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COMPARISON OF THERAPEUTIC EFFECTS OF MIRTAZAPINE AND CITALOPRAM ON OUT-PATIENTS WITH MAJOR DEPRESSIVE DISORDER WITH ANXIETY SYMPTOMS

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ABSTRACT

Objective: The purpose of the present study was to evaluate the efficacy of Mirtazapine and Citalopram on depressive and anxiety symptoms of patients with Major Depressive Disorder (MDD) with anxiety symptoms. **Method**: In a double blind randomized clinical trial, 64 subjects with MDD with anxiety symptoms were selected by DSM-IV-TR criteria and were divided in two groups (one with 20-40mg/day Citalopram and another with 15-30mg/day Mirtazapine). They were assessed according to the Beck rating Scales for anxiety and depression in the weeks 0, 2, 4 and 8 after treatment and in every visit they were assessed by weight and side effects of medication. **Results**: There were no significant differences between two groups according to the Beck rating Scales for anxiety (p=0/81) and depressive in base line, (P=0.84). In both groups the decline in depressive and anxiety symptoms was significant after 8weeks (P=0.001). In comparison between two groups, Mirtazapine was more effective than Citalopram in decline depressive and anxiety symptoms and was faster on effect onset (P=0.001). There was no significant differences in two groups in side effects of medication, weight and sedation after 8weeks (P=0.72). **Conclusion**: This study showed Mirtazapine versus Citalopram was more effective with faster effect onset on MDD with anxiety symptoms.

KEYWORDS: Depression, Anxiety, Mitrazapine, Citalopram.

INTRODUCTION

Mood disorders are very common and lifetime prevalence rates of them are 17% to that 20% of women and 10% of men are affected. Overall, 15% of patients with mood disorders may have attempted suicide in mood disorders and other diseases is high and has been shown That two-thirds of depressed patients suffer from anxiety symptoms are Also prominent symptoms of anxiety in the clinical course of patients with depression may be.[1]

Depression is the result of biochemical changes in the brain. It has been shown that about 70% of depressed patients respond to antidepressant medication. The main criterion for choosing medicine is patient or the patient's family response to a particular drug. If this is not possible it will be decided based on beneficial effects on prescribed medication to the patient's. Classes of available drugs are Tricyclics, SSRIs, MAOI, Mirtazapine, Venlafaxine and etc.[2] Fifth that there should be no interactions are between drugs and toxic potential be lower and finally have appropriate antidepressant effect and wide for the patient.[3] Depressive disorder occurs with other psychiatric disorders frequently. Depressed people have concomitant disorders such as pain, hyperactivity disorder and PTSD along with depression but the most important disorder in depression is anxiety symptoms. Currently there are no adequate studies which had compared the therapies method of major depressive disorder with anxiety symptoms. Most treatments used for that are selective serotonin reuptake inhibitors.[1]

This class of drugs widely used to treat major depressive disorder, obsessive-compulsive disorder, panic disorder, generalized anxiety disorder and social anxiety disorder.[2]

These drugs in addition to high health benefits have side effects including gastrointestinal disorders and sexual dysfunction can cause that the second complication (sexual dysfunction) also does not improve over time, which can be a risk factor for continuation of treatment.[2] These drugs can also cause a transient increase in anxiety symptoms like restlessness and agitation and insomnia leading to lack of regular drug use.[2]

Mirtazapine is a tetracyclic piperazinoazepine compound that was approved in 1960 for depression. Mirtazapine has no effect on monoamine reuptake. Therapeutic effect of this drug is inhibition of Alpha-2 adrenergic receptors and blocked post synaptic 5HT-2 and 5HT-3 serotonin receptors. This mechanism leads to flare of Serotonergic noradrenergic neurons that

this function is different from other antidepressants. Inhibition of serotonin receptor leads to the relief of insomnia and increasing appetite. Mirtazapine acts as an antagonist of histamine receptor. Also reduces the side effects such as agitation and nausea.[2]

Treatment with Mirtazapine reduces nighttime awakenings and increases total sleep time that most patients with depression and anxiety disorders suffer from.[2]
No cases of seizures and cardiac arrhythmias have been reported in treatment with Mirtazapine. The dose of this drug is 15-30 milligrams. The drug's half-life is about 30 hours and food has little effect on it.[2] Studies have shown that patients, who have been treated with Mirtazapine, have won faster health benefits than other antidepressants.

