

## Original Research Article

# Comparison of intravenous Acetaminophen and Morphine Sulfate for abdominal pain management in patients with acute abdomen

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## ABSTRACT

**Background:** Pain management is a crucial component in the postoperative care of patient. Opioids, which have been the mainstay of postoperative pain control for some time, are being used less because of significant adverse effects. Recently Intravenous acetaminophen that is an analgesic and antipyretic drug is used for reducing postoperative pain. Our Objective in this study was to use intravenous acetaminophen as an analgesic and antipyretic drug with the least complications and more safe than intravenous opioids for comparison with the effects of intravenous morphine sulfate in patients with acute abdominal surgery referred to emergency department of Fatemi Hospital.

**Methods:** 120 patients with acute abdomen will be assigned into the study by randomized allocation. Demographic data, pain severity in admission to the emergency department and 30 minutes after injection, vital signs in admission, side effects, and clinical findings will record questionnaires. The pain level, tenderness and the rebound tenderness of the patients will determine by the Visual Analog scale. The subjects will be divided into two groups A and B randomly. The intravenous acetaminophen (15 mg/kg/100cc normal saline in the form of intravenous infusion for 30 minutes) will be administered for group (A) and intravenous morphine sulphate (0.1 mg/kg Slow-acting intravenous injection for 1.5 to 2 minutes) will be administered for group (B). After 30, 60 and 90 minutes, the patient's pain is re-examined. Changes in the patient's pain, tenderness, rebound tenderness and side effects will documented in two groups and they will be compared. Finally, the collected data will be analyzed.

**Results:** The mean age of patients in acetaminophen group was 58.24±8.06 years with a mean age of 27-26 years and in morphine group was 56.7±7.63 years with age range of 34-69 years. There was no significant relationship between age and effect of intravenous acetaminophen and venous morphine sulphate (p=0.16). The mean of pain before injection of intravenous acetaminophen group was 8.92±1.25 and the mean pain before injection of morphine group was 8.80±1.35. There was no significant difference between the mean pain before injection of patients in the intravenous staphylococci group and the morphine group (p=0.049). The mean pain after injection of intravenous acetaminophen group was 4.46±1.25 and the mean pain after injection of the morphine group was 2.56±1.71. The mean pain after injection was significantly higher in patients with intravenous acetaminophen than in the morphine group (p<0.001).

**Conclusion:** Due to the effectiveness of morphine in relieving the pain of patients, it is recommended that doctors and associates use this painkiller to relieve pain in patients.

**Keywords:** Abdominal, Intravenous acetaminophen, Morphine sulphate, Pain, Patients

## INTRODUCTION

Acute abdomen is one of the most common urgent surgeries around the world and it is one the most important reasons of irritant and severe abdominal pain and unbearable in patients referring to emergency.<sup>1</sup> One of the duties of any physicians especially emergency Physicians, is sedation outpatients pain which is medical priority in novel emergency medicine. Pain sedation of patients with acute abdomen is an important matter.<sup>2</sup> but since the physical examination has an important role in diagnosis of acute abdomen with peritonitis symptoms such as Tenderness and rebound Tenderness, the admission of routine analgesics for pain sedation of these patients, may mask the symptoms and is not suggested in physical examination. Recent studies unlike previous hypothesis have proven the pain that the admission of intravenous opioids has no effect on therapeutic procedure and only decreases the pain in this patients.<sup>3</sup> Acetaminophen has been the main drug for sedating pain for some Long Years. Its Intravenous formulation has been used for adults and children extensively in Europe for more than 20 years. In United States, IV APAP has been granted by food and drug organization in the year 2010.<sup>4,5</sup> APAP analgesic mechanism has not been properly known.<sup>6</sup> Acetaminophen is rapidly absorbed and its maximum absorbed takes 1 hour. Its compellation takes 4 hours. When acetaminophen is absorbed, inhibits the production of E2 prostaglandins which brakes fever and causes numbness. The E2 prostaglandins production is being inhibited by two possible ways. One with cyclooxygenase 2 inhibition and the other with the inhibition membrane related prostaglandin production.<sup>7</sup> It has been reported that intravenous morphine usage is related to adult patients with acute abdominal pain with 12 percentages in diagnostic accuracy, however, as some findings demonstrate, morphine is a safe analgesic without compromising clinical diagnosis accuracy, is a controversial subject.<sup>8</sup> Morphine has some unpleasant side effects such as drowsiness, nausea and respiratory depression. It is a controlled drug which can affect much later from there time consumed or it can limit its own bioavailability in some settings.<sup>9</sup>

