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Effect of Preprocedural Intravenous Ibuprofen on Post-Repair Pain after Traumatic Wound Management: A Randomized Clinical Trial

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Abstract

Background: Wound repair cause extra pain and inflammation and can lead to post-repair discomfort in patients. Previous studies have indicated that pre-operative use of NSAIDs may reduce post-surgery pain; however, there is a dearth of data on traumatic wound repair.
Objectives: This study aimed to investigate the effect of intravenous Ibuprofen on patient satisfaction and pain relief following wound repair.
Methods: Based on the inclusion and exclusion criteria, 194 participants in this double-blind randomized controlled trial were randomly assigned to either intervention or control group. Ibuprofen 800 mg was infused in 100 cc normal saline before wound repair in the intervention group, while the control group received 100 cc normal saline. Numeric pain scores were recorded at the beginning of wound repair and 30 min after that. Patients' satisfaction with analgesia was also recorded 15 min after the drug infusion, during wound repair, and 6 h after the wound repair.
Results: Mean pain scores were similar in both groups during the wound repair, and before the application of local anesthesia (i.e. lidocaine). However, the mean pain score was significantly lower in patients who received Ibuprofen (3.86±1.93), compared to the control group (4.46±1.89), 30 min after the wound repair (P=0.043). Patients' satisfaction with pain management 6 h after the wound repair was higher in the intervention (P=0.000), compared to the control group.
Conclusion: Based on the obtained results, the application of IV Ibuprofen before the wound repair can reduce pain score after the wound repair and lead to improved patients' satisfaction.

Keywords: Emergency, Ibuprofen, Pain, Trauma, Wound

1. Background

Traumatic wounds are common causes of emergency visits to health care centers. Wound suturing was performed in 2.5% of all emergency visits in the US in 2016 that makes it the 4th most common procedure performed at emergency departments (ED) (1). Based on the evidence, patients' priorities in wound management include infection prevention, restoration of normal function, satisfactory cosmetic outcome, and minimal pain (2). Proper pain management can minimize physical and emotional damage. There are several pharmacological and non-pharmacological pain management methods for traumatic wounds including topical, local, and regional anesthesia. Moreover, oral, intravenous, intranasal, and respiratory analgesics are used as well (3, 4). Various studies are available on the application of local and regional anesthesia in wound repair procedure (3-8); however, there are limited data on post-repair pain. Cycloxigenase2 (COX2) is an inducible enzyme and its expression is increased by tissue injury. COX2 mediates inflammation, pain, fever, and carcinogenic responses by increased synthesis of pro-inflammatory prostaglandins. It is widely known that COX inhibition is responsible for non-steroidal anti-inflammatory drugs (NSAID) main anti-inflammatory and pain relief mechanism of action. However, the COX independent anti-inflammatory mechanisms have been discussed in some studies as well (9-10). In addition to tissue injury caused by the trauma, the process of wound management and repair (i.e. debridement, rubbing for irrigation, and suturing) can trigger an additional inflammatory response by excessive expression of COX2 and prostaglandins due to inevitable soft tissue damage. Therefore, it should be noted that the application of NSAIDs before suturing may decrease pain and inflammation after wound repair.

The results of previous studies indicated that preoperative use of NSAIDs can reduce postoperative pain (11-14); however, there is a dearth of data on traumatic wound repair.

The usual dose of Ibuprofen, as the most commonly used and most frequently prescribed NSAID, is 400-800 mg three times a day (15). Ibuprofen is available in oral and intravenous forms. The terminal half-life of IV ibuprofen appears to be slightly more than 2 h and consistent across all

dosing ranges (16). Like some other NSAIDs, there is evidence that the preoperative use of Ibuprofen is useful for the reduction of post-operative pain and the need for rescue analgesics (17-21).

2. Objectives

Therefore, this study aimed to investigate the effect of intravenous Ibuprofen on patient satisfaction and pain relief following the wound repair.

