

ISFAHAN UNIVERSITY OF MEDICAL SCIENCES
SCHOOL OF MEDICINE
EMERGENCY MEDICINE DEPARTMENT

Thesis For Obtaining The Specialty Degree In Emergency medicine

Title:

**The Comparison of the Analgesic Effect of Combining
Desmopressin with NSAID and Morphine with NSAID
in the Treatment of Renal Colic**

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Supervisor:

Dr. Saeid Majidinejad

(Assistant Professor of Emergency Medicine)

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تجربہ

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تحت عنوان: مقایسہ اثر ضد درد ترکیب دیکلوفنس و NSAID و ترکیب نرونین و NSAID در درمان زناں کرمی

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استاد راهنما: به راهنمایی: دکتر محمدی نزار

استاد مشاور: —

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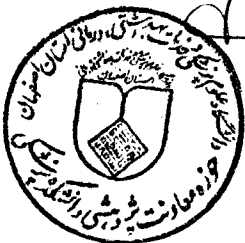
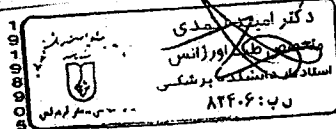
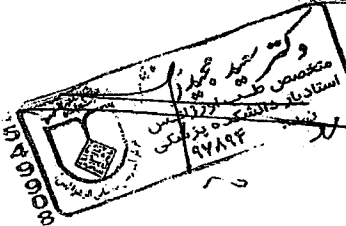
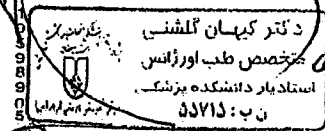
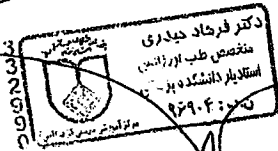
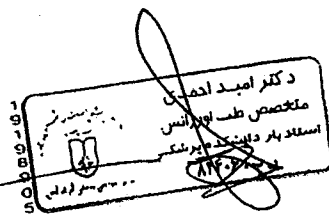
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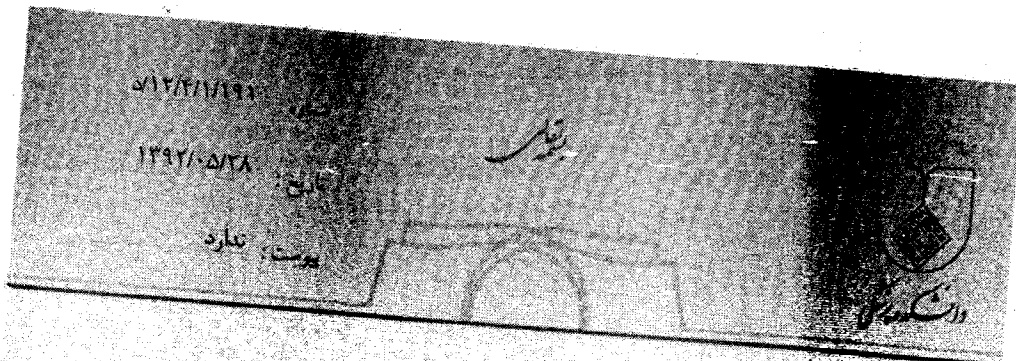
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معاون آموزش تخصصی دانشکده پزشکی:



در انعام




In the name of God

Dear Dr. Aakramoalsadat Razavizadeh

It is my pleasure to inform you as corresponding author and your colleagues " *Dr. Saeid Majidinejad (first author), Dr. Morteza Mazouchi* " that your manuscript entitled "*The Comparison of the Analgesic Effect of Combining Desmopressin with NSAID and Morphine with NSAID in the Treatment of Renal Colic*" has been accepted for publication in the journal of "*Advanced Biomedical Research*", Vol 2; No 4.

Thank you for submitting your article to this journal. We look forward to receiving your next precious articles.


