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Is Vilazodone Really the Answer to the Delay Associated with the Onset of Antidepressant Action of SSRIs? – A Randomised Control Trial

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Abstract **Aims and Objectives:** To assess and compare the onset of antidepressant actions of esitalopram, fluoxetine, sertraline and paroxetine with vilazodone. **Methodology:** One hundred and fifty patients diagnosed with Depression according to the DSM 5 criteria, seen in the Out-patient department of psychiatry at a tertiary care hospital, participated in the study after obtaining written and informed consent. Thirty patients each were randomly assigned to treatment with either of the following drugs: esitalopram, fluoxetine, sertraline, paroxetine and vilazodone. Montgomery Asberg Depression Rating Scale (MADRS) and Hamilton Depression Rating Scale (HAM-D) were applied on Day 1 to assess the baseline severity of Depressive features and again at week 1, week 2 and week 8 following initiation of treatment, to assess the extent of improvement, if any, along with onset of antidepressant action with various drugs. Results were tabulated using SPSS v20 and independent sample t tests were applied. **Results:** While all the drugs showed a decrease in depressive symptoms, Vilazodone was associated with significant differences between the day 1 and week 1 values of both MADRS and HAM-D scores as compared to other antidepressants in the study. **Conclusion:** The relatively faster onset of antidepressant action associated with Vilazodone can be useful in treating severe depression especially in those associated with suicidal tendencies and can thus be useful in achieving response and remission in patients suffering from Depression.

Keywords Vilazodone, Depression, MADRS, HAM-D

1. Introduction

According to the recent WHO 2017 statistics [1], approximately 300 million people suffer from Depression worldwide with females affected twice more commonly as compared to males. Prevalence of Depression varies worldwide – as high as 17% in the US to 9% in India [2]. The point prevalence of Depression in general out patients has been estimated to be 10%. The disability due to Depression has risen steadily with 2010 Global Burden of Disease study assigning it as the leading cause of disability, next only to HIV-AIDS [3]. This has prompted the World Health Organization (WHO) to include depression in the priority conditions listed in its Mental Health GAP action programme [4] (mhGAP) which aims to reduce the burden of selected mental illnesses.

The first antidepressants were Mono Amine Reuptake Inhibitors and Tricyclic Antidepressants, however the advent of Selective Serotonin Reuptake Inhibitor (SSRI) revolutionized the treatment of Depression and till date is the greatest discovery in the treatment of Depression. The introduction of SSRI markedly reduced suicide rates in both adults and adolescents, but they were not entirely free of burdensome side effects like increased sleep, gastric discomfort in the early stages and sexual adverse effects to name a few.

But the main drawback of SSRI agents is their delayed onset of action. An average of 2 weeks delay in the start of treatment with antidepressant agents and onset of clinical antidepressant action has been seen with almost all SSRIs, which forms the main setback of their clinical profile. This delay in the onset of action has been attributed to the time taken for the downregulation of somatodendritic 5HT1a receptors. With a view of developing a single drug which combines both the actions of 5HT1a agonism and SERT (Serotonin Transporter) antagonism, the molecule Vilazodone was developed (2011). Vilazodone shows partial agonism at the 5HT1a receptors which is why it is classified as Serotonin Partial Agonist Reuptake Inhibitor (SPARI) [5].

Studies conducted so far have been placebo control trials, comparing the efficacy of Vilazodone to placebo in the treatment of depression. This study aims to compare the antidepressant effect of Vilazodone with four of the SSRI antidepressant drugs – Esitalopram, Sertraline, Paroxetine

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and Fluoxetine with emphasis on the time taken for the onset of antidepressant action.

2. Methodology

The study was conducted on one hundred and fifty patients who visited the Outpatient department of Psychiatry at a tertiary care hospital located in western Uttar Pradesh which caters to a primarily rural and sub-urban population after obtaining approval form the Institute's Ethics Committee. Patients were diagnosed as suffering from depression on the basis of diagnostic criteria laid down by DSM-5, and only those who fulfilled these diagnostic criteria were included in the study. Patients were equally and randomly divided into five groups of thirty each to receive either of the five drugs: vilazodone, esitalopram, paroxetine, fluoxetine or sertraline. Patients were randomly assigned to each class after randomisation using paper chit method. Baseline values were noted on MADRS and HAM-D scales (day 1 scores) after which treatment with one of the above mentioned antidepressants was started. Follow up MADRS and HAM-D scores were taken after week 1, week 2 and lastly after week 8 of starting treatment. At the follow ups MADRS and HAM-D were administered to assess the efficacy and the relative onset of antidepressant actions of each drug.

