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A COMPARATIVE STUDY EVALUATING THE DEPRESSIVE SYMPTOMS AND FUNCTIONAL OUTCOME IN PATIENTS TREATED WITH SELECTIVE SEROTONIN REUPTAKE INHIBITORS V/S SEROTONIN–NOREPINEPHRINE REUPTAKE INHIBITORS AS ANTI-DEPRESSANT AGENTS IN MAJOR DEPRESSIVE DISORDER

Psychiatry

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KEYWORDS

INTRODUCTION

Being most common mental health disorder, Major depressive disorder, have affected approximately 350 million people all throughout the world at any time. In ranking among the cause of disability it has been ranked as major leading cause for disability in worldwide.(1) Major depressive disorder is debilitating disease and has and at least one individual depressive episode for minimum of two weeks and involves changed mood, decreased interest in surrounding and decreased pleasure specifically in activities which were earlier pleasurable along with changes in cognitive function and changes in vegetative symptoms(2). few of these patient might report guilt feelings and feelings of worthlessness or feeling of hopelessness, also patient reports of repetitive negative thoughts about individual self and their future(3). Taking consideration prevalence and the suffering, morbidity, dysfunction, and economic burden depression is major public health concern disorder. Depression being more common in women than men, report on global burden of disease suggests the point prevalence of unipolar depressive episodes is 1.9% for men and 3.2% for women, while the estimated one year prevalence to be 5.8% for men and 9.5% for women. Study says that if current trends for demographic and epidemiologic transitions continue by the year 2020, the burden of disease might increase up to 5.7% of total burden of the disease making it second leading cause of disability-adjusted life years (DALYs), second to ischemic heart disease.(4)

Selective serotonin reuptake inhibitors (SSRIs) and serotonin–norepinephrine reuptake inhibitors (SNRIs) are the first-line therapy for treating MDD because of their superior tolerability and safety profiles relative to monoamine oxidase inhibitors and tricyclic antidepressants.(6) Therapeutic application of these inhibitors is based on the monoamine hypothesis of depression. Unfortunately, over half of MDD patients do not achieve remission after a 12-week treatment with SSRIs. Studies have also shown that one-third of patients treated with successive antidepressant therapies do not achieve remission even after a 1-year intervention.(7) Thus in this study we attempt to examine the better treatment amongst two groups that can help to treat our patients and improve clinical outcome.

Aim and Objectives:

To study the effectiveness of SSRI and SNRI in treatment of Major Depressive Disorder. And to assess the clinical outcome and socio-demographic variables between the two groups.

Materials and Methods:

Prospective observational comparative study. Conducted on 90 willing participants of Major depressive disorder.

Sample Population:

Patients of Major depressive disorder visited the psychiatry Out Patient Department at Dhiraj Hospital. Both OPD and IPD patients were enrolled for the study. Two groups were divided, Group 1 was SSRI Group in which the patients SSRI were included and group 2 was SNRI Group the patients in this group were receiving SNRI as their primary anti-depressant agent. Inclusion Criteria includes: 1.Participants who are willing to give informed written consent for their participation. 2. Participants included between 18 to 60 years of age of both genders. 3.Patients who diagnosed as Major Depressive Disorder with Diagnostic and Statistical Manual fifth edition (DSM-V) by a trained psychiatrist receiving SSRI or SNRI as an anti-depressant agent. Exclusion Criteria includes: 1.Those participants who did not give written informed consent. 2.Patients having mental retardation or organic mental disorder. 3.Participants having serious debilitating medical or mental illness (as confirmed by clinical psychiatric interview).

METHODOLOGY:

Prior permission of Sumandeep Vidyapeeth Institutional Ethics Committee (SVIEC) has been taken to start the study. Prior written informed consent from participating patients had been taken. Patients were assured about confidentiality of their data & were explained to answer appropriately to the questions. Consecutives Patients (NEW Diagnosed) group having MDD and treatment naive were enrolled after confirming Inclusion and exclusion criteria from Psychiatric OPD and IPD setup, Dhiraj Hospital. Diagnosis of MDD was confirmed by SCID of DSM-V. All the patients and controls enrolled for study filled Performa containing demographic and other information and were assessed for severity of MDD and functioning using Hamilton Depression Rating Scale (HAM-D) and The World Health Organization Disability Assessment Schedule(WHODAS) at baseline, 6 weeks and 12 weeks.

