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ORIGINAL ARTICLE

Role of Memantine in the Management of Fibromyalgia: A Neuropharmacological Approach

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ABSTRACT

Background: Pharmacological treatment is one approach to managing fibromyalgia symptoms; however, selecting the appropriate medication is crucial to effectively minimizing patient discomfort**.**

Objective: To assess the role of memantine in the management of fibromyalgia.

Methodology: The study was ethically approved through the institutional review board. A cohort double blinded study was performed at Department of Neurology Services Institute of Medical Sciences, Services Hospital Lahore from 1st May 2023 to 31st October 2023. A total number of 200 patients were enrolled. The patients were confirmed cases of fibromyalgia and were within the age group of above 18 years. The diagnosis of fibromyalgia was done on the basis of clinical signs and symptoms. The patients were divided into two groups. Group memantine received maintenance dosage of memantine and group placebo (n=100) did not receive memantine. The patients who were receiving memantine got the dosage of 20 mg 1 tablet of 10 mg twice daily. The dose of 20 mg was titrated in a manner that patient received 5mg dose in week 1,10 mg in week 2, 15 mg in week 3 and 20 mg in week 4, continued as such till 12th week and were followed up for the outcomes. The follow-up of the patients (1st, 2nd week and at months) was planned up till a total of 3 month. A well-structured questionnaire was used for documenting the impact of the fibromyalgia through the administrated drug.

Results: The Fibromyalgia was found in 80% of the cases as severe (both groups cumulative) followed by 16% patients having moderate disease severity and only 2% with mild disease condition. There were majority of the females observed within groups with a number of 93% and 94% in group memantine and group placebo respectively. The mean age of the patients within both groups was 37.6±1.2 and 38.4±1.3 years. Around 84% of the total patients had an improvement in their disease condition.

Conclusion: Memantine administration improves the fibromyalgia condition and was observed to demonstrate positive outcomes in 84%of cases within 3 months as per FIQ scores.

Keywords: Role, Memantine, Management, Fibromyalgia, Neuropharmacological approach

INTRODUCTION

Fibromyalgia is considered as a highly common pain disorder which affects around more than 1-5% population globally. The symptoms are characterized by fatigue, sleep disturbance, insomnia as well as anxiety. There is various path of physiological mechanism which may result into the formation of fibromyalgia. Under the various mechanisms involved in the formation the abnormal signalling of the pain genetic predisposition and anomalies with the neuro-endocrine gland have been related with the formation of this disease.[1-4]

The treatment of fibromyalgia has been a highly focused area of research with several approved medications. These mediations success rate in terms of the efficacy of these drugs is yet to be investigated. Within various approaches of managing fibromyalgia, behavioral therapies, exercise, meditative therapy in addition to medication are commonly opted. The treatment of severe fibromyalgia cases where in chronic pain is formulated and initiates complexity is still under deep analysis and research.[5-7]

The management of fibromyalgia through pharmacological drugs is one of the methods for improving the symptoms. However, it is especially important to opt the appropriate medication for minimizing the patients associated clinical symptoms. As fibromyalgia is linked with depression therefore the use of anti-depressants has also been significantly researched.[8,9]

Under various drugs which have been used for the treatment of fibromyalgia, the applications of memantine have been suggestively studied in several articles including under various placebo control trials.[10] This study was designed to evaluate the efficacy of memantine in treating and clinically managing the fibromyalgia within patients of different ages. The results of this study guided roles and outcomes of administrating memantine for the benefits of the patients.

MATERIALS AND METHODS

The study was ethically approved through the institutional review board. A cohort double blinded study was performed at Department of Neurology Services Institute of Medical Sciences, Services Hospital Lahore from 1st May 2023 to 31st October 2023 over a period of 6 months. A total number of 200 patients were enrolled. The patients were confirmed cases of fibromyalgia and were within the age group of above 18 years. Sample size was generated by using 80% power of test, 95% confidence of interval and 5% margin of error with the prevalence of fibromyalgia taken as 33.3%.[11] The sample size calculator available on web was used for calculations. The patients were given an informed consent to approve before enrolling as participants. The patients who were below the age of 18 years and were undergoing treatment through medication for fibromyalgia and those who were receiving previous treatments were excluded from the study. Pregnant women as well as breast feeding mothers and hypersensitive patients to memantine were also excluded from the study. Those having any kind of co-morbidities related with liver kidney disease, immunological, respiratory or cardiovascular disease were also excluded. The diagnosis of fibromyalgia was done on the basis of clinical signs and symptoms. The patients were divided into two groups one which received the maintenance dosage: Group memantine (n=100) while the other were considered as placebos: Group placebo (n=100) and did not had memantine. The patients who were receiving memantine got the dosage in form of 20 mg 1 tablet of 10 mg twice daily. The dose of 20 mg was titrated in a manner that patient received 5mg dose in week 1, 10 mg in week 2, 15 mg in week 3 and 20 mg in week 4 (10 mg tablet twice daily) till 12th week and were followed up for the outcomes. The follow up of the patients (1st, 2nd week then monthly up to 3 months) was planned up till a total of 3 month. A well-structured questionnaire was used for documenting the impact of the fibromyalgia through the administrated drug. The positive outcome was based on improvement in the clinical variables from the baseline (in accordance with the weekly improvement) using FIQ20. The FIQ (10 question based) table was used for measuring the health status of patients suffering from fibromyalgia. The interpretations were made as 0-38 as mild effect while 39 -58 as moderate effect and59-100 as severe effect. Data was statistically analyzed by using SPSS-26.0 wherein Chi square tool was applied for interpreting the comparative results within drug administered and

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placebo group. P value less than 0.05 was considered as significant.

