ORIGINAL ARTICLE

ASSESSMENT OF EFFICACY AND ADVERSE EFFECTS OF TRAZODONE IN THE TREATMENT OF MAJOR DEPRESSIVE DISORDER

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Background: Major depressive disorder is a serious and disabling illness in the world and is common chronic and recurrent disorder. It is the fourth most important cause of worldwide loss in disability. **Methods:** This was prospective and open-label study, study conducted in JPMC, Karachi, to evaluate the efficacy and adverse effects in major depressive disorder individuals. A total of 40 patients irrespective of the gender, aged 18 years up to 65 years were enrolled from OPD of Psychiatry Department. Follow-up visits were carried out fortnightly after making evaluation of symptoms at baseline visit (day 0), follow-up continued till 90 days when the results were compiled. **Results:** Statistically significant ($p<0.05$) results were observed in all the parameters at the end of study, i.e., day 90. **Conclusion:** Among all the symptoms of major depressive disorder, trazodone proved to be more effective in controlling insomnia.

Keywords: Trazodone, major depressive disorder, side effects, anxiolytics

INTRODUCTION

Major depressive disorder is a common, chronic and recurrent disorder in the world, It is characterised by the usually sad mood, loss of interest or pleasure in normally routine activities, associated with disabling and co-morbidity on individuals to their families.[1] According to WHO the major depressive disorder to be the second most important worldwide cause of loss in disability-adjusted life years.[2] The ratio of prevalence rates in women to men is 1.5 to 2.5. In the National co-morbidity study, the life time prevalence of major depressive disorder in the US population was estimated to be 21.3% in women and 12.7% in men.[3] About 15% patients die with mood disorder by their own hand and 66% of all by suicides. Rate of suicide in Canada is higher than in united states.[4] The serotonergic system may play a key role in the pathogenesis of major depressive disorder and serotonin transporter (SERT) acts as a site of anti-depressant drug action.[5] In major depressive there are no specific abnormalities in genes that control the neurotransmitter or hormonal synthesis, but is heritable disease.[6] There are several neuropeptides which play role in the pathophysiology of major depressive disorder, these are vasopressin, endorphins particularly β-endorphins and gamma type endorphins and somatostatin.[7] Deficiency of monoamine neuro-transmitter levels was proposed as the underlying cause of depressive disorder over 40 years of age.[8]

MATERIAL AND METHODS

This was prospective and open-label study carried out in Department of Pharmacology and Therapeutics, Basic Medical Sciences Institute (BMSI), Karachi in collaboration with Department of Psychiatry, Jinnah Postgraduate Medical Centre, Karachi (JPMC). A total of 40 patients of either sex, age 18 years or more with insomnia, weight loss and sexual disturbance in major depressive disorder individuals were enrolled. All symptoms were assessed by Hamilton Depression rating scale. Patients were excluded having any other disease. Subjects were evaluated to determine eligibility for inclusion criteria. The study was extended over a period of 90 days. During treatment period patients were given trazodone 50 mg daily. The schedule of visits was the baseline visit at day 0, and on days 15, 30, 60 and day 90. The results were compiled and statistically analysed.

RESULTS

Forty patients were enrolled. Out of them 37 completed the study. Cure rate was (94.5%). All signs and symptoms were assessed by the Hamilton Depression Rating Scale from day 0 to day 90. The statistically significant results were observed from day 15 to day 90. In insomnia percentage reduction was on day 15, (32, 80%), on day 30, (23, 57.5%), on day 60, (5, 12.5%) and on day 90, (1, 2.7%). In weight loss, percentage reduction was decreased on day 60, (26, 65%) to day 90, (18, 48.6%). In sexual disturbance, percentage reduction was decreased from day 60, 26 (65%) which was also not improved and at day 90, (23, 62.1%) ($p<0.05$). (Figure-1).

The adverse effects observed from day 15 to day 90 were, in majority of patients (47.5%), dryness of mouth at day 15, which decreased significantly at the end of study while 5% had no any adverse effects. The other adverse effects of drug observed during study period are mentioned in Table-1.

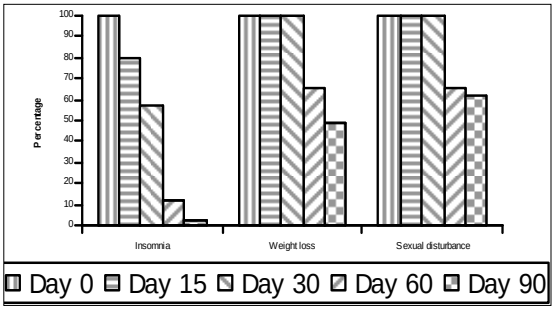

Figure-1: Percentage change in treatment of Trazodone from Day 0 through Day 90

Table-1: Adverse effects of Trazodone therapy from day 15 to day 90

Adverse effects	Day-15	Day-30	Day-60	Day-90
None	2 (5.0%)	3 (7.5%)	10 (25.0%)	15 (40.5%)
Dryness mouth	19 (47.5%)	24 (60.0%)	17 (42.5%)	11 (29.7%)
Nausea	7 (17.5%)	4 (10.0%)	3 (7.5%)	2 (5.4%)
Headache	8 (20.0%)	5 (12.5%)	6 (15.0%)	2 (5.4%)
Constipation	3 (7.5%)	3 (7.5%)	1 (2.5%)	1 (2.7%)
Tremor	1 (2.5%)	1 (2.5%)	3 (7.5%)	-

Adverse effects significantly decreased from day 15 through day 90 ($p<0.05$)

DISCUSSION

Trazodone is widely used in the Asia and Europe since the beginning of the 1980s for the treatment of major depressive disorder.[9] The therapeutic benefit of the drug is due to its ability to block postsynaptic 5-HT2A, receptors; its sedative property is probably due to its potent H_1 blocking activity. It also has a anxiolytic and hypnotic properties.[9,10] When given orally in a dose of 50 mg daily, it has been proved to be effective against insomnia patients of major depressive disorder with a fewer adverse effects.

Trazodone decreased insomnia from day 15 to day 90, [32 (80%) to 1, (2.7%)]. For weight loss and sexual disturbances, percentage reduction was decreased from day 60 to day 90 which was not an improvement ($p<0.05$). A few adverse effects were observed during study period including dryness of mouth, nausea, headache and constipation which were generally of mild to moderate intensity and not considered to be serious. Our study confirms the finding that the administration of a low dose of trazodone objectively improves sleep duration in patients who are being treated with antidepressants and have insomnia.[11]

It has been largely used more for its sedative than its antidepressant properties and may be the most commonly combined antidepressant with SSRTs.[12] Trazodone is well tolerated and its effects particularly in controlling the anxiety and sleep disturbances may be seen within first week of treatment.[13]

CONCLUSION

Trazodone proved to be more effective in controlling insomnia with some adverse effects among the other symptoms of major depressive disorder.

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