Current Pharmaceutical Views

Open Non Comparative Follow Up Study on Sertraline in Egyptian Patients Suffering from Major Depressive Disorder

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Abstract

Twenty nine adult Egyptian patients fulfilling the DSM-III-R criteria for major depression were included in this study. After a washout period of 7 days they were given sertraline tablets in a single daily dose of 50 mg. The dose was allowed to increase according to clinical response to 100 mg once daily after 4 weeks and to 200 mg once daily after another 2 weeks. Eight visits were scheduled for each patients on days -7, 0, 7, 14, 21, 28, 42 and 60 of treatment. Assessments were done using, Hamilton Depression and Anxiety scales and Clinical Global Impression scale. Side eftects were recorded at each visit. 27 patients (93.1%) completed the study. The results showed significant improvement over baseline by all scales measured. Side effects were reported in 13 patients (44.8%) which were all mild to moderate in severity except for one patient who discontinued due to manic symptoms. Sertraline was found effective, safe and well tolerated in the treatment of Egyptian patients with major depressive disorder.

Introduction

The place of selective serotonin reuptake inhibitors (SSRIs) in the treatment of major depressive disorder is now well established (Blier et al., 1990). The rapidity of onset of antidepressant effect as well as the side effect profile of SSRIs has gained them a wide acceptability in the treatment of major depressive disorders (Doogan and Caillard, 1988; Matilla et al., 1988). By enhancing serotonergic transmission and inducing down regulation of post- synaptic receptors, these agents provide effective antidepressant activity without the sedating, anticholinergic, or cardiotoxic reactions observed with standard tricyclic antidepressants (Schatzberg et al., 1987; and Fuller and Wong, 1987).

Sertraline, a naphethylamine derivative with a unique chemical structure, is a highly selective serotonin reuptake inhibitor. It is a very potent inhibitor of serotonin reuptake into brain synaptosomes, with only weak effects on the reuptake of dopamine and norepinephrine (Koe et al., 1983). Sertraline is slowly absorbed, with peak plasma concentrations occurring 6-8 hours after oral dosing. The elimination half life is about 26 hours which allows once daily dosing, meanwhile, steady state is reached rapidly within 7 days of the start of repeated daily dosing, which ensures no accumulation on repeating the dose (Warrington, 1991). Vessell in 1972, reported that inter-racial differences exist in how medications are metabolized in the body.

The aim of this work is to study the efficacy, and tolerability of Sertraline in the treatment of Egyptian patients with major depressive disorder.

Subjects and Methods

This was an open non-comparative study that included 29 adult patients of both sexes, aged between 18-70 years and

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suffering from major depressive disorder according to DSM-III-R criteria (American Psychiatric Association, 1987). The inclusion criteria were depressed patients with a total score on the Hamilton Rating Scale for Depression (HAM-D) (Hamilton, 1960) of 18 or more at the end of the washout period, and who had given informed oral consent to participate in the study. Adequate contraception was employed for females of child bearing potential. The exclusion criteria were all forms of secondary depression, pregnant or lactating females, patients taking concurrent psychotropic medications with the exception of short-acting benzodiazepines or chloral hydrate for insomnia only when indicated during the study. Patients with hypersensitivity or resistance to antidepressant drugs, electroconvulsive therapy in the 7 days before the start of the study, patients treated with lithium salts during 4 weeks prior to inclusion, and patients with physical or psychological dependence on drugs or alcohol were excluded. The exclusion criteria were also severe suicidal risk, patients who showed >25% improvement of HAM-D during the washout period and patients with significant renal, cardiac, or hepatic dysfunction.

After giving an informed oral consent to participate in the study, patients had a washout period of 7 days. A period of active treatment with Sertraline then started during which patients were treated as outpatients for 60 days. Eight visits were scheduled to each patient at days -7, 0, 7, 14, 21, 28, 42 and 60. No medication was allowed during the washout period.

Sertraline tablets were given as once daily dose of 50 mg with meals from day 1 to day 28. At day 28, if improvement was satisfactory with no side effects, the dose was maintained till the end of the study. If improvement was not satisfactory with no side effects, the dose was increased to 100 mg once daily. At day 42, if improvement was still not satisfactory, the dose was increased to 200 mg once daily until the end of the study (day 60).

