Comparison of Intranasal Desmopressin and Intramuscular Tramadol Versus Pethidine in Patients With Renal Colic

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Purpose: To study the safety and efficacy of intranasal desmopressin and intramuscular tramadol versus pethidine for treatment of renal colic.

Materials and Methods: A total of 90 adult patients who presented with renal colic to the emergency wards were recruited in this study. The patients were randomly assigned to receive 100 mg intramuscular tramadol, 40 μg intranasal desmopressin, or 40 μg intranasal desmopressin plus 100 mg intramuscular tramadol. The severity of the pain was assessed using Visual Analogue Scale.

Results: The studied patients consisted of 49 men and 41 women with the mean age of 35.20 $\pm$ 13.26 years (range, 16 to 82 years). There was no statistically significant difference regarding the mean age (F [2, 89] = 2.98, P = .056) and gender differences (x^2 = 3.3, df = 2, P = .19) in three groups. There was also no statistically significant difference considering pain relief in 3 studied groups (P = .2).

Conclusion: We concluded that narcotics such as pethidine can not be replaced by tramadol in patients with renal colic, but tramadol, desmopressin, or both in combination can reduce pethidine requirement.

Keywords: renal colic, tramadol, desmopressin

Urol J. 2010;7:148-51.
www.uj.unrc.ir

INTRODUCTION

Urinary stone is a common urological disease. Most patients present with sudden and severe pain while excreting a urinary calculus. The pain, called renal colic, can be localized in the flanks or refers to the inguinal and the genitalia areas depending on the place of the calculus in the urinary tract. Renal colic is caused by expansion of the renal capsule due to the passage of the calculus from the ureter which has a colic nature, ie, the pain of the patient exacerbates with each ureteral peristalsis trying to expel the calculus, then, the pain will decrease after some time and again this process will be repeated. Large stones logged in the renal pelvis may be painless, but can result in renal dysfunction. Hematuria may be another sign of the urinary calculus.[1]

Pain relief is the first issue which should be addressed in patients with renal colic. Spasmolytic drugs such as hyoscine and dicyclomine are traditionally prescribed for renal colic. There is no evidence that buscopon (hyoscine butylbromide) reduces the need for narcotics in renal colic.[2] Nonsteroidal anti-inflammatory drugs such as diclofenac, while inhibiting

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Received July 2009
Accepted February 2010

prostaglandins release, might be the next choice,[3,4] but its paranteral form is not available in Iran.

The common recommended treatment is narcotics such as pethidine or morphine, but they accompany with some side effects and difficulties. First, narcotics are not available in all the clinics, especially private clinics. Therefore, tramadol is used for treatment of renal colic in some clinics.[5,6] The second problem, with regard to prescription of narcotics, is related to their abuse.

There are other treatments for acute renal colic. Aminophylline infusion also reduces the pain and narcotics requirement.[7] Active topical heating is an easy way to alleviate the pain of patients suffering from renal colic in an emergency ward.[8] Tamsulosin (an alpha blocker) may be useful in provoking stone passage in patients without previous interventions such as transurethral ureterolithotripsy or extracorporeal shock wave lithotripsy.[9,10]

Kidney, ureter, and bladder x-ray (KUB), computed tomography (CT) scan, and ultrasonography are diagnostic tools for renal colic.[11] Accuracy of CT scan is more than ultrasonography.[12]

This study was performed to investigate the effectiveness of intramuscular tramadol, intranasal desmopressin,[13-15] or both in patients with renal colic.

MATERIALS AND METHODS

This clinical trial was carried out on 105 adult patients who presented with renal colic to the emergency wards of Imam Khomeini and Sina Hospitals, in Tabriz, Iran from February 2006 to October 2007.

Exclusion criteria were having taken any treatment before referring, being allergic to tramadol, or being hypertensive. The written informed consents were obtained form each patient. Patients who were consented were recruited in this study.

The presence of ureteral stone was confirmed using ultrasonography and KUB. The subjective symptom, pain, was evaluated by visual analogue scale. The visual analogue scale is a conventional 10-point pain scale with a score of 10 representing the worst pain.[16]

The study patients were randomly assigned into 3 groups according to the table of random numbers. The first group was treated with 100 mg intramuscular tramadol and their pain severity was subjectively and objectively examined every 10 minutes. The patient was asked to determine the severity of his or her pain at 10, 20, and 30 minutes after receiving the medication. The positive response was defined as complete pain relief after 30 minutes. In non-responsive patients, narcotics were administered.

The second group received 40 μg intranasal desmopressin and was monitored every 10 minutes. The third group received 40 μg intranasal desmopressin plus 100 mg intramuscular tramadol and was monitored every 10 minutes assessing the pain severity.

Of 105 patients, 15 subjects were not able to tolerate the pain for 30 minutes. Therefore, they left the study at the first minutes after therapeutic intervention and were treated with usual narcotics. Review of literature on the effects of different drugs on pain relief in renal colic determines that the required sample size with adequate power is 90. P values less than .05 were considered statistically significant.

