The Comparison of Apotel plus Low Dose of Morphine and Full Dose of Morphine in Pain Relief in Patients with Acute Renal Colic

Hamid Reza Morteza-Bagi MD[1], Mohsen Amjadi MD[2], Reyhaneh Mirzaii-Sousefidi MD[3]

Original Article

Abstract

Background: Renal colic is an acute flank pain which may radiate to the groin, lower abdomen, or external genitalia due to the passage of a urinary stones. Pain management is the most important task in emergency wards when a patient with renal colic attends. This study aims to compare intravenous acetaminophen plus a low dose of morphine with a full dose of morphine in renal colic.

Methods: In present randomized clinical trial, 100 patients with confirmed renal colic were recruited from the Emergency Ward of Imam Reza Teaching Hospital affiliated to Tabriz University of Medical Sciences, Iran, during a one-year period. These patients randomly received either intravenous acetaminophen (Apotel, 1 g) plus a low dose of morphine (n = 50), or a high dose of morphine (5 mg) (n = 50). Visual analogue scale (VAS) was used for reporting pain during 35 minutes. Side effects and rescue analgesic demand were recorded after 30 minutes.

Findings: The two groups were matched for the patients' age and gender. Intra-group analysis showed significant gradual decreases in pain intensity after 35 minutes for both groups. Inter-group analysis, however, did not show a significant difference between the two groups in this regard. There was no significant difference between the two groups in terms of side effects. The rate of rescue analgesic demand was 36% in the first and 40% in the second group (P = 0.68).

Conclusion: According to the results study, Apotel plus a low dose of morphine is at least as effective and safe as a full dose of morphine in patients with renal colic.

Keywords: Renal colic, Intravenous acetaminophen, Morphine

Citation: Morteza-Bagi HR, Amjadi M, Mirzaii-Sousefidi R. **The Comparison of Apotel plus Low Dose of Morphine and Full Dose of Morphine in Pain Relief in Patients with Acute Renal Colic.** Addict Health 2015; 7(1-2): 66-73.

Received: 19.09.2014 **Accepted:** 26.11.2014

1- Assistant Professor, Department of Emergency Medicine, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
2- Associate Professor, Department of Urology, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
3- Resident, Department of Emergency Medicine, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
Correspondence to: Reyhaneh Mirzaii-Sousefidi MD, Email: r.ms32@ymail.com

Introduction

Renal colic is a very common and important condition in medicine. In industrialized countries, 1-5% of the population is affected by this condition annually. The lifetime risk of developing this disease is estimated at 20% in men and 5-10% in women.[1] The most common cause of renal colic is the acute obstruction of the urinary tract by urinary system stones which often causes severe pain.[2,3] The first goal of renal colic treatment is to relieve the pain. Spasmolytic drugs such as hyoscyamine and dicycloverine are among the traditional medicines in this field.[4] Non-steroidal anti-inflammatory drug may also inhibit pain by inhibiting the release of prostaglandins in this situation. However, the injectable form of the drug is not available and causes many complications.[5,6]

Another standard treatment used in patients with acute renal colic is narcotic drugs such as morphine and pethidine. Despite the widespread use of these drugs, they have many problems, including side effects, lack of public access, and the possibility of drug-dependency.[7-10] A new drug used to control pain is intravenous acetaminophen. This antipyretic analgesic drug is used to relieve mild to moderate pain. The analgesic effect of acetaminophen is due to its raising of the pain threshold. Intravenous acetaminophen usually has few side effects and is well tolerated. Furthermore, unlike narcotic drugs, it does not develop drug-dependency.[11,12]

Bektas et al., in a study on patients diagnosed with renal colic, compared the efficacy and safety of the injectable form of paracetamol (46 patients) and morphine (49 patients). In this study, no significant differences were observed between the two medications regarding the effectiveness of pain management, complications, and rescue analgesic demand. Accordingly, the use of injectable paracetamol was recommended.[13] Serinken et al. conducted a similar study in this field. In this study, 38 patients received injectable paracetamol and 35 patients received morphine. Finally, it was shown that both drugs were similar in terms of treatment efficacy and safety.[14]

Given the high prevalence of renal colic and problems associated with its standard therapy (narcotic drug use), and the lack of similar studies in Iran, this study aimed to compare the efficacy and safety of intravenous acetaminophen (apotel) plus a low dose of morphine and full dose of morphine in these patients.