The data was collected and entered in MS Excel. Data was analysed using SPSS 20.0 and statistical differences in proportion were calculated using the chi square test, t-test and ANOVA.

The results were explained in the form of baseline identification and socioeconomic parameters of the subjects in all five drug groups (vilazodone, esitalopram, paroxetine, fluoxetine and sertraline) in terms of descriptive and inferential statistics.

Descriptive statistics were explained by frequencies, mean, standard deviation and range for numeric variables and by proportions and percentages for categorical variables in (vilazodone, esitalopram, paroxetine, fluoxetine and sertraline) groups. Inferential statistics were done by applying statistical test for significance testing by t test for continuous variables, univariate analysis wherever applicable and with 95% confidence intervals and Chi-square test for proportions and categorical variables. Following the derivation of initial results, post hoc analysis was done using Dunnett's Test. In post hoc analysis, vilazodone was taken as the control (J drug) and the other four drugs (I drug) were compared against it.

Table 1. Table showing descriptive statistics of MADRS scores and test of significance for mean difference across all test drugs at various time intervals

Female		N	Mean	SD	Std. Error	95% CI of diff.		Sig.
						Lower	Upper	
MADRS Day1	Vilazodone	16	19.313	5.3006	1.3251	16.488	22.137	**P=0.142 Non sig.**
	Escitalopram	19	23.263	7.7878	1.7866	19.510	27.017	
	Fluoxetine	21	19.476	5.8704	1.2810	16.804	22.148	
	Paroxetine	20	19.850	5.7881	1.2943	17.141	22.559	
	Sertraline	19	17.895	5.8679	1.3462	15.066	20.723	
	Total	95	19.968	6.3236	.6488	18.680	21.257	
MADRS Week 1	Vilazodone	16	14.313	5.4371	1.3593	11.415	17.210	**P=0.005 Sig.**
	Escitalopram	19	21.421	6.6859	1.5339	18.199	24.644	
	Fluoxetine	21	18.714	5.3679	1.1714	16.271	21.158	
	Paroxetine	20	19.350	5.1122	1.1431	16.957	21.743	
	Sertraline	19	16.684	5.8410	1.3400	13.869	19.499	
	Total	95	18.242	6.0577	.6215	17.008	19.476	
MADRS Week 2	Vilazodone	16	12.625	4.7871	1.1968	10.074	15.176	**P=0.006 Sig.**
	Escitalopram	19	19.632	6.9219	1.5880	16.295	22.968	
	Fluoxetine	21	16.286	5.1102	1.1151	13.960	18.612	
	Paroxetine	20	16.450	4.7181	1.0550	14.242	18.658	
	Sertraline	19	14.316	6.1829	1.4185	11.336	17.296	
	Total	95	15.979	5.9537	.6108	14.766	17.192	
MADRS Week 8	Vilazodone	16	10.063	3.9407	.9852	7.963	12.162	**P=0.024 Sig.**
	Escitalopram	19	15.632	7.0806	1.6244	12.219	19.044	
	Fluoxetine	21	11.476	4.4791	.9774	9.437	13.515	
	Paroxetine	20	12.150	4.9659	1.1104	9.826	14.474	
	Sertraline	19	10.684	6.0466	1.3872	7.770	13.599	
	Total	95	12.053	5.6613	.5808	10.899	13.206	

Table 2. Table showing descriptive statistics of MADRS scores and test of significance for mean difference across all test drugs at various time intervals

Male		N	Mean	SD	Std. Error	95% CI of diff.		Sig.
						Lower	Upper	
MADRS Day1	V	14	24.786	8.7370	2.3351	19.741	29.830	P>0.05 Non Sig.
	E	11	21.636	8.0904	2.4393	16.201	27.072	
	F	9	19.444	7.5682	2.5227	13.627	25.262	
	P	10	27.400	5.7388	1.8148	23.295	31.505	
	S	11	18.727	9.1661	2.7637	12.569	24.885	
	Total	55	22.545	8.3927	1.1317	20.277	24.814	
MADRS Week 1	V	14	17.857	7.1775	1.9183	13.713	22.001	P>0.05 Non Sig.
	E	11	18.818	7.0826	2.1355	14.060	23.576	
	F	9	21.222	4.8933	1.6311	17.461	24.984	
	P	10	26.200	5.7504	1.8184	22.086	30.314	
	S	11	19.909	8.0555	2.4288	14.497	25.321	
	Total	55	20.527	7.1644	.9660	18.590	22.464	
MADRS Week 2	V	14	14.643	7.0122	1.8741	10.594	18.692	P>0.05 Non Sig.
	E	11	18.273	6.9439	2.0937	13.608	22.938	
	F	9	17.000	6.0000	2.0000	12.388	21.612	
	P	10	22.100	6.0083	1.9000	17.802	26.398	
	S	11	18.091	7.5955	2.2901	12.988	23.194	
	Total	55	17.800	6.9984	.9437	15.908	19.692	
MADRS Week 8	V	14	10.786	5.8727	1.5696	7.395	14.177	P>0.05 Non Sig.
	E	11	14.909	7.1757	2.1636	10.088	19.730	
	F	9	12.889	7.7370	2.5790	6.942	18.836	
	P	10	16.800	7.5982	2.4028	11.365	22.235	
	S	11	12.636	5.1434	1.5508	9.181	16.092	
	Total	55	13.418	6.7651	.9122	11.589	15.247	