RESULTS:

In the current study total 80 participants 40 from SSRI group and 40 from SNRI group were taken.

Socio-demographic Variables		SSRI group N=40		SNRI group N=40		Comparative Values
		No.	%	No.	%	
Age	Range	21-51		18-52		t=0.553, p=0.290
	Mean	35.77		34.98		
	SD	7.52		8.48		
Gender	Female	17	42.5	19	47.50	x2=0.043, p=0.603
	Male	23	57.5	21	52.50	
Marital Status	Married	25	62.5	23	57.5	x2=2.003, p=0.321
	Unmarried	12	30	15	37.5	
	Separated	2	5	1	2.5	
	Divorced	1	2.5	1	2.5	
Residence	Rural	25	62.5	27	67.5	x2=0.051, p=0.764
	Urban	15	37.5	13	32.5	
Occupation	Skilled	32	80	33	82.5	x2=7.373, p=0.041
	Semiskilled	5	12.5	7	17.5	
	Unskilled	1	2.5	0	0	
Type of Family	Joint	33	82.5	31	77.5	x2=0.987, p=0.452
	Nuclear	7	17.5	9	22.5	

The mean age in the SSRI group was 35.77 years with a SD of 7.52, while in the SNRI group the mean age 34.98 with a SD 8.48. No any statistically significant difference observed (p=0.290). In both the groups number of male patients were slightly higher than female patients with a ratio of 1.22:1. Considering marital status majority of the patients in both the groups were married only few patients were seprated/divorced. Regarding residential area more than half of the

patients were from rural area including 25 (62.5%) from SSRI group and 27 (67.5%) from SNRI group, who belonged to rural areas of Gujarat and Madhya pradesh and 15 (37.5%) from SSRI group and 13 (32.5%) from SNRI group belonged to urban area. Majority of the patients in both the group were skilled considering the occupational status. In SSRI group, there were 33 (82.5%) patients who belonged to joint family and 7 (17.5%) patients belonged to nuclear family. In SNRI group, there were 31 (77.5%) patients who belonged to joint family and 9 (22.5%) patients belonged to nuclear family. Majority of the patients in both the groups belonged to joint family. No statistically significant difference (x2=0.886, p=0.346) were observed between two groups.Patients were assessed for severity of depression and daily functioning at regular interval from their first visit to psychiatry department till 12 weeks.

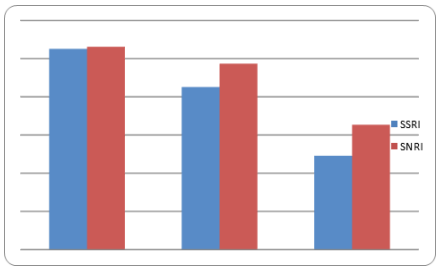

Figure 1 - Between groups analysis of HAMD score

Both the groups were assessed for their depressive symptoms using HAMD scale at baseline, 6 weeks and 12 weeks. At baseline HAMD scores in both the treatment arms were comparable. (P = 0.372). After 6 weeks there were significant improvement reported on HAMD scale in patients being treated with SSRI in comparison to patients in SNRI group(P = 0.001). However, by 12 weeks the difference in both the groups were much higher than before with a comparatively lower HAMD score in SSRI group in comparison to SNRI group (Figure 1).

Table 1 - HAMD scores on follow up

	SSRI Group		SNRI Group	
Visit	HAMD	P Value	HAMD	P Value
Baseline	26.28±3.11	0.000*	26.54±3.23	0.000*
6 weeks	21.28±3.65		24.34±4.21	
6 weeks	21.28±3.65	0.000*	24.34±4.21	0.000*
12 weeks	12.28±3.21		16.34±2.28	

Within group analysis showed that decrease in HAMD scores from baseline to subsequent visits in both arms was statistically significant (P < 0.0001). At the end of 12th week, the mean HAMD scores in both the groups were significantly decreased as compared to baseline showing improvement in depressive symptoms (P <0.0001) (Table 1).

Table 2 - Remission of depressive symptoms in both the groups

Visit	Remission	SSRI	SNRI	P value
6 weeks	Yes	12	8	x2 = 1.066 p value = 0.301
	No	28	32	
12 weeks	Yes	33	22	x2 = 7.04 p value = 0.007
	No	7	18	

Considering the remission rates after period of 6 weeks only 12 patients in SSRI group and 8 patients in SNRI group were found to have remission in depressive symptoms as defined as >50% improvement in HAMD scores, the difference was statistically found to be not significant. At the end of 12 weeks almost 33 patients out of 40 were found to have remission in SSRI group as compared to only 22 patients in SNRI group, with a statistically significant difference suggestive of better remission in depressive symptoms in patients treated with SSRI in comparison to SNRI treated patients.