Methods

In this randomized, double-blind clinical trial, 100 patients with a definite diagnosis of renal colic were randomly divided into 2 groups of 50 patients and were matched for age and gender. In one group, a low dose of acetaminophen injection plus morphine was administered to the patients. The other group received a full dose of morphine. Finally, pain intensity, possible complications, and the need for supplemental analgesic use in the two groups were compared. The location of the study was the emergency ward of the Imam Reza Teaching Hospital, Tabriz, Iran. The study duration was 12 months. From the beginning of June 2012 until the beginning of June 2013, the primary data collection and analysis of data was performed. A written informed consent was obtained from every patient before entering the study. This study was approved by the Ethics Committee of Tabriz University of Medical Sciences (Ethics Committee Act No. 9243).

Patients diagnosed with renal colic were consecutively recruited into the study. Patients were placed into one of the two treatment groups using stratified block randomization method using balanced randomized blocks with variable size. To maintain a balance between the two treatment groups, patients were randomized according to gender and age. Random allocation software sequence listing was separately made in these groups. Allocation of each of the categories was concealed in opaced sealed envelopes. In addition, the code for each of the treatments was written on paper in the order in which they were created by the software, and was placed in a box. This was a blinded experiment; thus, a code was given to each of the treatment groups and the person who performed the randomization process was not involved in other steps of the study. The participants received envelopes containing the treatment code, in the order of entering the study and according to their age and gender, and based on that the medicine was injected. Thus, neither the patient nor the administrator of the drug had any information about the injection and codes were disclosed only after statistical analysis. To explore the 2-unit difference (based on the visual

analog scale or VAS) between the two groups and considering the standard deviation (SD) of 2.5 units, the power of 95%, at least 35 patients in each group, is required.[13]

Finally, 100 patients (50 in each group) were enrolled in the study. The inclusion criteria included diagnosis of renal colic by ultrasound or abdominal radiography, and age of 18-50 years. Exclusion criteria included receiving any analgesic treatment before admission, allergies to medications, history of opioid dependency, high blood pressure, fever and chills, pregnancy, and intolerance of pain during the first 35 minutes of drug administration. In one group of patients, intravenous acetaminophen (apotel 1 g) plus a low dose of morphine was injected. The second group received 5 mg of morphine injected intravenously (total dose of morphine). Using a visual analogue scale (VAS) , the intensity of pain (pain scale of 10 units; 0 = no pain, 10 = maximum pain level) was measured at 0, 1, 5, 10, 15, 25, and 35 min after intravenous injection of the drugs. Patients who were unable to tolerate the pain within 35 minutes after administration of intravenous drugs were excluded from the study and were treated with common narcotic drugs. Data from the study were analyzed and compared using descriptive statistics (frequency, percentage, mean ± SD).

Moreover, the mean difference test, and chi-square or Fisher's exact tests were used for quantitative and qualitative variables, respectively. A repeated measure ANOVA was used to compare pain intensity between the two groups at specific time intervals. All statistical analyzes were performed using SPSS software (version 16, SPSS Inc., Chicago, IL, USA). P values of less than 0.05 were considered statistically significant.

Results

The mean age of the patients receiving apotel plus a low dose of morphine was 40.58 ± 13.45 (range: 19 to 50) years. The mean age of patients receiving full dose of morphine was 38.62 ± 10.35 (range: 20 to 50) years. Based on the results of Student's independent t-test, the mean age of patients was not significantly different between the groups (P = 0.42). In the group receiving apotel plus a low dose of morphine, 36 patients (72%) were male and 14 (28%) were female. In the group receiving a full dose of morphine, 38 patients (76%) were male and 12 (24%) were female. Based on the results of chi-square test, the two groups showed no statistically significant difference regarding gender (P = 0.65).