Fang and colleagues randomized double-blind study, which was carried out in 150 patients comparing antidepressants Mirtazapine and the rest paid in China. Patients were treated with 225 mg / daily of Venlafaxine and 55 patients treated with 45 mg of Mirtazapine, and 45 patients were treated with 20 mg of Paroxetine. Patients in the second, fourth and eighth weeks were compared. At the end, a 50 percent reduction in the Hamilton score and improve in the overall performance of the patients was observed. Three drugs had no significant advantage over the other.[4] Studies Goodnick and colleagues (1999), Thompson and colleagues (1999) and Lynvnn (1999), Pancreatin (2000), Huang and colleagues (2003), Watanabe et al. (2011) and Kim et al (2011) also confirmed the effectiveness of treatment with Mirtazapine.[5-11]

Another study in 2005in Iran Roozbeh Hospital and was conducted by Aghayan and colleagues showed that the amount of Mirtazapine, the Hamilton depression scores reduced mor.[12]

Given the high prevalence of major depressive disorder and its association with anxiety symptoms and make function for patients, finding the most appropriate treatment is important.

Study about Mirtazapine is not too much the application of this medicine in Iran is limited. Hence, this study investigates thetherapeutic impact of this drug in depressed patients with anxiety symptoms through comparing this drug with a widely used drug Such as Citalopram in Iran till its effectiveness be investigated.

METHOD

In this randomized, double-blind study 52 patients admitted to the Akhavan medical center and private clinic of two psychiatrists cooperating the plan that According to DSM-IV-TR diagnostic criteria for major depressive disorder and based on score 16 or higher in Beck Anxiety Inventory was put to them were included in the plan. Inclusion criteria were as follows: Diagnosis of depression based on the Beck Depression Inventory and the Hamilton scale with anxiety symptoms on the Beck Anxiety Inventory and the Hamilton 13 and higher, age between 18 and 65 and having no physical disorder.

Exclusion criteria included bipolar disorder, schizoaffective disorder, suicide, homicide, drug use; take shock in the past month, the difficulty in the use of psychiatric medications, pregnancy and breastfeeding, planning pregnancy physically unstable conditions.

Patients were randomly divided into two groups and by three clinical psychologists were asked to complete scales of depression and anxiety briefings and evaluate patients at weeks zero, two weeks later, four weeks later, and eight weeks after the intervention.

After selecting patients Mirtazapine was given to a group of patients with an initial dose of 15 mg per day which finally came up to 30 mg, and to the other group Citalopram with initial dose of 20 mg per day was given came up to 40 mg per day And patients at baseline and at weeks 2, 4 and 8 were compared.

Study was approved by the ethical committee of the University of Social Welfare and Rehabilitation on Sunday, February 12th of 2012 with No. 801 / A / 2/21384 and with the clinical trials number of IRCT-2012101811155N1 was recorded in Iran clinical trial.

Informed consent was obtained of all patients participating in the study; Patients in the group treated with Mirtazapine were explained that the cost of treatment until 8 weeks is on responsibility of the investigator and after that it is assumed on the patient. Patients could be excluded by their desire whenever they wanted and the Patient's information would be confidential. Hamilton and Beck Anxiety and Depression Inventory were used for the assessment. Beck Depression Inventory includes 21 articles. It has four options, which are numbered from 0 to 3. Scores from zero to 9 indicates Normal 10 to 16 is moderate depression 17 to 29 is mild depression and 30 to 63 indicates severe depression. In a study back in 1988 and Garbin ratio between the number of runs and the type of credit terms of 48

to 86 varied test. In 1996 Beck et al. reported Retest reliability coefficient within a week 0.93. Average correlation with the Beck Depression Inventory, Hamilton Psychiatric Rating Scale, Zung Self-Rating Scale, MMPI depression scale is over 0/60. Ghasmemzadeh and colleagues reported reliability 0/87 and validity of the content 74/0.[13]