Table 3. Table showing descriptive statistics and test of significance for mean of HAM-D scores across all test drugs at various time intervals

Female		N	Mean	SD	Std. Error	95% CI of diff.		Sig.
						Lower	Upper	
HAM-D Day1	V	16	16.625	3.3040	.8260	14.864	18.386	P=0.58 Non Sig.
	E	19	17.105	4.7480	1.0893	14.817	19.394	
	F	21	17.571	4.8639	1.0614	15.357	19.785	
	P	20	16.350	4.6029	1.0292	14.196	18.504	
	S	19	15.211	5.3601	1.2297	12.627	17.794	
	Total	95	16.589	4.6414	.4762	15.644	17.535	
HAM-D Week1	V	16	12.688	3.5160	.8790	10.814	14.561	P=0.026 Sig.
	E	19	15.789	4.6017	1.0557	13.572	18.007	
	F	21	17.190	4.5235	.9871	15.131	19.250	
	P	20	16.150	4.5105	1.0086	14.039	18.261	
	S	19	13.158	6.9463	1.5936	9.810	16.506	
	Total	95	15.126	5.1761	.5311	14.072	16.181	
HAM-D Week2	V	16	10.750	3.1728	.7932	9.059	12.441	P=0.022 Sig.
	E	19	14.263	4.8171	1.1051	11.941	16.585	
	F	21	15.286	4.1490	.9054	13.397	17.174	
	P	20	12.700	4.1180	.9208	10.773	14.627	
	S	19	12.158	5.3047	1.2170	9.601	14.715	
	Total	95	13.147	4.5848	.4704	12.213	14.081	
HAM-D Week8	V	16	8.250	2.7203	.6801	6.800	9.700	P=0.12 Non Sig.
	E	19	11.737	4.8171	1.1051	9.415	14.059	
	F	21	11.190	4.4454	.9701	9.167	13.214	
	P	20	9.500	4.4069	.9854	7.437	11.563	
	S	19	9.316	4.7382	1.0870	7.032	11.600	
	Total	95	10.074	4.4321	.4547	9.171	10.977	

Table 4. Table showing descriptive statistics of HAM - D scores and test of significance for mean difference across all test drugs at various time intervals

Male		N	Mean	SD	Std. Error	95% CI of diff.		Sig.
						Lower	Upper	
HAM-D Day1	V	14	20.357	6.0333	1.6125	16.874	23.841	**P=0.01 Sig.**
	E	11	16.091	5.2812	1.5923	12.543	19.639	
	F	9	16.111	2.0883	.6961	14.506	17.716	
	P	10	21.900	5.3635	1.6961	18.063	25.737	
	S	11	17.091	6.0902	1.8363	12.999	21.182	
	Total	55	18.436	5.6397	.7605	16.912	19.961	
HAM-D Week1	V	14	13.929	5.2545	1.4043	10.895	16.962	**P=0.005 Sig.**
	E	11	14.909	5.1856	1.5635	11.425	18.393	
	F	9	15.556	2.7437	.9146	13.447	17.665	
	P	10	21.200	5.0728	1.6042	17.571	24.829	
	S	11	16.273	5.9176	1.7842	12.297	20.248	
	Total	55	16.182	5.4674	.7372	14.704	17.660	
HAM-D Week2	V	14	11.357	4.6675	1.2474	8.662	14.052	**P=0.01 Sig.**
	E	11	14.273	5.4054	1.6298	10.641	17.904	
	F	9	12.333	2.8723	.9574	10.126	14.541	
	P	10	19.300	5.2504	1.6603	15.544	23.056	
	S	11	14.455	5.6633	1.7075	10.650	18.259	
	Total	55	14.164	5.4697	.7375	12.685	15.642	
HAM-D Week8	V	14	8.071	3.1247	.8351	6.267	9.876	**P=0.06 Non Sig.**
	E	11	11.364	6.0872	1.8354	7.274	15.453	
	F	9	9.000	3.8730	1.2910	6.023	11.977	
	P	10	13.100	5.2589	1.6630	9.338	16.862	
	S	11	8.636	4.3422	1.3092	5.719	11.553	
	Total	55	9.909	4.8161	.6494	8.607	11.211	