Visual analogue pain scale, at different levels in the two groups is summarized in table 1. Based on the results of Student's independent t-test, difference in mean baseline pain intensity of the groups was not statistically significant (P = 0.28). The mean change in pain intensity in both groups from baseline to 35 minutes is shown in figure 1. Based on the results of the repeated measurements, no statistically significant differences were observed between the two groups (P = 0.94). Percentage reduction of pain intensity compared to baseline in both groups at different times are summarized and compared in table 2. Accordingly, no significant differences were observed in any of the sections (P < 0.05). Complications and the need for supplemental analgesic drugs have been studied in both groups and are summarized and compared in table 3. Accordingly, none of the studied cases showed a statistically significant difference.

Table 1. Pain intensity based on the VAS during different time periods in the two evaluated groups

Variable / Time periods (minute)	Apotel + low dose of morphine	Apotel + full dose of morphine
	Mean ± SD (range)	Mean ± SD (range)
0	8.52 ± 0.89 (6-10)	8.32 ± 0.96 (7-10)
1	8.04 ± 0.97 (7-10)	8.30 ± 0.93 (6-10)
5	4.26 ± 1.08 (2-7)	6.86 ± 0.88 (5-8)
10	4.26 ± 1.08 (2-7)	3.90 ± 1.16 (1-7)
15	2.82 ± 1.02 (0-5)	2.76 ± 1.33 (0-5)
25	2.16 ± 1.31 (0-5)	1.94 ± 1.38 (0-5)
35	1.88 ± 1.27 (0-4)	1.98 ± 1.38 (0-4)

SD: Standard deviation; VAS: Visual analogue scale

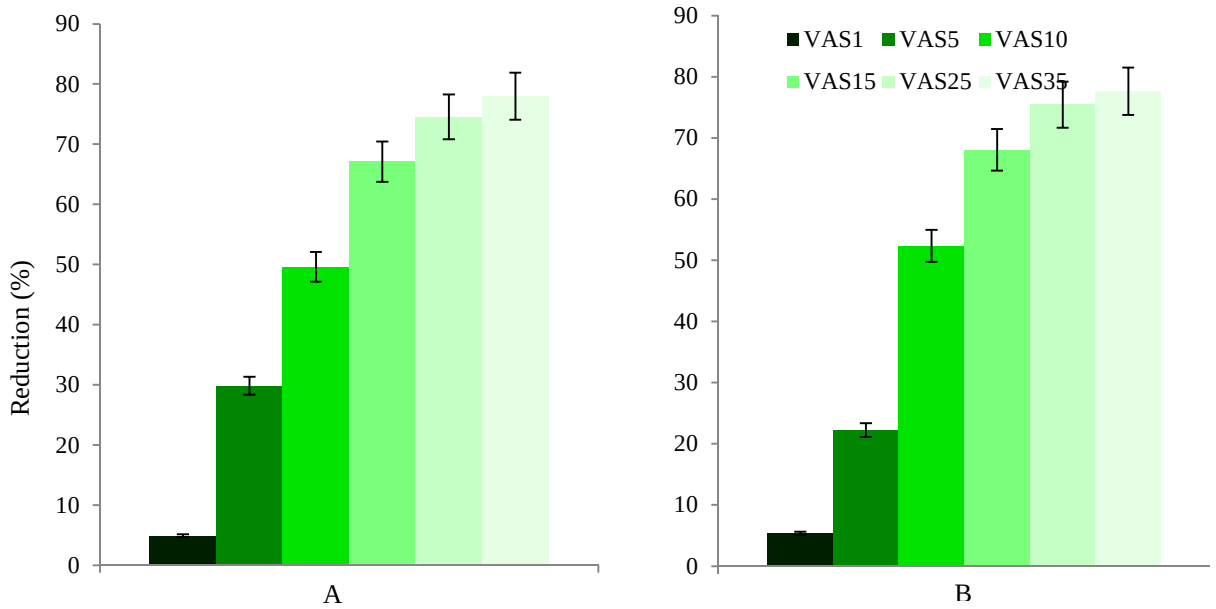

Figure 1. The mean change of pain intensity in the two evaluated groups in 0 to 35 minutes, A: morphine and B: Apotel morphine (comparison of percentage reduction in pain intensity to baseline in both groups)
VAS: Visual analogue scale