RESULTS

The studied patients consisted of 49 men and 41 women with the mean age of 35.20 $\pm$ 13.26 years (range, 16 to 82 years) (Table 1). Patients were similar in terms of baseline characteristics, including age (F [2, 89] = 2.98, P = .056) and sex (x^2 = 3.3, df = 2, P = .19).

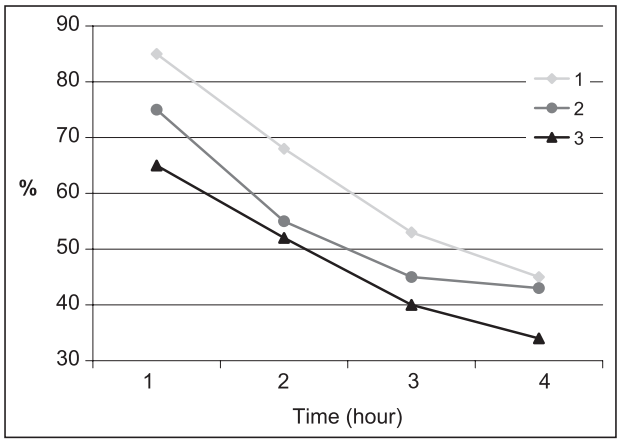
Repeated ANOVA measures showed that there was no statistically significant difference

Table 1. Age of the study patients

Treatment Group	Age range (years)	Mean Age ± Standard Deviation
1	16 to 82	37.13 ± 13.88
2	18 to 57	30.50 ± 10.11
3	19 to 75	37.96 ± 14.52

Table 2. Groups' difference considering need to pethidine after treatment intervention

Study groups (n)	Pethidine required (%)	Positive response (%)	*P*
Tramadol (30)	15 (50)	15 (50)	.05
Desmopressin (30)	10 (33.3)	20 (66.7)	.034
Tramadol plus desmopressin (30)	14 (46.7)	16 (53.3)	.071



Percentage of pain relief across study groups.

considering pain relief in 3 studied groups ($P = .2$) (Figure). This means that the effect of the 3 types of treatments was similar, with regard to patient's satisfaction, and none of them had superiority over others.

Of patients in tramadol, desmopressin, and tramadol plus desmopressin groups, 50%, 33.3%, and 46.7% required pethidine administration, respectively (Table 2). There was no significant differences between study groups ($x^2 = 1.90$, df = 2, $P = .38$). But the number of subjects needed pethidine after receiving desmopressin spray was lower than the other two groups ($P = .034$). Women were 10% more likely to need pethidine.

Adverse Events

Of patients who received desmopressin, 2 developed vertigo which resolved spontaneously within 10 minutes and one with the history of carpopedal spasm of the right hand experienced it, which was managed medically.

DISCUSSION

In a study by Moro and colleagues in 1999, the effect of desmopressin on acute ureteral obstruction was studied by measurement of intra-ureteral pressure in 24 rats. They found a significant reduction in intra-ureteral mean pressure.[14] This can explain the mechanism of pain relief with desmopressin administration.

Lopes and associates divided 61 patients with renal colic into 3 groups and treated them with desmopressin, diclofenac, or combination of both. They observed that all 3 treatment methods led to the pain relief, but desmopressin relieved the pain less than the other 2 modalities within 20 to 30 minutes. However, some patients showed complete response to desmopressin.[13] Our findings are consistent with that study.

In another study by Eray and coworkers in 2002, the effect of single dose of intramuscular tramadol was compared with mepridine in treating renal colic. Pain relief was achieved in both groups, but mepridine was more effective. Most patients required mepridine administration within 30 minutes.[6] In our study, 50% of the patients who received tramadol also required pethidine.

Constantinides and colleagues studied 108 patients with renal colic who received 40 μg intranasal desmopressin. Fifty-eight patients (53.7%) recovered within 30 minutes, while 44 patients (40.7%) did not respond to desmopressin and received prostaglandin inhibitor drugs, and 6 remainders required intramuscular pethidine.[15]

El-Sherif and associates compared the efficacy of intranasal desmopressin and intramuscular diclofenac sodium in renal colic management. They administered 40 μg intranasal desmopressin for 18 patients. The pain of 8 patients (44.4%) relieved completely within 30 minutes while 10 subjects required intramuscular diclofenac and their pain relieved completely within 30 minutes. Desmopressin plus diclofenac was effective for pain relief in more than 90% of the patients.[3]

We used both drugs separately and pethidine was used when the patients' pain did not improve. Drug combination resulted in a decrease in

pethidine administration. The number of subjects required pethidine in group 3 was more than group 2. We concluded that simultaneous administration of tramadol and desmopressin has no synergistic effect. However, further researches are required in this regard. We found that all three treatment regimens led to pain relief in renal colic, but pethidine was more effective than others.

CONCLUSION

Intranasal desmopressin relieved pain in about one third of the patients; thus, it is not as effective as narcotics. In addition, tramadol was more effective than desmopressin.

CONFLICT OF INTEREST

None declared.

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