MAGraine: Magnesium Compared to Conventional Therapy for Treatment of Migraines

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BACKGROUND

- **A migraine** is a chronic neurologic disease characterized by attacks of throbbing, often unilateral headache associated with photophobia, phonophobia, nausea, vomiting, and cutaneous allodynia[1]
- **Second most disabling neurologic condition:**
  - $27 billion cost due to loss of productivity in the United States (US) [1]
  - Over 1.2 million Emergency Department (ED) visits in the US [1]
- **Migraine in America Symptoms and Treatment Study:** 8.5% reported seeking medical attention at an ED or urgent care center in the previous 6 months
- Prompt and effective treatment improve patient outcomes and ED workflow
- Intravenous (IV) magnesium is an intracellular cation that may have a role in treatment of migraines by regulating vascular tone and affecting the function of serotonin[2]
- IV magnesium has been directly compared to placebo, metoclopramide, and prochlorperazine[2-3]
- To date, **no trial has evaluated all three agents** in a single population

STUDY OBJECTIVE

To compare the relative efficacy of magnesium, metoclopramide, and prochlorperazine in the treatment of headache and migraine in the ED

METHODS

IRB-approved, single center, prospective, double-blinded, randomized-controlled trial

Inclusion Criteria

- ≥ 18 years of age
- Presenting to ACMC ED
- Primary diagnosis of headache or migraine made by physician
- Treated in the ED from August 2019 to March 2020
- Able to provide informed consent

Exclusion Criteria

- Pregnancy—defined as a positive urine HCG
- Stated history of renal impairment
- Allergy or sensitivity to any study drugs
- Receiving QTc-prolonging medications
- Previously enrolled in this trial during a different patient encounter
- Absence of ED pharmacist

A total of **264 patients** were needed to detect a difference of **1.4 points** in pain scores to achieve a power of 80%. Due to enrollment termination related to COVID-19, **157 patients** were enrolled.

Statistical Analysis:

- **Normality:** Shapiro-Wilk test
- **Nominal:** Descriptive statistics
- **Categorical:** Chi Squared, Fisher's Exact test
- **Continuous:** One-way ANOVA, Kruskal Wallis
- **Statistical significance:** $p < 0.05$

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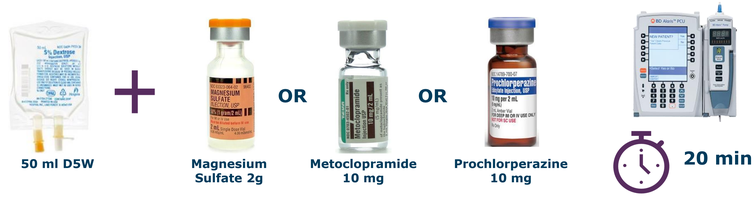
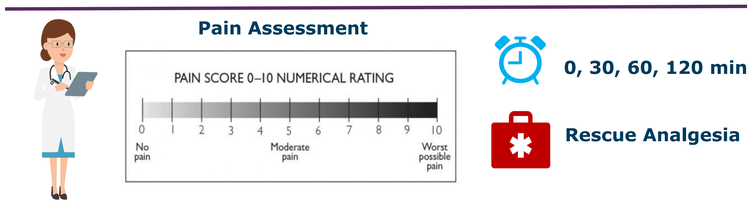
INTERVENTIONS





OUTCOMES

Primary Endpoints:

- Change in pain score from baseline to 30 minutes after initiation of infusion
  - **11-point Numeric Rating Scale (NRS)**

Secondary Endpoints:

- Change in pain score from baseline to 60 minutes and 120 minutes
- ED length of stay (LOS)
- Necessity for rescue analgesia

Safety Endpoints:

- Adverse events due to administration of study drug
  - **Magnesium:** hypotension, flushing
  - **Metoclopramide & prochlorperazine:** akathisia, dystonia, nausea, vomiting, dizziness, drowsiness
- Additional self-reported adverse effects

