07$	0.154
BMI (kg/m <sup>2</sup> )	$24.69 \pm 3.62$	$24.86 \pm 3.45$	0.881
Past medical history			
Pulmonary diseases	4 (2.9)	3 (2.2)	0.356
Kidney failure	6 (4.4)	7 (5.1)	
Cardiovascular disease	1 (0.7)	2 (1.5)	
Diabetes mellitus	3 (2.2)	5 (3.7)	
Digestive diseases	2 (1.5)	2 (1.5)	

BMI: Body mass index

90 min after the intervention ( $P > 0.05$ ). In contrast, patients' pain scores in each of the two groups were significantly reduced over time ( $P < 0.001$ ) [Table 3].

Finally, the complications observed were 7 (5.1%) cases of nausea, 4 (2.9%) cases of dizziness, and 2 (1.5%) cases of decreased SpO<sub>2</sub> in the morphine group and only 3 (2.2%) cases of dizziness in the ketorolac group. Although the occurrence percentage of complications was lower in the ketorolac group, no statistically significant difference was found between the two groups ( $P > 0.05$ ) [Table 4].

## DISCUSSION

The results of the present study revealed that patients' hemodynamic parameters including SBP, DBP, HR, RR, and SpO<sub>2</sub> before and after the intervention were not significantly different between the

**Table 2: Determination and comparison of patients' mean hemodynamic parameters in the two groups**

Variables	Morphine group	Ketorolac group	P#
<b>SBP (mmHg)</b>			
Baseline	11.66±0.78	11.37±1.58	0.067
T <sub>1</sub>	11.64±0.76	11.36±1.58	0.071
T <sub>2</sub>	11.52±0.70	11.35±1.57	0.253
T <sub>3</sub>	11.44±0.78	11.36±1.56	0.607
T <sub>4</sub>	11.42±0.74	11.38±1.55	0.803
T <sub>5</sub>	11.35±0.83	11.39±1.55	0.808
P*	0.771	0.286	
<b>DBP (mmHg)</b>			
Baseline	7.17±0.64	6.99±1.05	0.086
T <sub>1</sub>	7.15±0.63	6.99±1.04	0.120
T <sub>2</sub>	7.10±0.53	6.99±1.04	0.265
T <sub>3</sub>	7.09±0.53	6.99±1.03	0.331
T <sub>4</sub>	7.10±0.51	7.00±1.03	0.325
T <sub>5</sub>	7.10±0.51	7.00±1.02	0.325
P*	0.479	0.918	
<b>HR (bpm)</b>			
Baseline	68.83±5.08	67.50±9.34	0.146
T <sub>1</sub>	69.09±5.52	67.52±9.42	0.095
T <sub>2</sub>	68.96±5.39	67.57±9.45	0.136
T <sub>3</sub>	68.60±5.65	67.35±9.37	0.182
T <sub>4</sub>	72.96±51.70	67.21±9.35	0.203
T <sub>5</sub>	68.56±5.55	67.19±9.34	0.143
P*	0.874	0.854	
<b>PR (bpm)</b>			
Baseline	15.63±1.49	15.30±2.46	0.031
T <sub>1</sub>	15.65±1.55	15.56±2.47	0.280
T <sub>2</sub>	15.65±1.53	15.57±2.43	0.190
T <sub>3</sub>	15.58±1.52	15.57±2.43	0.370
T <sub>4</sub>	15.54±1.52	15.55±2.43	0.607
T <sub>5</sub>	15.54±1.52	15.06±2.43	0.053
P*	0.154	0.750	
<b>SpO2 (%)</b>			
Baseline	95.19±0.91	93.76±11.54	0.152
T <sub>1</sub>	95.16±0.90	93.75±11.52	0.157
T <sub>2</sub>	95.10±0.93	93.76±10.69	0.179
T <sub>3</sub>	95.08±0.92	93.75±11.06	0.180
T <sub>4</sub>	95.08±0.93	93.74±11.02	0.181
T <sub>5</sub>	95.08±0.93	93.74±11.10	0.179
P*	0.479	0.173	