3. Methods

3.1. Study design and setting

This double-blind randomized controlled trial was conducted at Haftome Tir Hospital, a major referral and trauma center in Tehran, Iran. Data gathering started in December 2018 and ended in April 2019. This trial was registered at the Iranian clinical trial registry (IRCT20120613010017N8). Informed consent was obtained from all participants before the enrollment in the study. The study was approved by the Ethics Committee of the Iran University of Medical Sciences, Tehran, Iran, and carried out according to the Declaration of Helsinki [1989].

3.2. Participants

The study participants included patients in the age range of 15-75 years who were referred to ED of Haftome Tir Hospital (with no companion) for the simple skin lacerations of at least 2 cm length major injury.

Patients with animal and human bites, blast injury, crush wounds, amputations, tendon injury, open fractures, intraarticular involvement, fingertip laceration, decreased level of consciousness, history of allergy to NSAIDs, ischemic heart disease, ischemic cerebral disease, history of gastric ulcer or gastrointestinal bleeding, vascular diseases, renal insufficiency, single kidney, renal transplant, as well as immune-compromised patients, and those who received any kind of analgesics or opium during last 18 hours were excluded from the study.

3.3. Sample size calculation

The sample size was calculated to be 86 for each group using G power software to detect a 50% or greater difference in the primary outcome between the two study groups, with an α and β of 0.05 and 0.1 (90% power), respectively.

3.4. Randomization and blinding

Randomization was performed using a computer-generated sequence table under the supervision of an emergency medicine physician who was in charge of the study. The process of patient selection and randomized allocation was performed by a PGY3 EM resident. The allocation was performed through the blind matching of the patient's number and package. Packages contained either 800 mg intravenous Ibuprofen or injectable sterile water (as a placebo). Attending emergency physician supervised package preparation and concealment session. After matching of patients and packages numbers, the emergency nurse prepared the injection solution containing Ibuprofen or placebo in IV infusion sets with the same appearance. Participants and research investigators (PGY3 EM residents) were blinded to the content and preparation of the injection solution. The data analyzer was also blinded in this study.

3.5. Intervention

The research investigator (PGY3 EM resident) enrolled eligible participants based on inclusion and exclusion criteria after triage and admission. Informed written consent was obtained from the participants after the study objectives were explained to them. Participants were then randomly assigned into two groups of intervention and control. The intervention group received an IV infusion set containing Ibuprofen 800 mg (Samen pharmaceutical Co., Iran) in 100 cc normal saline, and the placebo group received an IV infusion set containing 100 cc normal saline (both infused over 10 min).

Wound closure by suture was performed 2-3 min following 30 min local anesthesia conducted by lidocaine 2% injected at wound edges.

3.6. Outcome assessment

The study investigator (PGY3 resident) asked patients to report the severity of their pain using a numeric rating scale (0=no pain, 10=the most severe pain) at the beginning and 30 min after the wound closure. Patients' satisfaction with analgesia was also measured 15 min after drug infusion, during wound closure, and 6 h after wound closure using a verbal rating scale from 1 to 5 (1=Very bad, 2=Bad, 3=Rather bad, 4=Good, and 5=Excellent). Most patients were discharged from ED early after wound closure, and their satisfaction was recorded by phone call 6 h after the wound closure.Participants' demographic characteristics and outcome measures were recorded in pre-prepared data collection sheets.

3.7. Statistical analysis

Data were analyzed using SPSS software (SPSS, Inc., Chicago, IL; Version 23). Descriptive variables were presented as frequencies and means±SD. The normality of data distribution was tested using the Kolmogorov-Smirnov test. The parametric and non-parametric analysis was performed using the independent t-test and Mann-Whitney's test, respectively. A p-value less than 0.05 was considered statistically significant.

