

Comparing the analgesic effect of intravenous acetaminophen and morphine on patients with renal colic pain referring to the emergency department: A randomized controlled trial

Reza Azizkhani, Seyed Mehdi Pourafzali, Elahe Baloochestani¹, Babak Masoumi

Department of Emergency Medicine, School of Medicine, and ¹Department of Operating Room Nursing, Faculty of Nursing and Midwifery, Isfahan University of Medical Sciences, Isfahan, Iran

Background: Kidney stone is normally treated by opioids with a variety of side-effects including hypotension, respiratory depression and apnea, nausea and vomiting. Regarding less complications of intravenous acetaminophen, we aimed to compare it with intravenous morphine in management of renal colic pain. **Materials and Methods:** A randomized controlled clinical trial was applied with a convenience sampling method, as 124 patients suffering from renal colic pain were randomly assigned into two groups of 62 patients. Pain was assessed using visual analog scale ruler. Results were analyzed by SPSS.18 using the descriptive statistic, Chi-square, ANOVA, independent *t*-test and logistic regression. **Results:** According to the findings, 84 subjects (67.7%) were male. The mean age of participants were 39.06 (11.58). The mean of pain scores were not significantly different between two groups before administration of drugs ($P = 0.415$), while the more pain relief was achieved in morphine group after the intervention. Sex and age as influencing factors did not develop a significant difference in both groups. About the adverse effects, morphine had more complications and both groups showed a significant difference in occurrence of dizziness ($P = 0.000$) and hypotension ($P = 0.014$). **Conclusion:** Comparing intravenous morphine and acetaminophen in renal colic pain revealed that morphine can develop greater pain relief, but more complications such as dizziness and hypotension. Acetaminophen can be also be effective in renal colic pain, so it is concluded that acetaminophen can be administered as a less harmful drug for patients with renal colic pain.

Key words: Acetaminophen, emergency department, morphine, renal colic

How to cite this article: Azizkhani R, Pourafzali SM, Baloochestani E, Masoumi B. Comparing the analgesic effect of intravenous acetaminophen and morphine on patients with renal colic pain referring to the emergency department: A randomized controlled trial. *J Res Med Sci* 2013;18:772-6.

INTRODUCTION

Kidney stone is one of the common diseases of human society, which is demonstrated in the form of renal colic. Evidences indicate that renal colic is one of the most painful conditions that require urgent pain relief treatment.^[1,2] Patients suffering from renal colic do not usually recover from pain by using oral pain killers or rectal suppositories. Hence, a considerable percentage of these patients are admitted to the emergency department. A bothering and sharp pain is the most common characteristics of renal colic pain that wakes the patient up in the middle of the night. To achieve more pain relief, patients somehow take unusual positions such as squatting^[3] which are normally used as pain relievers in the emergency department are non-steroidal anti-inflammatory drugs and intravenous opioids. However, both of these classes of drugs have many side-effects.^[4] Another point in this regard which is worthy to be mentioned is that some patients with renal colic

complaint are drug addicted, so we have to administer higher dosage of analgesic drugs. According to the statistics provided by the US National Library website, the prevalence of kidney stones around the world in 2005 has been averagely around 140.1%, which is considerable. This issue suggests more attention to the field of prevention and treatment.^[5] According to the statistics of kidney stones incidence in Iran, 2.4 out of every 1000 people suffer from this pathologic condition, whereas it differs from 0.5 to 2 in every 1000 ones in other countries.^[6] Intravenous acetaminophen has been imported to our country and introduced with the brand of Apotel. In this regard, we decided to compare the effect of intravenous acetaminophen and morphine on renal colic pain.