Table 5. Descriptive statistics and Test of significance of mean MADRS Score between Vilazodone and Escitalopram at various time intervals

MADRS Score	Drug	N	Mean	SD	SEM	Mean diff.	Sig.	95% CI of diff	
								Lower	Upper
Day 1	Vilazodone	30	21.867	7.5143	1.3719	-0.80	P=0.680	-4.7584	3.1584
	Escitalopram	30	22.667	7.8007	1.4242				
Week 1	Vilazodone	30	15.967	6.4513	1.1778	**-4.50**	**P=0.011**	-7.9340	-1.0660
	Escitalopram	30	20.467	6.8316	1.2473				
Week 2	Vilazodone	30	13.567	5.9113	1.0793	**-5.56**	**P=0.001**	-8.8711	-2.2623
	Escitalopram	30	19.133	6.8417	1.2491				
Week 8	Vilazodone	30	10.400	4.8608	.8875	**-4.96**	**P=0.002**	-8.0812	-1.8522
	Escitalopram	30	15.367	6.9999	1.2780				

Table 6. Descriptive statistics and Test of significance of mean MADRS Score between Vilazodone and Fluoxetine at various time intervals

MADRS Score	Drug	N	Mean	SD	SEM	Mean diff.	Sig.	95% CI of diff	
								Lower	Upper
Day1	Vilazodone	30	21.867	7.5143	1.3719	2.4	P=0.185	-1.1814	5.9814
	Fluoxetine	30	1.467	6.2903	1.1484				
Week 1	Vilazodone	30	15.967	6.4513	1.1778	**-3.5**	**P=0.025**	-6.5459	-.4541
	Fluoxetine	30	19.467	5.2767	.9634				
Week 2	Vilazodone	30	13.567	5.9113	1.0793	**-2.9**	**P=0.048**	-5.8340	-.0327
	Fluoxetine	30	16.500	5.2964	.9670				
Week 8	Vilazodone	30	10.400	4.8608	.8875	-1.5	P=0.27	-4.1958	1.1958
	Fluoxetine	30	11.900	5.5482	1.0130				

Table 7. Descriptive statistics and Test of significance of mean MADRS Score between Vilazodone and Paroxetine at various time intervals

MADRS Score	Drug	N	Mean	SD	SEM	Mean diff.	Sig.	95% CI of diff	
								Lower	Upper
Day 1	Vilazodone	30	21.867	7.5143	1.3719	-.50	P=0.78	-4.1863	3.1863
	Paroxetine	30	22.367	6.7286	1.2285				
Week 1	Vilazodone	30	15.967	6.4513	1.1778	**-5.6**	**P=0.001**	-8.9313	-2.4020
	Paroxetine	30	21.633	6.1783	1.1280				
Week 2	Vilazodone	30	13.567	5.9113	1.0793	**-4.7**	**P=0.002**	-7.7819	-1.7514
	Paroxetine	30	18.333	5.7556	1.0508				
Week 8	Vilazodone	30	10.400	4.8608	.8875	**-3.3**	**P=0.026**	-6.1932	-.4068
	Paroxetine	30	13.700	6.2486	1.1408				

Table 8. Descriptive statistics and Test of significance of mean MADRS Score between Vilazodone and Sertraline at various time intervals

MADRS Score	Drug	N	Mean	SD	SEM	Mean diff.	Sig.	95% CI of diff	
								Lower	Upper
Day 1	Vilazodone	30	21.867	7.5143	1.3719	3.6	P>0.05	-.1133	7.4466
	Sertraline	30	18.200	7.1071	1.2976				
Week 1	Vilazodone	30	15.967	6.4513	1.1778	-1.9	P>0.05	-5.3219	1.5219
	Sertraline	30	17.867	6.7861	1.2390				
Week 2	Vilazodone	30	13.567	5.9113	1.0793	-2.1	P>0.05	-5.4425	1.1758
	Sertraline	30	15.700	6.8589	1.2523				
Week 8	Vilazodone	30	10.400	4.8608	.8875	-1.0	P>0.05	-3.7436	1.7436
	Sertraline	30	11.400	5.7211	1.0445				

