

## Preliminary Study of Pre-hospital Pain Management and Comparison of Pain Management Methods in Emergency Patients

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### ARTICLE INFO

#### Article history:

Received 09 October 2020

Revised 01 November 2020

Accepted 14 November 2020

#### Keywords:

Acetaminophen;  
Emergent patients;  
Ketorolac;  
Pain score;  
Pre-hospital

### ABSTRACT

**Background:** Pain is an unpleasant sensation in the body or mind. Uncontrolled pain can increase mortality and morbidity with its negative physiological effects. Effective pain management especially in emergency conditions is essential to keep the patient in optimal conditions and to achieve good clinical results. As most of the injured and traumatic conscious patients with acute pain in emergency situations, need control and perfect pain management during transfer to hospital essential to feel satisfied and improve the quality of service and to decrease mortality and morbidity. Due to some limitation to use opioid drugs in pre-hospital systems, the goal of this study was to evaluate the efficacy of non-opioids drugs in different doses on pre-hospital emergency traumatic conscious patients.

**Methods:** Infusion of 1 gr IV acetaminophen and 30 mg IV ketorolac were studied separately and in combination 500 mg acetaminophen and 15 mg ketorolac on 95 patients in three separate groups in the pre-hospital pain control system. Patient pain score was collected at 5 intervals.

**Results:** The results showed that there was no significant difference between the three groups in pain scores reduction finally ( $p > 0.05$ ). The rate of pain reduction in emergency department is very important and these criteria was significant ( $p < 0.05$ ).

**Conclusion:** The results of this study suggest that the combination of ketorolac and acetaminophen reduces pain more rapidly than either alone.

According to our findings we suggest a combination of apotel and ketorolac is injected in advance in moderate to severe conscious traumatic patient before any change in the position of patients if there are not any contraindications.

Pain is not a trivial phenomenon, but one of the greatest human problems that exists from the birth to the last stage of his or her life and suffers from the consequences [1-2].

In fact, pain is an unpleasant feeling and an emotional experience with real damage to the body tissue. Pain motivates us to get rid of the potentially destructive condition that has occurred to the affected part of the body in order to recover and prevent it from occurring in the future. Pain is the stimulation of the dissociative disorder in the peripheral nervous system or damage to the central nervous system or the environment [3].

Usually, the pain resolves immediately after the painful stimulus is removed and the body heals, but sometimes it continues to persist despite the removal of stimuli and the improvement of the body, the pain continues, and in some cases the pain increases due to the lack of recognizable conditions of injury or pathology. The result of an analgesic with minimal side effects is a serious concern in the treatment [4].

Pain leads to various reactions such as changes in the speed and depth of respiration, increased heart requirements, skeletal muscle contraction, muscle spasticity, coagulation, immunosuppression, and

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continuous catabolism. Inappropriate management of pain leads to an increase in the length of hospitalization, and patient dissatisfaction with medical care and ultimately leads to increased illness and increased mortality. Therefore, for proper management and control pain requires the assessment of pain and individual treatment based on observation of the patient's condition. Also, the costs of treatment and the consequences of the occupational and family affect the various aspects of the individual's life. For this reason, pain relief is one of the most important medical priorities [4].