RESULTS

The fibromyalgia was found in 80% of the cases as severe (both groups cumulative) followed by 16% patients having moderate disease severity and only 4% with mild disease condition (Table 1). In the present study there were majority of the females observed within groups with a number of 93% and 94% in group memantine and group placebo respectively The mean age of the patients within both groups was 37.6±1.2 and 38.4±1.3 years. Majority of the cases were reported within the age group of 39-48 years. There was no significant variance within both groups demographic information (Table 2).

Within the memantine group in the first week, 14% of the severe cases showed improvement while there was no case showing improvement in the placebo group within the first week. However, at the follow up a significant increase in the memantine group was observed with 28% severe cases showing improvement in second week and 40% severe cases showing improvement at the first month. In the similar group, the improvement of the disease symptoms was also observed in 30% and 2% of mild and moderate cases respectively at second week and 42% and 4% of mild and moderate cases in the first month respectively. The improvement rate did not significantly improve in the later follow up of second month and third month of the memantine group. The insignificant improvement was observed with an all the follow-up placebo group (Table 3).

The present study results interpreted that around 84% of the total patients had an improvement in their disease condition with 11% having no effect of the drug while 5% those wherein the disease condition deteriorated (Fig. 1).

Table 1: Disease severity with the enrolled patients (n=200)

Disease Severity	No. of Patients	Percentage
Mild	8	4.0
Moderate	32	16.0
Severe	160	80.0

Table 2: Gender and age distribution within groups (n=200)

Parameter	Group Memantine (n=100)	Group Placebo (n=100)
Gender		
Males	7 (7%)	6 (6%)
Females	93 (93%)	94 (94%)
Age (years)	37.6±1.2	38.4±1.3
18-28	5 (5%)	2 (2%)
29-38	11 (11%)	13 (13%)
39-48	53 (53%)	51 (51%)
49-58	21 (21%)	24 (24%)
>59	10 (10%)	10 (10%)

Table 3: FIQ score improvement over time: baseline to 3-month follow-up

Follow ups	Group Memantine (n=100)			Group Placebo (n=100)			P value
	Mild	Moderate	Severe	Mild	Moderate	Severe	
1st Week	--	--	14%	2%	1%	--	<0.001
2nd Week	30%	2%	28%	3%	2%	2%	
1st Month	42%	4%	40%	2%	2%	1%	
2nd Month	40%	3%	40%	1%	1%	--	
3rd Month	40%	4%	40%	--	--	--	

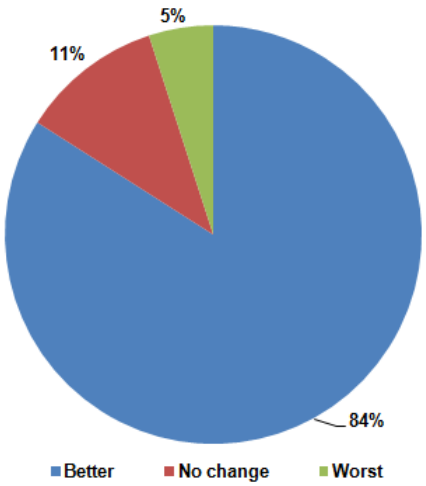

Fig. 1: Outcome of the drug efficacy

DISCUSSION

The current study aimed to assess the effectiveness of memantine in managing fibromyalgia symptoms. Previous research, including a randomized controlled trial involving 25 fibromyalgia patients, investigated the impact of memantine on brain metabolite levels. Results indicated that memantine administration led to increased cerebral glutamate metabolism and other metabolite activity, suggesting a possible therapeutic benefit in fibromyalgia.[12]

Numerous studies have evaluated N-methyl-D-aspartate (NMDA) receptor antagonists such as memantine, ketamine, amantadine, and dextromethorphan for their roles in treating neuropathic and chronic pain. One notable randomized controlled trial in Spain, lasting six months and involving 63 fibromyalgia patients who received 20 mg/day of memantine following a one-month titration period, showed significant improvements in pain severity, quality of life, overall functioning, and depression symptoms.[13-15]

In the present study, majority of the patients administered memantine reported better physical functioning by the final follow-up at three months. Additionally, 84% of patients experienced a reduction in pain and reported waking up feeling more refreshed. These patients indicated decreased difficulty in work-related tasks and less interference from fibromyalgia symptoms in daily activities. The same proportion also noted a reduction in stiffness. Furthermore, 60% of patients reported decreased fatigue and anxiety, and observed improvements in depression symptoms. Supporting these findings, a double-blind, randomized controlled trial conducted by Olivan-Blázquez[14] also highlighted the efficacy of memantine (20 mg/day post-titration) over a three-month period. Patients in that study showed notable improvements in cognitive function, depression, and overall health status.

In our trial, by the 2-week follow-up, 60% of patients already showed improvements in their Fibromyalgia Impact Questionnaire (FIQ) scores compared to baseline. By the end of 3 month, 84% had demonstrated progress in their FIQ scores. A statistical comparison between baseline and 3-month follow-up scores revealed a significant improvement indicating a highly significant effect. The comparable results have been reported in earlier studies.[15-18]

Importantly, a clinical study has consistently shown that memantine is well-tolerated, with a low incidence of adverse effects.[19] Our findings reinforce this, as no serious side effects were observed among participants throughout the trial.

CONCLUSION

Memantine administration improves the fibromyalgia symptoms and was observed to demonstrate positive outcomes in 84% of cases within 3 months as per FIQ scores.

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