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Original Contribution

Nebulized fentanyl vs intravenous morphine for ED patients with acute limb pain: a randomized clinical trial

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ABSTRACT

Objective: Intravenous morphine has been used as a common method of pain control in emergency care. Nebulized fentanyl is also an effective temporary substitute. This study was designed to compare the effectiveness of nebulized fentanyl with intravenous (IV) morphine on management of acute limb pain.
Methods: This was a placebo-controlled, double-blind randomized clinical trial. Ninety emergency department patients with moderate to severe pain aged 15 to 50 years were blocked randomized and enrolled in this study. Forty-seven patients in the experimental group received nebulized fentanyl (4 μg/kg) and IV normal saline as placebo, and the remaining 43 patients in the control group received IV morphine (0.1 mg/kg) and nebulized normal saline as placebo. All participants' pain scores were assessed by Numerical Rating Scale before and after intervention at 5-, 10-, 15-, 30-, 45-, and 60-minute intervals. Patients' vital sign and possible adverse effects were recorded respectively. Finally, all participants were assessed for their satisfaction.
Results: The mean initial pain score in the experimental group was 8.7 and 8.4 in the control group ($P = .1$). Pain relief in both groups after 5 and 10 minutes were similar ($P = .72$). Although the pain relief was significantly greater with fentanyl at 15 minutes, this difference is not clinically significant. Pain management in both groups was successful and was more than 3 scores reduction in Numerical Rating Scale. Patient satisfaction in both groups was similar. No adverse effects were reported in the experimental group.
Conclusion: This study suggests that nebulized fentanyl is a rapid, safe, and effective method for temporary control of acute limb pain in emergency department patients.

1. Introduction

Most emergency visits, up to 70%, are due to patients seeking relief from pain [1]. Although the patient easily describes the pain, managing that pain in overcrowded emergency departments is truly challenging. It is desirable to use a rapid, effective, and safe analgesic immediately after triage. Although intravenous (IV) morphine has been used as a common method of pain control in most emergency departments [1], its administration requires the insertion of an IV cannula. This can cause additional distress to the patient and can often be time consuming or unsuccessful. Between 12% and 26% of IV catheter insertions are unsuccessful in adults [2]. As a result, temporary and feasible methods for analgesic administration have been recently considered. One such method, nebulized fentanyl is a convenient and effective temporary relief, which has not been fully studied in adult emergency departments [3–5]. Fentanyl is a highly potent opioid with considerable lipid solubility. These features make it an ideal opioid to be administered through inhalation [6]. In this study, the effect of nebulized fentanyl has been compared with the IV administration of morphine in patients with acute pain due to limb trauma in the emergency department of Imam Khomeini Complex Hospital.

2. Methods

2.1. Trial design

This was a double-blind randomized clinical trial.

2.2. Participants

A convenience eligible sample of 90 fully cooperative patients aged 15 to 50 years presenting to the emergency department due to limb trauma with acute pain with Numerical Rating Scale (NRS) score above 5 were enrolled in the study. The numeric verbal scale ranges from 0 to 10, from no pain to most pain. After obtaining a written

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informed consent, patients were given a full instruction and reassurance about the process of their pain management and how to use the face mask.

2.3. Randomization

In this study, block randomization was used. Two sets of treatments were prepared and named package A (experimental) or package B (control). Block sizes were 2 by 2 (23 blocks of 4). Possible sequence for packages within each block was as follows: 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 23. At the end, blocks were set by using the generated sequence, and the packages within blocks were sequentially numbered from 1 to 90.

2.4. Allocation

Consecutive allocation was used in this study. The patients' sequences for allocation were generated by the triage time and date from 1 to 90. The caregiving team then matched the sequentially numbered identical packages from package 1 to package 90 to the consecutive patients, from patient 1 to patient 90.

2.5. Blinding

The size, content, and the sequence of treatment within blocks were masked and concealed from the participants, those administering the intervention, and those assessing the outcomes by the study supervisor. In the experimental treatment, 2 identical-labeled 10-cc syringes were placed, the first one contained fentanyl citrate with the label "nebulize 0.8 cc/kg in 2 to 3 minutes" and in the other syringe, normal saline as a placebo with the label "inject 0.1 cc/kg IV slowly." The control treatment also contained 2 identical 10-cc syringes, the first one contained normal saline as a placebo with the label of "nebulize 0.8 cc/kg in 2 to 3 minutes" and the other syringe contained morphine with the label "inject 0.1 cc/kg IV slowly."