Table 9. Table showing results of Dunnett's Test applied on MADRS scores across all test drugs at various time intervals in females

MADRS Score Female	(I) Drug	(J) Drug	Mean Difference (I-J)	Sig.
Day 1	Escitalopram	Vilazodone	3.9507	.185
	Fluoxetine	Vilazodone	.1637	1.000
	Paroxetine	Vilazodone	.5375	.997
	Sertraline	Vilazodone	-1.4178	.895
Week 1	**Escitalopram**	**Vilazodone**	**7.1086***	**.002**
	Fluoxetine	Vilazodone	4.4018	.071
	Paroxetine	Vilazodone	5.0375*	.034
	Sertraline	Vilazodone	2.3717	.536
Week 2	**Escitalopram**	**Vilazodone**	**7.0066***	**.001**
	Fluoxetine	Vilazodone	3.6607	.156
	Paroxetine	Vilazodone	3.8250	.136
	Sertraline	Vilazodone	1.6908	.772
Week 8	**Escitalopram**	**Vilazodone**	**5.5691***	**.012**
	Fluoxetine	Vilazodone	1.4137	.837
	Paroxetine	Vilazodone	2.0875	.592
	Sertraline	Vilazodone	.6217	.990

Table 10. Table showing results of Dunnett's Test applied on MADRS scores across all test drugs at various time intervals in males

MADRS Score Male	(I) Drug	(J) Drug	Mean Difference (I-J)	Sig.
Day 1	Escitalopram	Vilazodone	-3.1494	.753
	Fluoxetine	Vilazodone	-5.3413	.366
	Paroxetine	Vilazodone	2.6143	.863
	Sertraline	Vilazodone	-6.0584	.212

Week 1	Escitalopram	Vilazodone	.9610	.991
	Fluoxetine	Vilazodone	3.3651	.624
	Paroxetine	**Vilazodone**	**8.3429***	**.017**
	Sertraline	Vilazodone	2.0519	.881
Week 2	Escitalopram	Vilazodone	3.6299	.509
	Fluoxetine	Vilazodone	2.3571	.849
	Paroxetine	**Vilazodone**	**7.4571***	**.038**
	Sertraline	Vilazodone	3.4481	.554
Week 8	Escitalopram	Vilazodone	4.1234	.377
	Fluoxetine	Vilazodone	2.1032	.886
	Paroxetine	Vilazodone	6.0143	.114
	Sertraline	Vilazodone	1.8506	.908

Table 11. Table showing results of Dunnett's Test applied on HAM – D scores across all test drugs at various time intervals in males

HAM – D Male	(I) Drug	(J) Drug	Mean Difference (I-J)	Sig.
Day 1	Escitalopram	Vilazodone	-4.2662	.168
	Fluoxetine	Vilazodone	-4.2460	.212
	Paroxetine	Vilazodone	1.5429	.903
	Sertraline	Vilazodone	-3.2662	.383
Week 1	Escitalopram	Vilazodone	.9805	.972
	Fluoxetine	Vilazodone	1.6270	.878
	Paroxetine	**Vilazodone**	**7.2714**	**.004**
	Sertraline	Vilazodone	2.3442	.627
Week 2	Escitalopram	Vilazodone	2.9156	.414
	Fluoxetine	Vilazodone	.9762	.976
	Paroxetine	**Vilazodone**	**7.9429**	**.001**
	Sertraline	Vilazodone	3.0974	.360
Week 8	Escitalopram	Vilazodone	3.2922	.250
	Fluoxetine	Vilazodone	.9286	.974
	Paroxetine	**Vilazodone**	**5.0286**	**.039**
	Sertraline	Vilazodone	.5649	.995

Table 12. Table showing results of Dunnett's Test applied on HAM – D scores across all test drugs at various time intervals in females

HAM – D Female	(I) Drug	(J) Drug	Mean Difference (I-J)	Sig.
Day 1	Escitalopram	Vilazodone	.4803	.994
	Fluoxetine	Vilazodone	.9464	.923
	Paroxetine	Vilazodone	-.2750	.999
	Sertraline	Vilazodone	-1.4145	.768
Week 1	Escitalopram	Vilazodone	3.1020	.200
	Fluoxetine	**Vilazodone**	**4.5030**	**.026**
	Paroxetine	Vilazodone	3.4625	.124
	Sertraline	Vilazodone	.4704	.995
Week 2	Escitalopram	Vilazodone	3.5132	.066
	Fluoxetine	**Vilazodone**	**4.5357**	**.009**
	Paroxetine	Vilazodone	1.9500	.470
	Sertraline	Vilazodone	1.4079	.734
Week 8	Escitalopram	Vilazodone	3.4868	.064
	Fluoxetine	Vilazodone	2.9405	.133
	Paroxetine	Vilazodone	1.2500	.791
	Sertraline	Vilazodone	1.0658	.870