Shaghayegh Haghighi Javanmard
MD, PhD Editor in chief

The Comparison of the Analgesic Effect of Combining Desmopressin with NSAID and Morphine with NSAID in the Treatment of Renal Colic

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ABSTRACT:

Introduction: Pain relief is one of the most important basic medical skills. Renal colic pain is among the most severe pains which classic treatment is opioid injection and NSAID. Desmopressin is a new drug with an appropriate effect on sedation of colic pains. However, its advantage in pain relief over the others is a controversial issue. This study aimed to determine the efficacy of Desmopressin + Diclofenac compared to Morphine + Diclofenac in patients with renal colic.

Materials and methods: This clinical trial study was done in Al-Zahra Hospital, Isfahan in 2012 on 90 patients with renal colic divided into two groups. the first group received NSAID and nasal Desmopressin (40mg equivalent to 2puff in each nose) and the second group took the classical treatment of NSAID and morphine (0.1mg/kg). The rate of pain was assessed 10 minutes after taking drug by VAS. Data were analyzed by SPSS software.

Results: The mean difference of pain intensity in the group receiving morphine was 6.42 ± 1.9 and 5 ± 2.88 in the group receiving Desmopressin that shows a significant difference ($p = 0.007$). Pain intensity had significantly reduced after taking the drug compared to before ($p < 0.001$).

Conclusions: Desmopressin is an effective drug in the patients with renal colic pain relief and its easy administration, availability and lack of side complications is considerable. So it can be recommended as an acceptable and suitable treatment in these patients and even in outpatient treatment.

Key words: Renal colic, Desmopressin, Non-steroidal analgesic drugs, Morphine

Introduction:

The sedation of sever pains of renal colic is one of the difficulties for outpatient and emergency wards (1). Renal colic is created as a result of increasing pressure in the secondary urinary tract through a blockage in urinary tract that causes to increase prostaglandins production and diuresis which in turn can lead to increase pelvic pressure and pain (11).

About 12% of the population is affected by renal colic. Acute symptoms of the most patients are well improved through combining opioid with NSAID. However, the elders may have to take NSAID contraindications such as renal failure and peptic ulcer and using opioids certainly need to monitor patient in terms of respiratory depression and confusion resulting from (1).

Desmopressin is a drug that recently known as appropriate analgesia for renal colic considering to its nasal consumption and physiological effects on reducing the pain in renal colic patients (1). Many small stones at the end of urinary tract are removed by watchful waiting treatment for a period of 2-4 weeks. Meanwhile, patients should access an effective drug and treatment not require to use intravenous route for administration at home. It is assumed that Desmopressin causes to rapid pain reduction through reducing the diuresis. Some also believe that Desmopressin causes to secrete endorphin B in hypothalamus that may be another reason for central analgesic additional effect. Until now a few studies have been done on the effects of this drug on renal colic and given the lack of observing

significant analgesic effect of the drug in some studies and seeing the significant effect of Desmopressin in decreasing renal colic pain in some other studies and considering that in most studies, a significant effect has not been observed, small sizes have been studied which can be considered as one of the reasons in the failure to prove the efficacy of Desmopressin in reducing renal colic pain and according to the frequency of the population involved in renal colic and pain intensity and considering the consequences of the problem such as hospitalization cost and taking intravenous drug through admission fee and receiving medication through IV, problems from the repeated atherosclerosis in patients with renal colic, the absent period of the person from doing at the same amount of disorder in functional path of the community, involving emergency personnel, overusing opioids, dependency on opioid in frequent use and its complications such as respiratory depression and its deadly consequences, if Desmopressin efficacy is proved, and given safety of the drug and its ease of use and availability, even if this drug does not have quite efficacy for all patients, it can be a great help to save time and energy and in reducing morbidity and unpleasant feeling of tolerating repetitive pain in patients with renal colic. Therefore, the present study aimed at determining the efficacy of Desmopressin compared to the suppository of Diclofenac and Morphine along with Diclofenac in patients suffering from renal colic .