Baseline Assessments and Assessments during Therapy

At day -7 (screening), patients were assessed by history-taking, physical examination including vital signs, Hamilton Rating Scale for Depression (HAM-D) and Anxiety (HAM-A) (Hamilton 1959, 1960), Clinical Global Impression (CGI). At all visits, the following had been repeated, HAM-D, HAM-A, CGI, physical examination, side effects. Concomitant conditions with their medications were asked for and reported. Adverse events were looked for throughout the whole study period and were recorded with reference to their nature, severity, relation to the study drug and the outcome.

Statistical analysis was done using SPSSX package looking at T. test for probability, comparing significance of improvement between consecutive visits on total Hamilton depression and anxiety scales as well as separate items on each scale.

Results

29 adult patients attending an outpatient psychiatric clinic and suffering from major depressive disorder were included in this study. They were 10 males (34.5%) and 19 females (65.5%). Their ages ranged between 23-64 years with a mean age of 41.88 ± 10.04 years. Only two patients (6.9%) dropped out from the study prematurely, one male patient who showed poor response to therapy and one female patient who developed manic symptoms. At the end of the study, 27 patients (93.1%) were evaluated.

Clinical Efficacy

Improvement in total HAM-D scores is shown in table 1.

In the first item of the HAM-D a significant improvement was reached on visit 4 (day 14) (T = -13.3836 , d.f.= 28 p <0.0001) (Fig. 1).On The HAM-A scale total improvement was significant on visit 3 (day 7) T = -5.3645 (d.f. = 29 **p** <0.0001) (Fig. 2).

Insomnia was a common complaint among many patients with early insomnia being the highest rating on the Hamilton scale, the insomnia had improved by visit 4 on day 14 as the majority of patients (Fig. 3).

Subscales of Hamilton depression scale point to an improvement of individual symptoms (Figures 4,5,6,7,8,9).The final assessment on day 60 of the 27 patients who completed the study, showed that 21 patients (77.8%) were rated much improved and a further 6 patients (22.2%) were rated improved.

Of the 29 enrolled patients, 13 patients reported side effects (44.8%) (table 2). They were all mild to moderate in severity and did not necessitate interruption of therapy except one female patient (3.4%) who developed manic symptoms and discontinued the treatment.

Table (1)
Improvement in total HAM-D score.

Visit	HAM-D Score				
	Score	Mean	SD	Maximum	Minimum
1	29	28.79	5.86	18	40
2	29	27.96	5.85	19	45
3	29	23.10	5.23	11	31
4	28	18.67	7.22	06	32
5	28	12.81	6.51	03	26
6	28	12.35	8.10	02	29
7	**28**	8.50	6.65	**02**	24
8	27	6.18	5.76	02	20

Fig. 1: Change of depressed mood (HAM-D item 1) score during the study.

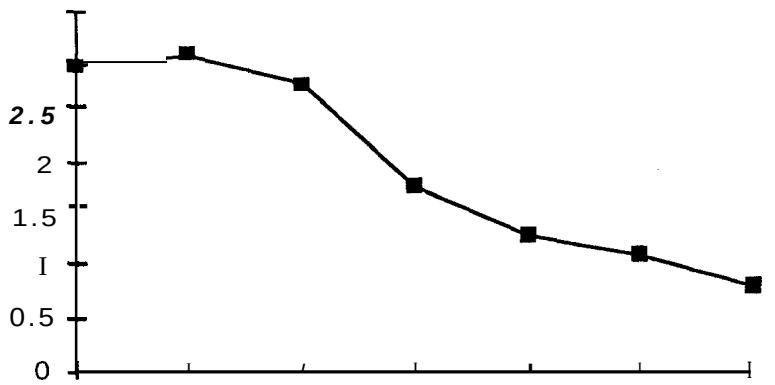


Fig. 2: Change in Total HAM-A anxiety score during the study.