Beck Anxiety Inventory is a 21-point scale in 1988 by Beck was designed to measure the severity of anxiety symptoms. In a study in 2009 conducted on 150 patients with clinical anxiety it was found that the Beck test had the validity of 0/72 and reliability of 0/83 and internal consistency of 0/92. In this questionnaire zero goes to option 1, option 2 score one, option 3 score two and option 4 score three. No anxiety for score of 0 to 7, 8 to 15 mild, 16 to 25 moderate and 26 to 63 is severe.[14]

To increase the reliability of data the Hamilton anxiety and depression questionnaires were used along the two above tools. Each question in the questionnaire is a sign which is graded on a grading scale 0 or 0-4. Frequency of response is considered as an overall score. Touzendeh Jani reported the correlation coefficient of depression scale 0.65 and Gharaie (1994) have reported a factor of 0.85 perennial anxiety scales.[15-16] To assess the weight the same digital weight was used of.

RESULTS

In this study, 52 patients were studied that 8 men (15.4%) and 44 women (84.6) in the Citalopram group 3 males (37.5) and Mirtazapine 5 males (62.5%) respectively. Also the number of women in the Citalopram group was 25 (56.8%) in the Mirtazapine group was 19 (43.2%), respectively. There were no significant differences between the two groups in terms of sex distribution (P = 0.31).

The mean age was 8.37 ± 39.26 and the lowest was 20 and most 57 years old. The mean age of Mirtazapine was 5.47 ± 38.00 and in the Citalopram group it was 10.21 ± 40.35 and differences in age between the two groups was not significant (P = 0.31).

In terms of marital status, 10 were single (19%), 39 patients were married (75%) and 3 patients (6%) were divorced. Marital differences were not significant (p> 0.05).

In terms of educational status10 patients were under high school diploma (19%), 16 diploma (31%) and 10 patients (19 %%) higher than diploma and 10 people without a degree (19%) respectively. Differences in educational level between the two groups were not significant (0.78).

Each group was compared before and after treatment at week zero to 8. Mirtazapine and Citalopram treatment in both groups before and two weeks after the first week and two weeks after treatment, the difference in weight between non-significant (P = 0.16), but the rest of the items were statistically significant (P = 0.001).

Drug side effects

13 patients in Mirtazapine group had drowsiness of which by continuing treatment were drowsiness of 10 of them was resolved, and 6 patients also experienced an increase in appetite. in Citalopram group 3 people experienced, decreased libido, 2 people decreased appetite, one person feeling of restlessness, dizziness and blurred vision in 2 patients and one patient experienced drowsiness also significant differences between the two drugs, the side effects were not observed.

Table-1: Comparison of the pre and post-test scores of both groups

	Time	BDI	P	BAI	P	HAM-D	P	HAM-A	P	Weight	P
Mirtazapine	Pre test	32/75 (3/65)		37/45 (7/40)		30/58 (4/31)		31/95 (6/12)		67/76 (5/79)	
	Second week	24/16 (2/16)	0/000	26/58 (3/63)	0/000	22/66 (3/65)	0/000	23/08 (2/84)	0/000	67/70 (6/02)	0/16
	Fourth week	18/17 (3/89)		21/2 (3/88)		17/87 (3/48)		18/91 (4/53)		68/70 (5/5)	
	Eights week	17/83 (3/02)		19/41 (3/20)		17/25 (3/03)		17/58 (3/72)		68/08 (5/54)	
Citaloperam	Pre test	30/53 (5/14)		37 (6/28)		28/85 (5/37)		32/07 (5/19)		68/95 (9/42)	
	Second week	27/10 (5/39)	0/015	30/46 (5/43)	0/015	24/50 (5/10)	0/000	26/92 (3/62)	0/000	68/90 (9/41)	0/66
	Fourth week	24/67 (4/49)		27/39 (4/77)		22/39 (4/18)		24/5 (3/77)		68/81 (9/034)	
	Eights week	22/31 (3/60)		24/75 (4/48)		20/64 (3)		22/58 (3/75)		68/95 (19/54)	