Material and methods:

The current study is a clinical trial study done in the emergency section of Al-Zahra Medical Center in 2012. Inclusion criteria included patients known with renal colic or renal colic typical pain referred to Al-Zahra Medical Center, aged less than 65 years, lack of suffering from blood pressure, and had no heart failure and informed consent to participate in the study. Also, Patients whom after study, their pains were not diagnosed as renal colic pain, other reason such as appendicitis, cases who were sensitive to Desmopressin and those who had received another analgesia at least 6 hours before referring were excluded from the study.

Using the formula for estimating the sample size to compare means and considering the level of 95% significance, test power of 80% ,standard deviation of pain intensity that is considered in the rate of 1.33 according to the following and also at least significant difference between both groups considered in the amount of 0.5, the size of studied sample was calculated in the number of 43 individuals that 45 were studied in both groups for more confidence.

Patients were divided into two groups. The randomization was done in the way that the first patient was randomly put in the group receiving Desmopressin and the second one was put in the morphine group and the rest of patients were consecutively distributed in the two mentioned groups. Both groups were initially evaluated by VAS in terms of pain rate, then, patients of group A received nasal Desmopressin with the dose of 40 mg equivalent to 2puffs in each

nose and NSAID. In the second group, patients were as the control group that used classical NSAID treatment and morphine with the dose of 0.1mg/kg.

The rate of pain was assessed by VAS at 10 minutes after receiving drug and the treatment was effective when pain reduced in the rate of at least 50% to the initial amount or score 3 out of VAS score 10. Information related to each patient in addition to demographic ones was recorded in a designed special questionnaire and analyzed using SPSS software version 20 after entering. The statistical tests used to analyze data included one-way ANOVA test, T student test, T paired test and Chi-square test. This study was registered in Isfahan medical school by code 390317

Results:

In the present study, 90 referred patients with renal colic pain were selected and randomly divided into two groups of receiving morphine and Desmopressin. The mean age of all patients was 36.3 ± 11.5 with a range of 16-72 years. Also, 64 (71.1%) patients were male and 26 (28.9%) patients were female. The mean age of male and female was 36.9 ± 10.1 and 34.8 ± 14.3 years, respectively and according to T test, there were no significant differences ($p = 0.42$). In Table 1, the age and sex distribution of the above-mentioned patients has been separately shown in both groups. According to the table, the mean age of patients receiving NSAID and Desmopressin was 35.6 ± 11.8 and in the group receiving NSAID and morphine, was 37 ± 11.2 years and according to t test, no significant difference was observed between both groups ($p = 0.59$). In terms of sex distribution, in two groups receiving NSAID with Desmopressin and NSAID with Morphine, 33 and 31 (73.3% vs. 68.9%) patients, respectively were male, and the rest were female with no significant differences according to Chi square test ($p = 0.64$).

Table 1: The age and sex distribution of patients in both groups

Variable	Group level	Morphine	Desmopressin	P
Age	Year	36.11 ± 6.35	35.11 ± 11.37	0.59
Sex	Male	33 (3.73%)	31(9.68%)	0.64
	Female	12(7.26%)	14(1.31%)	

In the group receiving Morphine and Desmopressin, the mean of pain intensity before the treatment was 9.04 ± 1 and 9.3 ± 0.91 , respectively and according to t test, there were no significant differences in both groups ($p = 0.27$). Also, in both groups receiving Morphine and Desmopressin, the mean of pain intensity after taking the drug was 2.62 ± 1.89 and 4.27 ± 3.09 , respectively and according to t test, it was significantly lower in the group receiving Morphine ($p = 0.003$). According to the obtained results, the mean difference of pain intensity was 6.42 ± 1.9 in the group receiving Morphine and 5 ± 2.88 in the group receiving Desmopressin and according to T test, the difference between both groups was not significant ($p = 0.007$). The mentioned results have been shown in Table 2. It should be noted that according to T paired test, in both groups, the pain intensity after taking the drug has been significantly reduced than before ($p < 0.001$). In Figure 1, the mean of pain intensity has been shown in both studied groups before and after drug consumption.