#Significance level obtained from the univariate analysis by adjusting for the age, sex, and additional dose of analgesia in comparison with the mean of the variable between the two groups in each of the studied times, \*Significance level obtained from the repeated measure analysis in comparison with the mean of variable changes over time in each of the two groups. T<sub>1</sub>: 5 min after the intervention, T<sub>2</sub>: 15 min after the intervention, T<sub>3</sub>: 30 min after the intervention, T<sub>4</sub>: 60 min after the intervention, T<sub>5</sub>: 90 min after intervention, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HR: Heart rate, SpO2: Oxygen saturation, PR: Pulse rate

two groups. In addition, changes in these parameters from before the intervention to 90 min after the intervention were not significant in each of the two groups over time. In fact, it can be stated that the administration of either morphine or ketorolac did not lead to significant fluctuations in patients' hemodynamic parameters,

and the patients were stable in terms of hemodynamic parameters. Therefore what matters to the researchers in this study was the result of the intervention in relieving patients' pain.

According to the results of the present study, the two groups had the same pain intensity at the beginning of the study and had no significant differences 5, 15, 30, 60, and 90 min after the administration of morphine or ketorolac. In fact, the role of the intervention in reducing patients' pain was palpable in both groups, and no distinction can be made between the effectiveness of the two drugs.

Consistent with the findings of the present study, Yazdani *et al.* stated that the effectiveness of the intravenous administration of ketorolac and morphine in relieving pain in patients with renal colic was not significantly different, and both drugs effectively reduced pain in patients up to 30 min after the administration.<sup>[17]</sup>

Furthermore, some other studies have evaluated the effectiveness of ketorolac and morphine alone and in combination in reducing pain caused by renal colic and indicated that the administration of morphine or ketorolac alone did not significantly differ in relieving patients' pain. In addition, they showed that the administration of an extra dose of analgesia over 40 min after the intervention was lower in the group receiving the combination of the two drugs as compared with the morphine and ketorolac alone groups.<sup>[7,16]</sup> In our study, to eliminate the effect of the extra dose of the painkiller, we adjusted this factor as a confounder in comparing patients' pain; however, no significant difference was found between the two groups in terms of the pain intensity.

Likewise, the results of Steinberg *et al.*'s study regarding the standardization of the pain management protocol for patients with renal colic in EDs revealed that the implementation of a protocol using 30 mg of ketorolac along with 0.5-1-1 mg/kg of morphine can be effective in reducing the duration of pain and causing analgesia.<sup>[15]</sup>

Although the results of the above-mentioned studies indicate the better effect of the combination of these two drugs in reducing patients' pain, still some studies have not found the combined administration of the two drugs to be superior to the administration of ketorolac alone and have not reported a significant difference in this regard.<sup>[18]</sup> In fact, the mentioned studies stated that the use of ketorolac alone can be as effective as the combination of ketorolac with morphine, and it is not required to add an additional drug to ketorolac.

In addition, a review study performed by Holdgate *et al.* revealed that NSAIDs, as compared to opioids, significantly reduced patients' pain.<sup>[14]</sup> Moreover, many studies have reported a faster reduction in the pain intensity following the administration of ketorolac as compared to other drugs such as pethidine, meperidine, and tramadol.<sup>[19,20]</sup>

It should be noted that one of the problems of NSAIDs was the lack of a product with the intravenous injection capability

**Table 3: Determination and comparison of patients' pain in the two groups**

Variables	Morphine group	Ketorolac group	P#
Pain			
Baseline	9.41±1.33	9.16±1.76	0.181
T <sub>1</sub>	9.27±1.43	9.04±1.78	0.256
T <sub>2</sub>	7.32±1.32	7.29±1.62	0.889
T <sub>3</sub>	4.80±1.60	5.02±1.58	0.268
T <sub>4</sub>	1.44±1.45	1.79±1.88	0.078
T <sub>5</sub>	0.01±0.17	0.07±0.39	0.154
P*	<0.001	<0.001	

#Significance level obtained from the univariate analysis by adjusting for the age, sex, and additional dose of analgesia in comparison with the mean of the variable between the two groups in each of the studied times, \*Significance level obtained from the repeated measure analysis in comparison with the mean of variable changes over time in each of the two groups. T<sub>1</sub>: 5 min after the intervention, T<sub>2</sub>: 15 min after the intervention, T<sub>3</sub>: 30 min after the intervention, T<sub>4</sub>: 60 min after the intervention, T<sub>5</sub>: 90 min after intervention

