EFFICACY OF MEMANTINE AS A PREVENTIVE AND THERAPEUTIC INTERVENTION FOR MIGRAINE AND TENSION TYPE HEADACHE

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ABSTRACT

Objective: To assess the efficacy of memantine as a preventive and therapeutic intervention for migraine and tension type headache. **Material and Methods:** This quasi experimental (pre and post experimental) was conducted for a period of 6 months. Patients were selected from a private tertiary care hospital setup a total of 44 patients receiving memantine, were selected through purposive sampling technique. Data was analysed using SPSS version 16.0 and associations were made using Chi square test with P value of less than 0.005 was taken as significant. **Results:** Out of 44 patients 35 (79.9%) were female and 9 (20.5%) were male which shows a very high occurrence of migraine and tension type headaches in females. Average age was found to be 32.6% Efficacy of the drug was observed to be 81.8% which is significantly high. The baseline MIDAS score when compared with score at 3 months follow up by applying Wilcoxon signed rank test showed mean ± S.D (39.52±21.27 vs. 6.72±6.41) where p=0.000 ≤0.005 which shows highly significant results. All 44 patients were known cases of migraine while 25% of them also suffered from tension type headache. Patients were treated on 10 mg dose of memantinea and were observed for the efficacy of the drug. Patients maintained their diaries of intensity of pain, distressing influence of pain and how it hindered their daily routine. Results show that intensity of pain fell significantly by the end of 3rd month of treatment while majority of the patients felt less distressed on their final follow up. By the end of the 3rd month the level of hindrance caused by the migraine pain in the daily routines of the patients also fell significantly. **Conclusion:** Memantine is effective as a preventive and therapeutic intervention for migraine and tension type headache.

INTRODUCTION

Memantine, an N-methyl D-aspartate (NMDA) receptor antagonist, works through its intrinsic blockade of afferent signals of pain transmission , known as the glutamate system, which is plays a major role in pathophysiology of tension type headaches (TTH) and migraine[1]. Memantine works as an uncompetitive low affinity open channel antagonist. Most importantly its dissociation rate is relatively faster so that it doe not accumulate in the synaptic channels hence does not interfere with normal synaptic transmission[2,3]. Thence can be used as an effective modality in prophylaxis and treatment for chronic pain disorders including chronic headaches and migraine. During the recent decade memantine has evolved as an revolutionary drug in treatment of chronic pain states[4]. Its efficacy as a neuroprotective drug has been demonstrated through various researches[5]. Studies have proven that menantine has its excellent effects on D2 receptors as well preventing its sensitization during a manic attack hence can be used as drug of choice for bipolar disorder.[6] Recent works are being done to evaluate it effectiveness in demented disorders such as Alzhiemers[7]. The aforementioned wide variety of uses in the field of medicine has greatly increased the interest of researchers in this revolutionary drug. Our area of interest is to find out efficacy of memantine in prophylaxis and treatment of migraine and tension type headaches as marked by decrease in frequency and increase in patients self reporting of symptomatology.

METHODS

This quasi experimental (pre and post experimental) was conducted in the year 2014 for time duration of 6 months . Patients were selected in a private setup tertiary care hospital . All statistical analyses were done using SPSS software version 16.0. A sample of 44 was calculated for this study by taking a confidence interval of 5 while 95% confidence level was considered with p≤0.005.

Inclusion Criteria:

All patients known to have migraine for more than 1 year

of duration and at least one migraine attack per month were included in the study. All patients above 15 years and below 65 years of age were included in the study.

Exclusion Criteria:

Patients on any other drug are not to be considered.

