



EVALUATION OF EFFICACY AND ADVERSE EFFECTS OF PAROXETINE IN THE TREATMENT OF MAJOR DEPRESSIVE DISORDER PATIENTS.

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ABSTRACT... Major depressive disorder is a serious and disabling disease in world; it is a most common chronic and recurrent disorder with fourth cause of loss in disability in the worldwide. **Objectives:** To evaluate the efficacy and adverse effects of Paroxetine in major depressive disorder patients. **Study Design:** Open Labeled study. **Setting:** Department of Psychiatry, Chandka Medical College Hospital Larkano. **Period:** Three months (August to October 2019). **Material & Methods:** Total 40 patients of either sex were enrolled from OPD of Psychiatric department with age of 18 to 65 years. Follow-up visits were carried out fortnightly after making evaluation on symptoms at base line visit (day 0) continued till 90 days, and then results were compiled. The SPSS-16 version was used for the analysis of data. **Results:** Paroxetine is highly significant ($p=0.001$) to decrease the symptoms of depression during treatment of 90 days. **Conclusion:** In this study, Paroxetine is more effective drug to decrease the symptoms like, weight loss, sexual disturbance, insomnia and with less adverse effects in patients of major depressive disorder.

Key words: Major Depressive Disorder, Paroxetine.

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INTRODUCTION

Major depressive disorder (MDD) is a medical condition that is characterized by persistent feelings of sadness, loss of interest in routine life activities, fatigue, sleep disturbance, poor concentration, suicidal ideas, feeling worthless, and loss of appetite for at least one month.¹ The patients with more than eight or nine MDD symptoms with impaired functioning in daily routine activities and thinking of suicidal ideas.²

Disability is major cause of depression in the worldwide by 2020, and also causes very economic burden to the health system.³ The patients with suffering from psychological, physical and social disorders have more chances of depression and anxiety.⁴ Depression may be affect of all ages, including children and adolescents with their different sign/symptoms and causes.^{5,6} The major involvement of Serotonergic neurons in the pathogenesis of major depression and Serotonin Transporter (SERT) works as a site

of antidepressant drug action.⁷ It also plays an important role in learning and memory by interacting with the different neurotransmitters such as; cholinergic, glutamergic, dopaminergic or GABAergic systems.⁸

There are no specific abnormalities in genes that control the neurotransmitter or hormonal synthesis in patients of major depressive disorders but heritable character is related. Many postmortem studies have showed that reduce the volume of serotonin transporter (SERT) areas of brains in depressive disorder patients and 80% reduced serotonin transporter binding after the one month treatment of Paroxetine.⁹ The nor-epinephrine transporter is located in the plasma membrane of noradrenergic nerve fibres where it works as uptake to norepinephrine.¹⁰ Psychiatric and physical processes are regulated through the involvement of nor-epinephrine, the locus ceruleus synthesizes and release the norepinephrine (NE), that regulate different

functions like as emotions , stress, attention and memory power.¹¹

Life time prevalence most commonly occurs in female patients of depression, in general population it varies from 17-25%, and develops at any time of age but almost begins between the 20-45 years of age.¹² It mostly occurs in Japan (3%) and (17%) in America, and also has been proving that 15% of patients commits suicide having severe depression episodes.¹³

The prevalence of major depressive disorder in Pakistani community among men is varied from 26.5% to 27% and among women from 11.5% to 52%.¹⁴ Gadit et al; reported that 47% prevalence of depression is among the people of Karachi city, Pakistan, this is the highest depression rate with numerous causes.¹⁵

MATERIAL & METHODS

Total 40 diagnosed patients 22 (55.0 %) female and 18 (45.0 %) male) of major depressive disorder were enrolled from the department of psychiatry OPD Chandka Medical College Hospital, Larkano for period of three months (August to October 2019). The patients were included with aged 18 to 65 years of either sex with present of symptoms from one month and not receiving treatment before run of study, and all the patients were eligible for the enrolment after taking their written consent to complete the full course of therapy. Patients were excluded with ideas of suicide, psychosis, epilepsy, chronic illness or any major psychiatric disorder. The parameters of study were insomnia, weight loss and sexual disturbance assessed by Hamilton depression of rating scale. The schedule of visits were as follows, baseline visit (day 0), 30, 60, and last visit at day 90. Paroxetine 20 mg per day was given for 90 days. The observation of each follow up was noted during the study.

