

# Comparison the Efficiency of Morphine, Propofol and Fentanyl for Controlling Acute Renal Colic in patients admitted to hospital: A Randomized Double-Blind Clinical Trial

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## ABSTRACT

**Background:** Acute renal colic (ARC) is known as a widespread urological emergency that its prevalence commonly increases in relation to kidney stone disease. The different agents are commonly used for relieving pain. This study, for first time, compared effect of propofol and fentanyl in controlling ARC of patients admitted to the Shahid Mohammadi Hospital (Bandar Abbas-Iran).

**Methods:** A total of 150 eligible patients were randomly selected from patients referred to Shahid Mohammadi hospital, Bandar Abbas. The basal pain values of the patients were investigated by the Visual Analogue Scale (VAS) in values from 0 up to 10 at the 0th, (immediately before drug administration), 15th, and 30th minutes. Value of zero means lack of pain and 10 means the most pain. Demographic characteristics were also recorded.

**Results:** The results showed that most patients studies were male and middle age. Our findings did not show significant difference between groups for VAS0 ( $P>0.05$ ). The results showed that mean for VAS0 was 8.80, 2.42, 5.05 and 9.01 for Morphine, Fentanyl and Propofol groups and total, respectively. There was significant difference between Morphine with Propofol and Fentanyl for VAS30 ( $P<0.05$ ). The results showed that values for VAS30 were 2.85, 1.19 and 3.52 for Morphine, Fentanyl and Propofol groups, respectively.

**Conclusion:** Thus, fentanyl had the best response for controlling pain in patients with ARC. It can be suggested to use fentanyl for controlling ARC in emergency department instead of morphine and other conventional agents with higher side effects.

**Keywords:** Acute renal colic, Fentanyl, Morphine, Propofol

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## INTRODUCTION

Acute renal colic (ARC) is known as a widespread urological emergency that its prevalence commonly increases in relation to kidney stone disease and it is commonly diagnosed and alleviated its pain in emergency and hospitals<sup>1</sup>. ARC implicates on an acute renal colic pain in the flanks which is due to the passage of a stone from the ureter. The classic condition for ARC is a pain radiating from the flanks up to the groin which is often accompanied with hematuria and vomiting<sup>2</sup>. Pains referred associated to ARC are attributed to blockage of the urinary flow by kidney stone, raised pressure in the urinary tract wall, smooth muscle spasms in the ureter, edema and inflammation near the stone site, raised in peristalsis, and pressure of the proximal stone<sup>3,4</sup>. ARC pain is often reported as the worst pain the patients experienced the different pains<sup>5</sup>. The most patients ask an agent for relieving from the hospital, but health workers is to follow find a fast-acting treatment without side effects and/or lower side effect<sup>6</sup>. Fluids and pain relief therapy are commonly used for relieving pain<sup>7</sup>, however, non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used for pain relief due to non-addictive and having fewer side effects<sup>8</sup>. Morphine sulfate is used in the treatment of RC<sup>9</sup> and the most studies have compared morphine sulfate with NSAIDs<sup>10,11</sup>. Not only morphine sulfate, but also analgesics are extensively used through intravenous (IV) and intramuscular (IM) routes in the emergency department<sup>1</sup>. Propofol (2, 6-diisopropylphenol), a sedative agents, is commonly used in emergency

medicine for relieving pain, but it has disadvantages such as loss of airway reflexes, hypoventilation, apnea, and hypoxia<sup>12</sup>. However, it prevents renal injury via down-regulating inducible nitric oxide synthase expression<sup>13</sup>. Fentanyl, an opioid analgesic, is known to have high solubility in fat and it is commonly administered by traditional parenteral route<sup>1</sup>. It is commonly used as an effective analgesic under emergency conditions<sup>14,15</sup> and also has lower side effects<sup>15</sup>. The effects of fentanyl are started immediately and end early<sup>6</sup>.

So far, any study has not been conducted to compare the effects of morphine, propofol and fentanyl on RC. This study, for first time, compared effect of propofol and fentanyl in controlling ARC of patients admitted to the Shahid Mohammadi Hospital (Bandar Abbas-Iran).