**Table 4: Determination and comparison of the frequency distribution of complications in patients in the two groups**

Complications	Morphine group (%)	Ketorolac group (%)	P#
Nausea	7 (5.1)	0 (0)	0.054
Dizziness	4 (2.9)	3 (2.2)	0.702
Decreased SpO <sub>2</sub>	2 (1.5)	0 (0)	0.156

#Significance level obtained from Chi-square test. SpO<sub>2</sub>: Oxygen saturation

because the intramuscular injection or the oral administration coincides with increasing the duration of action and more pain tolerance in the patient. However, the entry of ketorolac as the intravenous injection product into the drug market has led to the introduction of this drug as a preferred drug in the treatment of patients with renal colic.<sup>[21]</sup>

Another benefit of ketorolac over opioids is the significant reduction in the drug complications. Moreover, the complications of dependence and reduction of drug action in long-term use, which occur in opioids, are not an issue following the continuous use of ketorolac. However, it should be mentioned that Ketorolac has its own complications and contraindications such that this drug reduces renal blood flow and glomerular filtration and is not recommended in patients with renal insufficiency.<sup>[21]</sup> In general, ketorolac has received more attention due to the benefits of NSAIDs, especially ketorolac, over the opioids, its limited cases of contraindications, and the occurrence of fewer complications.

The results of this study in evaluating the occurrence of drug complications revealed that a total of 13 patients in the morphine group and 3 patients in the ketorolac group had drug complications including nausea, dizziness, and decreased SPO<sub>2</sub>. Therefore, although the occurrence of complications was generally low in both groups, the occurrence of complications was lower in the ketorolac group as compared with the morphine group.

In line with the findings of the present study, the results of another study reported higher drug complications in the morphine group as compared to the ketorolac group.<sup>[7]</sup> Although they had the complication of dry mouth in the morphine group, the mentioned complication was not observed in our study. In many other studies, no significant difference was found between ketorolac and morphine groups in terms of the occurrence of drug complications.<sup>[14,17,18]</sup> Ghuman *et al.* also stated that most complications were observed in the morphine group, followed by the two drug combination groups, and finally the ketorolac alone group.<sup>[16]</sup>

In general, considering that both ketorolac and morphine had similar effect in terms of the stability of the patients' hemodynamic status and the occurrence of complications was not significantly different between the two groups, it can be stated that although both ketorolac and morphine have a significant effect on reducing the target patients' pain intensity, ketorolac can be considered as a significantly effective drug in relieving pain in patients with renal colic due to the benefits of NSAIDs. Although attention to the mentioned issue and the large sample size were the strengths of the present study, the lack of the combination of the two drugs and the lack of attention to the drug onset of action can be considered as the weaknesses of the present study. Therefore, it is suggested that future studies evaluate the effect of each of these drugs and their combination as well as the use of different doses to reduce the pain caused by renal colic or other acute pains.

## CONCLUSION

According to the results of the present study, there was no significant difference between morphine and ketorolac in terms of changes in patients' hemodynamic parameters. Moreover, these two drugs had similar effectiveness in terms of relieving pain in patients with renal colic. In addition, patients' pain scores in the two groups decreased significantly over 90 min after the intervention, and no significant difference was found between the two groups in any of the evaluated times. Finally, although the occurrence of complications in the morphine group was higher than that of the ketorolac group, this difference was not statistically significant due to the few complications reported in this study. Therefore, it can be generally mentioned that ketorolac may be safer and more reliable than morphine in reducing pain in target patients due to the similar hemodynamic stability in both groups, the higher possibility of the occurrence of complications in the morphine group as compared with the ketorolac group, and the similar efficacy of the two drugs.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