RESULTS

In this study total 37 (92.7%) out of 40 patients in which male 18 (45%) & female 22 (55%) completed the treatment and 3 (7.5%) patients left out due to non compliance of treatment as shown in Figure-1 & Table-I. Finally statistical analysis applied to 37

(92.7%) patients, who completed study protocol. Paroxetine 20 mg tablet per day was given to the patients for 90 days. The follow up visits were from day 30, to day 90. The observation of each follow up was noted during the study. Parameters of study were insomnia, weight loss and sexual disturbance assessed by Hamilton depression of rating scale. During the treatment decreases MEAN+SEM Hamilton rating score from day-0 to-90 6 ± 0.00 (100%) 0.6 ± 0.55 (10%) respectively ($p=0.001$) as shown in Table-II. The results showed that the cure rate of Paroxetine in the study was 100 %. After completion of study the significant results were observed from day 30 to day 90. The percentage reduction in insomnia patients was 35 (85%) on day 30, 26 (65%) on day 60 and 24 (64.8%) on day 90 ($p=0.001$). In patients of weight loss no percentage reduction was 39 (97.5%) on day 30, 24 (60%) on day 60 and 17 (45.9%) on day 90 ($p=0.001$). In sexual disturbance percentage reduction was 28 (70%) on day 30, 25 (60%) on day 60 and 17 (45.9%) on day 90 ($p=0.001$), as shown in Table-III and Figure-2.

During the treatment no such serious adverse effect was developed in patients but some minor adverse effects were observed such as; dryness of mouth, nausea and vomiting, headache and abdominal cramps and noted from day 15 to 90. No any major adverse effects 15 (37.5% and 28 (75%) were observed during the treatment, that is highly significant ($p=0.001^{**}$), shown in Table-IV.

Characteristics	Paroxetine (n=40)
Remained in study	37 (92.7%)
Left out	3 (7.5%)
Cured	36 (97%)
Male patients	18 (45%)
Female patients	22 (55%)
Age 30-39 years	20 (50%)
40-49 years	6 (15%)
50 years and above	14 (35%)
Mean \pm SEM	42.6 ± 1.45

Table-I. Demographic, remained in study & left out patients

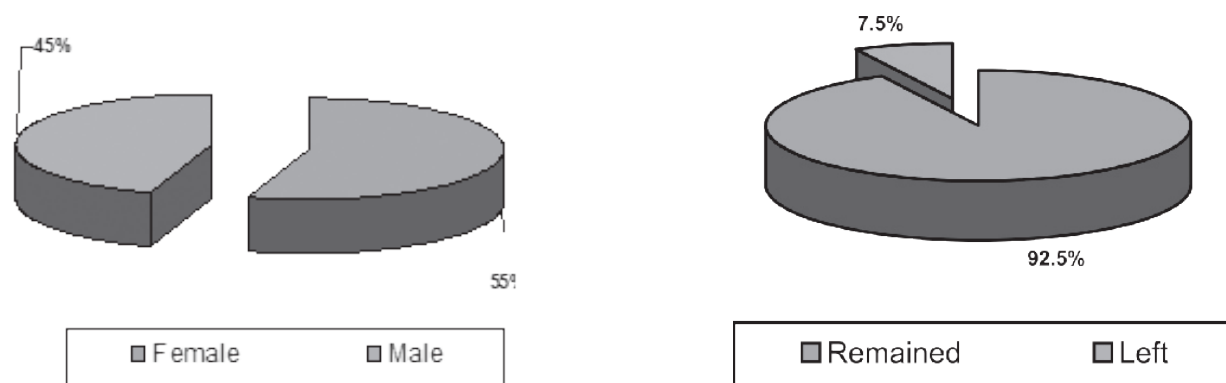


Figure-1. Demographic, remained & left out patients

Follow-up visit	Hamilton score Mean±SEM	Percentage	Percentage decrease 0-90	P-value			
				day 0-30	day 30-60	day 60-90	day 0-90
Base line	6±0.00	100%					
Day 30	3.1±0.79	50%	90%	0.001**	0.001**	0.001**	0.001**
Day 60	1.4±1.06	23.33%					
Day 90	0.6±0.55	10%					

Table-II. Hamilton rating score decrease (%)

Parameters	Day- 0	Day- 30	Day 60	Day 90	% decrease Day 0-90	P-Value			
						Day 0-30	Day 30-60	Day 60-90	Day 0-90
Insomnia	40 (100%)	35 (85%)	26 (65%)	24 (64.8%)	40%	0.034	0.039	1.000	0.001**
Weight loss	40 (100%)	39 (97.5%)	24 (60%)	17 (45.9%)	57.5%	1.000	0.001**	0.179	0.001**
Sexual disturbance	40 (100%)	28 (70%)	25 (62.5%)	17 (45.9%)	57.5%	0.001**	0.478	0.116	0.001**

Table-III. Parameters decrease (%)

