

Renal Colic Pain Relief by Intranasal DesmopressinSeyed seifollah Moosavi beladi¹, Ali Asgari Darian², Arash Forouzan², Hossein Kalantar³, Kambiz Masoumi²¹Nephrologist, Department of Internal Medicine, Ahwaz Jundishapur University of Medical Sciences, Khoozestan, Iran.²Emergency Medicine Consultant, Department of Emergency Medicine, Ahwaz Jundishapur University of Medical Sciences, Khoozestan, Iran.³General Physician, Imam Khomeini General Hospital, Ahwaz Jundishapur University of Medical Sciences, Khoozestan, Iran.Kami_masoumi@yahoo.com

Abstract: The relief of acute pain is key in the modern practice of emergency medicine. Pain is the most common complaint of emergency department patients, seen in one half to three quarters of all patients. According to some last studies desmopressin acts quickly, has no apparent adverse effects, reduces the need for supplemental analgesic medications, and may be the only immediate therapy necessary for some patients²⁵. Therefore in the present study, we have conducted to assess the efficacy of intranasal desmopressin in patients with acute renal colic. In this inventional study, patients 18-55 years old with probably acute renal colic based on history, physical exam and past medical history came to emergency department of Imam khomeini Hospital of Ahwaz Jundishapour University of Medical Sciences were evaluated randomly. we evaluated recorded information in SPSS software and analyzed them by "Paired t test" (p-value<0.05). Seventy patients were evaluated in this study including 12 female (17.1%) and 58 male (82.8%) with mean age 33.7±10.1. Comparison of pain score in zero and 30 min (efficacy of desmopressin alone) with "paired t test" showed significant results (p-value <0.00001). It has been suggested that an antidiuretic hormone 24 (ADH)-induced decrease in diuresis could contribute to the rapid relief of pain in renal colic.

[Moosavi beladi. SS, Asgari Darian . A, Forouzan. A, Kalantar. H, Masoumi. K. **Renal Colic Pain Relief by Intranasal Desmopressin.** *Life Sci J* 2012;9(4):3354-3358]. (ISSN: 1097-8135). <http://www.lifesciencesite.com>. 495

Keywords: Desmopressin, Acute renal colic

1. Introduction

"The relief of acute pain is key in the modern practice of emergency medicine.¹" Pain is the most common complaint of emergency department patients, seen in one half to three quarters of all patients. Satisfaction with emergency care often depends on the techniques and timeliness of analgesia as well as the discharge plans for pain relief.²⁻³ Methods must be not only effective but also safe. In reality, physicians often prescribe a suboptimal drug in an inadequate dose at an excessive interval or via an inappropriate route. Pain relief is best addressed with a plan that incorporates administration, nurses, and clinicians. Acute renal colic pain is probably the most excruciatingly painful event a person can endure. Renal colic affects approximately 1.2 million people each year and accounts for approximately 1% of all hospital admissions. The ED physician are often the first to see and evaluate these patients. While proper diagnosis, prompt initial treatment especially pain relief, and appropriate consultations and substantial patient education are clearly the primary responsibility of the emergency physician. Many medications are used for relieving pain in renal colic and helping to passage of renal stone: Narcotics & Opiates, NSAIDs, Antiduretics, Alfa blockers, Ca

channel blocker, Steroids, Anticholinergics, *Narcotics and opioids* are the mainstay of medical therapy for patients with acute renal colic is parenteral narcotic analgesics. They are inexpensive and quite effective. Some diverse effects represent. Choosing any particular agent tends to be somewhat arbitrary. Morphine, meperidine (Demerol) is the most commonly used. NSAIDs²⁴ have been used in the management of renal colic as effective factors for several years. Sodium diclofenace is a products which was used by injection in pain management .It has been suggested that an antidiuretic hormone (ADH)-induced decrease in diuresis could contribute to the rapid relief of pain in renal colic.⁸⁻⁹⁻¹² Desmopressin(1-desamino-8-D-arginine vasopressin) is a synthetic structural analog of ADH. The mechanism by which desmopressin relieves acute renal colic pain is unclear, but probably manifold.¹¹ Studies using desmopressin therapy for up to a few years have shown no toxic reactions or significant changes in laboratory values²⁰. According to some last studies desmopressin acts quickly, has no apparent adverse effects, reduces the need for supplemental analgesic medications, and may be the only immediate therapy necessary for some patients. Therefore, in the present study, we have conducted to

assess the efficacy of intranasal desmopressin in patients with acute renal colic.