There are different methods to evaluate patient's pain severity. In this study authors use visual analogue scale (VAS) to evaluate patient's pain severity. VAS is as 10 centimeter line, with one end for patient without pain and the other end patients with the most severe pain. The patient indicates his /her own pain severity with a dot on the spectrum.<sup>10</sup> According to the mentioned contents above it is being understood that the injection of opioid in patients with acute abdominal pain, not also it doesn't mask the sign and deteriorate the patient's diagnosis, but also it causes more comfort and less pain in patient. But as it is obvious the morphine sulfate drug has some serious side effects such as respiratory depression and reduction in blood pressure, the point of our study is to use venous Acetaminophen as an analgesic and antipyretic drug with the lowest side effects and safer

than intravenous opioids for comparing with intravenous morphine sulfate effects on patients with acute abdomen referring to the emergency ward of Fatemi Hospital of Ardabil.

## METHODS

This study was clinical trial and has been done in the Ardabil Fatemi Hospital in Mar 2017-Mar 2018. The study population was the patients who referred to the Fatemi Hospital. 120 patients were determined in 2 groups each 60 with considering alpha 5% and power 80% for detecting an effect size of 0.5 and standard deviation by using open epi software for each group with 60 patients. The aim of this random double blind clinical trial was to compare the morphine sulfate drug and intentional Acetaminophen in controlling the pain of the patients with acute abdomen who referred to the emergency ward of Fatemi Hospital of Ardabil. Patients with acute abdomen were randomly entered to the study. The demographic information, pain severity at the entering point, side effects after injection, vital signs at the entering point, side effects and clinical findings were registered in the questioners' form.

### *Inclusion criteria*

The patients above 18 year-olds, stable hemodynamics, acute abdominal pain with colic essence.

### *Exclusion criteria*

Sensitivity to morphine or other opioids, proved or possible pregnancies, breastfeeding, under 12 year old, addiction to any kind of opioids and receiving analgesics in 6 hours before referring emergency department. (after primary studies done by surgical or non-surgical methods and acute abdomen diagnosis, before the surgery, patients pain severity in the normal condition and the tenderness and rebound tenderness severity was determined by visual analog scale. Then the patient received one of the two following drugs: intravenous Acetaminophen (15 mg/kg in 100cc normal saline serum, IV infusion in 30minutes) or IV morphine sulfate (0.1mg per kg, slow IV infusion in 1.5 to 2 minutes) then after 30 minutes, patients pain was reevaluated. The changes in pain severity, tenderness rebound tenderness and side effects in both groups were registered and compared with each other.

Intravenous Acetaminophen or intravenous morphine sulfate reception was ascertained by blocked randomization and it was done as double-blind randomization meaning that both Intern and the patient did not know about the coded drug, which in coordination whit one of the nurses who was the same in the study of every patient, 6 block drugs with proper coding were prepared randomly and injected by the Intern. The drugs kind was known by the codes and after wards this code was written on top of the information collection form.

