"Efficacy of Memantine compared to sodium Valproate as prophylactic treatment for Episodic Migraine" A controlled randomized pilot clinical trial

A controlled randomized clinical trial

NCT04698525

ID 74-19

Study Protocol document date: February 15, 2019.

Statistical Analysis Plan document date: January 15, 2020.

Informed Consent Form document date: February 15, 2019.

STATISTICAL ANALYSIS PLAN

Sample size calculation

Normal distribution model: $x=Z(^{c}/_{100})^{2}\, r(100\text{-}r)$. $n=^{N\,x}/_{((N\text{-}1)E^{2}+x)}$ $E=Sqrt[^{(N-n)x}/_{n(N\text{-}1)}]$.
With a margin of error of 5%, a confidence level of 95%, with a prevalence of migraine in the general population of the State of San Luis Potosi of 271800 with a distribution response of 15%.[19] The recommended sample size is 196 participants. Because a pilot study will be conducted, 10% of the sample size will be taken to make it representative, a sample size of 20 participants for each group is decided.[20]

Descriptive statistical analysis of the variables of interest will be performed. For continuous variables, analysis will be performed using the student's t-test. The number of participants (n) and the final analysis was calculated using R (56). Alpha, the probability of type 1 error was set to 0.05 and the power was set to 0.8 which resulted in the probability of a type 2 error of 0.2, given that we limited to 20 participants per treatment, delta was estimated with this restriction.

The aim of this study was to assess the efficacy of memantine and compared sodium valproate in the prophylactic treatment of migraine.

Study design

A single center, doble-blinded, controlled, randomized pilot clinical trial.
The present study was designed as a randomized, double-blind, controlled pilot trial. It was authorized by the Research and Ethic Committee in February 2019, with the ID 74-19 and register in Clinical Trials from INH with the NCT04698525.
The study was conducted from July 2019 to November 2020 at Neurology service at Hospital Central Dr. Ignacio Morones Prieto, San Luis Potosí, México.

Inclusion criteria

Men and women from 18 to 65 years old.
Diagnosis of migraine according to the ICHD-III of the IHS at least one year before the study.
To have at least 4-14 migraine attacks per month.
Not receiving prophylactic treatment for migraine
Sign informed consent

Exclusion criteria

Pregnant or lactating patients.
Patients with another type of non-migraine headache.
Allergy to Sodium Valproate and/or Memantine
Being a carrier of systemic disease (infectious, immunological, or metabolic processes) or cardiovascular (myocardial, coronary, or valvular disease) prevents their participation in the study.

Primary outcomes

The primary outcome was the difference in change from baseline in the monthly attack frequency at week 12 between the two groups (using migraine diary).

Secondary outcomes

1. Evaluate the response rate to treatment.
2. Evaluate migraine disability using MIDAS (Migraine Disability Assessment) before and after treatment.
3. Identify adverse effects to sodium valproate and memantine.

Statical analysis.

Statistical analysis

Descriptive statistical analysis of the variables of interest will be carried out.
For continuous variables, their research will be analyzed using the t-student test.
First, the number of participants (n) and the final analysis were calculated using R (56).
Alpha, the probability of a type 1 error was set to 0.05.
The power was set to 0.8, resulting in a type 2 error of 0.2.
Since we were limited to 20 participants per treatment, the delta was estimated with this restriction.
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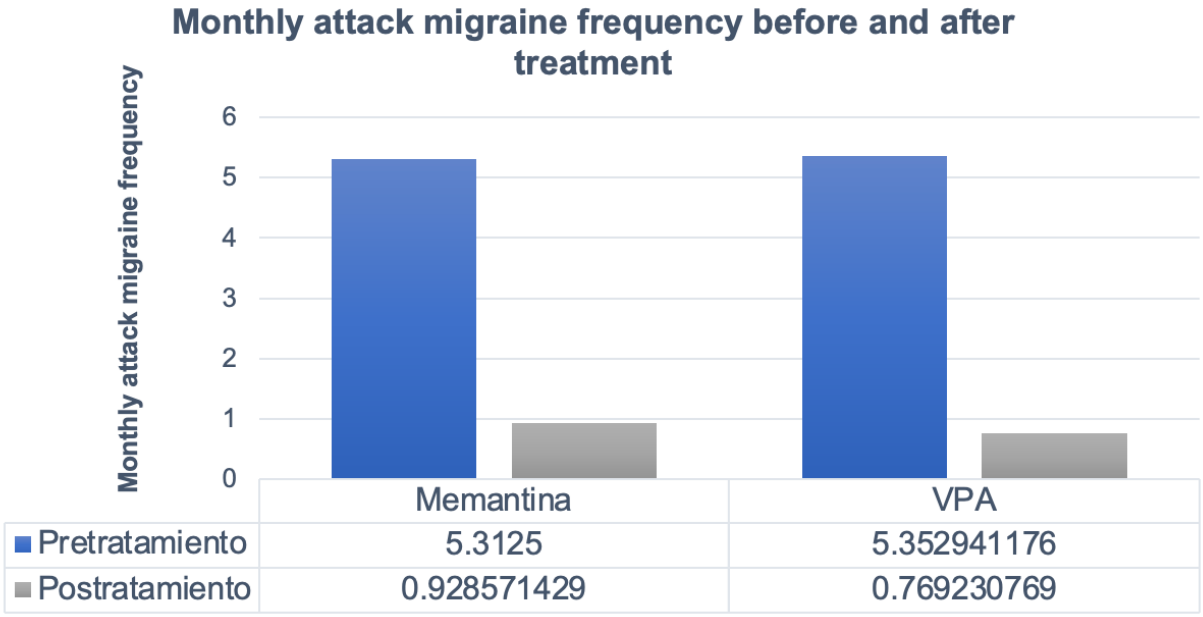
Results