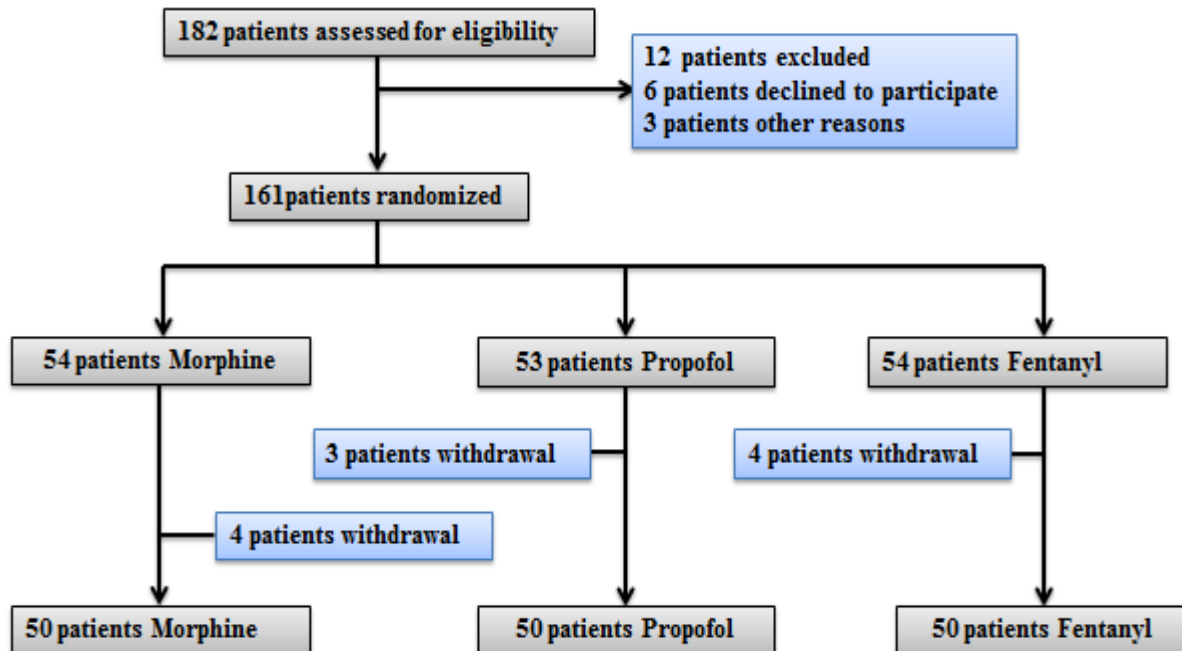
## METHODS

A randomized double-blind clinical study was conducted in the Shahid Mohammadi hospital, Bandar Abbas from December 2018 and February 2018. A total of 150 eligible patients were randomly selected from patients referred to Shahid Mohammadi hospital, Bandar Abbas, using the following criteria. The inclusion criteria were as follows; 1) Consent of patients for participation in the study, 2) Patients aged between 18-70 years, 3) Patients must have medium and/or severe pain (Score of  $>5$ ), 4) Non-responding to treatment of anti-pain in the Emergency and 5) Whose diagnosis of RC were confirmed by urinary analysis, KUB image, sonography and CT scan. Exclusion

criteria included: 1) Patients did not have tendency for participation in this study, 2) Patients not diagnosed with RC as a result of imaging and laboratory tests, 3) Patients with history of cardiovascular, blood pressure, liver, paroxysm Pregnant women, nursing mothers, and consumption of psychotherapy drugs, 4) Allergy to egg and 5) The use of sedative drugs 6 h before of bedridden.

Out of 150 patients, 50 patients were assigned to the Morphine group, 50 patients to Propofol group and the rest patients to Fentanyl group (n=50). In the current study, 181 patients were initially selected and 31 patients withdrew during the trial, as illustrated in Figure 1

. Figure 1 Trial profile.