Then changes in patient's pain, Tenderness rebound Tenderness register and the collected information was analyzed. Data with Entered into SPSS program after coding and then by using descriptive and analytical statistical method by using T-Test exam and Chi-square exam, quantitative and qualitative data was analyzed. Significant level was considered lower than 0.05. By respecting Ethical considerations, all personal information of patient was kept confidentially by the physician and director of study and no patient's name is said in the study. No cost was received from the patient's for doing laboratory exams. This study was done after getting the approval of ethical committee. Consent form was received from the Patients. The Approval of ethical committee of Ardabil University of medical science for this thesis (IR-ARUMS-REC1396.87) was received and also the study was registered in IRCT number of IRCT2017110427097N5.

## RESULTS

All of 120 patients with acute abdomen was divided randomly into two groups, group A received IV acetaminophen (15mg/kg in 100cc IV infusion in 30 minutes) group B received IV Morphine Sulfate (0.1 mg/kg, slow IV injection in 1.5 to 2 minutes). In Group A there were 28 males (46.66%) and 32 females (53.33%) and in group B there were 29 males (48.33%) and 31 females (51.66%). There were no significant relations between patient's gender and intravenous acetaminophen and Morphine Sulfate efficacy ( $p=0.31$ ). The average age of patients in group A was  $58.24\pm 8.06$  with the range of 26-74 years and in group B was  $56.7\pm 7.63$  years with the range of 34-69 years. There was no significant correlation between age and the efficacy of intravenous acetaminophen and Morphine Sulfate efficacy ( $p=0.31$ ).

In group A 10% had College education, 25% intermediate education, 43.34% Elementary education and 21.66% were illiterate. There was no significant correlation between the patient education and the efficacy of intravenous acetaminophen and Morphine Sulfate. ( $p>0.05$ ) and from group B, 11.66% had College education, 28.33% intermediate education, 41.67% elementary education and 18.34% were illiterate. From group A 45% of the patients were housewives, 26.67% were self-employed, 3.33% were fears and 25% were employees or retired.

Most of the patients were housewives. This was no significant correlation between the patient's job and efficacy of IV acetaminophen and Morphine Sulfate ( $p>0.05$ ), and from group B 40% were housewives, 28.34% were self-employed, 13.34% employees and 18.33% retired. Most of the patients were housewives; the average pain severity was measured before injection in male and female patients. The average amount of pain before injection in males was significantly lower than the females ( $p=0.006$ ) (Table 1).

**Table 1: Average pain severity before injection in male and female patients.**

Patients	Mean $\pm$ SD	p value
Male	8.69 $\pm$ 1.29	p=0.006
Female	9.17 $\pm$ 1.27	

The average of pain severity before injection IV acetaminophen group was  $8.92\pm 1.25$  and the average of pain severity before injection in morphine group was  $8.80\pm 1.35$ . There were no significant differences between the pain severity mean before injection. In IV acetaminophen group and Morphine group ( $p=0.489$ ) In IV acetaminophen group The Pain severity mean before injection in IV acetaminophen group patient was  $8.92\pm 1.25$  and the pain severity mean after injection in IV Acetaminophen group patients was  $4.46\pm 1.25$ .

There was no significant sedation in pain severity mean after the injection in IV acetaminophen group patients comparing to after injection ( $p<0.001$ ).

In morphine group, the pain severity means before injection was  $8.80\pm 1.35$  and the pain severity mean after injection was  $2.56\pm 1.71$ . There was no significant sedation in pain severity mean before injection in morphine group patients comparing to after injection ( $p<0.001$ ) (table 2).

**Table 2: Average pain before and after injection in groups.**

Groups	Acetaminophen	Morphine	p value
Average pain before injection	8.92 $\pm$ 1.25	8.80 $\pm$ 1.35	p=0.489
Average pain after injection	4.46 $\pm$ 1.25	2.56 $\pm$ 1.71	p<0.001

The nausea rate ( $p=0.617$ ) and vomit rate ( $p=0.266$ ) after injection had no significant differences into study groups. Was lowered significantly in injection of acetaminophen group ( $p<0.001$ ).