## REFERENCES

1. Patti L, Leslie SW. Acute Renal Colic. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2021.
2. Amer T, Osman B, Johnstone A, Mariappan M, Gupta A, Brattis N, *et al.* Medical expulsive therapy for ureteric stones: Analysing the evidence from systematic reviews and meta-analysis of powered double-blinded randomised controlled trials. *Arab J Urol* 2017;15:83-93.
3. Akbari H, Foroughian M, Abiri S, Kalani N, Rayatdoost E, Safaei M, *et al.* Comparing the analgesic effect of aminophylline and hyoscine with morphine on renal colic: A randomized clinical trial. *Front Emerg Med* 2020;4:e85.
4. Aydin ME, Ahiskalioglu A, Tekin E, Ozkaya F, Ahiskalioglu EO, Bayramoglu A. Relief of refractory renal colic in emergency department: A novel indication for ultrasound guided erector spinae plane block. *Am J Emerg Med* 2019;37:794.e1-3.
5. Ziyae AM, Simfroush N, Zand S. Renal colic: Pathophysiology, diagnosis and treatment. *J Islamic Repub Iran Med Council* 2017;24:412-22.
6. Reza KB, Safarinezhad MR, Markazi MN, Valimanesh HA, Abd EM. The comparison of the efficacy of common pain management in acute renal colic. *Ann Mil and Health Sci Res*; 2004;381-6.
7. Hosseinijad SM, Amini Ahidashti H, Bozorgi F, Goli Khatir I, Montazar SH, Jahanian F, *et al.* Efficacy and safety of combination therapy with ketorolac and morphine in patient with acute renal colic; A triple-blind randomized controlled clinical trial. *Bull Emerg Trauma* 2017;5:165-70.
8. Farnia MR, Jalali A, Vahidi E, Momeni M, Seyedhosseini J, Saeedi M. Comparison of intranasal ketamine versus IV morphine in reducing pain in patients with renal colic. *Am J Emerg Med* 2017;35:434-7.
9. Holdgate A, Pollock T. Nonsteroidal anti-inflammatory drugs (NSAIDs) versus opioids for acute renal colic. *Cochrane Database Sys Rev* 2004;1:CD004137.
10. Machado GC, Maher CG, Ferreira PH, Day RO, Pinheiro MB, Ferreira ML. Non-steroidal anti-inflammatory drugs for spinal pain: A systematic review and meta-analysis. *Ann Rheum Dis* 2017;76:1269-78.
11. Singla N, Singla S, Minkowitz HS, Moodie J, Brown C. Intranasal ketorolac for acute postoperative pain. *Curr Med Res Opin* 2010;26:1915-23.
12. Shirazi M, Salehipour M, Afrasiabi MA, Aminsharifi A. analgesic effects and safety of desmopressin, tramadol and indomethacin in patients with acute renal colic; a randomized clinical trial. *Bull Emerg Trauma* 2015;3:41-5.
13. Shaker SH, Mosadegh R, Jalali F, Zavareh M. Comparison of intravenous morphine and ketorolac in renal colic patients admitted to Firoozgar and Hazrat Rasoul e Akram hospitals. *J Anesthesiol and Pain*; 2016;7:40-8.
14. Holdgate A, Pollock T. Systematic review of the relative efficacy of non-steroidal anti-inflammatory drugs and opioids in the treatment of acute renal colic. *BMJ* 2004;328:1401.
15. Steinberg PL, Nangia AK, Curtis K. A standardized pain management protocol improves timeliness of analgesia among emergency department patients with renal colic. *Qual Manag Health Care* 2011;20:30-6.
16. Ghuman J, Vadera R. Ketorolac and morphine for analgesia in acute renal colic: Is this combination more effective than monotherapy? *CJEM* 2008;10:66-8.
17. Yazdani R, Saeedi M, Amirshakari T, Bordbar G, Tabibzadeh A. Intravenous paracetamol, morphine, or ketorolac for the treatment of renal colic: A randomized double blind clinical trial. *J Res Med Dent Sci* 2018;6:169-73.
18. Safdar B, Degutis LC, Landry K, Vedere SR, Moscovitz HC, D'Onofrio G. Intravenous morphine plus ketorolac is superior to either drug alone for treatment of acute renal colic. *Ann Emerg Med* 2006;48:173-81.
19. Lin F, Li SQ, Yuan Y, Zhang L, Chen JY. Clinical observation of ketorolac tromethamine combined with pethidine hydrochloride in the treatment of renal colic. *China Pharm* 2012;5:12.
20. 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;73:583-95.
21. Eidinejad L, Bahreini M, Ahmadi A, Yazdchi M, Thiruganasambandamoorthy V, Mirfazaelian H. Comparison of intravenous ketorolac at three doses for treating renal colic in the emergency department: A noninferiority randomized controlled trial. *Acad Emerg Med* 2021;28:768-75.