

Use of memantine in adults with migraine without aura

Hena Arif

Clinical Question

The clinical question this paper will aim to address is does the administration of memantine reduce the occurrence of migraines per month in adults with migraine without aura in comparison to placebo. The primary research article referenced in this paper consists of a randomized double-blind placebo-controlled study with a sample size of 60 in Tehran, Iran carried out by Tehran University of Medical Sciences referenced below. The aforementioned paper will be critically analyzed in order to deduce a clear recommendation to answer if memantine should be used in this setting.

Introduction

Migraine without aura is a recurrent headache disorder and is a common type of migraine which does not elicit any transient sensory changes or vision obstruction. This type of migraine does not start and stop with the headache and consists of different phases. Migraines are a leading cause of emergency visits to the hospital as well as outpatient care. It is a huge economic burden as well as a social burden for affected patients. There are a variety of medications being used for this condition which mainly consist of acute medication and preventative medication. Many of the common therapies used for migraines without aura have undesirable side effects or may cause fetal harm and with women being the majority of people affected, that is very inconvenient.

In recent years, however, the use of a drug called memantine for migraine prevention has been garnering a lot of popularity. Memantine is a glutaminergic NMDA receptor antagonist and noncompetitively binds to the receptor. Its use is deemed as an option for migraine prophylaxis and is thought to reduce migraine severity, length, and frequency compared to no treatment. This is desirable because memantine is thought to have minimal side effects such as dizziness, confusion, headaches, etc. and is also category B in pregnancy, deeming its use acceptable in pregnancy. Migraines are a substantial concern in healthcare and with memantine's unique mechanism and minimal side effect profile, it can be a promising intervention in this area.

Search Strategy

The search strategy to find the answer to this question involved searching on Google Scholar for a randomized controlled clinical trial focused on comparing memantine use in adults with migraine without aura compared to placebo with regards to reduction in migraine occurrence per month as the main efficacy parameter. An article with those criteria was chosen and analyzed for clinical and practical significance.

Critical Appraisal

The study is a randomized control trial which is the gold standard for comparing efficacy. The comparator was not an effective preventative medication itself and the sample size was small which weakens the study. The study was double blinded which adds to its authenticity and the method of blinding was explained extensively as well. Parameters such as sleep and quality of life were also improved in the treatment group, suggesting that the change may be of value to the patients. The duration of the study was short and unable to track long term effects. The sample size was 60 with 30 adults allocated in either the treatment or placebo group. The minimum number of migraines per month had to be more than two and the maximum number of migraines

was eliminated, broadening the eligibility criteria. There were also a few dropouts from each group.

The statistical tests run are least square regression analysis for continuous outcomes and logistic regression analysis for dichotomous outcomes which was apt for both outcomes. Regression analysis helps describe the impact between the predictor and outcome variables. A p-value of less than 0.05% was obtained deeming the reduction in migraine frequency clinically significant.

Also, to note was that the use of acute medication was greater in the treatment group with many subjects using triptans and some ergot derivatives while nobody in the placebo group used those medications. One thing to consider would be that acute medication could have also been controlled for or at least remained consistent among the two groups.

Impression of Study

This study is a decent and notable attempt in answering the research question presented. It is one of the few randomized controlled trials attempting to answer this question. The results do seem to be clinically significant, but there are inherent weaknesses embedded in the study. The study must be replicated with increased sample size and compared to an active comparator for a longer duration to deduce a stronger recommendation for the use of memantine. It may have been hard to get a big sample size for this research question. Out of 403 people, only 60 were eligible which may indicate the eligibility criteria may have been too stringent even though the requirements seemed reasonable.

The statistical tests performed were correct and the study was double blinded. There did not seem to be any biases present there. The parameters evaluated were also valid outcomes to judge migraine treatment.

Overall, the study sets a good base but requires a lot more validation. It indicates that there may be a link between the predictor and effector variable meaning memantine can possibly be used in this area but lacks certain qualities to be able to make a strong recommendation.

Clinical Recommendation

Based on the research done, memantine does seem to have the potential of being an effective and well tolerated preventative therapy for adults with migraine without aura. Although the study clearly needs replication, memantine still does seem to be a possible alternative for adults in reducing the migraine frequency and even duration per month compared to placebo. It can be used in individuals who cannot take or tolerate conventional preventative therapies such as pregnant patients. It can possibly be used in patients who have severe and frequent migraines and are not finding standard therapies effective. In short, memantine may be used for these groups of patients as there is some evidence of efficacy and safety proposed by this study. This study should be further investigated in order to give a stronger recommendation for the use of memantine in adults with migraine without aura.

References

Noruzzadeh R, Modabbernia A, Aghamollai V, Ghaffarpour M, Harichian MH, Salahi S, et al. Memantine for Prophylactic Treatment of Migraine without Aura: A randomized Double-Blind Placebo-Controlled Study. *Headache*. 2016 Dec 06; 56: 95-103

Mistry, VM, Morizio, PL, Pepin, MJ, Bryan, WE, Brown, JN. Role of memantine in the prophylactic treatment of episodic migraine: A systematic review. *Headache*. 2021 Aug 05; 61: 1207-1214

Mondia MWL, Espiritu AI, Bolaños ML, and Jr AAR. Memantine for Episodic Migraine: A Systematic Review and Meta-analysis. *Acta Medica Philippina*. 2021 May 28;