Opioids and NSAIDs (nonsteroidal anti-inflammatory drugs) are the most commonly used drugs to relieve pain, and their use has a long history. In this regard, many studies have been conducted to investigate the mechanism of the performance of these compounds. Many studies have shown that the use of opioids to reduce pain can lead to complications such as constipation, nausea, and respiratory depression [5]. Subsequently, NSAIDs such as ketorolac and diclofenac replaced opioids. In 1996, Stein et al. examined the effectiveness of ketorolac compared to diclofenac ampoules. Their study showed that the rate of pain reduction in both groups was approximately the same [6]. In 2000, in a systematic study, Jelinek et al. showed that taking ketorolac could reduce pain in cancer patients with minimal side effects as much as taking morphine [7]. Many studies have examined the effect of injectable acetaminophen on pain relief after surgery. In 2010, immediately after confirming the administration of acetaminophen by the American Food and Drug Administration, Dr. Wininger et al. conducted extensive research on the efficacy of various injectable acetaminophen dosages in reducing pain after abdominal laparoscopic surgery. Their study showed that different regimens of acetaminophen were effective in reducing postoperative pain [8]. Combination therapy can be used with regard to the different conditions of patients and the limitation of immediate pain relief. This method was first introduced in the early nineties by Kehlet et al. [9]. In 2002, Hyllested et al. reviewed a qualitative overview of the effectiveness of acetaminophen compared to NSAIDs after surgery [10]. The aim of their study was to compare the analgesic effects and complications of acetaminophen and other postoperative NSAIDs, compare the effects of these compounds in combination and separately and finally discuss how side effects of NSAIDs and acetaminophen in the face of their analgesic effects. The result of their study, given the limited number of samples, showed that NSAIDs are clearly effective after dental surgery, whereas in orthopedic surgeries the efficacy of acetaminophen and NSAIDs are the same. The notable point in their studies is that the addition of acetaminophen to NSAIDs increases their analgesic effect [10]. In 2002, Livshits et al., examined and compared the effects of ibuprofen and acetaminophen on abortion patients with a

double-blind randomized study. According to the results of their study, ibuprofen is statistically significant in reducing postoperative pain after abortion compared to acetaminophen [11].

According to studies on the use of non-opioids compounds to reduce pain and low complications of these compounds, the need to use these compounds in pre-hospital and hospital research is clear. In this study, for the first time, control of pre-hospital pain using acetaminophen and ketorolac, is discussed. The main goal of this study is to evaluate the effects of the compounds mentioned in order to reduce pain individually and in combination in injured traumatic patients.

## Methods

This study is a blind randomized clinical trial that was conducted at Hamadan Medical Center for Accidents traumatic conscious patients in the emergency department of Besat Hospital, during 6 months. After the approval of the ethics committee and obtaining written consent, 95 patients who had the entrance criteria entered the study. These patients were randomly allocated to the three groups using a random number table. Two groups include 35 and one group includes 25 cases. The first groups (35 patients) were injected 30 mg ketorolac intravenously to reduce the pain in a 1 to 2 minute period. The second group (35 patients) were infused 1 g acetaminophen (appendix) diluted in 100 ml of normal saline serum and to measure pain after 10 minutes. To the third group (25 patients), 500 mg acetaminophen (appendix) and 15 mg ketorolac were injected intravenously over a period of 10 minutes.

Inclusion criteria include all traumatic conscious patients between 16-80 years of age. Exclusion criteria were unconscious and non-traumatic patients, contraindication to use NSAID and apotel such as history of GI bleeding or Liver disease and or other limitations. Pain scores were determined at 5 intervals before injection and the times 20, 30, 60 and 120 minutes after injection. The collected data included respiratory rate, systolic blood pressure, diastolic blood pressure, heart rate and numeric rating scale (NRS). 10 steps NRS was used to measure pain score. Data were analyzed using SPSS software. The Repeated Measure Anova test was used to analyze the data at different time intervals and Bonferroni test was used in Post-hoc test. In conclusion, p values less than 0.05 were considered as statistically significant.

## Results

In the first group, 35 patients were present, of which 26 were male (75%) and 9 were female (25%). The age

range was 38-83 years old. All traumatic conscious patients who suffered from acute pain, were injected with 30 mg of ketorolac. The mean respiratory rate, systolic blood pressure, diastolic blood pressure, heart rate, and

pain reduction score (NRS) were recorded for all patients in the first group at a time interval of 120 minutes in (Table 1).