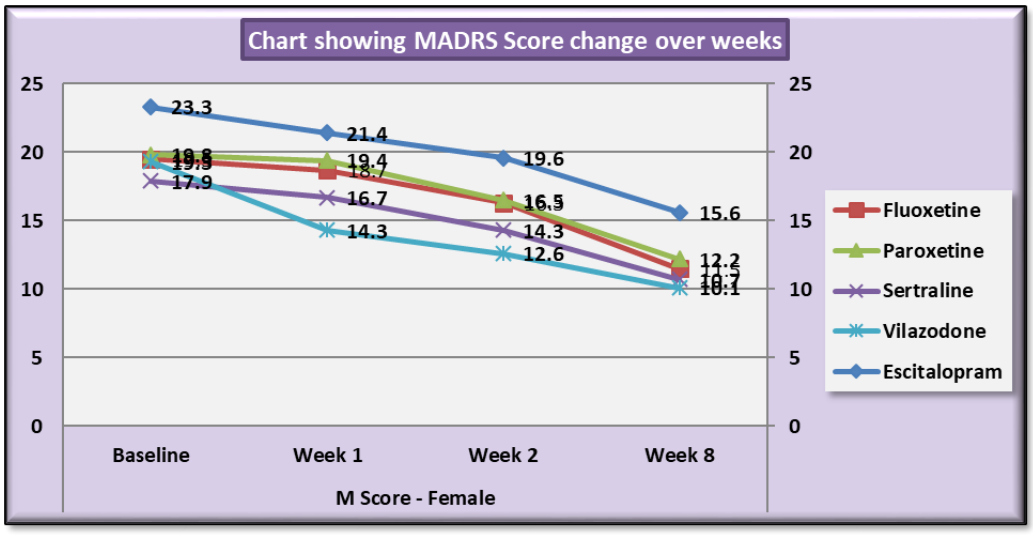

Chart 1. Line Graph showing changes in mean MADRS score during the course of the study in females

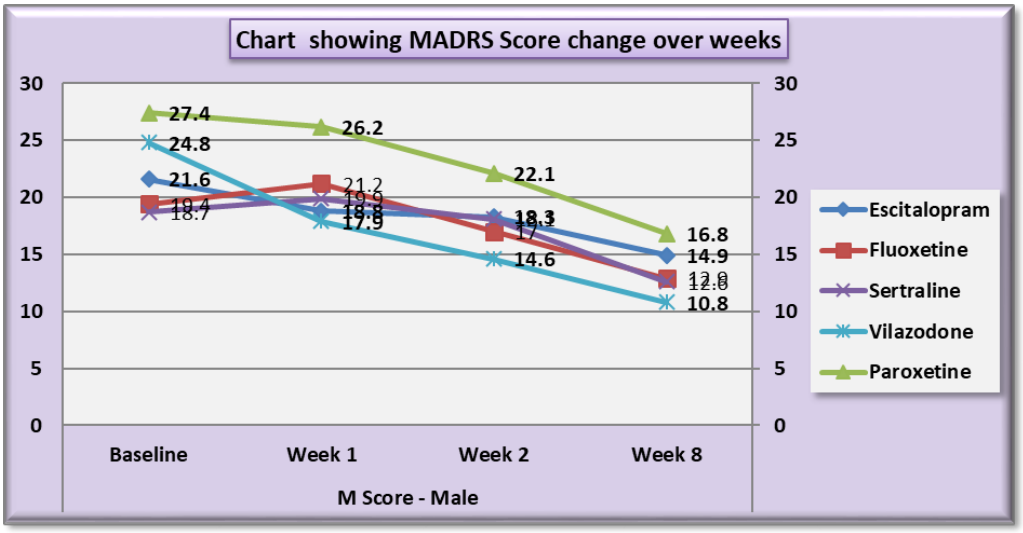

Chart 2. Line Graph showing changes in mean MADRS score during the course of the study in males

