Official Title: A Randomized, Placebo-Controlled, Double-Blind Study of the Effects of Magnesium Compared to Conventional Therapy on Acute Migraine

NCT05967442

Date: 9/10/2020

Study Protocol and Statistical Analysis Plan

Study Design and Setting

This study was a single-center, prospective, double-blinded, randomized-controlled, three-armed trial comparing magnesium, metoclopramide, and prochlorperazine for the treatment of migraine. This trial was conducted in a large, level 1 trauma, tertiary-care medical center ED near Chicago, Illinois from August of 2019 through March of 2020.

Selection of Participants

Patients greater than or equal to 18 years of age presenting to the ED with a chief complaint of migraine or headache while an ED pharmacist was present were eligible for inclusion in this study. Migraine diagnosis was determined by an ED physician after thorough examination to rule out migraine mimics or headache conditions where traditional migraine therapy would be deemed inappropriate. Patients were required to have the ability to provide informed consent. Exclusion criteria included pregnancy, a stated history of renal impairment, allergy or sensitivity to any of the study drugs, or receipt of any of the study drugs prior to Enrollment.

Interventions

Following assessment for study eligibility, patients were consented by the ED pharmacist. Patients were randomized to receive one of three study drugs (magnesium sulfate 2 g, metoclopramide 10 mg, or prochlorperazine 10 mg) via computer randomization. Study drug randomization and preparation was the responsibility of the IV room pharmacist who was not part of the study. The ED pharmacists, physicians, and nurses participating in administration of the medications were blinded to which drug was selected. Magnesium sulfate 2 g/50 mL D5W, prochlorperazine 10 mg/50 mL D5W, or metoclopramide 10 mg/50 mL D5W was then administered as an IV infusion over 20 min.

Measurements and outcomes

The primary outcome of this study was change in pain from baseline to 30 min after initiation of infusion. Pain was assessed by the ED pharmacist using the 11-point Numeric Rating Scale (NRS) and recorded on a data collection tool. NRS is a validated tool commonly used to measure different types of pain [15]. Secondary endpoints included change in pain score from baseline to 60 min and 120 min after initiation of infusion (as defined on a 11-point NRS), ED length of stay, and necessity for rescue analgesia at any time following the study drug administration. Safety endpoints included monitoring for common adverse effects related to the study drugs—primarily hypotension, flushing, akathisia, dystonia, nausea, vomiting, dizziness, drowsiness, or other self-reported adverse effects [16-18]. Patient baseline characteristics were also collected, which included patient-reported past medical history and analgesic use prior to presenting to the ED.

Analysis

A sample size of 264 subjects (88 subjects per treatment arm) was calculated to detect a difference of 1.4 points in the NRS between groups to achieve a power of 80% [19]. Statistical significance was defined a priori as $p < 0.05$, and normality was assessed using the Shapiro-Wilk test. Descriptive statistics were used for nominal data, while ordinal and categorical data were evaluated using Mann-Whitney U and Pearson's $\chi 2$, respectively. Between-group comparisons were made using one-way ANOVA and Kruskal-Wallis, as appropriate for all continuous data. A post hoc non-inferiority analysis of the primary endpoint was conducted using Welch's t-test with a non-inferiority margin of 1.4. Data analysis was performed through SAS software for Windows (Version 9.4).