2. Material and Methods

In this intentional study, patients 18-55 years old with probably acute renal colic based on history, physical exam and past medical history came to emergency department of Imam khomeini Hospital of Ahvaz Jundishapour University of Medical Sciences were evaluated randomly if they have no history of hypertension, coronary artery disease, rhinitis, influenza, coagulopathy, anticoagulant therapy, peptic ulcer, bronchial asthma, azotemia, hepatic failure, pregnancy use of other analgesics during the 4 hours before our treatment, receiving α -blockers before admission, addiction, surgery on kidneys or ureters, intravenous fluid therapy just before admission and took written consent at the first. There was no control group for ethical issues. A visual analogue scale (VAS) was used to assess the intensity of pain; this consisted of a 10-cm horizontal scale ranging from 'no pain' (VAS=1) to 'unbearable pain'(VAS=10), with values recorded to the nearest millimeter. Patients received 40 micrograms DDAVP intranasal of available product (4puff, each puff equivalent to 10 micrograms and alternately in each nostril of nose). Pain score was recorded at 15, 30, 45 and 60 minutes after DDAVP administration by VAS. At 30 min, sodium diclofenac 75 mg intramuscular was injected if any degree of pain. At 45 min, morphine sulfate 5 mg intravenously administered if pain score was greater than 5. Ultimately, at 60 min, morphine sulfate 5 mg intravenously injected again if any degree of pain. Additional doses of opioids were used if no response to last drugs. With pain intensity equal or less than 2 score, each patient was dischargeable based on situation. During study, probable side effects were observed. At the end, we evaluated recorded information in SPSS software and analyzed them by "Paired t test" (p-value<0.05).

3. Results

Seventy patients were evaluated in this study including 12 female (17.1%) and 58 male (82.8%) with mean age 33.7 ± 10.1 . In this study, Mean and Standard deviation of pain score in 0, 15, 30, 45 and 60 minutes was represented in Table1.

Table-1

Pain minute	n	Min	Max	\bar{X}	SD
Pain0	70	10	10	10	0.0
Pain 15	70	1	10	8.1	1.66
Pain 30	70	1	10	5.95	1.65
Pain45	70	1	7	4.32	1.4
Pain60	70	1	5	2.04	0.99

Two patients (2.8%) in 30 min have no pain and discharged home in 60 min without sodium diclofenac or morphin sulfate administration. Others received 75 mg diclofenac IM in 30 min that 21 patients (30%) have no pain in 60 min and discharged without opioid injection. During study, 47 patients (65.7%) were given opioid. From this, 14 patients had pain score greater than 5 in 45 min and received 5 mg morphin IV but only one person have no pain in 60 min and in 13 patients (18.5%) was administered second dose of morphin in 60 min. 34 patients received one dose of morphin (48.5%) alone. There is no side effect during study. Comparison of pain score in zero and 30 min (efficacy of desmopressin alone) with "paired t test" showed significant results (p-value < 0.00001). (Table-2).

Table-2

Time	\bar{X}	SP	p-value
0	10	0.0	0.00001
30	5.95	1.65	

Also, results of comparison of pain score decrease in zero and 45 min and between 30 and 45 min (synergism of desmopressin and sodium diclofenac together with no opioid) was significant (p-value < 0/00001). (Table-3,4)

Table-3

Time	\bar{X}	SD	n	p-value
T ₀	10	0	68	0.00001
T ₄₅	4.42	1.29	68	

Table-4

Time	\bar{X}	SD	n	p-value
T ₃₀	6.1	1.43	68	0.00001
T ₄₅	4.4	1.29	68	

4. Discussions

It has been suggested that an antidiuretic hormone²⁴ (ADH)-induced decrease in diuresis could contribute to the rapid relief of pain in renal colic.^{8, 9-12} Desmopressin is a synthetic structural analog of ADH. Compared with ADH, it has a greater antidiuretic effect, a longer duration of action, and reduced vasopressor activity. It is a first-line drug for replacement therapy in central diabetes insipidus and in the treatment of nocturnal enuresis.¹³⁻¹⁵ The mechanism by which desmopressin relieves acute renal colic pain is unclear, but probably manifold.¹¹ The antidiuretic effect of desmopressin is probably responsible for its efficacy in the treatment of renal colic.^{11,17} Desmopressin suppresses the spontaneous contractions of circular smooth muscle fibers in the renal pelvis of rabbits.¹⁸ The same effect might be possible in humans. Some investigators have reported on the role of desmopressin in stimulating the secretion of B-endorphins by the hypothalamus, which could explain a possible additional central