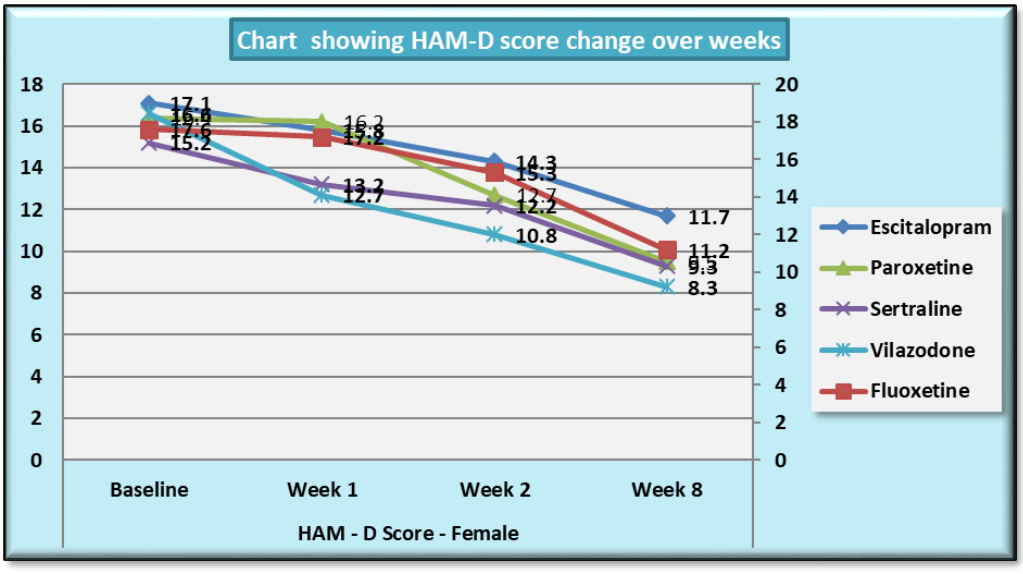

Chart 3. Line Graph showing changes in mean HAM-D score during the course of the study in females

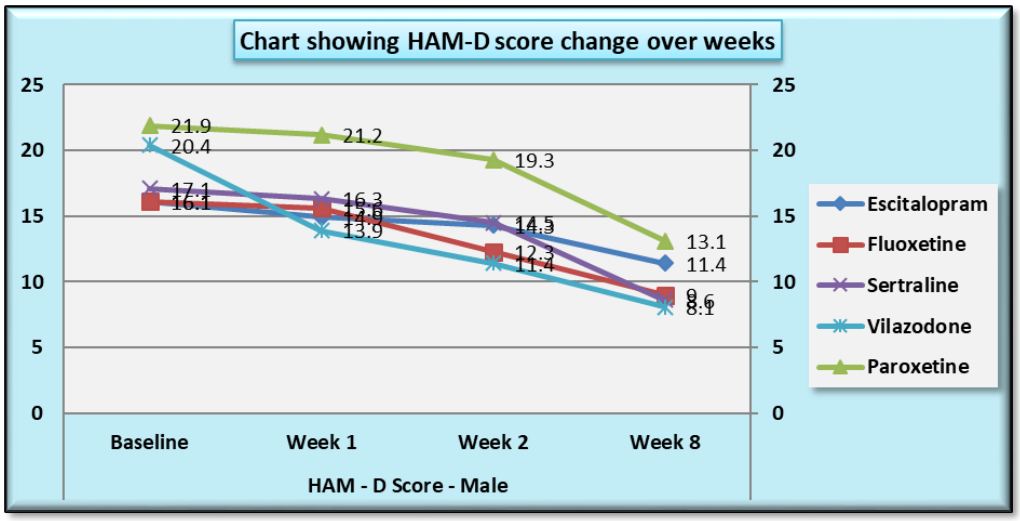

Chart 4. Line Graph showing changes in mean HAM-D score during the course of the study in males

3. Results

The number of females was almost twice the number of males amongst the sample size of the study (females N=95 and males N=55). In this study no specific age group showed significantly higher rates of depression as compared to other age groups. Many sociodemographic factors such as unemployment, lack of social and familial support have also been positively linked to depression [6]. In this study no significant association between the occurrence of depression and various socio demographic factors was noted.

The study revealed that there was no significant difference in the treatment of depression with either of the five drugs used in the study (Tables 1, 2, 3, 4). Mean HAM-D and MADRS scores reductions were comparable in all five drug groups (Charts 1, 2, 3, 4). The findings that Vilazodone has a relatively rapid onset of action was seen in this study when it was compared directly with esitalopram, fluoxetine, paroxetine and sertraline. There was a significant reduction in week 1 values of MADRS scores in patients belonging to the vilazodone group as compared to the other groups (Tables 5, 6, 7, 8). These findings were also replicated on the HAM-D scores at week 1.