Demographic characteristics such as age, sex, weight, history of ureteral stones, diabetes, HTN, cardiovascular diseases, hematuria, UTI and renal hydronephrosis were registered. The basal pain values of the patients were evaluated via the Visual Analogue Scale (VAS) in values from 0 up to 10 at the 0th, (immediately before drug administration), 15th, and 30th minutes. Value of zero as lack of pain and 10 as the most pain was considered.

The drugs used in this study were numbered on the basis of alphabetical order, A, B, C, ... . The drugs were assigned to one of the study groups on the basis the alphabetical words. The drugs were prepared by someone outside the hospital. Drug administration was conducted by a nurse in the hospital. The nurse administrated the drug by iv, infusion and slow routes during 5 minutes. The Propofol and Fentanyl were prepared from Braun Melsungen and Darou Pakhsh, respectively. The lowest administration levels for drugs were as follows; Fentanyl (2µg/kg body weight), Propofol (0.30 µg/kg body weight) and morphine (0.10 mg/kg body weight). Following administration of drugs, the VAS was assessed in 10 and 30 minutes after administration.

For investigating the data, the data were analyzed by the Chi square test, T-independent and ANOVA procedure.

We used SPSS 22.0 software for analysis of data.  $P < 0.05$  was considered significant.

## RESULTS

The results showed that 34 patients (68%) and 16 patients (32%) were man and woman in morphine group, 29 patients (58%) and 21 patients (42%) were man and woman in Fentanyl group and 28 patients (56%) and 22 patients (44%) were man and woman in Propofol group. Also, the means of age and weight were 33.61 years and 73.16 kg. The results also showed that 21 patients (42%), 27 patients (54%) and 24 patients (48%) had ureteral stones in Morphine, Fentanyl and Propofol groups, respectively. The results also showed that 3 patients (6%), 4 patients (8%) and 2 patients (4%) had hydronephrosis history in Morphine, Fentanyl and Propofol groups, respectively. In addition, 3 patients (6%), 7 patients (14%) and 3 patients (6%) had diabetes in Morphine, Fentanyl and Propofol groups, respectively. In addition, the results also showed that hematuria was 38(76%), 48(96%) and 48(96%) in Morphine, Fentanyl and Propofol groups, respectively. The most percentage UTI (38%) was observed in Fentanyl group ( $P < 0.05$ ).

Table 1 Demographic characteristics and history of disorders inpatients studied

	Morphine	Fentanyl	Propofol
Sexuality (Man)	34 (68%)	29 (58%)	28 (56%)
Sexuality (Woman)	16 (32%)	21 (42%)	22 (44%)
Ureteral stones	21 (42%)	27 (54%)	24 (48%)
Hydronephrosis history	3 (6%)	4 (8%)	2 (4%)
HTN	5 (10%)	6 (12%)	10 (20%)
Diabetes	3 (6%)	7 (14%)	3 (6%)
Cardiovascular	0 (0%)	0 (0%)	1 (2%)
Hematuria	38 (76%)	48 (96%)	48 (96%)
UTI	17 (34%)	19 (38%)	16 (32%)

**The pain values:** The data for comparison of VAS values at the 0th 15th and 30th minutes in patients with ARC are reported in Table 2. Our findings showed that all the groups VAS value was significantly higher in VAS0 compared to VAS10 and VAS30 ( $P<0.05$ ). The results showed, as VAS increases from 0 to 30, the mean decreases ( $P<0.05$ ). Our findings did not show significant difference between groups for VAS0 ( $P>0.05$ ). The results showed that mean for VAS0 was 8.80, 2.42, 5.05 and 9.01 for Morphine, Fentanyl and Propofol groups and total, respectively. There was significant difference between Morphine with Propofol and Fentanyl for VAS30 ( $P<0.05$ ). The results showed that values for VAS30 were 2.85, 1.19 and 3.52 for Morphine, Fentanyl and Propofol groups, respectively. The values for VAS30 was 2.85, 1.19 and 3.52 for morphine, fentanyl and propofol groups, respectively. The lowest value was observed for Fentanyl and the highest value was observed in Propofol group for VAS30.