4. Results

In total, 230 patients attended ED with traumatic lacerations from whom 34 patients were excluded based on the exclusion criteria. Afterward, 97 patients were assigned to each group of intervention and control using a random assignment approach. CONSORT flow diagram and baseline characteristics are provided in Figure1 and Table 1, respectively. The mean±SD age of participants was 35.52±12.83, and the majority (90.2%) of them were male. The mean±SD time interval from the injury to ED attendance was 97.7±85.98 min. It is worth mentioning that, 29.9%, 24.4%, 19.5%, and 15.8% of patients were presented with the scalp, upper limb, lower limb, and face lacerations, respectively.

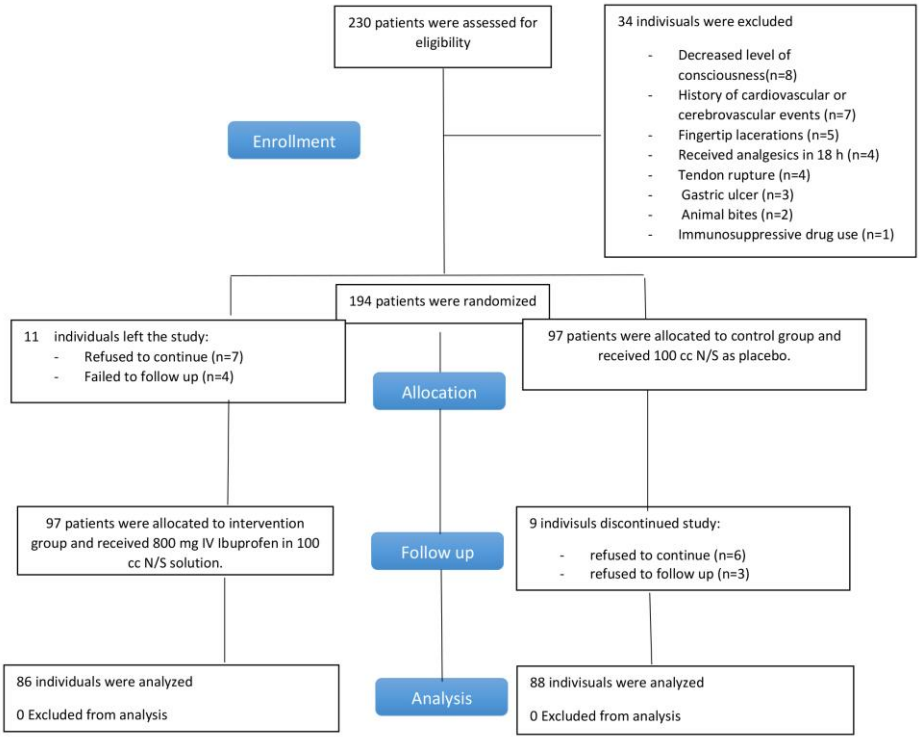

Figure1.CONSORT flow diagram

Table 1. Baseline characteristics

	Intervention Group	Placebo Group	P-Value
Age	33.71±12.64	37.71±12.80	0.04
Male			
Gender	85(81%)	72(91%)	0.714
Female	10(19%)	7(9%)	
Wound length	6.58±4.87	6.01±2.46	0.356
Wound depth	1.08±0.85	1.22±0.60	0.263

Table 2. Pain score in intervention and placebo groups

	Intervention Group	Placebo Group	P-Value
Pain score during wound closure	6.91±1.19	6.86±1.37	0.819
Pain score 30 min after wound closure	3.86±1.93	4.46±1.89	0.043
Patients' satisfaction 15 min after drug injection	1.44±0.52	1.44±0.59	0.991
Patients' satisfaction during wound closure	2.79±0.97	2.51±0.86	0.335
Patients' satisfaction 6 h after wound closure	3.98±1.02	3.20±1.15	0.000

The mean±SD pain scores during the wound repair and before the application of local anesthesia (i.e. lidocaine) were similar in both intervention (6.91±1.19) and control (6.86±1.37) groups (P=0.81). However, the mean±SD pain score was significantly lower in patients who received Ibuprofen (3.86±1.93), compared to those who received placebo (4.46±1.89), 30 min after the wound repair (P=0.043). There was no statistically significant difference in patients' satisfaction of pain management 15 min after infusion and during the wound repair. However, the patients' satisfaction with pain management was higher in the intervention (3.98±1.02) compared to control group (3.21±1.15) 6 h after the wound repair. The difference between two groups in terms of pain severity was statistically significant (P=0.000). Table 2 presents the study results in detail.