Table 2. Percentage of reduction in pain intensity compared to the baseline in both groups evaluated at different time periods

Variable / Time periods (minute)	Apotel + low dose of morphine Mean ± SD	Apotel + full dose of morphine Mean ± SD	P
1	4.27 ± 1.01	2.28 ± 1.13	0.19
5	29.86 ± 2.86	23.15 ± 2.59	0.09
10	49.61 ± 12.94	52.76 ± 14.52	0.26
15	67.10 ± 11.17	67.09 ± 16.05	0.98
25	74.78 ± 14.97	75.81 ± 16.19	0.74
35	78.03 ± 14.27	77.64 ± 16.42	0.90

SD: Standard deviation

Table 3. Complications and the need for supplemental analgesic drugs were studied in two groups

Variable / Complications	Apotel + low dose of morphine n (%)	Apotel + full dose of morphine n (%)	P
Nausea and vomiting	13 (26)	16 (32)	0.51
Headache	3 (6)	1 (2)	0.62
Dry mouth	4 (8)	4 (8)	0.64
Any complications	19 (38)	22 (44)	0.54
The need for supplemental analgesic drugs	18 (36)	20 (40)	0.68

Discussion

In this study, the efficacy and possible complications of intravenous acetaminophen in combination with a low dose of morphine was evaluated and compared with a full dose of morphine in patients admitted to the emergency ward of Imam Reza Teaching Hospital. Intravenous acetaminophen was first introduced in 80 countries and was approved by the Food and Drug Administration (FDA) of the USA in 2010.[15]

Recently, the use of this form of medication to relieve pain and fever in different conditions has been studied. For example, the efficacy of the intravenous form of acetaminophen and its ability to reduce the dose of intravenous morphine for pain relief of traumatic limb,[16] environmental damage pain,[17] and pain after tooth extraction,[11,18] orthopedic joint replacement of the hip or knee,[19] and heart surgery[20] were mainly studied.

However, studies on the effect of this drug on patients with renal colic are very few. In the first study in this area, Bektas et al. studied 146 patients with renal colic admitted to the emergency ward of a hospital in Turkey.[13] The patients were divided into 3 groups: 46 patients receiving a single dose of intravenous paracetamol (1 g), 49 patients receiving intravenous morphine (1 mg weight per kg body weight), and 51 patients receiving placebo. In this study, the mean reduction in pain based on the VAS during the 30 minutes after injection in the intravenous paracetamol group was 43 mm and in the group receiving morphine was 40 mm. Although both drugs, compared with placebo in reducing pain of the patients after 30 minutes, were more successful than placebo, no statistically significant differences were reported between the two groups of paracetamol and morphine in this regard. The study also found that the need for analgesic drugs after 30 minutes in both groups was similar; 45% in the paracetamol group versus 49% in the morphine group and 67% in the placebo group.[13]

In the current study, however, pain reduction, based on VAS over time, was significant in both groups, but no significant differences were found between the two groups. On the other hand, the need for analgesic drugs after 30 minutes, in both groups showed no statistically significant difference (36% in the acetaminophen plus morphine group versus 40% in full dose of morphine group P = 0.68).

In a similar study, Serinken et al. reported the same results. In this study, the first group (n = 83) received a single dose of intravenous paracetamol (1 g), while the second group received a dose of 0.1 mg of morphine injection based on body weight per kg (n = 35). The mean reduction of pain at 30 minutes, based on the VAS, in the first group was 63.7 mm and in the second group 56.6 mm, which were significantly different. Furthermore, the need for analgesic drugs 30 minutes after administration of the drug were similar in both groups.[14]

Based on the results of these studies and the present study, intravenous acetaminophen was similar to a full dose of intravenous morphine in terms of reduction of renal colic pain. This reveals the clinical importance and effectiveness of this medication. Due to the similarity of intravenous acetaminophen and morphine in terms of clinical efficacy in reducing pain, it appears that one of the factors in clinical decision making is its side effects and frequency.