MATERIALS AND METHODS

This study is a randomized double-blind clinical trial conducted on patients with renal colic pain complaint in Al-Zahra Hospital affiliated to the Isfahan University

Address for correspondence: Dr. Seyed Mehdi Pourafzali, Department of Emergency Medicine, Isfahan University of Medical Sciences, Isfahan, Iran. E-mail: pourafzali@resident.mui.ac.ir

Received: 14-03-2013; **Revised:** 06-07-2013; **Accepted:** 12-08-2013

of Medical Science in 2012. A convenience sampling method was applied, as 124 patients, referring to the emergency ward with a renal colic pain complaints were selected. Subjects were randomly assigned into two groups of 62 patients marked as intravenous acetaminophen (1 gr Amp, Authorized by Cobel Darou Co, Iran) and morphine (10 mg Amp, Darou Pakhsh Co, Iran) groups. For the purpose of conducting this research, ethical approval from Research Ethics Committees of Isfahan University of Medical Sciences was obtained. All samples were tended to participate and signed a written informed consent. They included to the study only if they aged 15-80 years and had a weight of 60-80 kg for the purpose of applying fixed dosage of the drugs, which is 0.1 mg/kg for intravenous morphine and 15 mg/kg for intravenous acetaminophen. In addition, patients whose pain was caused merely by renal colic were included to the study. Those subjects who were addicted, allergic to opioids and acetaminophen, those who had received any types of analgesic drugs within previous 6 h, cases of kidney transplantation, patients with known heart failure, liver failure, respiratory failure, renal failure, cases of blindness and physical disabilities who were not able to communicate, excluded from the study. In order to get more accurate data, a history of previous illness, addiction and medication of the patients were evaluated. Once the diagnosis was confirmed by means of urine analysis, ultrasonography and also applying inclusion criteria, patients were randomly allocated into two groups, one by one by using a table of random numbers. In continue, patient's pain was assessed by using a visual analog scale (VAS) ruler, which rates the amount of pain from 0 to 10 based on patient's confession. At the beginning of each shift, two protocols were prepared by a nurse and labeled as Drug A and Drug B. The specified dosage for morphine, based on patient's weight, was 0.1 mg/kg and also 15 mg/kg for acetaminophen. Since the rapid injection of morphine can result in histamine release, therefore it must be infused slowly within 15 min. Moreover, intravenous acetaminophen should be infused slowly as well as morphine. The nurse, who was in charge of infusing a pain reliever, was unaware of the type of drug in each protocol. At the end of the study, types of infused drugs were determined depending upon the date of drug administration. Patient's pain was checked out twice: Exactly before receiving the pain reliever and 30 min later.

All collected data were analyzed by SPSS [PASW statistics 18 software IBM(®)] and statistical tests such as descriptive statistic, Chi-square, ANOVA, independent *t*-test and logistic regression.

RESULTS

Results of this study indicate that most of the participants were male. In other words, frequency of male and female

samples, depending upon the type of pain reliever, were (67.7%) and also (32.3%), respectively. Demographic variables are presented in Table 1.

According to this table, none of the influencing factors such as sex, age and weight could make a statistically significant difference between morphine and acetaminophen groups.

Comparing the mean of pain score between two groups of intravenous morphine and acetaminophen indicated that despite the difference in the minimum of pain scores in acetaminophen group (2.70 ± 1.78) and morphine group (5.0 ± 1.04), no statistically significant difference was found between two groups before the intervention ($P = 0.514$).

After taking the pain reliever, the mean of pain score in morphine group was (0.75 ± 1.31) and in acetaminophen group was (2.41 ± 3.29), which revealed a statistically significant difference in compare to the time of before intervention. In other words, morphine ($P = 0.001$) and acetaminophen ($P = 0.014$) have been effective, separately.

Comparing the mean differences between two group by means of independent *t*-test have shown a significant difference after the intervention ($P = 0.000$). Hence, morphine has been more effective than acetaminophen in reducing renal colic pain.

For the purpose of comparing mean pain scores between two groups, after controlling the influence of factors such as sex, age and weight, ANOVA testing was applied. The reason for using ANOVA is that patients' pain has been a quantitative continuous variable assessed by VAS scale and also used for variable such as age, which is classified in to more than two groups (under 30 years, 30-40 years, 40-50 years and older than 50 year).

