

ORIGINAL RESEARCH

Comparison of the Analgesic Effect of Intravenous Acetaminophen and Morphine Sulfate in Rib Fracture; a Randomized Double-Blind Clinical Trial

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Abstract

Introduction: Rib fracture is one of the common causes of trauma disabilities in many events and the outcome of these patients are very extensive from temporary pain management to long-term significant disability. Control and management of the pain in such patients is one of the most important challenges in emergency departments. Thus, the aim of the present study was assessing the efficacy of IV acetaminophen in pain control of patients with rib fracture. **Methods:** In this double-blind clinical trial, 54 patients over 18 years of age, referred to two educational hospitals with rib fracture, were entered. Patients were randomly categorized in two groups of morphine sulfate (0.1 milligram per kilogram of body weight) and IV acetaminophen (1gram), as single-dose infused in 100 cc normal saline. The pain severity was measured by numeric rating scale (NRS) on arrival and 30 minutes after drug administration. At least three scores reduction was reported as therapeutic success. **Results:** The mean and standard deviation of patients' age was 41.2 ± 14.1 years. There is no difference in gender ($p=0.24$) and age frequency ($p=0.77$) between groups. 30 minutes after drug administration the mean of pain severity were 5.5 ± 2.3 and 4.9 ± 1.7 in morphine and acetaminophen groups, respectively ($p=0.23$). Success rate in morphine and acetaminophen groups were 58.6% (95% CI: 39.6-77.7) and 80% (95% CI: 63.2-96.7), respectively, ($p=0.09$). Only 3 (5.6%) patients had dizziness ($p=0.44$) and other effects were not seen in any of patients. **Conclusion:** The findings of the present study shows that intravenous acetaminophen and morphine have the same therapeutic value in relieving the pain of rib fracture. The success rate after 30 minutes drug administration were 80% and 58.6% in acetaminophen and morphine groups, respectively. Presentation of side effects was similar in both groups.

Key words: Acetaminophen; morphine; pain management; rib fractures

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Introduction:

Rib fracture is one of the common causes of trauma disabilities in many events such as traffic accidents, falling, occupational events, and intentional traumas (1-4). The outcome of these patients are very extensive from temporary pain management to long-term significant disability (1, 5, 6). Recent studies showed that prolonged pain in the chest wall of patients with rib fracture is more prevalent than previously thought, so that about 60% of them suffer from long-term pain and disability (1, 7). Patients with rib fracture have severe pain during breathing, speaking, coughing, and even body movements (3, 8). Thus, rapid pain control has high priority to reduce the risk of pulmonary and systemic effects derived from the fracture such as decrease the respiratory effort which leads to hypoxia,

atelectasis, and even pneumonia (9). The presence guidelines recommend using opioids for these patients, but tolerance, probability of breathing depression, and other side effects of these products limit their use. Consequently, the recent studies have searched to find alternative or auxiliary treatments for decreasing such side effects. Intravenous (IV) acetaminophen, given the Food and Drug Administration confirmation in 2010 to management of mild to moderate pains, is introduced as an auxiliary drug to treatment of moderate to severe pains. Although acetaminophen causes to relieve the pain significantly and improving opioid sparing effects, it does not reduce the adverse effects arise from opioids such as vomiting and nausea (10). However, recent researches have declared that with considering economical and clinical evidences, administration of IV acetaminophen



should not be replaced by rectal or oral form unless for the patient cannot take it through these ways. But, rapid pain relief in trauma patients is an indication for IV administration based on which new protocols have been presented to introduce it as the first-line therapy in patients with rib fracture (9). Another indication of this drug is the patients who cannot tolerate non-opioid analgesic or antipyretic drugs (11). Since the pain is a main obstacle to examination, diagnosis, and treatment, control and management of the pain in trauma patients, especially in those with rib fracture, is one of the most important challenges in emergency departments (12, 13). In all studies, non-opioid analgesic drugs are presented as a therapeutic indication in trauma cases and their IV form such as acetaminophen is more considered by physicians in critical conditions (9). Nevertheless, these findings have not yet been published to show their therapeutic value. Thus, the aim of the present study was assessing the efficacy of IV acetaminophen in pain control of patients with rib fracture.