In the study by Bektas et al., at least one complication was reported in 24% of patients receiving paracetamol and 33% receiving morphine. No statistically significant difference was observed in this respect. Nausea and vomiting, headache, dry mouth, and other complications were reported in 15, 2, 7, and 9 percent of the patients receiving paracetamol, respectively. These cases in the group receiving morphine were 18, 2, 8, and 20 percent, respectively. In addition, 2% of patients in the group receiving morphine reported cases of urinary retention. The rate of complications were similar in the two groups.[13]

In the present study, nausea and vomiting, headache, dry mouth, and at least one complication were reported in 26, 6, 8, and 38 percent of the cases in the group receiving acetaminophen plus a low dose of morphine, respectively. Furthermore, in the group receiving a total dose of morphine they were reported in 32, 2, 8, and 44 percent of cases, respectively. The frequency percentage of the cases in the two groups was not statistically significant. In the study by Serinken et al., complications related to the treatments were observed in 5.3% of the cases in the paracetamol group and in 14.3% of the cases in the morphine group, which were statistically similar.[14]

The results in this area show that although the frequency percentage of complications associated with the treatment in intravenous acetaminophen group was apparently lower than that of the morphine group, this difference was not statistically significant. These results emphasize the safety of this drug in patients with renal colic. Based on the results on the effectiveness of intravenous acetaminophen in reducing renal colic pain and its safety, it appears that the third factor that can influence clinical decision making is the cost. Although this was not compared in this study or previous studies, earlier studies have shown that the benefits of intravenous acetaminophen pharmacokinetics compared to similar analgesics, such as no steroidal anti-inflammatory drugs and opioids, justify the higher costs.[21]

However, for a direct comparison and better valuation, further studies are necessary. The current study compared the combination of intravenous acetaminophen and low doses of morphine in patients with renal colic to the effect of

high doses of morphine. Thus, the role of this drug in reducing the dose of morphine was emphasized. The role of lowering the dose of morphine by intravenous acetaminophen in surgical patients was also emphasized.[22,23] However, the current study was the first in this field on patients with renal colic; therefore, more clinical trials can help in obtaining definite results and correct clinical decision making.

Conclusion

Changes in pain intensity (based on a numerical visual scale) and incidence of complications in patients with renal colic treated with intravenous acetaminophen plus low doses of morphine, and total doses of morphine did not have a significant difference. Changes in pain intensity (based on a numerical visual scale) and incidence of complications in patients with renal colic treated with intravenous acetaminophen plus moderate doses of morphine, and total doses of morphine based on the gender of the patients did not have a statistically significant difference.

Changes in pain intensity (based on a numerical visual scale) in patients with renal colic treated with intravenous acetaminophen plus moderate doses of morphine, and total doses of morphine based on the age of the patients did not have a statistically significant difference. Regarding the complications, the frequency percentage of the headaches in patients older than 50 years receiving full dose of morphine was significantly higher. In other cases, there was no statistically significant difference.

Conflict of Interests

The Authors have no conflict of interest.

Acknowledgements

Our appreciation goes to the respectful supervisor Dr. Hamidreza Morteza Beigi for his assistance in this research, the consultant professor Dr. Mohsen Amjadi for his assistance in the development of the study plan, and all our colleagues at Imam Reza Teaching Hospital. Hopefully this project is successful in the treatment of patients with renal colic.