analgesic effect of the drug.¹⁹ A central mechanism in producing an analgesic effect could also be a valid hypothesis. Whether this therapy significantly affects eventual stone passage is unknown. It is available as a nasal spray (usual dose of 40 mcg, with 10 mcg per spray) and as an intravenous injection (4 mcg/mL, with 1 mL the usual dose). DDAVP Nasal spray delivers 500 mcg doses. For 10 mcg dose, administer in one nostril. Any solution remaining after 50 doses should be discarded. Pump must be primed prior to first use. The biphasic half-lives for intranasal DDAVP are 7.8 and 75.5 minutes for the fast and slow phases. Generally, only one dose is administered.²⁵ Studies using desmopressin therapy for up to a few years have shown no toxic reactions or significant changes in laboratory values²⁰.

Ahmed E. El sherrif and et al⁶ Evaluated a total of 18 patients with acute renal colic due to stone disease that received 40 microgram desmopressin intranasal spray with encouraging results. There was a significant decrease in the colic pain intensity from an initial mean visual analogue score of 67 plus/minus 17 mm. to 39 plus/minus 36 mm within 30 minutes (p less than 0.001). Eight patients (44.4 percent) had complete pain relief within 30 minutes of administering intranasal desmopressin spray. Nine of 10 patients who required intramuscular diclofenac sodium achieved complete pain relief within another 30 minutes. In other words, when intranasal desmopressin spray was administered before diclofenac sodium, 94.4 percent of the patients achieved complete pain relief and were discharged home.

Constantinides .C et al²¹ after a study concluded that the simplicity and effectiveness of intranasal desmopressin spray in treating renal colic makes this simple method a useful means of confronting a frequent and disturbing urological problem.

T. LOPES, J.S et al²⁰ assessed the efficacy of desmopressin nasal spray compared with diclofenac given intramuscularly in patients with acute renal colic caused by urolithiasis. The study included 61 patients randomized into three different groups; group A received desmopressin (40 mg, nasal spray), group B diclofenac (75 mg) intramuscularly and group C, both desmopressin and diclofenac. Pain was assessed using a visual analogue scale (a 10-cm horizontal scale ranging from 'no pain' to 'unbearable pain') at baseline, 10, 20 and 30 min after administering the treatments. Results On admission, the pain level was the same in all three groups. At 10 min the pain decreased in all groups to a level that was not significantly different. At 20 min groups B and C had similar mean pain levels (3.7), whereas in group A it was 5.0. At 30 min, groups B and C scored 2±3, and group A 5.6. All three treatments were

equally effective at 10 and 20 min but at 30 min there was a stabilization/slight increase in pain level in group A.

Pourmund .G et al²² in a clinical trial study, from Feb 1997 to Mar 1998, assessed 60 patients (21 male and 39 female with mean age of 36.3 years) who presented with acute Renal colic to emergency ward and received no medication enrolled in this study. Due to ethical law no control group could be selected. The pain severity was taken by percent with patient's permission. The pain intensity was between 0% (no pain at all) to 100% (the most severe pain ever imagined). 40 microgram intranasal DDAVP started and pain severity evaluated at 10, 20, and 30 min. Side effects were noted. If the patient's pain did not subside after 30min, 75 mg diclofenac was administered intramuscularly; if this was ineffective the patient was admitted to the ward and narcotics was administered (morphine or prthedine). The mean of pain severity was 89% in our patients with renal colic. After 30 minutes 30 patients (50%) had no pain. In 15 patients the pain decreased significantly. The mean pain intensity was 30.66% (p<0.001), and no other medication was used. Fifteen patients (25%) had some degree of pain (mean 54%, p<0.05), which was significantly decreased, but needed to use diclofenac or narcotics to relieve pain. None of them continued to have loin pain to necessitate admission to the emergency ward. The patients reported no side effects.

