Comparison of the Effectiveness of Dexmedetomidine and Morphine Sulfate in the Management of Acute Renal Colic Pain

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Abstract--- Introduction: One of the most important problems in emergency departments is relieving pain in patients with renal colic. The aim of this study was to compare the efficacy of dexmedetomidine and morphine sulfate in the management of acute renal colic pain.
Methods: This clinical trial study was performed on 200 patients with acute renal colic pain. Patients were divided into two groups, the first group was injected with dexmedetomidine 1 µg/kg IV, and the second group was injected with morphine at a concentration of 0.1 mg/kg IV and ketorolac. Pain intensity was measured at the time of admission and during the experiment, and the findings were recorded in a questionnaire. The results were analyzed by SPSS.
Results: The onset time of analgesic effect was less than 30 minutes in the dexmedetomidine group and between 30 and 60 minutes in the morphine group. The onset time of the analgesic effect of dexmedetomidine injection was significantly shorter compared to the group of patients that received morphine injection (p-value = 0.001). Also, the duration of analgesia in most patients in group 1 was below 10 minutes, and in the morphine group this amount was less than 20 minutes, and the difference was statistically significant (p-value = 0.001).
Discussion: The use of dexmedetomidine is effective in relieving renal colic pain and has more benefits than morphine and can be a good substitute for morphine.

Keywords: Renal Colic, Dexmedetomidine, Morphine, Renal Patients.

I. Introduction

Renal colic refers to one or more acute and short-term painful attacks associated with nausea and vomiting due to movement and excretion of kidney stones (1). The main cause of renal colic pain is the passage of stones through the collecting system of the kidneys, sudden dilation of the collecting system, pelvis, and ureter, which leads to increased pressure behind the obstruction site and causes the main symptoms of renal colic (2); also, the site of the pain is not directly related to the location of the stone (3). Associated symptoms can be nausea and vomiting, hematuria (microscopic or gross), dysuria, and frequent urination. Pain relief is one of the best treatments in the acute stage because most urinary stones heal with expected treatment (4).

Drugs used in acute renal colic are divided into two main categories of nonsteroidal anti-inflammatory drugs (NSAIDs) and narcotics (5, 6). Narcotics, especially morphine, are associated with various side effects such as dependence, nausea, vomiting, constipation, drowsiness, at higher doses, respiratory failure, and hypotension (7, 8). Dexmedetomidine is an imidazole drug that is water-soluble and has no active metabolite (9, 10). This drug has a high protein binding (94%) and therefore in patients with severe renal problems, due to reduced plasma protein binding, the sedative effect of this drug is stronger (11). In dexmedetomidine sedation, the patient can be easily awakened and the patient is able to cooperate and obey instructions (12). Dexmedetomidine reduces opioid use (more than 50%) in the postoperative phase and reduces opioid-induced muscle rigidity. Therefore, in emergency conditions, it can be a suitable alternative to opioids (more commonly, morphine) in the management of acute renal colic pain in patients (13). In this study, a comparison was performed between dexmedetomidine and morphine sulfate in the management of acute renal colic pain in patients referred to the emergency department of Shahid Beheshti University of Medical Sciences of Iran.

II. Methods

Study Population

All patients with acute renal colic pain who were referred to the emergency department of Shohadaye Tajrish Hospital in 2019 and underwent pain control treatment with dexmedetomidine, were included in this study.

Inclusion and Exclusion Criteria

Inclusion criteria were all patients with acute renal colic pain caused by renal stones according to clinical examination, patients with moderate and severe pain scores, aged more than 18 years and less than 60 years, patients in whom urinary stones have been duly recorded by ultrasound or CT scan, and patients who did not receive analgesic injection before referring to the emergency department. Exclusion criteria included patients with severe hepatic impairment and hypertension without medical treatment, patients with uncontrolled hypertension undergoing medical treatment, patients with systolic blood pressure less than 90 mmHg on arrival, and patients with a history of beta-blockers use in the past 24 hours and a history of allergies to Alpha-adrenergic drugs, as well as those over 60 years of age and morphine-sensitive.

Randomization and Blinding

In this study, patients were randomly divided into two groups of 100. The first group of patients received dexmedetomidine to reduce colic pain and the second group of patients received morphine. In this study, the double-dummy blinding method was implemented, and the prescriber (researcher) and the patient were not aware of the contents of the drug.