The mean of pain score in both morphine and acetaminophen groups, considering different age classifications, showed that in acetaminophen group, patients aged 41-50 years developed the least effectiveness after receiving the pain reliever, but no significant difference was found between the classified age groups ($P = 0.604$). In the case of morphine,

Table 1: Demographic variables in morphine and acetaminophen groups

Variable	Group		P value
	Morphine	Acetaminophen	
Sex (frequency)			
Female, %	32.3	32.3	$P=0.315$
Male, %	67.7	67.7	
Age (year) (mean [SD])	39.73 (11.62)	38.40 (11.60)	$P=0.444$
Weight (kg) (mean [SD])	69.16 (7.31)	68.35 (6.08)	$P=0.242$

SD=Standard deviation

no significant difference was proved between two different classified age groups ($P = 0.799$).

Respecting the sex factor, no significant difference was found in morphine ($P = 0.482$) and acetaminophen ($P = 0.486$) groups separately, but in acetaminophen group females have experienced a little bit more pain relief than males.

According to the weight factor, no significant difference was found between different classified weight groups in acetaminophen ($P = 0.608$) and morphine ($P = 0.731$) groups separately.

Finally, it was found that there is a statistically significant difference between two interventional groups by controlling these influencing variables.

In order to determine the amount that these factors such as type of medication, age, sex and weight influence renal colic pain, logistic regression was applied [Table 2].

Results indicates that type of medication has been an efficient factor in reducing pain in both groups ($P = 0.000$), although variables such as age ($P = 0.288$), sex ($P = 0.898$) and weight ($P = 0.180$) did not make a significant difference.

In order to determine complications developed by morphine and acetaminophen in two groups, the Chi-square test was applied. The frequency of side-effects caused by the medications is presented separately in Table 3.

Table 2: Logistic regression analysis of factors affecting renal colic pain

Predictive variable	Logistic regression coefficients	Test statistic	P value
Constant value	-2.57	-2.33	0.021
Prescribed drug	-2.28	-4.66	0.000
Ultrasonography report	-1.26	-2.54	0.012
Age group	0.012	0.149	0.882
Weight group	0.111	1.35	0.180
Sex group	-0.011	0.129	0.898

Table 3: The frequency of side-effects caused by the medications

Complications	Group				P value
	Morphine		Acetaminophen		
	Frequency	Percent	Frequency	Percent	
Vomiting	1	1.61	0	0	0.50
Arterial hypotension	6	9.7	0	0	0.014
Dizziness	15	24.2	0	0	0.000

Chi-square test indicates that no significant relationship between vomiting and the type of medication have been proved ($P = 0.50$).

Considering hypotension as a complication, there was a significant difference between two intervention groups ($P = 0.014$), as presented in Table 2. Furthermore, both groups developed a significant difference ($P = 0.000$), as far as dizziness as a side-effect in concerned. Results suggest that morphine is more likely to cause symptoms of dizziness and arterial hypotension.

DISCUSSION

Results of this study with the aim of comparing the analgesic effect of intravenous morphine and acetaminophen (Apotel) on renal colic pain indicates that both medication types have been effective to reduce pain, although morphine has been more effective in compare to acetaminophen. This interventional study on determining and comparing the efficacy of acetaminophen and morphine on renal colic is a completely new one in Iran.

Results of searches in all medical libraries and electronic magazines showed that so far few studies have been published on this subject.

Bektas *et al.* from the Department of Emergency Medicine of University of Akdeniz in Turkey aimed to evaluate the analgesic efficacy and safety of intravenous single-dose acetaminophen and morphine for treatment of renal colic. About 165 subjects out of 645 met the inclusion criteria, but finally 146 ones remained. The prescribed doses of acetaminophen (15 mg/kg), morphine (0.1 mg/kg) and placebo (normal saline solution) administered for patients presenting to the emergency department. Results of this study revealed that there was significant differences in the mean of pain intensity reductions in compare with placebo for acetaminophen ($P = 0.005$) and morphine ($P = 0.050$). However, no difference has been found between acetaminophen and morphine ($P = 0.740$). Similar to our study, this study shows the positive impact of both morphine and acetaminophen on reducing renal colic pain.^[7]