References

1. Balaji KC, Menon M. Mechanism of stone formation. Urol Clin North Am 1997; 24(1): 1-11.
2. Labrecque M, Dostaler LP, Rousselle R, Nguyen T, Poirier S. Efficacy of nonsteroidal anti-inflammatory drugs in the treatment of acute renal colic. A meta-analysis. Arch Intern Med 1994; 154(12): 1381-7.
3. Kobayashi T, Nishizawa K, Mitsumori K, Ogura K. Impact of date of onset on the absence of hematuria in patients with acute renal colic. J Urol 2003; 170(4 Pt 1): 1093-6.
4. Holdgate A, Oh CM. Is there a role for antimuscarinics in renal colic? A randomized controlled trial. J Urol 2005; 174(2): 572-5.
5. el-Sherif 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(5): 1395-8.
6. Wein AJ, Kavoussi LR, Novick AC, Partin AW. Campbell-Walsh Urology. 9th ed. Philadelphia, PA: Saunders; 2007. p. 1211-15.
7. Grond S, Sablotzki A. Clinical pharmacology of tramadol. Clin Pharmacokinet 2004; 43(13): 879-923.
8. Eray O, Cete Y, Oktay C, Karsli B, Akca S, Cete N, et al. Intravenous single-dose tramadol versus meperidine for pain relief in renal colic. Eur J Anaesthesiol 2002; 19(5): 368-70.
9. Lennon GM, Bourke J, Ryan PC, Fitzpatrick JM. Pharmacological options for the treatment of acute ureteric colic. An in vitro experimental study. Br J Urol 1993; 71(4): 401-7.
10. Ginifer C, Kelly AM. Administration of rectal indomethacin does not reduce the requirement for intravenous narcotic analgesia in acute renal colic. Eur J Emerg Med 1996; 3(2): 92-4.
11. Moller PL, Juhl GI, Payen-Champenois C, Skoglund LA. Intravenous acetaminophen (paracetamol): comparable analgesic efficacy, but better local safety than its prodrug, propacetamol, for postoperative pain after third molar surgery. Anesth Analg 2005; 101(1): 90-6, table.
12. Murat I, Baujard C, Foussat C, Guyot E, Petel H, Rod B, et al. Tolerance and analgesic efficacy of a new i.v. paracetamol solution in children after inguinal hernia repair. Paediatr Anaesth 2005; 15(8): 663-70.
13. Bektas F, Eken C, Karadeniz O, Goksu E, Cubuk M, Cete Y. Intravenous paracetamol or morphine for the treatment of renal colic: a randomized, placebo-controlled trial. Ann Emerg Med 2009; 54(4): 568-74.
14. Serinken M, Eken C, Turkcuer I, Elicabuk H, Uyanik E, Schultz CH. Intravenous paracetamol versus morphine for renal colic in the emergency

department: a randomised double-blind controlled trial. Emerg Med J 2012; 29(11): 902-5.
15. Jahr JS, Lee VK. Intravenous acetaminophen. Anesthesiol Clin 2010; 28(4): 619-45.
16. Craig M, Jeavons R, Probert J, Benger J. Randomised comparison of intravenous paracetamol and intravenous morphine for acute traumatic limb pain in the emergency department. Emerg Med J 2012; 29(1): 37-9.
17. Hoogewijs J, Diltoer MW, Hubloue I, Spapen HD, Camu F, Corne L, et al. A prospective, open, single blind, randomized study comparing four analgesics in the treatment of peripheral injury in the emergency department. Eur J Emerg Med 2000; 7(2): 119-23.
18. Van AH, Thys L, Veekman L, Buerkle H. Assessing analgesia in single and repeated administrations of propacetamol for postoperative pain: comparison with morphine after dental surgery. Anesth Analg 2004; 98(1): 159-65, table.
19. Sinatra RS, Jahr JS, Reynolds LW, Viscusi ER, Groudine SB, Payen-Champenois C. Efficacy and safety of single and repeated administration of 1 gram intravenous acetaminophen injection (paracetamol) for pain management after major orthopedic surgery. Anesthesiology 2005; 102(4): 822-31.
20. Cattabriga I, Pacini D, Lamazza G, Talarico F, Di BR, Grillone G, et al. Intravenous paracetamol as adjunctive treatment for postoperative pain after cardiac surgery: a double blind randomized controlled trial. Eur J Cardiothorac Surg 2007; 32(3): 527-31.
21. Kwiatkowski JL, Walker PL. Intravenous acetaminophen in the emergency department. J Emerg Nurs 2013; 39(1): 92-6.
22. Pettersson PH, Jakobsson J, Owall A. Intravenous acetaminophen reduced the use of opioids compared with oral administration after coronary artery bypass grafting. J Cardiothorac Vasc Anesth 2005; 19(3): 306-9.
23. Maund E, McDaid C, Rice S, Wright K, Jenkins B, Woolacott N. Paracetamol and selective and non-selective non-steroidal anti-inflammatory drugs for the reduction in morphine-related side-effects after major surgery: a systematic review. Br J Anaesth 2011; 106(3): 292-7.