Study Protocol

After obtaining the necessary permits to implement the project, the research was conducted as a controlled clinical trial. The drugs were pre-prepared, coded, and labeled, and then were infused into patients according to a random table. The initial doses of the drugs in two groups were morphine IV 0.1 mg/kg with a maximum dose of 5 mg and ketorolac, 30 mg intramuscularly in the fifth minute of treatment, and dexmedetomidine at a dose of 1 µg/kg IV. For simulation, a micro-set was used for intravenous injection of drugs, and the drug was diluted to 100 cc with normal saline so that it could not be identified by the researcher at the time of injection. The medication was infused slowly within 10 minutes, and in case of insufficiency, the patient was excluded from the study. The pain was measured by NRS scale in each group at 0 (baseline), 5, 10, 20, 30, and 60 minutes after receiving the drug.

The onset of action of the drug was immediately recorded by defining when the patient indicated a reduction in pain. A reduction of at least 3 points in pain intensity was considered a success in pain control. Patients were fully monitored during and after receiving the drug and all vital signs were recorded.

The patients were monitored for the occurrence of side effects (hypotension, respiratory depression) and in case of any complication, the case and the time of occurrence and dose of the drug were recorded in addition to appropriate treatment. The dose required for the onset of the effect and the time required for recovery were recorded.

Random Exclusion

During the study, in group one, 6 patients were excluded from the study due to lack of pain treatment with dexmedetomidine, 16 patients due to mild pain, and 8 patients due to lack of diagnosis of stones. (Figure 1).

Study Variables

According to the Stone Scoring system, which includes 1- patient gender 2- duration of pain 3- patient's race (black or white race) 4- nausea and vomiting 5- hematuria, the score of patients was initially measured and recorded. The maximum score that can be obtained in this system is 13 and based on this, patients were classified into three groups including low risk (score 0-5), moderate risk (score 6-9), and high risk (score 10-13). High-risk patients necessarily underwent spiral CT-scan of the abdomen and pelvis without contrast and with 3 mm cuts, and the presence of stone, stone location, number of stones, and stone density were recorded based on the Hounsfield number.

Statistical Analysis

Mean, standard deviation, minimum, maximum, and first, middle, and third quarters were used for descriptive analysis of quantitative data, and frequency and percentage were used for descriptive analysis of qualitative data. Spearman correlation test or Pearson correlation test were used to examine the linear relationship between variables. T-test or Mann-Whitney non-parametric test (depending on the distribution of variables) were used to compare continuous variables between the two groups. To investigate the relationship between nominal variables, the Chi-square test or Fisher's exact test (depending on the data) was used. SPSS statistical software 20.0.0 was used to analyze the data and all tests were two-way and the significance level was considered to be 0.05.

Ethical Considerations

Researchers confirm that at all stages of the research were conducted in accordance with Helsinki Declaration. The general course of treatment of the patients was not changed and no time cost was imposed on the patients.

Patients were able to leave the study whenever they wished. Data confidentiality was generally maintained and no individual reports were published. All aspect of the work covered in this study has been conducted with the ethical approval obtained from Shahid Beheshti University of Medical Sciences (SBMU) ethics committee (IR.SBMU.MSP.REC.1398.157).