Table 1. Baseline Demographic and Clinical Characteristics

Characteristic	Memantine	Sodium Valproate	*p*
Female sex – no (%) *Male sex – no (%)*	13(81.25%) 3 (18.75%)	13 (76.47%) 4 (23.52%)	0.54*
Age	31.18 ±10.94§	31.58 ± 7.51§	0.91*
A family history of migraine (%)	10 (62.5%)	9 (52.94%)	0.82*
Clinical characteristics			
Photophobia - no (%)	14 (87.50%)	16 (94.12%)	0.48*
Phonophobia - no (%)	16 (100%)	10 (58.82%)	0.60*
Nausea - no (%)	14 (87.5%)	17 (100%)	0.23*
Disability activities of daily living	15 (93.75%)	16 (94.12%)	0.74*
Migraine without aura	13 (81.25%)	13 (76.47%)	0.54*
Migraine with aura	3 (18.75%)	4 (23.52%)	

* Fisher's exact test
§ Plus–minus values are means ±SD

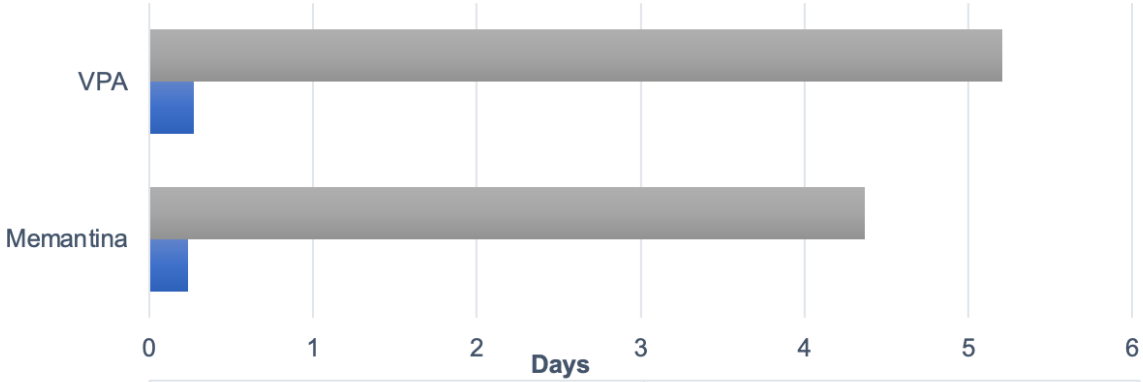
PRIMARY OUTCOME



Secondary outcome

Evaluate the response rate to the treatment

Figure 2. Days with migraine before and after treatment



	Memantina	VPA
Pretratamiento	4.36875	5.205882353
Postratamiento	0.237142857	0.27384615

Adverse Events

Table 2. Adverse Events According to Group

	Memantine (n=17)	Sodium Valproate (n=16)	Clinical severity CTCAE*
Any adverse event	8	7	
Somnolence	4	6	Grade 1-Mild
poor concentration	2	0	Grade 1-Mild
Parasomnia	0	1	Grade 1-Mild
Dizziness	2	0	Grade 1-Mild

CTCAE v5.0 Common Terminology Criteria for Adverse Events

Conclusions

This double blind randomized clinical trial is the only pilot study where Memantine is compared to Sodium Valproate as prophylactic treatment for migraine.
The response of both groups was dramatic and significant ($p< 0.05$) to the management they received, with a clear difference in the number of attacks, duration of four, intensity (EVA), and disability caused by the attack (MIDAS)
Memantine could be considered as a prophylactic treatment option in migraine.
The adverse events were frequent but mild and transient for both groups.