After injection the pain severity mean in IV acetaminophen group patient's was  $4.46\pm 1.25$  and hip pain severity mean after injection in Morphine group patients was  $2.56\pm 1.71$ .

The after injection pain severity mean in IV acetaminophen group was significantly higher than the morphine group ( $p<0.001$ ). In IV acetaminophen group, the before injection pain severity mean was  $8.92\pm 1.25$ . There was a significant reduction in after injection pain in acetaminophen group ( $p<0.001$ ). In morphine group, the before injection pain severity mean was  $8.80\pm 1.35$  and the after injection pain severity mean was  $2.56\pm 1.71$ . There was

a significant reduction in after injection pain in morphine group ( $p < 0.001$ ) (table 3).

**Table 3: Results of treatment regimens of patients before and after intervention.**

Groups	Average pain before injection	Average pain after injection	p value
Acetaminophen	8.92±1.25	4.46±1.25	$p < 0.001$
morphine	8.80±1.35	2.56±1.71	$p < 0.001$

By considering the results of this study, the pain severity mean changes were assessed in 30,60 and 90 minutes and there was a significant correlation in pain severity marks after 30 minutes ( $p < 0.001$ ), after 60 minutes ( $p < 0.001$ ) and after 90 minutes ( $p = 0.002$ ) (Table 4).

**Table 4: Mean pain after injection in 30, 60 and 90 minutes.**

Groups	Acetaminophen	Morphine	p value
30 minutes	4.46±1.25	2.56±1.71	$p < 0.001$
60 minutes	2.88±1.40	1.46±1.14	$p < 0.001$
90 minutes	2.01±1.88	1.28±1.21	$p = 0.002$

## DISCUSSION

Findings indicated that before injection pain severity mean in IV acetaminophen group was 8.92±1.25 and the before injection pain severity mean in morphine group was 8.80±1.35. There were no significant differences between the before injection pain severity means in IV acetaminophen group vs morphine group ( $p = 0.489$ ). The after injection pain severity mean in IV acetaminophen group was 4.46±1.25 and the after injection pain severity mean in morphine group patients was 2.56±1.71. The After injection pain severity in IV acetaminophen group was significantly higher than the morphine group patients ( $p < 0.001$ ). Pain is the most common chief complaint in any kind of disease. Although the essence, location and the cause of pain is different in each case but the pain was the primary chief complaint in almost half of the patients referring to Physicians.<sup>9</sup>

Studies has always indicated that the 30-40% of post-surgical patients have moderate to severe levels of pain. The feeling of distress, suffering and torment due to sensitization of nerve ending is the result of an objective or personal Multi Factor Phenomenon which is under the influence of physiological, cultural, psychological and social factors.<sup>11</sup>

There has been a lot of effort through time to reduce, control or Ablate pain. The current medical guidelines for controlling pain in surgery are dependent on analgesics and opioids and NSAIDs.

In Control of pain other than narcotics (opioids) then non-opioidal drugs are also used. Most of the patients feel itchiness, nausea and vomiting after the epidural morphine administration. Usually to eliminate the complications, Naloxone or Diphenhydramine is used. Preventing or reducing complications is an important clinical goal. Also, intramuscular administration only reduces the patient's pain for a short time and it is not usually accompanied with the complications discussed before. About 11% of the patients who received post-surgical intramuscular morphine have no need to be sedated in first 24 hours. Respiratory depression happens in 0.25% of the cases. It seems that intrathecal morphine is more effective than the intramuscular form, but the complications are the same.<sup>12,13</sup>

