Pakistan Journal of Neurological Sciences (PJNS)

Volume 16 | Issue 1 Article 3

June 2021

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THE MIDAS SCORE AFTER MEMANTINE IN PATIENTS WITH MIGRAINE AT A TERTIARY CARE HOSPITAL.

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Date of submission: *August 28, 2020* ***Date of revision:*** *January 25, 2021* ***Date of acceptance:*** *February 04, 2021*

ABSTRACT

INTRODUCTION: Memantine has been suggested as a migraine prophylaxis therapy in some observational studies.

OBJECTIVE: To determine the mean change in MIDAS score after Memantine in patients having migraine.
SAMPLING TECHNIQUE: Non-probability, consecutive sampling.

Methods: This study was conducted in the Neurology department, Bolan Medical Complex Hospital, Quetta. January 2017 to January 2018. All patients in the outpatient department of Bolan medical complex hospital, Quetta, with the diagnosis of migraine were enrolled in the current study after informed consent.

RESULTS: A total of 68 patients with a mean age of 32.32 ± 8.44years were enrolled in the study. Gender distribution of the patients showed that most of the patients were female. Most of the patients had a duration of symptoms of >3± 2.11 years. Before starting treatment, the mean MIDAS score was age group 18-30 years 43.53 ± 13.36 and at the end of treatment was 9.86 ± 6.28 (P=0.005). 31-45 years age group before MIDAS score was 43.73 ± 8.83 and treatment after MIDAS score 9.31±3.36. The difference in MIDAS scores before and after treatment was assessed.

CONCLUSION: The current small cohort has been effective in predicting that the use of Memantine may lead to the improvement in MIDAS score regarding the management of Migraines; however, large-scale studies are needed to validate this current study's results further.

KEYWORDS: Migraine; Memantine; Headache; MIDAS

INTRODUCTION

Migraine is the second most common brain disorder [(1)]. According to a report by World Health Organization, migraine is ranked as 19th among all diseases causing disability[(1)]. Migraine and other benign recurrent headache disorders are major public health problems. They are associated with substantial personal suffering, disability, and societal expense [(2)].Moreover, Migraine is a common disease, and various therapeutic options are currently available[(2)]. The most commonly used treatments for migraines include triptans, analgesics like NSAIDS, ergot derivatives, and antiemetics. However, the recent advances have raised the bar and options. Ubrogepant, which is an oral calcitonin gene-related peptide (CGRP) receptor antagonist and monoclonal antibiotic receptor antagonist, has been showing significant improvement in symptoms in recent trials [(3, 4)]. Additionally, the Memantine had been recently introduced for the treatment of migraines [(5)]. It is an uncompetitive antagonist of N-methyl-D-aspartate (NMDA) receptors, approved in the USA and many countries worldwide to treat migraines [(5)]. It is currently administered twice daily as an immediate-release formulation, with a maximum recommended 20 mg/day [(6)]. Khalid S et al. conducted a study which described that after treatment of migraine for 3 months by Memantine, the mean Migraine Disability Assessment Scale (MIDAS) score was found to be 6.72 ± 6.41 vs. 39.52 ± 21.27, which was noted before starting the treatment (P= 0.00) [(7)]. As Memantine is a relatively newer drug and only a few studies are available in the literature regarding the role of Memantine for migraine

management [8]. Recently published studies have emphasized the role of Memantine for migraines with promising results [7-9]. The current study aims to observe the effects of Memantine on migraine management in a tertiary care hospital.

MATERIAL AND METHODS

After authorization from the institutional ethical board, all outpatient general neurology clinic patients diagnosed with Migraine were enrolled in the research study, and written consent was obtained. The inclusion criteria included patients with the diagnosis of migraine, patients with age groups 18-45. Exclusion criteria included patients already taking Memantine, patients with known psychiatric disorders, anti-depressants, and analgesics. Patients were assured regarding confidentiality for an anticipated better outcome. Patients fulfilling the inclusion criteria having migraines were assessed and were asked to fill MIDAS score [7-10]. After that, Memantine was started as 5mg for the 1st week, 10mg for the 2nd week, 15mg for the 3rd week, and 20mg for the 4th week. They were maintained at a dose of 20mg till the end of 3 months. All these patients were asked to maintain a headache diary. At the end of 3-months of treatment, they were asked for a MIDAS score again. The collected data, including age, gender, and duration of symptoms, were entered and analyzed accordingly using SPSS version 20 through its statistical program. Mean and standard deviation was calculated for quantitative variables like age, age at the time of diagnosis of migraine, and MIDAS score. Frequencies and percentages were calculated for qualitative variables like gender. Mean MIDAS score was calculated both before and end of the treatments, and student t-test was applied for comparison. Effect modifiers like age, gender, and duration since treatment were addressed through stratification using an independent sample t-test. P-value <0.05 was considered significant.

