The Journal of Emergency Medicine, Vol. 49, No. 3, pp. 326–334, 2015
Published by Elsevier Inc.

0736-4679/$ - see front matter

ELSEVIER

http://dx.doi.org/10.1016/j.jemermed.2015.03.023

Pharmacology in Emergency Medicine

# A RANDOMIZED CONTROLLED TRIAL OF INTRAVENOUS HALOPERIDOL VS. INTRAVENOUS METOCLOPRAMIDE FOR ACUTE MIGRAINE THERAPY IN THE EMERGENCY DEPARTMENT

Matthew E. Gaffigan, MD,* David I. Bruner, MD,† Courtney Wason, BS,* Amy Pritchard, DO,‡ and Kenneth Frumkin, MD, PHD*

*Naval Medical Center Portsmouth, Portsmouth, Virginia, †Naval Medical Center San Diego, San Diego, California, and ‡Naval Hospital Camp Pendleton, Camp Pendleton, California

*Reprint Address:* David I. Bruner, MD, Naval Medical Center San Diego, 8022 Paseo del Ocaso, La Jolla, CA 92037

☐ **Abstract—Background: Emergency Department (ED) headache patients are commonly treated with neuroleptic antiemetics like metoclopramide. Haloperidol has been shown to be effective for migraine treatment. Study Objective: Our study compared the use of metoclopramide vs. haloperidol to treat ED migraine patients. Methods: A prospective, double-blinded, randomized control trial of 64 adults aged 18–50 years with migraine headache and no recognized risks for QT-prolongation. Haloperidol 5 mg or metoclopramide 10 mg was given intravenously after 25 mg diphenhydramine. Pain, nausea, restlessness (akathisia), and sedation were assessed with 100-mm visual analog scales (VAS) at baseline and every 20 min, to a maximum of 80 min. The need for rescue medications, side effects, and subject satisfaction were recorded. QTc intervals were measured prior to and after treatment. Follow-up calls after 48 h assessed satisfaction and recurrent or persistent symptoms. Results: Thirty-one subjects received haloperidol, 33 metoclopramide. The groups were similar on all VAS measurements, side effects, and in their satisfaction with therapy. Pain relief averaged 53 mm VAS over both groups, with equal times to maximum improvement. Subjects receiving haloperidol required rescue medication significantly less often (3% vs. 24%, $p < 0.02$). Mean QTcs were equal and normal in the two groups and did not change after treatment. In telephone follow-up, 90% of subjects contacted were "happy with the medication" they had received, with haloperidol-treated subjects experiencing more restlessness (43% vs. 10%). Conclusions: Intravenous haloperidol is as safe and effective as metoclopramide for the ED treatment of migraine headaches, with less frequent need for rescue medications. Published by Elsevier Inc.**

☐ **Keywords—migraine; haloperidol; pain management**

## INTRODUCTION

### *Background*

Headache accounts for 2–5% of emergency department (ED) visits and is the fifth most common ED chief complaint (1). Current first-line ED therapies typically include a dopamine receptor antagonist like prochlorperazine or metoclopramide, often combined with diphenhydramine. Studies have shown these medications to be safe and more effective than opiates, nonsteroidal anti-inflammatory medications, and sumatriptan (2–5).

This study was presented at the American Academy of Emergency Medicine Scientific Assembly Resident Research Forum in February 2014, and it won first place. It was also presented at the Naval Medical Center Portsmouth local research competition for 2014 and won first place. It was then presented at a Navy-wide research competition and placed third.

The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States Government.

RECEIVED: 30 October 2014; FINAL SUBMISSION RECEIVED: 9 March 2015;
ACCEPTED: 24 March 2015

Haloperidol is another venerable dopamine antagonist, of the butyrophenone class. Like other neuroleptic antiemetics, haloperidol has been reported to be effective in the treatment of nausea and migraine headaches (5–9). When neuroleptics are used alone, side effects (most commonly akathisia) can limit their usefulness. The addition of i.v. diphenhydramine can help reduce this side effect (10,11).

*Importance*

Over the last several years, nationwide shortages of antiemetics have narrowed the range of therapies available to emergency physicians for treating headaches (12). The frequency of medication allergies, plus strong recommendations to forego opiate use for headaches further limit our options (13). A new, readily available, safe and effective option for ED migraine treatment would potentially benefit large numbers of patients.

*Goals of the Investigation*

Our goal was to compare the efficacy of intravenous haloperidol with intravenous metoclopramide (both in combination with diphenhydramine) for the treatment of acute migraine headache in the ED. The primary outcome measure was pain relief, measured using a visual analog scale (VAS). A difference in pain relief of 13 mm between the two groups was considered a priori to be clinically significant.

Secondary outcome measures included time to maximal pain relief; the use of rescue medication; VAS measurements of nausea, sedation, and anxiety/restlessness (akathisia); electrocardiographic Q-T intervals prior to and after treatment; and responses to a follow-up telephone questionnaire.

## MATERIALS AND METHODS

*Study Design and Setting*

We conducted a prospective, double-blinded, randomized, controlled trial on a convenience sample of patients presenting to the ED from June 2013 to February 2014 with a chief complaint of migraine headache. The medical center's Institutional Review Board approved this study. The design and analysis closely resembles that of Kostic et al., which compared prochlorperazine with sumatriptan for migraine relief in the ED (2).

The setting was the ED of a 360-bed U.S. Department of Defense teaching hospital with an emergency medicine residency and an annual census of 75,000 patients.

**Table 1. Inclusion Criteria (14)**

| Inclusion Criteria |
|---|
| Ages 18 to 50 years |
| At least two of the following: |
| Unilateral location |
| Throbbing character |
| Worsening pain with routine activity |
| Moderate to severe intensity |
| At least one of the following features: |
| Nausea or vomiting |
| Photophobia or phonophobia |

*Selection of Participants*

Adult patients ages 18–50 years, presenting with their typical migraine headache, were identified by the triage nurse or their assigned provider as potential subjects. Those meeting the Modified International Headache Society's criteria for migraine (Table 1) were offered participation by their treating physician or a research coordinator when present (2,14). Exclusion criteria are listed in Table 2.

*Interventions*

All subjects provided written informed consent. Patients declining enrollment received standard migraine therapy at the discretion of the treating physician. After informed consent was obtained, each subject had a peripheral intravenous (i.v.) catheter placed and a bolus infusion of 1000 mL of normal saline begun. A point-of-care whole blood electrolyte panel (Istat9; Abbott Point-of-Care, East Windsor, NJ) was drawn, a cardiac monitor was placed, and an electrocardiogram (ECG) completed. Female patients provided a urine sample for a point-of-care pregnancy test. Diphenhydramine 25 mg i.v. was administered, followed by the study medication. All parties were blinded as to the study medication administered: metoclopramide 10 mg i.v., or haloperidol 5 mg i.v. Both were given over 2 min. Subjects were assigned to one of the two arms by means of a random-numbers table generated and maintained by the pharmacy. Study medications were provided in identical coded syringes. Vital signs (blood pressure, pulse, respiratory rate, oral temperature, and oxygen saturation) were assessed at triage, during the course of care (per ED protocol), and prior to discharge. Per protocol, subjects were to remain on cardiac monitors throughout their ED stay, and a repeat ECG was to be completed prior to discharge.

*Methods of Measurement*

The time of study-medication delivery was considered Time 0. Pain, nausea, restlessness (akathisia), and sedation were each assessed via separate 100-mm nonhatched VAS presented to the subject at 0, 20, 40, 60, and 80 min.