Table 3 - Between group analysis of WHODAS score

Visits	SSRI	SNRI	P Value
Baseline	15.78 ± 3.18	15.88 ± 3.27	0.451
6 weeks	13.28 ± 3.09	14.38 ± 3.11	0.087
12 weeks	5.25 ± 2.67	9.25 ± 2.81	0.0001

Between groups comparison of WHODAS score showed that at baseline both the groups were having almost similar functioning (P = 0.451) while during the first follow up at the end of 6 weeks showed improvement in WHODAS scoring suggestive of better functional outcome. However at the end of 12 weeks follow up the functioning was comparable in both the groups and in SSRI group outcome was better in comparison to SNRI group with lower WHODAS score in SSRI than SNRI group (P <0.0001) (Table 3).

DISCUSSION:

The results from this pooled analysis show that patients treated with SSRI is superior in improving depressive symptoms and functional outcome than patients treated with the SNRI anti depressant agents. The SSRI treated patients had significantly lower HAMD scores at end of 12 weeks compared with the SNRI-treated patients, with a statistically significant value.

Kornstein et al., 2009 study showed, a pooled analysis of four RCTs comparing escitalopram, which is SSRI, to SNRIs found evidence for superiority of escitalopram in efficacy and tolerability(7), as did a pooled analysis of the two escitalopram versus duloxetine trials reported in the study by Lam et al., 2008(8). Kennedy et al. (2009) conducted a meta-analysis of all published escitalopram trials and found a significant advantage of escitalopram on the treatment difference in MADRS scores against all comparators (n=16 studies), SSRI comparators (n=12 studies) and SNRI comparators (n=4 studies). In that study the odds ratios in favour of escitalopram over SNRIs (venlafaxine XR and duloxetine) were 1.63 for response (P=0.0007) and 1.45 for remission (P=0.0088)(9). Which is similar to what results were obtained in the present analysis. Suggestive of that the superiority of SSRI compared with SNRIs in improving depressive symptoms on HAMD scale over 12 weeks of period.

However, a meta-analysis of MDD clinical trials conducted by Papakostas et al. (2007), who reported an number needed to treat of 24 for response with SNRI instead of SSRI treatment, and suggested that SNRI antidepressants may be more effective than SSRIs in the treatment of MDD(10). Supporting the same, a study by Martinez etal.,showed that the number of patients needed to treat to achieve QIDS-SR (Quick Inventory of Depressive Symptomatology) remission in one additional patient treated with duloxetine instead of an SSRI was 25, and the number needed to treat was 15 for one additional patient to respond. These results suggest that duloxetine, which is an SNRI agent, may have a modest advantage over the SSRIs included in this study in the treatment of MDD(11).

A study conducted by Nemeroff et al. showed an overall difference in remission rates of 5-9% favouring venlafaxine(12), also similarly a study conducted by Thase et al. reported a 7-3% difference favouring duloxetine over SSRIs(13). However in our study remission rates of SSRI was higher than SNRI showing higher improvement in depressive symptoms in patients treated with SSRI as compared to SNRI, which might be due to limitations of group study rather than considering individual drugs for the same. Considering the functional outcome SSRI group at the end of 12 weeks was found to have better functioning as compared to SNRI group which could be due to improvement in depressive symptoms severity and remission of the symptoms being higher in SSRI group than SNRI treated patient group.

Limitations of the study includes: (1) As this study has taken place in one hospital premises making it difficult to generalize the findings to other part of country. (2) Patients were followed for 12 weeks only, hence recurrence of the depressive episode could not be assessed. (3) Retrospective subjective questionnaire were used which might include chances of biases. (4) Treatment groups were taken rather than comparing individual drugs, specific drug cannot be commented upon.

CONCLUSION:

In present study it was found that patients treated with SSRI as their anti depressant agent had higher decrease in depressive symptoms as compared to SNRI groups, remission rates in SSRI groups were found to be higher than SNRI group. The SSRI group was found to have better functional outcome in comparison with SNRI group.

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