**Table 1- Mean changes in respiratory rate, blood pressure, heart rate, and NRS for 120 minutes after injection of 30 mg ketorolac for the first group of 35 patients.**

Time	respiratory rate	std	blood pressure(sys)	std	blood pressure(dias)	std	heart rate	std	NRS	std
T0	16.34	1.32	117.42	10.87	77.00	6.77	72.77	5.78	8.88	1.69
T20	16.14	1.03	116.71	10.28	78.00	6.20	71.25	5.51	5.95	2.33
T30	16.00	0.64	117.00	9.71	76.00	5.66	70.68	4.84	5.17	2.46
T60	15.85	0.49	118.71	8.85	76.71	5.41	71.45	4.59	4.22	2.64
T120	15.68	0.67	119.57	9.10	77.81	5.59	70.37	5.17	4.21	2.62

According to Table 1, the changes in respiratory rate per minute were significantly different ( $p < 0.05$ ). The important point about the changes in blood pressure in the periods considered is that the patients' physical condition and their genetic history is a determinant factor, and according to Table 1, there is a significant difference between the pressure data blood is not seen. According to the analysis performed due to pain, at first, the number of beats is high, then the decrease in pain is a downward trend ( $p < 0.05$ ).

According to the results of Table 1, decrease in the mean score of pain in the range of 0 to 60 minutes is quite

tangible, and after 60 minutes, this criterion is slowed down.

In the second group, 35 patients were present, 20 men (57%) and 15 women (43%). The age range of the group was 35-77 years old. All of the patients traumatic conscious who suffered from acute pain, were injected 1 g acetaminophen. The mean respiratory rate, systolic blood pressure, diastolic blood pressure, heart rate and pain reduction score (NRS) were recorded for all patients in the second group in the time interval of 120 minutes in (Table 2).

**Table 2- Mean changes in respiratory rate, blood pressure, heart rate, and NRS for 120 minutes after 1g acetaminophen injection for the second group consisting of 35 patients**

Time	respiratory rate	std	blood pressure(sys)	std	blood pressure(dias)	std	heart rate	std	NRS	std
T0	15.88	2.11	112.14	7.30	74.14	5.62	73.97	6.05	8.88	1.64
T20	15.94	1.86	112.42	7.60	74.28	4.22	72.40	5.91	6.67	1.63
T30	15.85	1.16	114.85	8.70	74.28	4.22	71.51	5.40	5.38	1.68
T60	16.02	0.89	115.14	8.86	75.71	5.02	71.37	4.86	3.57	1.54
T120	15.77	0.89	114.57	8.77	74.57	5.05	70.74	5.64	3.41	1.71

According to Table 2, respiration rate per minute, changes in blood pressure at different times in the second group did not have a significant difference. Noteworthy in Table 2, pulse changes at different times are significantly different, due to the pain of the patient at the start of the drug injection and then the reduction of pain that reduces anxiety and pulse. According to the analysis, the pain score of patients in the second group at different times has a significant change due to the analgesic effect of acetaminophen.

In the third group, 25 patients were present: 14 men (56%) and 11 women (44%) had an age range of 35-76 years. Patients received 500 mg intravenous acetaminophen plus 15 mg intravenous ketorolac. The mean respiratory rate, systolic blood pressure, diastolic blood pressure, heart rate and pain reduction score (NRS) were recorded for all patients in the third group in the time interval of 120 minutes in (Table 3).