Methods:

Study design and setting

In this double-blind study, 54 patients over 18 years of age, referred to two educational hospitals with rib fracture, were entered and randomly categorized in two groups. The protocol of the study was confirmed by Ethical Committee of Esfahan University of Medical Sciences and consent form given from patients. During the study, all researchers observed the declaration of Helsinki. The study was registered in Iranian registry of clinical trial (IRCT number: IRCT2015042812072N2). Inclusion criteria were presence one or two rib fractures confirmed

by chest radiography, normal level of consciousness (Glasgow Coma scale of 15), weight range between 60-100 kg, and pain score >4 centimeters based on Numeric Rating Scale (14). Excluded criteria were dissatisfaction toward participation, background pulmonary problems, history of taking analgesic or opioid drugs, addiction, history of liver or kidney diseases, head trauma, pregnancy, history of taking monoamine oxidase, hypnotic and sedative drugs, as well as phenobarbital and isoniazid, respiratory arrest on arrival and repeated vomiting and nausea. Patients was sequentially entered to the study and randomization was done using computer generated sets of random allocations by a physician who did not involve in data gathering. All emergency staff included physicians, nurses, and researches were blind to the study. To ensure from blindness status, drugs were prepared as clear solutions in dark packs and only the person prepared them was aware from their content. Drug packs were coded and delivered to the drug prescribers. For doing the study as double blind, preparation and injection of solutions as well as record of results were separately performed by three physicians who did not in touch with each other during the study. Information regarding IV drugs was accessible to therapeutic staff only when side effects or other clinical changes happened to the patient. Patients were randomly categorized in two groups of morphine sulfate (0.1 milligram per kilogram of body weight, single-dose, and infused in 100 cc normal saline) and IV acetaminophen (1gram, single-dose, and infused in 100 cc normal saline). If the pain was not relieved after the first 30 minutes, a rescue dose of morphine was injected by a trained physician,

Table 1: Demographic data of studied patients based on administered drug

Variables	Morphine	acetaminophen	P
Age (Mean ± SD)	41.3 ± 14.1	41.0 ± 14.3	0.77*
Weight (Kilogram)	65.4 ± 2.9	64.9 ± 3.0	0.76*
Gender			
Female	10 (34.5)	5 (20.0)	
Male	19 (65.5)	20 (80.0)	0.24
Reason of Fracture			
Road traffic injury	21 (72.4)	12 (48.0)	0.25#
Falling <5 meters	5 (17.2)	8 (32.0)	
Falling >5 meters	0 (0.0)	1 (4.0)	
Direct trauma	3 (10.3)	4 (16.0)	
Fracture frequency			
One	20 (71.4)	15 (60.0)	0.38*
Two	8 (28.6)	10 (40.0)	
Co-injury			
No	25 (89.3)	25 (100.0)	0.49#
Pneumothorax	2 (7.1)	0 (0.0)	
Hemothorax	1 (3.6)	0 (0.0)	
Baseline pain severity (Mean ± SD)	8.6 ± 1.6	9.2 ± 1.3	0.19

*, Based on Mann-Whitney U test; #, Based on Fisher's exact test; SD: Standard deviation; Pain severity measured by numeric rating scale.



considered as a treatment failure. The patient was continuously monitored and vital signs (body temperature, blood pressure, respiratory rate, and pulse rate), level of arterial oxygen saturation, and drug side effects were recorded. The pain severity was measured by Numeric Rating Scale on arrival and 30 minutes after drug administration. In addition, adverse effects of drugs including vomiting and nausea, respiratory depression (respiratory rate less than 10 times per minute) and dizziness were evaluated. The primary outcome was defined as decreasing the pain severity that at least three scores reduction was reported as therapeutic success. Presentation of side effects was also considered as secondary outcome. With considering 95% confidence interval ($\alpha=0.05$), 80% power ($\beta=0.2$), and 1.65 standard deviation, with 1.3 centimeters reduction in pain severity because of drug efficacy ($d=1.3$), the sample volume was calculated 25 subjects in each group (15).

Statistical analysis

Data was analyzed using SPSS 11.0 version. Pain severity was showed as mean and standard deviation as well as successful rate as frequency and percentage. Mann-Whitney U test was applied for assessing the difference of quantitative and rating factors, while Chi-square and Fisher's exact tests for qualitative and numerical ones. $P < 0.05$ was statistically significant.

Results:

54 patients were entered, 29 cases in morphine group and 25 ones in acetaminophen, 39 (72.2%) cases was male. The mean and standard deviation of patients' age was 41.2 ± 14.1 years. There is no difference in gender ($p=0.24$) and age frequency ($p=0.77$) between groups. Table 1 shows demographic data of the studied patients.