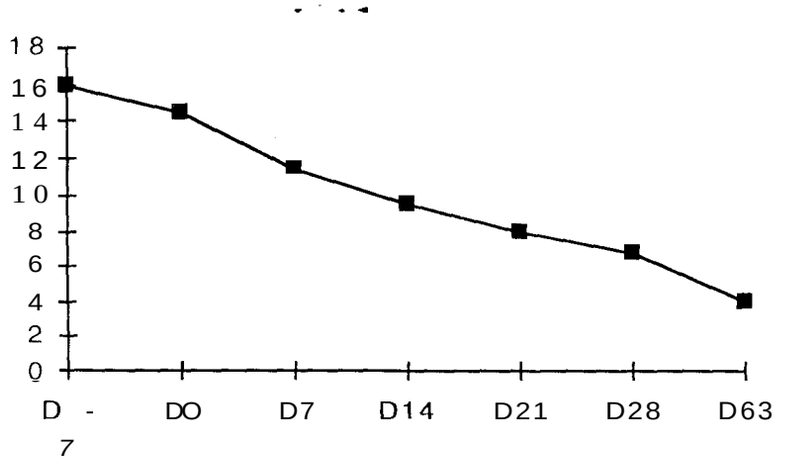


Fig. 3: Change of HAM-D insomnia score during the study.

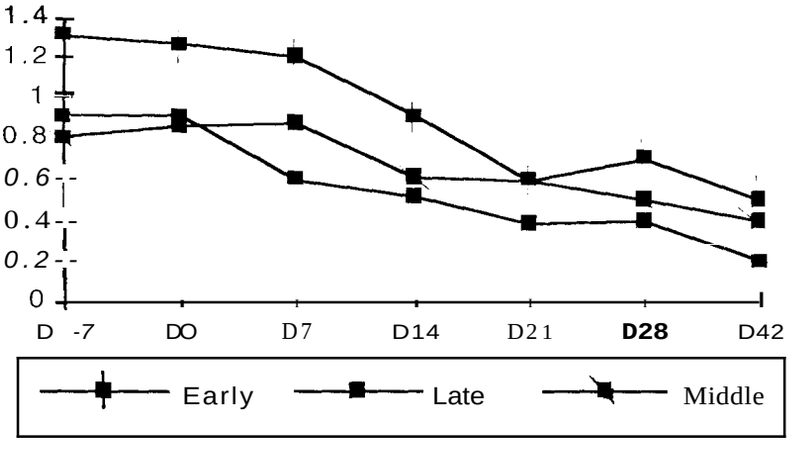


Fig.4: Change in helpness, hopelessness and worthlessness score during the study.

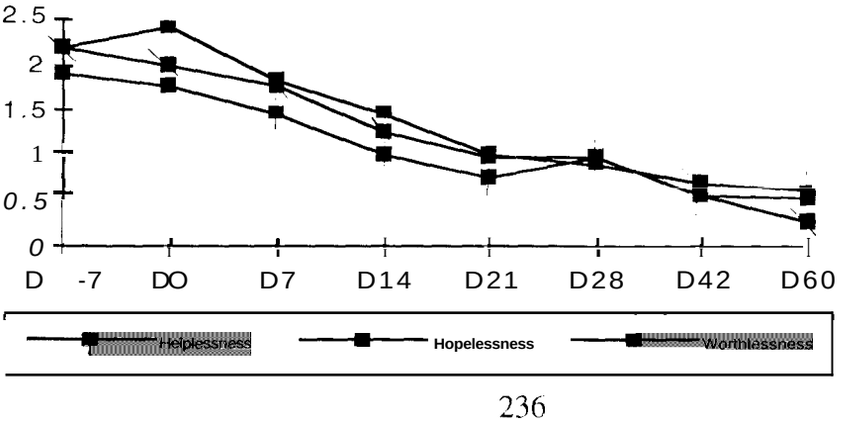


Fig.5: Change of aqitation score during the study.