Table 1: baseline characteristic

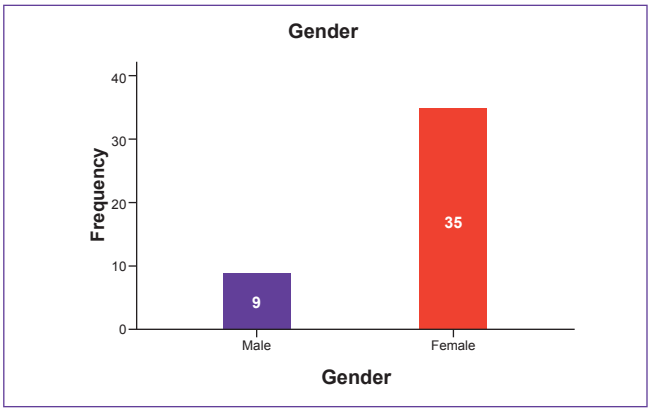
Variable	Frequency (%)	Mean ± S.D	Range(Min/max)
Gender			
Male	9 (20.5%)		
Female	35 (79.5%)		
Age		32.6±10.32	15/65
Efficacy	36 (81.8%)		
Diagnosis			
migraine	20		
migraine+TTH	(45.45%)		
migraine changing to seizures	11 (25%)		
others	3 (6.81%)		
	10 (22.7%)		
Missed work or school (no. of days)		6.81±7.15	0/30
Productivity at work/school reduced by half		6.88±5.52	0/20
Could not perform household chores		9.97±6.36	0/33
Productivity reduced by half in household work		10.52±6.06	3/32
Missed leisure activities		5.86±4.84	0/20
Average headache days		14.39±6.41	1/32

The proforma was well explained and self interviewed . Out of 44 patients, gender distribution of Male = 9 (20.5%) and Female= 35 (79.5%) . with chronic migraine and tension type headache were studied. At baseline , study patients were on regular memantine. We added memantine, 5mg per day with weekly increases of 5mg (up to a maximum of 20mg per day), as tolerated. The average dose of memantine was 19.25mg per day across all study patients and ranged from 10 to 20mg. Patients kept headache diaries for migraines and TTH, as well as pain scores. Evaluations were conducted after one month of therapy for those being treated with 20mg dose of memantine. For those on a lesser, maximally tolerated dose of memantine, evaluations were conducted after at least 1.5 to 2 months' therapy. The average length of treatment, including the initial titration of memantine dosage, was 6 months, with an average daily dosage of 19.25mg (ranging from 10 to 20mg/day). Dose of menantine was increased for acute migraine attacks management. For descriptive stasitics frequency and percentages were calculated while association was made using chi square.

RESULTS

All statistical analyses were done using SPSS software version 16.0. A sample of 44 was calculated for this study by taking a confidence interval of 5 while 95% confidence level was considered with $p \leq 0.005$.

Figure: 1



All 44 patients were known cases of migraine while 25% of them also suffered from tension type headache as shown in table 1. Patients were treated on 10 mg dose of memantine and were observed for the efficacy of the drug. Patients maintained their diaries of intensity of pain, distressing influence of pain and how it hindered their daily routine.

Table 2: Frequency of pain intensity, distress and interference at baseline and after 3 months follow up

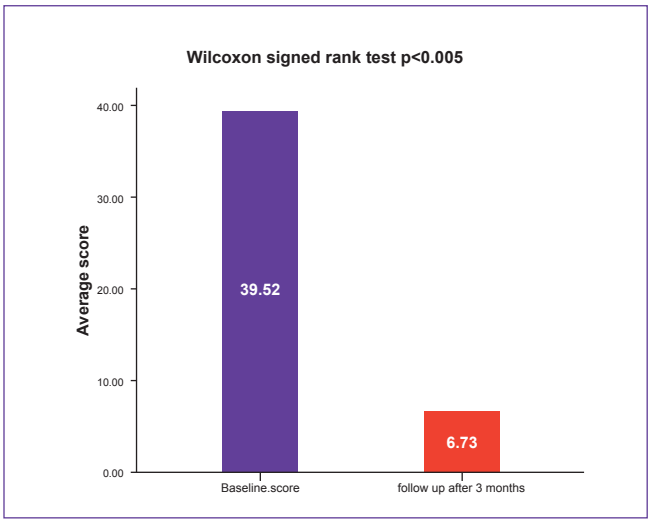
Variable	Frequency (%)
How intense is your pain now?	
Moderate pain	4 (9.1%)
Severe pain	15(34.1%)
Extreme pain	25(56.8%)
How intense was your pain on average last week?	
Moderate pain	13 (29.5%)
Severe pain	15 (34.1%)
Extreme pain	16 (36.4%)
How distressing is your pain now?	
Mild	2 (4.5%)
Moderate	6 (13.6%)
Severe	25 (56.8%)
Extreme	11 (25%)
How distressing was your pain on the average last week?	3 (6.8%)
Mild	7 (15.9%)
Moderate	25 (56.8%)
Severe	9 (20.5%)
Extreme	
How your pain interferes with your normal routines?	1 (2.3%)
Mild	12 (27.3%)
Moderate	26 (59.1%)
Severe	5 (11.4%)
Extreme	
At 3 months follow up: How intense is your pain now?	
No pain	1 (2.3%)
Mild	15 (34.1%)
Moderate	19 (43.2%)
Severe	8 (18.2%)
Extreme	1 (2.3%)
At 3 months follow up: How intense was your pain on the average last week?	
No pain	1 (2.3%)
Mild	11 (25%)
Moderate	18 (40.9%)
Severe	13 (29.5%)
Extreme	1 (2.3%)
At 3 months follow up: How distressing is your pain now?	
No distress	3 (6.8%)
Mild	14 (31.8%)
Moderate	20 (45.5%)
Severe	6 (13.6%)
Extreme	1 (2.3%)
At 3 months follow up: How distressing was your pain on the average last	