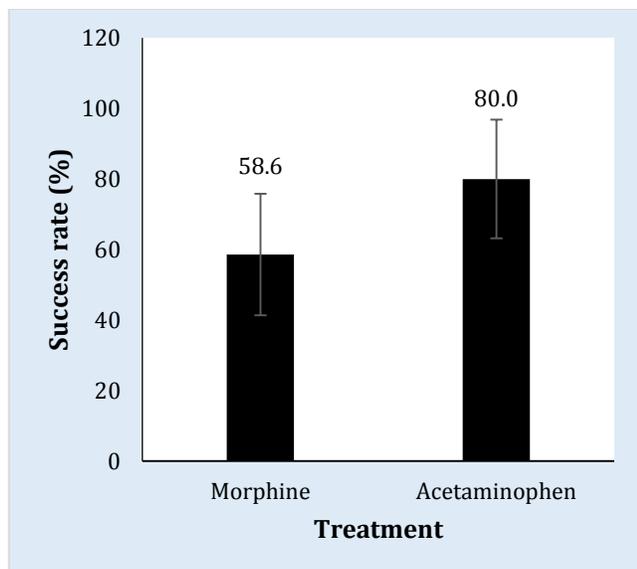


Figure 1: The success rate of morphine and acetaminophen in reducing the pain of fractures. Data is shown as percentage with 95% confidence interval.

The mean of pain severity on arrival were 8.6 ± 1.6 and 9.2 ± 1.3 in morphine and acetaminophen groups ($p=0.19$), respectively. 30 minutes after drug administration this mean were 5.5 ± 2.3 and 4.9 ± 1.7 in morphine and acetaminophen groups, respectively ($p=0.23$). Success rate in morphine and acetaminophen groups were 58.6% (95% CI: 39.6-77.7) and 80% (95% CI: 63.2-96.7), respectively, ($p=0.09$) (Figure 1). Only 3 (5.6%) patients had dizziness, 1 (3.5%) case in morphine group and 2 (8%) ones in acetaminophen ($p=0.44$). Other effects were not seen in any of patients.

Discussion:

The findings of the present study showed that IV acetaminophen and morphine have the same therapeutic value in relieving the pain of rib fracture. The pain of rib fracture may lead to exacerbate the lung injuries in chest trauma. Thus, administration of an analgesic and sedative drug has priority for these patients to improving the breathing, cough reflex, and respiratory physiotherapy (16). A review article in 2003 showed that presentation of a safe and effected method as a standard tool to decrease the pain of rib fracture is complicated. Therefore, having enough knowledge regarding strong and weak points of each drug is essential for physician to choose the appropriate medication according to clinical conditions and patient's status (17). Only one protocol in 2014 was published that considered the role of IV acetaminophen in pain management of rib fracture (fracture in three ribs or more). This protocol, which was written based on the experiences of a therapeutic center, showed that IV acetaminophen is the first-line therapy in such patients (9). Similar to this guideline, the present study declared that using IV acetaminophen as single-dose can be an appropriate medication for patients with rib fracture. The success rate reported for this drug in this study was 80% that although did not have significant difference with morphine (58.6%), it had more improvement rate, clinically. Even with supposing the same rate of success between the two drugs, using IV acetaminophen because of clinical (lesser side effects and contraindications) and economical (being cheaper) aspects are more rational. Also, in Tsang et al. study, it was declared that administration of IV acetaminophen with morphine causes to decrease the dose of morphine significantly, while both treatment protocols (acetaminophen with morphine and morphine alone) have the same efficacy in reducing the pain (18). Moreover, Zare et al. showed that administration of IV acetaminophen and oral oxycodone have more efficacy than morphine in pain management, but they have more side effects in compare to morphine (19). Finally, no difference was seen between side effects of drugs in two groups, representative the safety of acetaminophen in relieving the pain of rib fracture. Paydar and colleagues also stated that during one year using IV acetaminophen in patients



with rib fracture, no cases of hypotension, respiratory depression, loss of consciousness, and etc. was observed (9). Small sample size was the limitation of this study; if the number of patients was more, maybe the difference between success rate of acetaminophen and morphine would be significant in pain relieving of rib fracture. In addition, lacking of placebo was considered as another limitation of the present project, which because of ethical issues there was no possible to cancel the medication.

Conclusion:

The findings of the present study shows that IV acetaminophen and morphine have the same therapeutic value in relieving the pain of rib fracture. The success rate after 30 minutes drug administration were 80% and 58.6% in acetaminophen and morphine groups, respectively. Presentation of side effects was similar in both groups.

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Conflict of interest:

None

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Authors' contributions:

All authors met four criteria for authorship contribution based on recommendations of the International Committee of Medical Journal Editors.

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