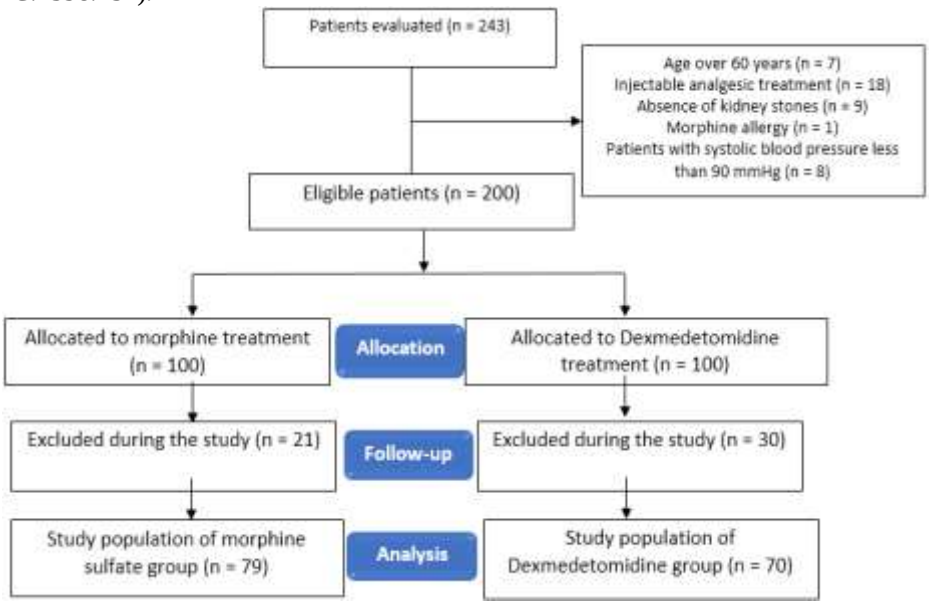

Figure 1: Flowchart of Patients Studied

III. Results

In the present clinical trial study, the mean age of patients in the dexmedetomidine group was 42.48 years and in the morphine group was 43.91 years. Of the 70 patients in the dexmedetomidine group, 48 were female and 22 were male, and of the 79 patients in the morphine group, 52 were female and 27 were male. The relationship between the two groups was not statistically significant (p-value = 0.735). Also, 5 patients in the first group had a history of drug use and 65 patients had no history of drug use. In the second group, 8 people had a history of drug use and 71 people did not have a history of drug use. There was no significant relationship between the two groups regarding the history of drug use (p-value = 0.384). However, in terms of the history of the underlying diseases, there was a significant relationship between the two groups, so that the frequency of underlying diseases in the first group was higher than the patients in the second group (Table 1).

Table 1: Investigation of Contextual Variables in Both Groups

Variable		Dexmedetomidine group	Morphine group	p
Age (years)	Mean	42.38	43.91	0.735
Gender	Female	48	52	0.720
	Male	24	27	
History of drug use	Yes	5	8	0.384
	No	65	71	
History underlying diseases	Yes	21	25	0.007
	No	49	54	
Severity of pain	Moderate	18	29	0.288
	Severe	52	50	

Of the total patients in the dexmedetomidine group, 16 had nausea, 9 had vomiting, 7 had dizziness, and 14 had headaches, and no other complication was observed in the other patients. In contrast, 19 patients in the morphine group experienced nausea, 13 had vomiting, 14 had dizziness, and 7 had headaches, and no other complication was observed in the other patients. The incidence of side effects in the morphine group was significantly higher than in the dexmedetomidine group (p-value = 0.007).

Among the 70 patients in the first group (dexmedetomidine), 14 reported a reduction in pain after 5 minutes, 37 patients after 10 minutes, and 12 patients after 20 minutes after the injection. Also, in the second group, 12 patients reported pain relief after 5 minutes, 14 patients after 10 minutes, 37 patients after 20 minutes, and 4 patients after 60

minutes following the injection. Duration of pain relief after dexmedetomidine injection was significantly shorter than pain relief after morphine injection (p-value = 0.001) (Table 2).

Table 2: Evaluation of the duration of Analgesia in the Two Groups

	Time	Dexmedetomidine group	Morphine group	p
Analgesic effect after injection	After 5 minutes	14	12	0.001
	After 10 minutes	37	14	
	After 20 minutes	12	37	
	After 30 minutes	7	12	
	After 60 minutes	0	4	
Duration of analgesia		17.21	24.16	0.000

In the dexmedetomidine group, the onset time of analgesic effect was under 30 minutes in 54 patients, between 30 and 60 minutes in 13 patients, and 3 patients did not respond to dexmedetomidine injection. In the morphine group, the onset time of analgesic effect was under 30 minutes in 32 people, 30 to 60 minutes in 38 people, and 9 people did not respond to morphine. In general, the difference between the two groups was statistically significant (p-value = 0.001). In the first group, the dose required to achieve analgesia was below 5 µg for 47 patients and above 5 µg in 23 patients. Also in the second group, the dose required to achieve analgesia was below 5 mg for 43 patients and above 5 mg for 36 patients. This difference was not statistically significant.

Also, in the dexmedetomidine group, the recovery time was less than 10 minutes in 32 patients, 10 to 15 minutes in 33 patients, and more than 15 minutes in 5 patients, while in the morphine group, the recovery time was less than 10 minutes in 23 patients, between 10 and 15 minutes in 39 patients, and 15 minutes in 17 patients. The difference between the two groups in terms of recovery time was statistically significant so that the recovery time in the dexmedetomidine group was less than the morphine group (p-value = 0.006).

Table 3: Evaluation of the Onset Time of Analgesic Effect, the Required Dose, and the Recovery Time in Both Groups

		Dexmedetomidine group	Morphine group	p
The onset time of analgesic effect	Under 30 minutes	54	32	0.000
	30 to 60 minutes	13	38	
	No response	3	0	
Required dose	Under 5mg	47	43	0.121
	Over 5mg	23	36	
Recovery time	Under 10 minutes	32	23	0.006
	10 to 15 minutes	33	39	
	Over 15 minutes	5	17	

Also, in the performed studies, it was found that the most frequent location of stones in the studied patients in both groups was the ureter, but no significant difference was observed between the two groups in terms of this variable (p-value = 0.26).