In another study by Atef and Fawaz in Cairo with the aim of evaluating analgesic efficacy and safety of intravenous paracetamol in adult patients undergoing tonsillectomy, 76 patients have been randomly divided into two groups of 38 people, one group receiving intravenous acetaminophen 1 g and another just normal saline 0.9% (placebo), Immediately, after surgery and in a 6 h interval. The two groups have been evaluated within 24 h. In the group that received intravenous acetaminophen, in compared with the group

that had received saline, patients significantly improved more pain relief and less need for pethidine have been acquired. Results of this study show that intravenous acetaminophen could well reduce postoperative pain and need for Opioids.^[8]

In a meta-analysis study by Remy *et al.* on clinical trials with the aim of determining the morphine-sparing effect of acetaminophen using patient-controlled analgesia (PCA) with morphine and evaluating its effects on opioid-related adverse effects in Medline and the Cochrane Library search, seven prospective randomized controlled trials have been chosen finally, including 265 patients in the group with PCA morphine plus acetaminophen and 226 patients in the group with PCA morphine alone. Results of this meta-analysis revealed that there is no significant correlation between reduction of morphine-related side-effects and increasing patient satisfaction by using acetaminophen as a combination therapy with morphine.^[9]

Fijalkowska *et al.* in their study with the aim of evaluating the efficacy of intravenous acetaminophen in patients after gynecological surgery, have chosen 92 women scheduled for laparotomy or laparoscopy in the age of 20-69 years and allocated them into two groups. In both groups, 15 min before the end of anesthesia and 6 h after surgery, 1 g intravenous acetaminophen has been used. Results of this study indicated that the mean pain score in the laparotomy group and laparoscopy group have been 5/5 and 4/5, respectively. Results of this study indicate that acetaminophen as an activator of serotonin and also inhibitor of cyclooxygenase III and nitric oxide can significantly reduce the need for opioids after the surgery. However, injectable acetaminophen has no side-effects and also is well-tolerated. On the other hand, because of its rapid onset, it's a suitable drug for after surgery pain.^[10]

Van Aken *et al.* conducted a double-blind study with the aim of comparing analgesic effects of 2 g intravenous acetaminophen, 10 mg intramuscular morphine and placebo in patients undergoing third molar surgery. They reached to this conclusion that both intravenous acetaminophen and intramuscular morphine have been effective in controlling pain. Results revealed that the mean of pain score have not been significantly different between these two experimental groups.^[11]

Based on the results of the present study, intravenous morphine and intravenous acetaminophen could independently make changes in the mean pain scores and reduce renal colic pain in patients. However, comparing the mean scores between these two groups

show that morphine is more effective in reducing pain than intravenous acetaminophen although has more side effects. Hence it can be concluded that intravenous acetaminophen is safer and also effective treatment that can be administered for patients with renal colic. It's an appropriate alternative or supplement for Opioids. It seems that more research is needed in this field to confirm this suggestion.

CONCLUSION

From this research study, we found out that although opioids such as morphine has been approved to be effective in management of renal colic pain, but intravenous acetaminophen can be effective as well, especially with less harmful complications. Many studied around the word confirms the effectiveness of morphine in this way, but our study is somehow a new one that shows intravenous acetaminophen (Apotel) can be effectively administered for these patients.

ACKNOWLEDGMENTS

This article has been originated from a medical thesis which has been approved by Deputy of Research of Isfahan University of Medical Sciences with research number 389456. The Clinical Trial Identifier for this Article is NCT01906762. Financial support for this project has been done by the University Research Council and also the Presidential Department of Science and Technology. Researcher expresses his appreciation and give thanks to all who have participated and helped in any way to fulfill this research project.

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Source of Support: MUI Deputy of Research, Presidential Department of Science and Technology. **Conflict of Interest:** None declared.