Analysis also revealed that reductions in MADRS scores in females were more significant in all treatment groups as compared to males. Amongst females, esitalopram showed significant minimal reductions in week 1, week 2 and week 8 MADRS scores (p=.002, p=0.001 and p=0.012 respectively) (Table 9). Amongst males, paroxetine showed significantly minimal reductions in MADRS scores at week 1 and week 2 as compared to vilazodone (p=0.17 and p=0.38 respectively) (Table 10). While comparing the onset of antidepressant action on the basis of changes in week1 and week 2 MADRS scores, sertraline was most comparable to vilazodone.

While similar findings were duplicated in the score reductions of HAM-D in males, paroxetine showed significantly less reductions at week 1, week 2 and week 8 (p=0.004, p=0.001 and p=0.039 respectively) (Table 11), results of HAM-D post-hoc analysis differed in females with fluoxetine showing most significant difference as compared to vilazodone (p=0.026 at week 1 and p=0.009 at week 2) (Table 12).

4. Discussion

The classical treatment of depression has involved the initiation of treatment with a single antidepressant agent, and either switching or augmenting the existing regimen only if no response is observed after a period of 4-6 weeks of observation. But evidences started emerging in the mid to late 2000s that initiating the antidepressant regimen with two drugs right from the beginning was seen to be associated with better response and lower remission rates [7]. This led to particular exploration of drugs which had more than one mechanism of action against depression in their pharmacological profile. Vilazodone is the result of such further experimentations as it combines the classical SERT inhibition with partial agonism at the 5HT1a receptors, which is seen in many atypical antipsychotics as well as the anxiolytic Buspirone.

The first randomised trials which showed the efficacy of Vilazodone in patients with depression were conducted by Rickels et al in 2009 and Khan et al in 2011. Both these trials demonstrated superior efficacy of Vilazodone against placebo in patients with depression [8, 9]. This prompted further long term trials to study the efficacy and tolerability of Vilazodone in depression.

Robinson et al (2011) [10] conducted a multicentric study at 52 different centres in the US on patients with MDD. The study showed that clinical improvement in depressive symptoms was seen across MADRS, CGI-S (Clinical Global Impressions - Severity) and CGI-I (Clinical Global Impressions - Illness), with a maximal change after 8 weeks of treatment which continued throughout the year.

Khan et al (2014) [11] published a report on analysing the effectiveness of Vilazodone against the different symptoms of depression. They reported that the mean MADRS score of

the patients at the start of treatment was 31.4. The mean MADRS score at the end of 8 week treatment was 21.1 ($p<0.0001$). Statistically significant improvement was seen as early as week 1 after initiating treatment with Vilazodone ($p<0.01$).

According to a placebo controlled trial conducted by Croft et al (2014) [12], primary efficacy outcomes of Vilazodone using MADRS and CGI-S were significantly better than those in the placebo group ($p<0.00001$, effect size=0.54). While many such other studies have shown similar results, such as Citrome et al [13], McCormack in 2015 [14], most of the available data compares Vilazodone with placebo in patients suffering from Depression.

Rele et al (2015) [15] conducted a double blind randomised trial on 60 subjects suffering from DSM-IV-TR MDD (Major Depressive Disorder). Patients receiving treatment with other antidepressants - fluoxetine, Esitalopram, citalopram, paroxetine, sertraline or venlafaxine – were randomised to three groups of varying doses of Vilazodone. All three arms of the study reported significant reductions in mean MADRS, CGI-S, CGI-I and HAM-D scores despite differing dosing schedules.

Vilazodone has been directly compared with another antidepressant (paroxetine) in only one known study conducted by Eyre et al [16]. In this study both Vilazodone and Paroxetine showed significant decrease in HAM-D scores, however no significant differences were observed between the two groups.

5. Conclusions

To our knowledge, this was the first study to directly compare Vilazodone with other popular SSRI drugs as opposed to the placebo control trials. Whilst our study has shown similar results as the work which has been previously done on the subject, our study also attempted to evaluate the lag of onset of antidepressant action associated with SSRIs. This lag of onset can be very unsettling in patients struggling with severe depression or in those with suicidal ideation. Thus as per the results of this study, Vilazodone can be effectively used as a first line antidepressant in these patients. However similar long term longitudinal trials are required in this area for a better understanding of the drug and its unique mechanism of action.

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