Results

Demographic:

A total of 68 patients were included in the study. The mean age of the patients was found to be 32.3 ± 8.3 years. Patients were further categorized according to age groups into 2 groups (18-30 years and 31-45 years). (Table 1) Most of the patient were female 61.8% (N= 42) compared to male 38.2% (N= 26). (Table 2) Most of the patients in the current study had a duration of symptoms of >3 years were 45 (66.3%), with the mean duration of symptoms in the overall cohort was found as 4.4 ± 2.1 years (Table 3).

Outcomes:

Within the age group of 18-30 years, the MIDAS score before the start of treatment was 43.53 ± 13.36, and at the end of treatment was 9.86 ± 6.28 (P=0.00). For the age group 31-45 years, the MIDAS score before the treatment started was 43.73 ± 8.83, and after the treatment, the MIDAS score was 9.31±3.36. The difference in MIDAS score before and after treatment was assessed, and it was stratified for age, gender, and duration of symptoms. All results are summarized in Table 4.

TABLE No. 1 Age DISTRIBUTION (N=68)

Age groups	No. of patients	%
18-30 Years	30	43.7%
31-45 Years	38	55.7%
Total	**68**	**100**
Mean ± SD	**32.3 ± 8.4years**	

Abbreviations: N= Number; SD= Standard deviation

TABLE No. 2 GENDER DISTRIBUTION (n=68)

Gender	No. of patients	%age
Male	26	38.2%
Female	42	61.8%
Total	**68**	**100**

Abbreviations: N= Number

TABLE No. 3 Distribution of patients according to duration of symptoms (N=68)

Duration of symptoms	No. of patients	%
<3 years	23	33.7%
>3 years	45	66.3%
Total	**34**	**100**
Mean+SD	**4.4 ± 2.1 years**	

Abbreviations: N= Number; SD= Standard deviation

Table 4: Means and SD Deviation Stratification of Difference in MIDAS score according to age groups, gender and duration of symptoms

	MIDAS score before treatment	MIDAS score after treatment	P-Value
Age groups			
18-30 Years	43.53 ± 13.36	9.86 ± 6.28	0.00
31-45 Years	43.73 ± 8.83	9.31 ± 3.36	0.00
Gender			
Male	50.96 ± 7.72	9.92 ± 4.85	0.00
Female	38.83 ± 9.81	9.28 ± 4.77	0.00
Duration since symptoms			
<3 years	49.00 ± 9.33	11.33 ± 4.83	0.00
>3 years	40.72 ± 10.72	8.59 ± 4.60	0.00

Discussion

Migraine is associated with economic burden, disability and poor quality of life. Despite these challenges majority of patients avoid or delay taking medications due to side effects and cost. (8-10) There are many options available for migraine prophylaxis with emerging data related to glutamate modulators. [11] Increased levels of glutamate in CSF of migraine patients suggest a pathophysiological link. Few open label studies have suggested Memantine (Glutamate N Methyl aspartate receptor antagonist) may be useful in migraine patients. [12-16] In one open label study of 60 patients more than half of patients showed 50% reduction in migraine pain frequency.[9] These studies are limited being non-randomized, unblinded with varying eligibility criteria and outcome measures. Use of valproate is associated with substantial side effects especially among women [13-14]. Topiramate and venlafaxine are also associated with many limiting side effects especially among young migraine patients. In our study, Memantine was associated with minimal side effects and its onset of action was brief (only 3 days) as compared to longer periods with other migraine prophylaxis agents. Additionally, being a category B risk for pregnancy it may be suitable for pregnant migraine sufferers. Our study has several limitations including sample size , lack of randomization and unblinded outcome assessment. Despite these limitations this is first study to our knowledge in Pakistan. Larger, randomized controlled studies are required to prove efficacy of this treatment in refractory migraine patients.

Conclusion

In our small cohort study, the Memantine has shown an excellent improvement in MIDAS score regarding the management of Migraine; however, the current study results need to be explored further with well-powered study and randomized control trials.

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Conflict of interest: Author declares no conflict of interest.
Funding disclosure: Nil

Author's contribution:
Ihsan ul Haq zarkoon; data collection, data analysis, manuscript writing, manuscript review
Wazir Akbar; data collection, data analysis, manuscript writing, manuscript review
Noor Ahmad Khosa; concept, data analysis, manuscript review