5. Discussion

Based on the obtained results, the use of IV Ibuprofen before wound closure was effective in the reduction of postoperative pain measured 30 min after the wound repair and increase of patients' satisfaction with analgesia 6 h after the wound repair. However, the use of IV Ibuprofen before wound closure was not effective in the reduction of pain at the time of wound repair, and the improvement of patients' satisfaction 15 min after infusion of IV Ibuprofen and during the wound repair. Based on previous studies on the pharmacokinetics of IV Ibuprofen, CSF concentration reached the peak within 30 to 38 min after the infusion (16, 22), and plasma concentration may take 1 h to reach the peak depending on infusion speed (23). This can explain how Ibuprofen showed more efficacy in late outcomes in this study.

Traumatic wound repair is a procedure accompanied by extra tissue damage, irrigated wound, and debridement. Suturing itself can cause inflammation, pain, and significant discomfort after the wound closure is completed. However, there is a dearth of data concerning pain reduction methods after wound repair. Our knowledge about the effect of NSAIDs on postoperative pain is limited to studies conducted on surgical wounds, and there are still some controversies over this issue. However, the results of another meta-analysis performed by Nir et al. including studies on different kinds of medication for pre-operative analgesias (e.g., opioids, NSAIDs, Gabapentin, Pregabalin, Clonidine, and Dextromethorphan) showed that although COX 2 inhibitor class of NSAIDs were effective in the reduction of post-operative pain and rescue analgesics requirement, other classes of NSAIDs, including propionic acid class failed to show effectiveness in this regard. Four studies among the included studies in this meta-analysis used Ibuprofen in gynecology and dental surgeries (14). Singla N et al. conducted a multi-center RCT which showed that IV Ibuprofen 800 mg used before the surgery and every 6 h after the surgery is effective in reducing pain in orthopedic surgeries. The findings showed that early postoperative pain would be significantly reduced in the group of intervention, compared to placebo after the patients received the single pre-operative dose of Ibuprofen (17). Moss JR et al. applied a single dose of 10mg/kg IV Ibuprofen on 161 pediatric patients undergoing tonsillectomy before the induction of anesthesia which reduced the need for postoperative rescue analgesics (19). The application of single-dose IV Ibuprofen 400 mg in another study showed that pre-operative Ibuprofen reduces postoperative pain measured by visual analog scale within a few minutes and up to 24 h after the surgery, and patients who received Ibuprofen required lower opioid and other analgesics after the surgery (21).

The results obtained in this study were consistent with the findings of most previous studies; although, this seems to be the first study on pre-operative use of Ibuprofen on traumatic wounds.

Limitation

Regarding the limitation of the present study, it should be noted that due to the fact that initial pain scores had not been recorded, it was not possible to calculate the change in pain severity following the traumatic wound repair. The probable side effects of Ibuprofen were not recorded as well. We are planning to conduct other studies in the future that lack the limitations of the present study in order to provide more evidence on this issue.

Therefore, regarding the lack of knowledge on pain management after traumatic wound repair, further studies on different classes of NSAIDs and other analgesics seem to be necessary.

6. Conclusion

Based on the obtained results, IV Ibuprofen is effective for the reduction of pain after the wound repair procedure in the emergency department of hospitals and health centers.

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Footnotes

Authors' Contribution: HBG and MHR contributed to the acquisition of data, drafting the article, and interpretation of data. HS, EM, HBG and NA contributed to the conception and design and interpretation of data. All authors contributed to the initiation of the research and interpretation of data. HS, HBG and MHR contributed to the analysis and interpretation of data. NA and EM contributed to drafting the article and revising it critically for important intellectual content. All authors have read and approved the final version of the manuscript.

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