RESULTS

Table 1: Patient Baseline Characteristics

	Magnesium (n=61)	Metoclopramide (n=44)	Prochlorperazine (n=52)	p Value
Age, median (IQR)	34 (27-48)	37.5 (29.5-48)	37.5 (27-47.5)	0.67
BMI, median (IQR)	31.2 (25.5-35.9)	30.1 (26.2-34.4)	33.4 (26.5-36.2)	0.52
Female sex, No. (%)	44 (72)	33 (75)	46 (88)	0.09
Race, No.(%)				
White	30 (49)	23 (52)	14 (27)	0.02
Black	25 (41)	16 (36)	28 (54)	0.19
Comorbidities, No. (%)				
Hypertension				
Diabetes	15 (25)	10 (23)	15 (29)	0.78
Asthma	8 (13)	7 (16)	5 (10)	0.65
Migraine/Headache	4 (6.5)	6 (14)	7 (13)	0.39
Gastrointestinal	17 (28)	13 (29.5)	19 (36.5)	0.59
Disorders	5 (8)	5 (11)	4 (8)	0.79
Aneurysm/ICH	3 (5)	3 (7)	3 (6)	0.92
Depression/Anxiety	7 (11.5)	5 (11)	3 (6)	0.63
Aura, No. (%)	18 (29.5)	14 (32)	20 (38.5)	0.52

RESULTS

Figure 1: Median Pain Scores

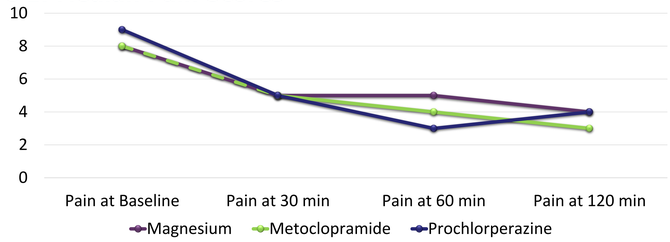


Table 2: Change in Median Pain Scores

	Magnesium (n=61)	Metoclopramide (n=44)	Prochlorperazine (n=52)	p Value
Change in Pain Score at 30 min, median (IQR)	-3 (1-4.25)	-3 (1-4)	-3 (1-5)	0.71
	Magnesium (n=56)	**Metoclopramide (n=37)**	**Prochlorperazine (n=39)**	**p Value**
Change in Pain Score at 60 min, median (IQR)	-4 (2-6)	-3 (2-5)	-4.5 (2-7)	0.27
	Magnesium (n=30)	**Metoclopramide (n=16)**	**Prochlorperazine (n=25)**	**p Value**
Change in Pain Score at 120 min, median (IQR)	-4 (2.25-7)	-4 (2-7.25)	-3 (3-7.75)	0.66

Table 3: Medication Administration

	Magnesium (n=61)	Metoclopramide (n=44)	Prochlorperazine (n=52)	p Value
Patient Reported Medication Administration Prior to Admission, No. (%)	29 (47.5)	19 (43)	24 (46)	<0.01
Received Medications in ED Prior to Study Drug, No. (%)	49 (80)	38 (86)	40 (77)	0.50
Need for Rescue Analgesia, No. (%)	26 (43)	15 (34)	17 (33)	0.50

Table 4: ED Length of Stay

	Magnesium (n=61)	Metoclopramide (n=44)	Prochlorperazine (n=52)	p Value
ED LOS (min), median (IQR)	325 (274-410)	308 (263.5-403)	332 (268.5-391)	0.84
Time from Study Drug Administration to Discharge (min), median (IQR)	139 (98-208)	122.5 (93-175)	140.5 (92.8-230.3)	0.39

Table 5: Adverse Events

	Magnesium (n=61)	Metoclopramide (n=44)	Prochlorperazine (n=52)	p Value
Total Adverse Events, No. (%)	3 (5)	2 (4.5)	6 (11.5)	0.51

CONCLUSIONS

- Primary endpoint: No difference in change in median pain scores at 30 minutes
- Prochlorperazine may have a greater effect at alleviating migraines at 1 hour
- Patients in the magnesium group required more rescue analgesia
- More adverse effects were seen in the prochlorperazine group

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