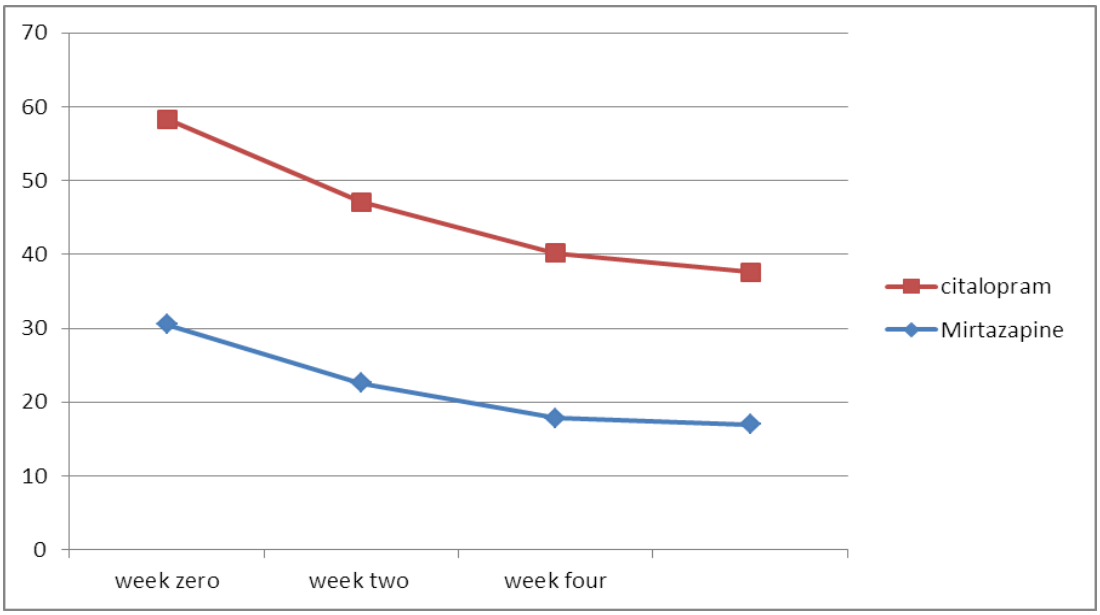

Figure 1: Reduction of scores of two treatment groups based on the Hamilton anxiety scale

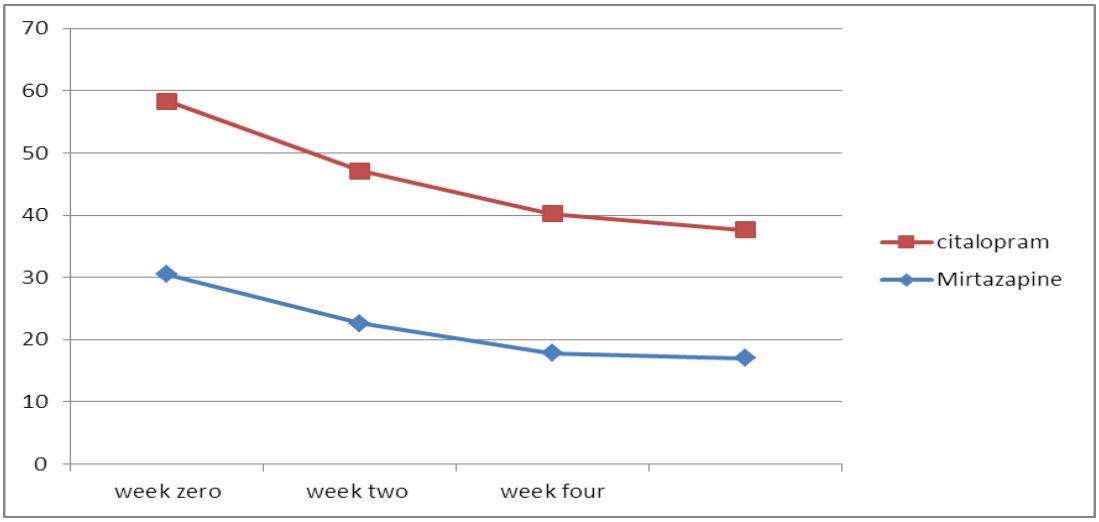

Figure 2: Reduction of the two treatment groups based on the Hamilton depression scale

DISCUSSION AND CONCLUSION

According to previous studies, we conducted this study to investigate the medication Citalopram and Mirtazapine in depressed patients with anxiety symptoms. Previous studies have shown that the effect Mirtazapine in terms of being an antidepressant is in tier of older antidepressant drugs such as Citalopram, paroxetine and venlafaxine (17-20). Other studies have also shown that it is more powerful anxiolytic drugs.[21]