In the present study, if the pain intensity reduced at least 50% at 10 minutes after administrating the drug, it was considered as an improvement that on this basis, after receiving the drug, 24 patients (26.7%) had effective reduction in pain that in the group receiving NSAID, this effective reduction in pain was in 5 patients and in the group receiving Desmopressin was in 19 patients (11.1% vs. 42.2%). In other words, in the groups receiving Desmopressin, the pain intensity has been reduced in higher rate at 10 minutes after receiving the drug. Chi square test also showed that in the group receiving

Desmopressin, improvement has been significantly greater than that in the group receiving Morphine ($p = 0.001$). The results have been shown in Table 3.

Table 2: the pain intensity in patients in both groups before and after consuming drug

Time	Morphine	Desmopressin	P
Before Taking Drug	9.04±1	9.3±0.91	0.27
After Taking Drugs	2.26±1.89	4.27±3.09	0.003
Difference	6.42±1.9	5±2.88	0.007
P	<0.001	<0.001	

Figure 1: The mean of pain intensity in both groups before and after drug administration.

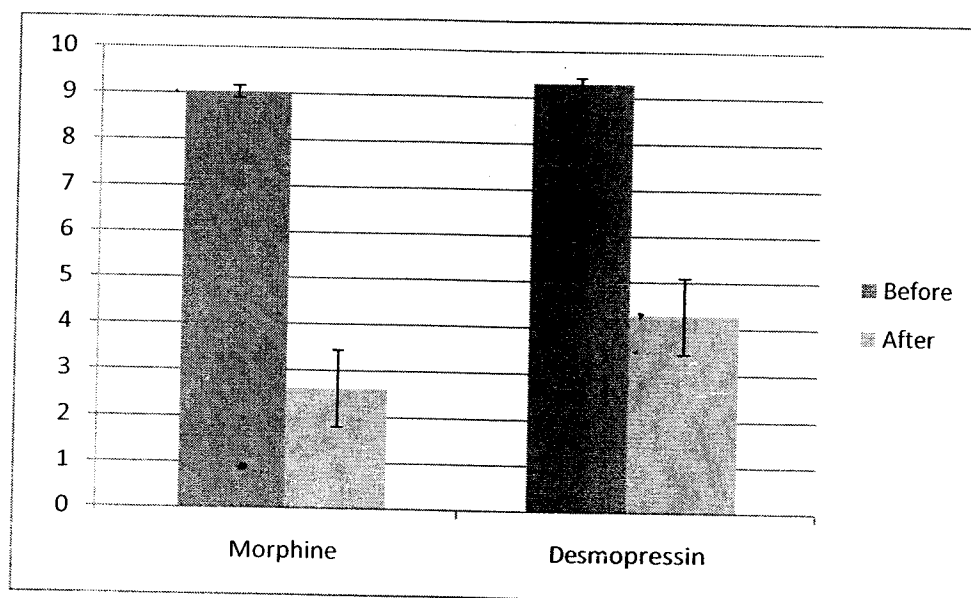


Table 3: Frequency distribution of improving pain in both groups

Group	Morphine		Desmopressin		Total	
	n	%	n	%	n	%
Effective pain relief	5	11.1	19	42.2	24	26.7
Relevant pain relief	40	88.9	26	57.8	66	73.3
Total	45	100	45	100	90	100

P=0.001

The mean of changes in pain intensity was 5.92 ± 2.53 and 5.19 ± 2.48 , respectively in the studied male and female and according to the t test; changes in pain intensity were not significantly different based on sex. Also, according to the Pearson correlation test, there was no significant relationship between age and changes in pain intensity ($p = 0.79$). According to the mentioned test, between age and changes in pain intensity, the correlation was -0.03. Doing ANOVA test with replicated observations on the mentioned data also showed that the age and sex of patients had no effect on changes in pain intensity.