**Table 3- Mean changes in respiratory rate, blood pressure, heart rate, and NRS for 120 minutes after injection of 500 mg acetaminophen and 15 mg ketorolac for the third group of 25 patients.**

Time	respiratory rate	std	blood pressure(sys)	std	blood pressure(dias)	std	heart rate	std	NRS	std
T0	17.16	1.24	112.20	13.07	72.40	5.42	73.96	6.14	8.88	1.56
T20	16.16	0.98	111.00	9.35	72.20	3.84	70.80	5.55	5.34	2.53
T30	15.88	1.05	112.20	8.54	74.20	4.49	69.4	4.80	4.04	2.83
T60	15.72	1.17	114.00	7.90	73.40	4.01	68.00	5.03	3.64	3.05
T120	15.72	1.17	115.20	7.96	75.40	3.79	66.96	4.65	3.44	3.08

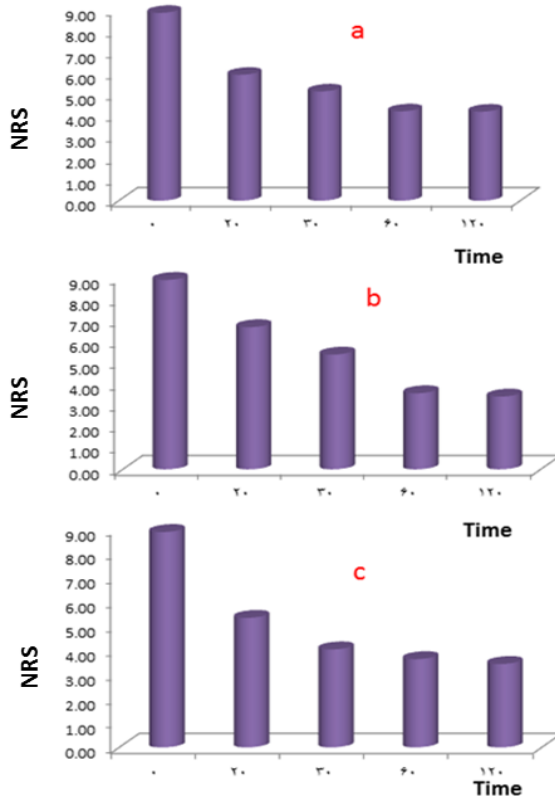
According to Table 3, respiratory rate, changes in blood pressure and heart rate at different times were significantly different in the third group, which is due to pain reduction in patients ( $p < 0.05$ ). According to the analysis, the pain score at different times has a significant difference.

To confirm the accuracy of the data in Tables 1-3, a separate test was used to examine the data on respiratory rate, systolic and diastolic blood pressure, and number of heart pulses and reduction of pain score. Separation results showed that injection of 30 mg ketorolac in the first group, 1 g acetaminophen in the second group, and the combination 500 mg acetaminophen and 15 mg ketorolac reduced the pain in the patients under study, which was in the Supporting Information referred to.

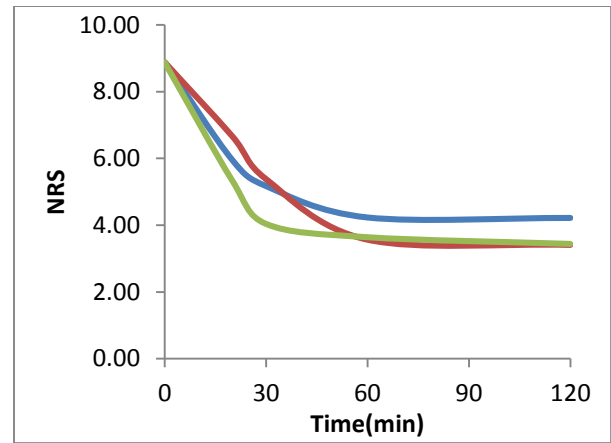
### Discussion

In this study, the efficacy of non-opioid drugs in different doses on pre-hospital emergency traumatic conscious patients was evaluated. These patients were randomly allocated to the three groups using a random number table. Two groups include 35 and one group includes 25 cases. Graphic data of (Figure 1-2) provide a good comparison basis for reducing pain scores in all three study groups.