Abdol-Reza Kheirollahi et al²³ in a clinical trial, Studied analgesic effect of hyoscine N-butyl bromide and desmopressin combination in comparison with hyoscine N-butyl bromide alone in patients with acute renal colic induced by urinary stones. In The study included 114 patients randomly allocated in two groups (A and B). Patients in group A received 20 mg intramuscular hyoscine N-butyl bromide at admission time and patients in group B received 20 µg of intranasal desmopressin in combination with 20 mg intramuscular hyoscine N-butyl bromide. A visual analogue scale (VAS; a 10-cm horizontal scale ranging from "zero or no pain" to "10 or unbearable pain") was hired to assess the patients' pain severity at baseline, 30 and 60 minutes after the treatments. On admission, the pain level was similar in both groups (group A: 8.95 ± 0.11 and group B: 8.95 ± 0.12). In group A, the mean of pain level showed a decrease after 30 minutes (group A: 7.26 ± 0.25 and group B: 5.95 ± 0.28) but further decreasing did not occur; however in group B, the pain consistently decreased and the mean after 60 minutes was significantly decreased (group A: 6.80 ± 0.31 and group B: 3.71 ± 0.31). No side effects were detected in this study.

Roshani.A et al²⁴ determined the effect of the combination of intranasal desmopressin spray and diclofenac sodium suppository on acute renal colic and compare it with diclofenac sodium suppository assessed a total of 150 patients aged 15-65 years referred to their hospital with acute renal colic were included in a double-blind controlled clinical trial study. Patients in group 1 received desmopressin, 40 micg intranasally plus diclofenac sodium suppository 100 mg and patients in group 2 received diclofenac sodium suppository 100 mg plus a placebo spray consisting of normal saline 0.9%. Significant differences were found in the pain scores at 15 and 30 minutes between the 2 groups ($P < .05$). Also, significant differences were found in the mean pain scores in the first 15 and first 30 minutes after treatment between the 2 groups ($P < 0.05$). Of the patients in group 1, 37.3% had no pain relief and required pethidine. However, this rate in group 2 was 69.3%. In 17 cases, they prescribed pethidine within 20 minutes after treatment, and these patients were excluded from their study.

Also, results of our study showed that DDAVP administration (40 micg intranasal spray) can cause effective pain relief in acute renal colic and its association with sodium diclofenac resulting in better and more relief of pain with no need or low dose of morphin that ultimately may cause early discharge and more satisfaction for patient.

Desmopressin acts quickly, has no apparent adverse effects, reduces the need for supplemental analgesic medications, and may be the only immediate therapy necessary for some patients. While some of the human studies lack adequate controls and further studies must be conducted, desmopressin therapy currently appears to be a promising alternative or adjunct to analgesic medications in patients with acute renal colic, especially in patients in whom narcotics cannot be used or in whom the pain is unusually resistant to standard medical treatment.

Other issues which need to be explored include: confirmation of last studies, the optimum dosage, method of use (i.e. in an ambulatory setting), whether there is a reduction in the need for diagnostic or therapeutic interventions and whether it reduces the rate of hospital admissions. That there seem to be some patients who do not respond or respond only minimally to desmopressin needs further clarification; characteristics should be identified in this group which might explain their lack of response.

Corresponding Author:

Kambiz Masoumi Emergency medicine consultant, Department of Emergency Medicine, Imam Khomeini General Hospital, Ahwaz jundishapur university of medical sciences, Khoozestan, Iran.