Discussion and conclusion:

The main objective of the present study was to compare effects of Desmopressin and Morphine on the treatment of renal colic pains in patients referring to the emergency of Al-Zahra Medical Center. Patients assigned to the two treatment groups with no significant differences in terms of age and sex distribution, so the confounding effect of such variables has been more likely neutralized and the observed difference is probably related to the effect of the used drug. According to the obtained results, before intervening in two mentioned groups, the mean of pain intensity was not significantly different, although in the group receiving Morphine, the mean difference of pain intensity was higher compared to the group receiving Desmopressin.

Yet according to the obtained results, the effective reduction in pain was higher in the group receiving Desmopressin so that if at 10 minutes after administrating the drug, the pain intensity decreased at least 50%, it was considered as an improvement that on this basis, 26.7% patients had an effective reduction in pain after receiving the drug that in the group receiving Morphine, the effective reduction in pain was 11.1% and in the group receiving Desmopressin was 42.2%. In other words, at 10 minutes after receiving the drug, the pain intensity has declined in higher rate in the group receiving Desmopressin.

However, the results obtained from our study is not consistent with the study conducted by Beigi and Rafieian so that in their study done

on Desmopressin and Pethidine, Desmopressin was not effective in reducing the pain of renal colic patients but the pain intensity in patients receiving Pethidine had significantly reduced at 10 minutes after the injection (1). Difference between our study and their research may be due to factors such as the type of consuming opium and the technique of evaluating the pain intensity.

In 2010, in Hazhir et al study, three groups of patients with renal colic were treated by intramuscular Tramadol, nasal Desmopressin and Desmopressin associated with Tramadol that no significant differences were observed between three groups in reducing pain and in this study, it was concluded that although Tramadol cannot be replaced with Pethidine, taking Tramadol and Desmopressin or both together can reduce the need for opioid pethidine in patients (2).

The effect of Desmopressin alone on the reduction of renal colic pain has been examined in the study by Constantinides that according to the obtained results, using the drug had a significant effect in reducing pain, but in the study, Desmopressin had not been compared with another drug (7).

In his study, Lopes compared three groups of patients receiving Desmopressin + Diclofenac, alone Desmopressin and alone intramuscular conclude that the reduction of pain was similar in all three groups at 10 and 20 minutes after receiving the drug, however; 30 minutes after treatment, mild increasing in pain was found in the group receiving Desmopressin (8). While in comparing Diclofenac and Desmopressin, Sheriff concluded that Desmopressin was more

effective than Diclofenac at 30min after Desmopressin (1). In another study by Ibrahim et al in Baghdad, at 10, 20 and 30 minutes after receiving the drug, the reduction of pain was not different in three groups under treatment with Desmopressin, Diclofenac and both together at 10 and 20 minutes while at 30 minutes, the effect of two compositions of pharmaceuticals and Diclofenac alone was better than Desmopressin alone (9).

In 2010, Roshani compared the effect of Diclofenac alone with Diclofenac and Desmopressin that was an indicator of the significant pain reduction in the treatment of two drugs together (10).

According to the obtained results from this study and comparing them with other studies, it can be said that although Desmopressin has not proved effect compared with opium drugs and in this field, there is need for further study, given the appropriate and acceptable response of some patients and that Desmopressin is a drug with easy and accessible administration technique without significant side complications while the side effects of opium drugs and the incidence of dependence on long-term usage are the problems in renal colic treatment, taking Desmopressin can be recommended as an acceptable and appropriate treatment in these patients and the pain intensity and as a result hospital referring and treatment costs can be reduced by Desmopressin administration with NSAID to treat outpatients and in-home patients.

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CONSORT Flow Diagram

