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Pain management of acute limb trauma patients with intravenous lidocaine in emergency department☆,☆☆

Shervin Farahmand [a], Hadid Hamrah [b], Mona Arbab [c], Mojtaba Sedaghat [d], Hamed Basir Ghafouri [e], Shahram Bagheri-Hariri [f,*]

[a] Emergency Medicine Department, Tehran University of Medical Sciences, Tehran, Iran
[b] Tehran University of Medical Sciences, Tehran, Iran
[c] General Surgery Department, Brigham and Women's Hospital, Boston, MA, USA
[d] Community Medicine Department, Tehran University of Medical Sciences, Tehran, Iran
[e] Trauma and Injury Research Center, Iran University of Medical Sciences, Tehran, Iran
[f] Emergency Medicine Department, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Introduction: This study was designed to assess the possible superiority of intravenous lidocaine to morphine for pain management.
Methods: This was a randomized double blind controlled superiority trial, carried on in the emergency department (ED). Traumatic patients older than 18-year-old with the complaint of acute pain greater than 4 on a numeric rating scale (NRS) from 0 to 10 on their extremities were eligible. One group received IV lidocaine (1.5 mg/kg), and the other received IV morphine (0.1 mg/kg). Pain scores and adverse effects were assessed at 15, 30, 45 and 60 minutes and patients' satisfaction was evaluated two hours later. A minimum pain score reduction of 1.3 from baseline was considered clinically significant.
Results: Fifty patients with the mean age of 31.28 ± 8.7 were enrolled (78% male). The demographic characteristics and pain scores of the two groups was similar. The on-arrival mean pain scores in two groups were, lidocaine: 7.9 ± 1.4 and morphine: 8.0 ± 1.4 ($p = 0.57$) and after 1 hour were, lidocaine: 2.28 ± 1.2 and morphine: 3.2 ± 1.7. Although the pain score decreased significantly in both group ($p = 0.027$), there were not any clinically and statistically significant difference between the two groups ($p = 0.77$). Patients' satisfaction with pain management in both groups were almost similar ($p = 0.49$).
Conclusion: The reduction in pain score using IV lidocaine is not superior to IV morphine in adult ED patients with traumatic limb pain.

1. Introduction

Pain is one of the most common complaints of traumatic patients visiting the emergency departments (ED). Although sufficient pain management is crucial, up to half of patients believe more could be done to alleviate their pain [1]. Many studies have been done in this era as well as ongoing ones to evaluate the efficacy of pain management in traumatic patients using different medications along with various techniques. However, it seems that, there is significant mismanagement in this regard [2]. For instance, Karmakar et al. reported that fear of respiratory depression, confronting drug (opioid) seeking behavior and fear of hemodynamic instability have led to insufficient pain management in patients with multiple rib fractures [3,4]. On the other hand, lack of sufficient pain management might result in unexpected responses like releasing inflammatory cytokines, cortisol, and catecholamines that could lead to higher morbidity and mortality [5]. From the perspective of emergency medicine (EM), the main goal in pain management is finding a rapid, safe and efficient analgesic. There are a variety of medications for pain management in the ED including acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDS), and opioids. Each one has its own onset of action and side effects.

Lidocaine is well-known as a local anesthetic agent that is being used to control pain due to its anti-inflammatory, antihyperalgesic and analgesic properties [6]. But intravenous (IV) lidocaine administration has recently been taken into consideration in this regard. For example, IV lidocaine has been used to reduce pain in patients with renal colic andafterlaparoscopy and laparotomy. These studies have supported that IV lidocaine can reduce the intensity of post-operative pain, decrease the need for opioids and other analgesics, and result in shorter

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* Corresponding author.
E-mail address: hariri@sina.tums.ac.ir (S. Bagheri-Hariri).

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hospital length of stay and lower morbidity [7-10]. Lidocaine has not been reported as a potential drug of abuse. The major reported side effects are headache and shivering although cardiovascular, gastrointestinal and respiratory effects have been rarely reported and should still be taken into account.

Considering the above, the current study was designed to test the hypothesis that IV lidocaine was superior to IV morphine for pain reduction in patients with acute traumatic limb pain visiting the ED.

2. Material and methods

2.1. Study design

This study was a randomized double blind superiority clinical trial conducted during June 2014 in the ED of a referral hospital and trauma center, in Tehran, Iran. The study protocol was approved by the ethical committee of Tehran University of Medical Sciences. The patients were included after obtaining informed consent. The study was registered and approved by the Iranian clinical trial registry (IRCT2014080518698N1 at http://www.irct.ir).

2.2. Participants

Trauma patients older than 18-year-old, came to the ED in person or were transferred by the emergency medical service (EMS), with acute extremity injury and a pain score >4 on a 0–10 numerical rating scale (NRS) were considered eligible for enrollment.