Results in table 1 show that intensity of pain fell significantly by the end of 3rd month of treatment while majority of the patients felt less distressed on their final follow up. By the end of the 3rd month the level of hindrance caused by the migraine pain in the daily routines of the patients also fell significantly. Out of 44 patients 35 (79.9%) were female and 9 (20.5%) were male which shows a very high occurrence of migraine and tension type headaches in females. Average age was found to be 32.6% Efficacy of the drug was observed to be 81.8% which is significantly high, only 20% of the patients required the increment of 5mg in the prior adjusted dose. The baseline MIDAS score when compared with score at 3 months follow up by applying Wilcoxon signed rank test showed mean ± S.D (39.52±21.27 vs. 6.72±6.41) where p=0.000 ≤0.005 which shows highly significant result (as shown in fig:2).

Table 3: Comparison of baseline scores with follow up after 3 months

Variables	mean±S.D	p-value
Baseline score vs. followup after 3 months	39.52±21.27 vs. 6.72±6.41	0.000

Figure:1



DISCUSSION

This study sought to explain the efficacy of memantine in the prevention and treatment of migraine and tension type headache. Studies have elucilated that memantine works by blocking N-methyl-D-aspartate (NMDA) glutamate receptors that are excitatory amino acids , play an intrinsic role in pain transmission,long-term potentiation and central sensitization. Therefore, blockade of NMDA helps in reducing the central barrage of afferent signals that might contribute to maintenance of migraine states. Agents whose activity, in part, impinges on the glutamate system are already in use for migraine prophylaxis[1] As compared to other similar researches the participants mainly comprised of females proving a worldwide female dominance in incidence of chronic migraine and tension type headache[7,1]. Our subjects were classified according to the type and nature of chronic tension headache. Comprising of migraine alone, migraine along with tension type headache, migraine changing to seizures and others in coherence to other researches[8]. An initial dose of 10mg memantine was started and the patients were asked to maintain a headache diary so this helps in keeping proper record and effectiveness of drug in every individual patients.[9]. As per patients self reporting in their headache diary the interference of pain with routine work markedly reduces in frequency from 59% to 40% (p<0.005). this was observed in other researches headache frequency was reduced from 21.8 days at baseline to 16.1 (P < .01) at 3 months10. When patients reported after 3 months follow up there was a significant reduction in frequency of occurrence of symptoms, statistically proven as 39.52±21.27 vs. 6.72±6.41 (baseline vs follow up).

CONCLUSION

Memantine is effective as a preventive and therapeutic intervention for migraine and tension type headache.

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Author's Contribution:
Dr. Sidra Sattar: Study concept and design, protocol writing, data collection, data analysis, manuscript writing, manuscript review
Dr. Bashir Soomro: Data collection, data analysis, manuscript writing, manuscript review