Table 4: Location of Renal Stones in the Patients of Both Groups

	Location of renal stones	Number of patients	p
Dexmedetomidine group	Renal calyx	17	0.26
	Ureter	26	
	Urinary bladder	19	
	Both calyx and bladder	8	
Morphine group	Renal calyx	19	
	Ureter	27	
	Urinary bladder	25	
	Both calyx and bladder	8	

IV. Discussion

Annually, about 1.2 million people worldwide suffer from renal colic, which accounts for about 1% of hospital admissions (14). Renal colic is a severe pain that starts suddenly in the flanks and spreads to the groin. This pain recurs intermittently in the patient and its intensity increases constantly (13). The basic principles of renal colic treatment are to reduce and alleviate the patient's pain and eliminate water and electrolyte disorders, and the only definitive treatment is to eliminate the source of pain, which is the cause of the obstruction; however, all efforts at the beginning of the referral revolve around the relief of pain and its temporary treatment (15). Pain due to kidney

stones not only increases the rate of disease but also has many economic consequences on society and also leads to exorbitant health costs.

Non-opioid drugs also play a major role in the treatment of renal colic by inhibiting cyclooxygenase and thus inhibiting the production of prostaglandins, and therefore the mechanism of pain relief in them is different from narcotic drugs. One of these drugs is dexmedetomidine. (16).

Numerous studies have been performed comparing the effectiveness of opioids and non-opioids in relieving renal colic pain. In 2016, Lundorf et al. examined the effect of dexmedetomidine in the treatment of acute pain caused by surgery. They stated that the use of dexmedetomidine was effective in relieving pain after surgery and demonstrated better results compared to opioids (17).

In 2020, Cornett et al. conducted a study on the efficacy of dexmedetomidine and concluded that the use of high-dose dexmedetomidine leads to increased blood pressure (18). In 2013, Bekker et al. studied the use of dexmedetomidine in reducing pain and reported the side effects of hypoxia or nausea, vomiting, dry mouth, and headache, following the use of this medication; However, they acknowledged that dexmedetomidine induced lower complications for the nervous system because it does not suppress respiratory function even at high doses (15). In our study, it was found that fewer patients in the dexmedetomidine group had side effects such as nausea, vomiting, and headache after the injection, in comparison with the second group who received morphine sulfate, and these findings were consistent with the results of the study by Bekker et al.

In a study performed in 2014, Lee et al. stated that a concentration of 0.5 µg/kg of dexmedetomidine in combination with propofol could be a suitable dosage for pain relief when controlling hemodynamic changes (19). In our study, in order to reduce acute renal colic pain, a concentration of less than 5 µg/kg of dexmedetomidine was used for group 1, and the results indicated that most patients reported the onset time of the analgesic effect of this medication to be under 30 minutes after injection; while the onset time of the analgesic effect of morphine was reported to be 30 to 60 minutes after injection. Therefore, it can be said that dexmedetomidine injection can be effective in the treatment of acute renal colic pain.

According to the results of this study, patients who were injected with dexmedetomidine had a shorter recovery time compared to patients in group 2 who received morphine.

The present study is in fact a step towards evaluating the effectiveness of dexmedetomidine injection in comparison with a similar injection of corticosteroids in the treatment of acute renal colic pain. Similar to other clinical trials that were conducted on injections for the treatment of acute renal colic, patients in both groups showed short-term improvement after enrollment in this study, however, patients in the dexmedetomidine group demonstrated a longer improvement in function compared to the morphine group.

V. Study Limitations

Due to the expensiveness of drug and its lack of availability in all emergency centers, this research was conducted only in two emergency centers. The age range of the individuals and the prevalence of the COVID-19 were other issues that limited the target population in this study. Because, as a result of COVID-19 pandemic, patients were less often admitted to the emergency department and due to the crowding of emergency centers, most of the patients did not return for follow-up. In some cases, the patients were excluded from the study because they did not go for follow-up after the pain relief.

VI. Conclusion

Considering that the analgesic efficacy of dexmedetomidine was better than morphine and also considering the fewer side effects of dexmedetomidine compared to morphine, this drug can be a suitable alternative to morphine to reduce pain in renal colic patients referred to the emergency department.

Conflict of Interest

The authors of this article have not reported any conflict of interest.

Authors' Contribution

A.M: Conception and study design, analysis and interpretation of data, drafting the article.

M.A: Study conduction, data collection, drafting the article and revising.

A.R: Analysis and interpretation of data, drafting the article or revising.

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