مقایسه اثر درمانی آپوتل و دوز متوسط مورفین با فوق دوز مورفین در تسکین درد بیماران مبتلا به کولیک کلیوی حاد

دکتر حمیدرضا مرتضی بیگی[۱]، دکتر محسن امجدی[۲]، دکتر ریحانه میرزایی سوسفیدی[۳]

مقاله پژوهشی

چکیده

مقدمه: کولیک کلیوی درد پهلوی حادی است که می‌تواند به کفل، بخش پایینی شکم یا ناحیه تناسلی خارجی انتشار یابد و ناشی از عبور سنگ‌های دستگاه ادراری می‌باشد. مهم‌ترین وظیفه در بخش اورژانس در مواجهه با بیمار مبتلا به کولیک کلیوی، کنترل درد است. هدف از این مطالعه، مقایسه استامینوفن وریدی به همراه مورفین با دوز پایین و مورفین با دوز کامل در کولیک کلیوی بود.

روش‌ها: در کارآزمایی بالینی تصادفی حاضر، ۱۰۰ بیمار با تشخیص قطعی کولیک کلیوی در بخش اورژانس مرکز آموزشی- درمانی امام رضا (ع) تبریز طی مدت یک سال بررسی شدند. این بیماران به طور تصادفی استامینوفن تزریقی (آپوتل ۱ گرم) همراه با دوز پایین مورفین (۵۰ نفر) یا مورفین با دوز کامل (۵ میلی‌گرم) (۵۰ نفر) دریافت کردند. مقیاس چشمی آنالوگ (Visual analogue scale یا VAS) جهت گزارش شدت درد تا ۳۵ دقیقه بعد به کار گرفته شد و عوارض و نیاز به ضد درد کمکی تا دقیقه ۳۰ ثبت گردید.

یافته‌ها: بیماران دو گروه از نظر سن و جنس همسان بودند. مقایسه داخل گروهی نشان داد که شدت درد به طور معنی‌داری به تدریج تا دقیقه ۳۵ در هر دو گروه کاهش یافت. با این وجود، در مقایسه بین گروهی تفاوت آماری معنی‌داری از این نظر بین دو گروه مشاهده نشد. از نظر عوارض جانبی بین دو گروه تفاوت آماری معنی‌داری وجود نداشت. میزان نیاز به داروی ضد درد کمکی در گروه اول ۳۶ درصد و در گروه دوم ۴۰ درصد بود (P = ۰/۶۸).

نتیجه‌گیری: بر اساس نتایج مطالعه، آپوتل و مورفین با دوز پایین حداقل به همان میزان مورفین با دوز کامل در کولیک کلیوی مؤثر و ایمن می‌باشد.

واژگان کلیدی: کولیک کلیوی، استامینوفن داخل وریدی، مورفین

ارجاع: مرتضی بیگی حمیدرضا، امجدی محسن، میرزایی سوسفیدی ریحانه. **مقایسه اثر درمانی آپوتل و دوز متوسط مورفین با فوق دوز مورفین در تسکین درد بیماران مبتلا به کولیک کلیوی حاد.** مجله اعتیاد و سلامت ۱۳۹۴؛ ۷ (۲-۱): ۷۳-۶۶.

تاریخ دریافت: ۹۳/۶/۲۸ **تاریخ پذیرش:** ۹۳/۹/۵

۱- استادیار، گروه طب اورژانس، دانشکده پزشکی، دانشگاه علوم پزشکی تبریز، تبریز، ایران
۲- دانشیار، گروه ارولوژی، دانشکده پزشکی، دانشگاه علوم پزشکی تبریز، تبریز، ایران
۳- دستیار، گروه طب اورژانس، دانشکده پزشکی، دانشگاه علوم پزشکی تبریز، تبریز، ایران
نویسنده مسؤول: دکتر ریحانه میرزایی سوسفیدی Email: r.ms32@ymail.com