2.6. Interventions

Patients were randomized to receive either nebulized fentanyl plus IV placebo or IV morphine plus nebulized placebo for their temporary pain management. In both groups, the nebulized drug was administered first, in 2 to 3 minutes depending on its dosage, followed by the slow injection of the IV drug in 2 minutes. The dose for nebulized fentanyl was 4 μg/kg from an IV solution with the concentration of 50 μg/mL, and the dose for IV morphine was 0.1 mg/kg from an IV solution with the concentration of 1 mg/mL. The placebo in both groups was normal saline.

Ultrasonic nebulizers were used in this study (Hikoneb home-type; Kare Medical and Analytical Devices Ltd, Ankara, Turkey [7]). The nebulizers had a high nebulizing performance and low-energy consumption and were capable of nebulizing a small amount of drugs (5-10 mL) in less than 5 minutes. The Continuous mode was selected during the nebulization period. In order to prevent fentanyl vapor accumulation in the experimental group, a highly sealed (disposable silicon) face mask in the well-ventilated room was used.

2.7. Outcome

An absolute reduction of pain score from the baseline in NRS was considered as the primary outcome of this study. All participants' pain

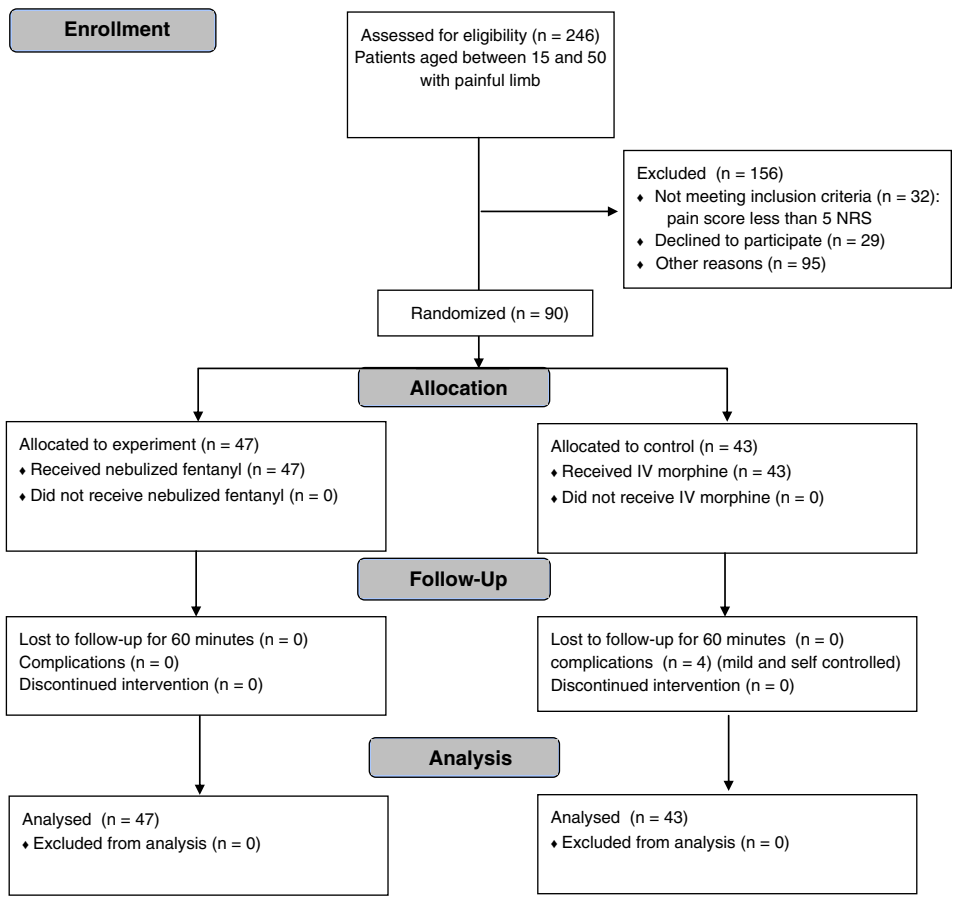

Fig. 1. CONSORT diagram of the study.