Patients with any alteration in the level of consciousness (Glasgow coma scale (GCS) < 15), hemodynamic instability, history of opioid use, alcohol or any sedative-hypnotic drug use in the past 48 h, history of chronic disease including cardiac, renal or hepatic diseases, history of asthma, epilepsy, and history of allergic reaction to lidocaine or morphine were excluded.

2.3. Sample size calculation

Based on a similar previous study, we estimated a study sample size of 25 patients in each group [11].

This sample size would give 80% power to detect a minimally important difference of 1.3 points on the NRS at the level of 5% significance. [12].

2.4. Randomization

Block randomization was used in this study. Block sizes were 2 by 2 (13 blocks). The acceptable sequences for packages within each block were: AABB (1), ABAB (2), BBAA (3), BABA (4), BAAB (5), and ABBA (6). Each acceptable possibility of the blocks had been marked from 1 to 6 as above. Then a dice was used to generate the sequence of the blocks from 1 to 13. In the end, blocks were set by means of the generated sequence from 1 to 13, then packages within blocks were sequentially numbered from 1 to 50. Concealment was completed by wiping off the letter A and B on the syringes and then each package was sealed with tape. Participants were consecutively numbered from 1 to 50 considering the time of triage. Allocation was performed by blindly matching the patient's number and package. Randomization sequence and concealment were performed by the study supervisor (EM attending). Allocation and matching of the number of participants to the package number in order to receive the intervention was performed by the study investigators (EM residents). Participants, research investigators (EM residents) and nurses were blinded to the content and the sequence of treatment within blocks.

2.5. Intervention

Eligible patients were first triaged and admitted in the ED. Parallel to standard and routine ED management, such as limb immobilization in a temporary splint, the study investigators (designated and trained emergency medicine residents) explained the purpose and method of study of the patients, evaluated the patients for the exclusion criteria and obtaining informed consent.

Two sets of 25 sterile, colourless and ready-to-inject 10cm^3 syringes were prepared and named syringe A (lidocaine) and syringe B (morphine sulphate) before concealment. Syringes A contained 150 mg lidocaine (15 mg/ml lidocaine) with a therapeutic dose of 1.5 mg/kg IV with the posted label "inject 1 ml/10 kg IV slowly over 2-3 minutes". Syringe B contained 10 mg morphine (1 mg/ml MS) with the therapeutic dose of 0.1 mg/kg with the posted instruction label as "inject 1 ml/10 kg IV slowly over 2–3 min". The contents of both sets of syringes looked identical (clear). Then, each of them were put in identical and sterile packages.

2.6. Outcome assessment

The primary hypothesis was that compared with IV morphine, IV lidocaine would reduce the pain at 60 min by >1.3 points. Based on the existing literature, an absolute reduction of 1.3 point on the NRS, or a 30% relative reduction in pain score from baseline, are considered clinically significant. [13].

The secondary outcome was any subjective reports of possible adverse effects and the patients' overall satisfaction with their pain management.

Pain scores were assessed using the NRS in the current study (with a minimum of 0, no pain, to a maximum of 10, the worst pain ever). All participants' pain scores were assessed before and after intervention at 15, 30, 45 and 60-min by the investigator. If the NRS scores remained >5 or the relative risk reduction in pain score was <30% from baseline after the first 15 min or at any other time-point and the patients requested additional analgesia, a fixed dose of 50 μg fentanyl was given intravenously as the rescue dose in both groups.

During the observation period, the vital signs (blood pressure, pulse oximetry, respiratory rate and heart rate) were monitored and recorded by emergency medicine residents and nursing staff. Participants were constantly monitored for adverse effects, such as nausea, vomiting, vertigo, pruritus and decreased level of consciousness. After 60 min, patients were asked how satisfied they were with their pain management during the past one hour. All participants expressed their satisfaction for pain management based on the 6-item Likert scale from very satisfied to very dissatisfied.

2.7. Statistical analysis

All data were gathered on individual data sheets for each subject (appendix 1) and were analyzed by SPSS version 16, Chicago, SPSS Inc., using the Kruskal Wallis, Wilcoxon, paired *t*-test and repeated measures ANOVA.

3. Results

From 143 subjects with acute limb trauma who visited the ED in Jun 2016, 93 subjects were eligible to participate in this study. Based on the exclusion criteria, 43 subjects were excluded, and 50 subjects signed the written informed consent and enrolled in the study. In the next step, 25 patients were randomly assigned to the lidocaine group and 25 patients were assigned to the morphine group. Fig. 1 shows the CONSORT flowchart of study patients.

Fifty patients with the mean age of 31.28 ± 8.7 years were enrolled (78% male). Baseline characteristics of studied patients are reported in Table 1. Considering gender, age, weight and height, there was not a

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