**Figure 1- Comparison of NRS in a) first group, b) second group, and c) third group**



**Figure 2- Comparison of NRS at different times between the three groups, blue: Ketorolac NRS, red: Acetaminophen NRS and green: Combination NRS**

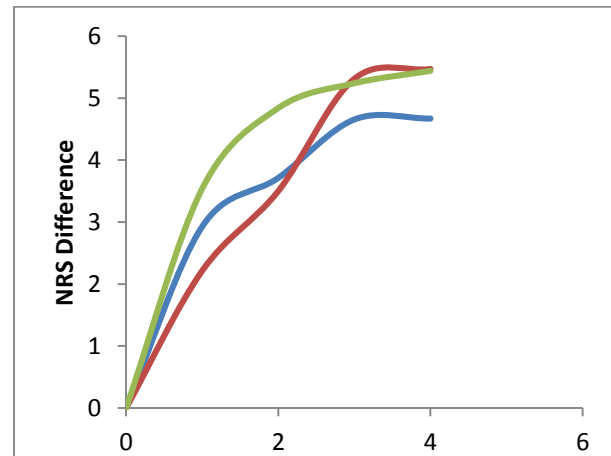


According to Figure 1 and 2, there was no significant difference over all between the three groups in reducing pain scores ( $p > 0.05$ ). Another way to compare pain scores in the three experimental groups is using T-test and One Way Anova test. According to the results of these tests, pain scores at different times between the three groups were compared.

No significant difference was found between the groups ( $p > 0.05$ ), as the rate of pain reduction in the emergency department is of high importance, compared to the rate of reduction in the rate of pain reduction.

According to (Figure 3), the rate of pain reduction was significantly different between groups ( $p < 0.05$ ).

**Figure 3- Comparison of the rate of NRS in the three groups, blue: Ketorolac NRS, red: Acetaminophen NRS and green: Combination NRS**



According to the slope of Figure 3, it is concluded that the combination of ketorolac and acetaminophen reduces pain more rapidly than either alone.

Similar research has been done with our study, which often confirms the results of our study.

In 2013, Anand et al. examined the effect of 1000 mg venous acetaminophen compared to 30 mg ketorolac in reducing pain in patients undergoing parathyroid gland surgery. Regarding the results of their study, the mean VAS in the two groups was not significantly different. However, ketorolac was significantly more effective in decreasing the amount of pain compared to acetaminophen in longer intervals after surgery [12].

In 2016, Mamoun et al. studied intravenous acetaminophen analgesia after cardiac surgery using a randomized, blinded, controlled superiority trial. The results of their study showed that intravenous acetaminophen can be an effective analgesic aid in patients recovering from median sternotomy [13].

Kayhan et al. in an interesting study compared intravenous ibuprofen and acetaminophen for postoperative multimodal pain management in bariatric surgery. The results of their study showed that intravenous ibuprofen may be a good alternative to intravenous acetaminophen as part of postoperative analgesia in patients undergoing bariatric surgery [14].

In 2020, Xie et al. compared low pre-emptive oral doses of celecoxib versus acetaminophen for postoperative pain management after third molar surgery. The results of their study showed that celecoxib has a significant analgesic effect and can reduce postoperative pain relief after the removal of the third molar [15].

## Conclusion

In the present study, there was no significant difference between the three experimental groups in reducing pain scores. It is noteworthy that patients who received both ketorolac and acetaminophen had greater pain reduction rates than the groups receiving either drug individually. Pain relief has a significant role in pain relief in the emergency system. According to the results of this study, it can be used to reduce pain rapidly if there is no inhibition in patients receiving any of the injectable acetaminophen drugs. Our studies also showed that in all three groups, in addition to decreasing pain score, respiratory rate per minute and pulse rate were significantly reduced by drug injection, this can prevent unintended complications from acute pain and we suggest in advance be injected combination of apotel and ketorolac in moderate to severe conscious traumatic patient before any change in the position of patients if there are not any contraindications.

## Acknowledgments

The authors would like to acknowledge the Hamadan University of Medical Sciences and Tehran Medical Sciences, Islamic Azad University.

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