Adverse effects	Day-15	Day-30	Day-60	Day-90	P-Value			
					D15-30	D30-60	D60-90	D15-90
No adverse effects	15 (37.5%)	21 (52.5%)	26 (65.0%)	28 (75.7%)	0.177	0.256	0.329	0.001**
Dryness of mouth	5 (12.5%)	3 (7.5%)	-	1 (2.7%)	0.709	0.239	1.000	0.202
Nusea & vomiting	9 (22.5%)	5 (12.5%)	3 (7.5%)	-	0.239	0.709	0.239	0.004
Headache	10 (25.0%)	7 (17.5%)	7 (17.5%)	1 (2.7%)	0.412	1.000	0.062	0.003
Abdominal cramps	6 (15.0%)	4 (10.0%)	1 (2.5%)	-	0.498	0.356	0.356	0.003

Table-IV. Adverse effects of paroxetine (%)

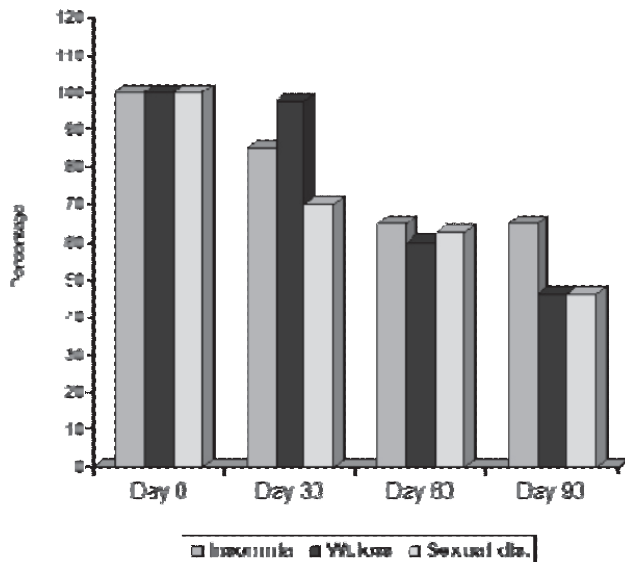


Figure-2. Parameters decrease in major depressive disorder patients.

DISCUSSION

This study matches with the study of Kasper et al. (2005), who observed the effects of SSRIs on sleep architecture at the beginning of treatment, as sedative therapy for insomnia and another study which observed that the paroxetine appears to be more sedating than the other SSRIs.^{16,17} Our study show the results of weight loss observed from day 30 to day 90, and 100% patients having weight loss on base line visit, the results were significant ($p < 0.05$) i.e. 60% on day 60, and 45.9% on day 90.

Some studies showed that weight gain is less likely occurs when the SSRIs are used for short time duration.¹⁸ In randomized, double blind 6 months clinical trial observed that the weight gain is more developed with paroxetine other than sertraline during continuation therapy, and another randomized trial also reported there is largest weight gain with paroxetine as compared with other SSRIs.¹⁹ The mechanism of SSRIs to increase the weight may be due to recovery from major depressive disorder or relationship with improvement of patient's psychiatric symptoms.²⁰

Sexual disturbance cases were observed, from day 0 to day 90 at the end of study period. During treatment of paroxetine sexual disturbance was

observed on day 0 (100%), patients having sexual disturbance, the results were significant on day 60 (62.5%) and 45.9% on day 90. When compared the both groups, the results of paroxetine were statistically significant ($P < 0.05$). Model et al. conducted a direct comparison of the sexual functions related with Bupropion and fluoxetine, sertraline and paroxetine. The patients treated with bupropion have significant improvements in libido, arousal and orgasm intensity and duration.²¹ The results of this trial are also nearer to our results. The efficacy of paroxetine is over all better to controlling the symptoms i.e. weight loss and sexual disturbance of major depressive disorder.²² Headache, nausea & vomiting, dizziness, nervousness, tremor, constipation, dry mouth and asthenia are common side effects of paroxetine.²³

The use of SSRIs was associated with significant improved the sexual functions. Only 27% of patients have no sexual problems.²⁴ The physiological mechanism of normal sexual response includes a combination of neurogenic, psychogenic, vascular, and hormonal factors that are co-ordinated by the hypothalamus, limbic system, and cerebral cortex centres. Blockage of the peripheral α -adrenergic and cholinergic receptors in the genitourinary tract impairs sexual function.²⁵ Sexual dysfunction is a common rare side effect (inability to ejaculate, delay ejaculation and anorgasmia) than the other SSRIs.²⁶

CONCLUSION

In this study, it has been proved that the efficacy of paroxetine in the treatment of major depressive disorder symptoms of weight loss, insomnia and sexual disturbance were significantly improved and less adverse effects were observed.

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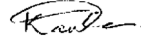

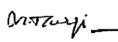

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Friendship is an art of keeping **distance**
while **love** is an art of **intimacy**.

”

“Sigmund Freud”

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