In this study, patients were treated for 8 weeks. The results showed that both drugs reduced the Hamilton and Beck scores were obtained based on the criteria and the difference between the scores obtained before and after treatment of depression and anxiety in both groups was significant. But in comparison between Mirtazapine and Citalopram medication Mirtazapine significantly in the two weeks after the treatment was to reduce symptoms of depression and anxiety in patients that represents a faster response to treatment in the Mirtazapine group. also Mirtazapine showed that it is more effective in reducing symptoms in patients than Citalopram in 8 weeks for treatment And difference between Hamilton and Beck scores on measures in two, four and eight weeks after treatment in Mirtazapine group was significantly lower than that of Citalopram. The results of our study was consistent with of study Watanabe et al in 2011 in a study that compared the Mirtazapine and other antidepressant And Mirtazapine showed a faster effect and also being more effective with fewer side effects than other antidepressants.[9]

A study byn Gardner et al that compared the effects of Mirtazapine and the other antidepressants in adult patients showed that the Mirtazapine medication is more effective in reducing symptoms of depression and anxiety.[22] However, another study in 2008 by Kang et al comparing Mirtazapine and Venlafaxine in the treatment of major depression and somatic symptoms in patients with major depression showed that both drugs have similar effects and there is no significant difference between the two drugs.[23] Another study by Blair that also examined the effect of Mirtazapine and Paroxetine in Depression Indicated that Mirtazapine Mono therapy is less effective than the combination with Paroxetine and the combination of these two drugs is better tolerated.[24]

Antidepressants and anti-anxiety medications have side effects; this is also squeezed into because of nature of the performance. Studies have shown that a wide range of side effects that may occur from use of these drugs that has caused even some of these drugs are totally excluded.[25,31] Watanabe et al study showed that patients in Mirtazapine group had an increase in appetite, weight gain and drowsiness that was more than the SSRI drugs (9) that is similar to results obtained in our study.

In our study, in Mirtazapine group 13 patients had drowsiness of which were by continuing therapy drowsiness of 10 of them was resolved and 6 in have also had increase appetite. In Citalopram group 3 people experienced, decreased libido, 2 people decreased appetite, one person feeling of restlessness, dizziness and blurred vision in 2 patients and one patient

experienced drowsiness. The study of Hong also showed that both Fluoxetine and medication Mirtazapine are acceptable in terms of the side effects However, this study showed that nausea and influenza-like symptoms in Fluoxetine were more and symptoms of weight gain and drowsiness was more in Mirtazapine than Fluoxetine that was Similar to our results in terms of considerably rising of appetite and weight gain and drowsiness in the Mirtazapine group.[11] These results also were shown by the study of Zhelofy and colleagues. In their study they found that sleep problems are significantly greater than Venlafaxine in the treatment with Mirtazapine.[18] Watanabe study in 2010 comparing Mirtazapine and other antidepressants in the study showed that Mirtazapine is entirely appropriate and it is intolerable side effects and suggested that physicians can inform patients properly Patients in the low frequency of these events will encourage patients to use the drug. In this study, the most important side effects Similar to our study Increased appetite, fatigue and drowsiness was less common side effects such as constipation, nausea and vomiting however also been reported.[28]

From strengths of our study was that the Mirtazapine and Citalopram groups in terms of sex, educational level, marital status and weight at baseline did not vary significantly which indicates The appropriateness of the study design, matched properly, reduce the bias and precision study the results From the present study is to compare the two groups.

On the other hand, our study had a major limitation that causes the results have not the necessary generalization and that was the sample size was small. Another problem is that in use of drugs that are produced in different factories and different efficacy and side effects caused by the different needs of different and sometimes contradictory results from studies that reported from different countries. For this reason it is suggested that future studies from larger sample size to be used and prescribed drug in several study be construction of a unit factory So much to offer and compare the results with confidence and precision action.

CONCLUSION

In summary, our study showed that Mirtazapine compared with Citalopram in the treatment of anxiety and depression was the most rapidly effective and the treatment was effective. The significant difference between the two drugs, the side effects were not observed.

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