In 2012 Criag and et al had studied the comparison of Clinical effect of IV paracetamol and IV morphine in limb traumatic patients with moderate to severe pain. Is east double blinded randomized study was done an emergency Ward of Britain. The patients were between 16 to 65 years old with traumatic limp and with the moderate to severe pain (pain score of 7 and more) who received 1 gr IV paracetamol or 10 mg IV Morphine Sulfate in more than 15 minutes. The results were found by primary measurement of pain score in Visual analogue scale at 0.5,15,30,60 minutes after the drug usage. The need for Breaking Free of analgesics and their complications were registered. 55 patients were selected in over 10 months. There were no significant differences between the analgesics in both paracetamol and morphine group in different timelines. The side effects were much higher in morphine group. The results of this study indicate the IV paracetamol causes analgesia in comparison with IV morphine in a level of limb traumatic patients.<sup>9</sup> the study above is the same as the current study. In 2012 Aghamohammadi and et al had published a study with this goal debt consideration has no effect on precious findings in physical examination. This double blinded randomized clinical trial was done on 120 patients over 12-year-old who administered to emergency Ward of a hospital with acute abdomen. Patient randomly divided into 2 groups: IV Placebo group and morphine groups: pain score, change into tenderness and also change into the rebound tenderness were measured based on pain score scale after morphine or placebo. Statistically there was a significant difference between pain score by considering pain score mean. There was a significant difference between both groups after drug administration in Tenderness and the rebound Tenderness prevalence. (the fact is the consumption of narcotics reduces the pain in patients with acute abdomen, they have no desire to eliminate the diagnostic data of physical examination, such as Tenderness and rebound Tenderness) surprisingly, all the acute abdomen cases had rebound Tenderness after morphine administration. Therefore, this research suggests the prudent use of morphine in patients with acute abdomen study about is collaborative with our study.<sup>14</sup>

In 2012 in a study done by Serinken and et al in emergency medicine department by assessing the effect of IV acetaminophen in pain treatment of patients with renal colic in comparison with Morphine, he concluded IV acetaminophen was effective like morphine in patients in production and it caused pain reduction in patients.<sup>15</sup>

In a study done by Morgan and et al, by assessing the IV acetaminophen function in patients pain reduction they concluded that IV acetaminophen is an effective in patient pain reduction and in renal colic patients there was a significant reduction in pain.<sup>16</sup>

Our study assumes the results of the study above the IV acetaminophen use in patient's cause's pain reduction and this reduction was significant.

Mc Daid and et al, concluded that IV acetaminophen use in post-surgical patients is effective and do the use of it reduces the consumption of narcotic sedatives such as morphine, and its complications.<sup>17</sup> In a study done by Babl and et al, in the Royal Hospital of Melbourne-Australia in Year 2011, assessment of IV acetaminophen in patient's pain sedation in emergency, he concluded that the use of IV acetaminophen is effective for pain sedation the decreases they need of narcotics sedative consumption in these patients.<sup>18</sup> In a study done by Winger and et al in Phoenix university in America's Arizona in year 2010, which day assessment of IV acetaminophen effect on patient's abdominal pain sedation, earlier to surgery, they concluded that IV acetaminophen use in these patients significantly decreases the pain.<sup>19</sup> In a study done by moon and et al in Anesthesia and pain in department of Banpordang University of South Korean in Zoll, with the assessment of IV acetaminophen analgesics effect they concluded that this drug was effective in controlling patients pain.<sup>20</sup>

In a study of Grissa and et al, are you as a termination was more effective in controlling patient's pain with renal colic than intramuscular Piroxicam and it significantly decreased the pain in patients.<sup>21</sup>

By considering the effectiveness of IV acetaminophen inpatient pain sedation, suggested to use this sedative for patient's pain sedation and to study more about IV acetaminophen and comparison of it with other drugs in larger statistical Society.

## CONCLUSION

The result of our study indicated that morphin is effective in reducing patients pain with abdominal pain and however the amount of reduction in patients receiving the morphin was significantly higher than the patients receiving iv acetaminophen and it was significantly reduced comparing to before injection in patients receiving iv acetaminophen this indicates the effectiveness of this drug in patients pain sedation.

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