Intranasal Lidocaine in Acute Treatment of Migraine: A Randomized Controlled Trial

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Study objective: The study aims to evaluate the efficacy and safety of intranasal lidocaine administration for migraine treatment.

Methods: This single-center, double-blind, randomized, controlled trial was conducted in a tertiary care emergency department. Included patients met the migraine criteria of the International Headache Society. Patients were randomized to intranasal lidocaine or saline solution; all participants received 10 mg of intravenous metoclopramide. Patient pain intensity was assessed with an 11-point numeric rating scale score. The primary outcome measure was the change in pain scores at 15 minutes; secondary outcomes were changes in pain intensity after pain onset and need for rescue medication.

Results: Patients (n=162) were randomized into 2 groups with similar baseline migraine characteristics and numeric rating scale scores. The median reduction in numeric rating scale score at 15 minutes was 3 (interquartile range [IQR] 2 to 5) for the lidocaine group and 2 (IQR 1 to 4) for the saline solution group (median difference=1.0; 95% confidence interval 0.1 to 2.1). The reduction in pain score at 30 minutes was 4 (IQR 3 to 7) for the lidocaine group and 5 (IQR 2 to 7) for the saline solution group (median difference=1.0; 95% confidence interval 0.1 to 2.1). Need for rescue medication did not differ between the groups, and local irritation was the most common adverse event in the lidocaine group.

Conclusion: Although intranasal lidocaine was found no more efficacious than normal saline solution in our study, future studies should focus on patients who present earlier after headache onset. [Ann Emerg Med. 2016;■:1-9.]

Please see page XX for the Editor's Capsule Summary of this article.

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INTRODUCTION

Background

Headache is a frequent presentation to the emergency department (ED). The statistics on the prevalence and burden of headache disorders in the United States indicate that headache is the fourth leading cause of visits to the ED, accounting for 3.1% of all visits. In all ambulatory care settings, migraine accounts for 0.5% of all presentations.[1]

Current meta-analyses and systematic reviews reveal that abortive treatment of migraine consists of numerous medications, including triptans,[2] nonsteroidal anti-inflammatory drugs,[3-5] acetaminophen,[6] aspirin,[7] and antiemetics.[8] These medications are widely used in the acute treatment of migraine, but uncertainty remains in regard to the comparative efficacy of presently available drugs. Intranasal administration is now viewed as effective in the treatment of acute migraine because of its rapid effectiveness, lack of need for an injection site, and rare adverse reactions.[9]

Importance

The entire pathophysiologic mechanism of migraine and its therapeutic pathways is not clearly understood. Activation of the trigeminovascular system and central brain sites is one of the suggested mechanisms involved in migraine pathogenesis.[10] The sphenopalatine ganglion may have a pivotal role in the cranial parasympathetic outflow through the release of neuropeptides and may contribute to migraine pain by activating or sensitizing intracranial nociceptors.[10-12] Reducing this parasympathetic outflow to brain sites by blocking the sphenopalatine ganglion was previously studied as a migraine treatment using different application methods.[10,11,13] The sphenopalatine ganglion is located in an accessible region through both nostrils; thus, local

Editor's Capsule Summary

What is already known on this topic

Intranasal lidocaine may reduce pain from migraine headache.

What question this study addressed

In migraine patients receiving protocol-based analgesic care, did intranasal lidocaine reduce pain?

What this study adds to our knowledge

In this randomized clinical trial of patients arriving between 5 and 7 hours after onset, intranasal lidocaine performed similarly to placebo in reducing pain while causing additional local irritation.

How this is relevant to clinical practice

Better treatments are needed for the emergency department management of headache. Clinical trials of intranasal lidocaine are conflicting, but the treatment has biologic promise.

Research we would like to see

A larger randomized clinical trial focused on patients arriving earlier after headache onset.

anesthetics may affect the ganglion and prevent its signal transmission.[11,13]

The parasympathetic outflow theory suggests that early interventions affecting the sphenopalatine ganglion might be more beneficial when delivered through an intranasal route in early-presenting migraineurs.[14] In contrast, late presenters might not derive the same benefits if vasodilation and the effects on deep brain tissues involved in migraine attack have already occurred because peripheral nerve blocks might have no effect on pain control.

The efficacy of intranasal lidocaine versus placebo was evaluated in 3 randomized trials of migraine headache.[10,11,15] However, drug administration methods and outcome measures were different in each study and the results were conflicting.

Goals of This Investigation

The aim of the present trial was to investigate the efficacy and safety of an intranasal 10% lidocaine treatment compared with placebo for patients presenting to the ED with migraine headache and receiving intravenous metoclopramide as part of standard care. Also, we aimed to evaluate the relationship between pain onset and the efficacy of lidocaine.

MATERIALS AND METHODS

Study Design and Setting

This single-center, prospective, double-blind, placebo-controlled, randomized trial was carried out with patients with acute migraine attack. Results are reported according to the Consolidated Standards of Reporting Trials guideline. The study was conducted from January to October 2014 in an academic ED with an annual census of approximately 45,000 patients per year. The efficacy and safety of intranasal lidocaine were compared with those of intranasal normal saline solution in the acute treatment of migraine. This study was performed in accordance with the tenets of the Declaration of Helsinki, and institutional review board approval was obtained. Although this trial was not registered in a clinical trial database, the study protocol was previously declared to the institutional review board. The patients were asked to sign an informed consent form before their enrollment in the study.

Selection of Participants

Patients older than 18 years who presented to the ED with acute headache and who met International Headache Society criteria for migraine[16] were included in the study. Patients were excluded if they refused to give informed consent; had received any analgesic drug within 6 hours before the ED visit; had any hemodynamic abnormality, documented allergy to the study drugs, or meningismus symptoms; or were pregnant. Because most patients with pain do not receive any medication before an ED visit in Turkey, we specified any analgesic use within 6 hours as an exclusion criterion.

Interventions

The randomization schedule was generated with a computer-based program (http://www.randomization.com).[17] Eligible patients were randomly assigned in a 1:1 ratio to receive either a single intranasal dose of 10% lidocaine (Xylocaine 10% Pump Spray; Astra Zeneca İlaç San., İstanbul, Turkey) (1 puff=10 mg) or normal saline solution (1 puff of intranasal 0.9% saline solution spray). The placebo vial was prepared beforehand by a study nurse, and it was identical in appearance and color to the drug vial. If the patient had a unilateral headache, the study drug was administered as 1 puff in the ipsilateral nostril, in accordance with the Barre method.[10] Briefly, the patient was asked to lie supine, with the head dangling from the edge of the bed. The patient's head was turned 30 degrees toward the side with the headache, the application was performed with the patient in this position, and the patient was asked to hold the position for 30 seconds (Figure 1). If