Table 2: Comparison of VAS values at the 0th 10th and 30th minutes in patients with ARC

AS	Mean	P-values	
<b>Morphine</b>			
0	8.80	Vs Fentanyl=0.884	Vs Propofol=0.999
10	3.66	Vs Fentanyl=0.000	Vs Propofol=0.287
30	2.85	Vs Fentanyl=0.000	Vs Propofol=0.000
<b>Fentanyl</b>			
0	9.04	Vs Morphine=0.804	Vs Propofol=0.818
10	2.42	Vs Morphine=0.000	Vs Propofol=0.000
30	1.19	Vs Morphine=0.000	Vs Propofol=0.000
<b>Propofol</b>			
0	9.23	Vs Morphine=0.999	Vs Fentanyl=0.818
10	5.05	Vs Morphine=0.287	Vs Fentanyl=0.000
30	3.52	Vs Morphine=0.008	Vs Fentanyl=0.000
<b>Total</b>			
0	9.01	0.778	
10	3.62	0.000	
30	2.69	0.000	

**DISCUSSION**

On the basis of our knowledge, this study is the first study for comparison the efficacy of fentanyl and propofol in controlling ARC and in patients referred to hospital. On the basis of previous reports, prevalence of renal colic was 1 million patients in the United States, 7-9% of emergency ambulatory in European country<sup>16</sup> and totally between 12% and 15% in all over world<sup>17</sup>. The results also showed that most patients studies were male and middle age. Parallel to our findings, several studies showed that the most

patients referred to the hospital for treatment of renal colic were middle age and man<sup>18,19</sup>.

The results for pain scores showed that the best responses were observed in fentanyl, morphine and propofol for controlling ARC. Morphine sulphate is a commonly used as opioid analgesic in neonatal intensive care unit<sup>20</sup>. The present study showed positive effects of morphine for decreasing pain. However, a study showed that administration of morphine caused reversible hydronephrosis with ARC in extremely premature infants<sup>20</sup>. Other study showed that morphine may be related to toxicity in patients with ARC<sup>21</sup>. It can be stated that morphine can alleviate pain and may have side effects. Propofol showed the lowest efficiency for controlling ARC. Propofol is usually used in combination with ketamine as ketofol. Previous studies have reported that ketofol can efficiently induce sedation compared to ketofol with propofol<sup>22-24</sup>. A study showed that propofol was related to higher incidence of hypotension, but patients satisfied from propofol and ketofol<sup>25</sup>. In a meta-analysis, it was concluded that ketamine-propofol as an effective combination for decreasing some complications and suggested it as an appropriate substitution instead of propofol<sup>26</sup>. It seems that propofol in combination with other agents such as ketamine have better efficiency. In the current study, a combination of propofol and ketamine may have better efficiency. Our findings showed that Fentanyl could significantly decrease the VAS. There are some studies showing that different forms of fentanyl are compared with each other or with morphine. Parallel to our findings, a study compared the outcome of IV morphine (0.1mg/kg) and nebulized fentanyl (2 µg/kg) on the basis of VAS scores at the 10th, 20th, 30th, and 40th minutes and reported that nebulized fentanyl could have significant analgesia at all-time intervals<sup>15</sup>. Other study compared intravenous lidocaine and fentanyl in ARC and showed that the mean for pain severity was not significant between fentanyl and lidocaine in the different times following administration<sup>27</sup>.

**CONCLUSION**

This randomized double-blind clinical trial aimed to compare the efficiency of morphine, propofol and fentanyl for controlling ARC in patients admitted to hospital. In sum, fentanyl had the best response for controlling pain in patients with ARC. It can be suggested to use fentanyl for controlling ARC in emergency department instead of morphine and other conventional agents with higher side effects.

**Ethical Approval:** Approval for this study was obtained from Hormozgan University of Medical Sciences, Bandar Abbas, Iran.

**Conflict of Interests:** The authors declared no conflict of interest.

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