Email: Kami_masoumi@yahoo.com

References

- 1-Ducharme J. Acute pain in pain control: state of the art. *Ann Emerg Med* 2000;35:592.
- 2-Fosnocht DE, Swanson ER, Bossert P. Patient expectations for pain medication delivery. *Am J Emerg Med* 2001;19:399.
- 3-Weisman SJ, Bernstein B, Schechter NL. Consequences of inadequate analgesia during painful procedures in children. *Arch Pediatr Adolesc Med* 1998;152:147.
- 4-Bry PH, Dahl JL. The new JCAHO pain standards: Implications for pain management nurses. *Pain Mgmt Nurs* 2000; 1:3.
- 5- Nuss GR, Rockly JD, Assimos DG. Adjunctive therapy to promote stone passage. *Rev Urol.* 2005;7:67-74.
- 6-El-sheriff AE, Salem M, Yahia H, Al-Sharkawy WA, Al-Sayrafi M. Treatment of renal colic by desmopressin intranasal spray and diclofenac sodium. *J Urol* 1995 ; 153:1395-1398.
- 7-Marumo F, Edelman IS. Effect of Ca²⁺ and prostaglandin E1 on vasopressin activation of renal adenyl cyclase. *J Clin Invest.* 1971; 50:1613-1620.
- 8-Teichman JM. Clinical practice: Acute renal colic from ureteral calculus. *N Engl J Med.* 2004;350:684-693.
- 9-Lopes T, Dias JS, Marcelino J, Varela J, Riberio S, Dias J. An assessment of the clinical efficacy of intranasal desmopressin spray in the treatment of renal colic. *Br J Urol.* 2001;87:322-325.
- 10-Holdgate A, Pollock T. Systemic review of the relative efficacy of non-steroidal anti-inflammatory drugs and opioids in the treatment of acute renal colic. *BMJ.* 2004;328:1401.
- 11-El-sheriff AE, Salem M, Yahia H, Alsharkwy WAS, Alsayrafi M. Treatment of renal colic by desmopressin intranasal spray and diclofenac sodium. *J Urol.* 1995; 153:1395-1398.
- 12-Grenabo L, Aurell M, Delin K, Holmlund D, Sjodin JG. Antidiuretic hormone levels and the effect of indomethacin on ureteral colic. *J Urol.* 1983;129: 941-943.
- 13-Naghizadeh S, Kefi A, Dogan HS, Burgu B, Akdogan B, Tekgul S. Effectiveness of oral desmopressin therapy in posterior urethral valve patients with polyuria and detection of factors affecting the therapy. *Eur Urol* 2005; 48:819-825.
- 14-Triantafyllidis A, Charalambous S, Papatsoris AG, Papathanasiou C, Kalaitzis C, Rombis V et

- al. Management of nocturnal enuresis in Greek children. *Pediatr Nephrol* 2005;20:1343-1345.
- 15-Robinson AG. DDAVP in the treatment of central diabetes insipidus. *N Engl J Med* 1976;294:507-511.
- 16-Miller K, Goldberg S, Atkin B. Nocturnal enuresis: Experience with long-term use of intranasally administered desmopressin. *J Pediatr* 1989;114:723-726.
- 17-Moro U, De Stefuni S, Crisci A, De Antoni P, Scott CA, Selli C. Evaluation of desmopressin in acute ureteral obstruction. *Urol Int* 1999;62:8-11.
- 18-Kimoto Y, Constantinou CE. Effect of (1-desamino-8-D-arginine) vasopressin and papaverin on rabbit renal pelvis. *Eur J Pharmacol* 1990;175:359-362.
- 19-Kohl RL. Beta-endorphine and arginine vasopressin following stressful sensory stimuli in man. *Aviat Space Environ Med.* 1992;63: 986-993.
- 20-Lopes T, Dias J, Marcelino J, Varela J, Ribeiro S, Dias J. An assessment of the clinical efficacy of intranasal desmopressin spray in the treatment of renal colic *BJU International* (2001), 87, 322-325.
- 21- Constantinides C, Kapralos V, Manousakas T, Mitropoulos D, Alamanis C, Dimopoulos C. Management of renal colic with intranasal desmopressin spray. *Acta Urol Belg.* 1998 Dec;66(4):1-3.
- 22- Pourmund.G, Mansoori D, Mehraei A. EFFECT OF NASAL DESMOPRESSIN IN TREATMENT OF ACUTE RENAL COLIC . *European Urology Supplements* 2 (2003) No. 1, pp. 81
- 23- *Kheirollahi A.R, Tehrani M, Bashashati M.* A comparison of the effect of intranasal desmopressin and intramuscularhyoscine N-butyl bromide combination with intramuscular hyoscine N-butyl bromide alone in acute renal colic. *JRMS/ July & August 2010; Vol 15, No 4.*
- 24- Roshani .A, Falahatkar S, Khosropanah Iradj, Atrkarroshan Z, Zarkami T, Palizkar Maryam, et al. Assessment of Clinical Efficacy of Intranasal Desmopressin Spray and Diclofenac Sodium Suppository in Treatment of Renal Colic Versus Diclofenac Sodium Alone. *UROLOGY* 75 (3), 2010.540-542.

11/12/2012