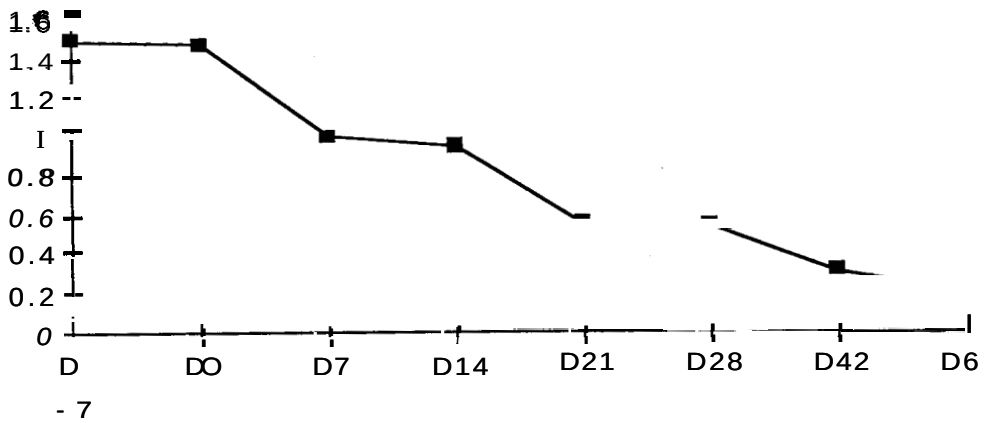


Fig.6: Change of suicidal ideas score during the study.

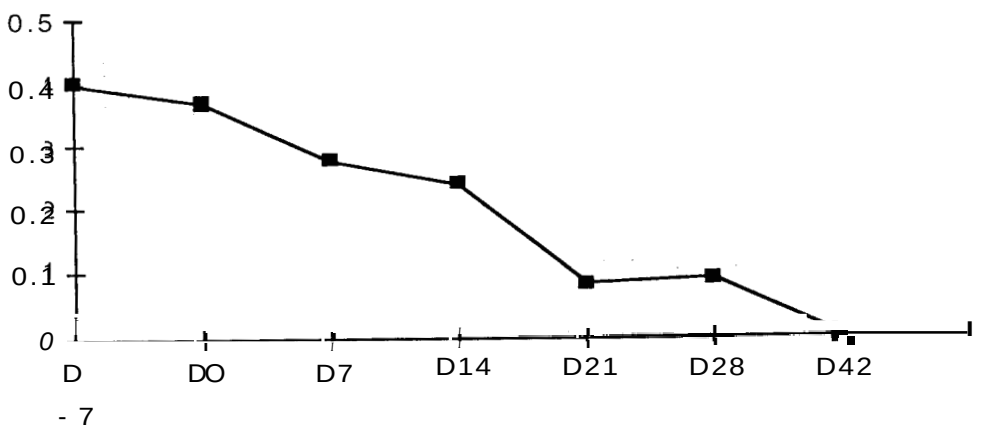


Fig.7: Change of feelings of guilt score during the study.

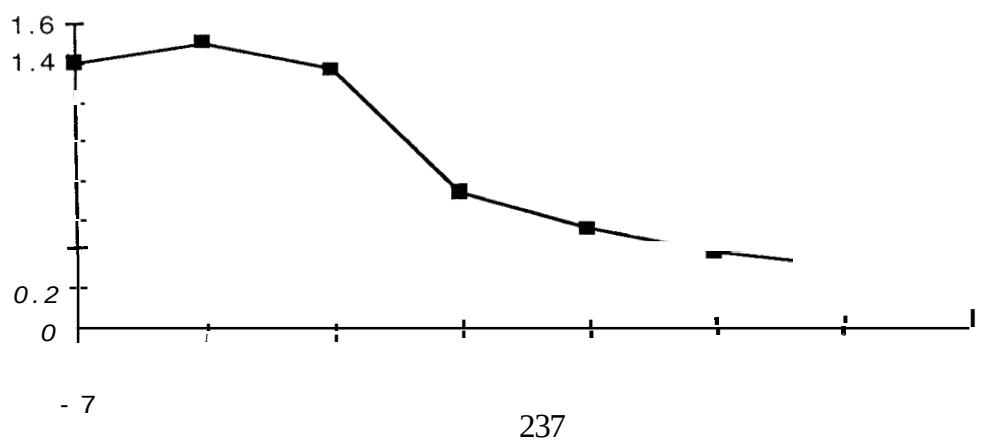


Fig.8: Change of retardation score during the study.

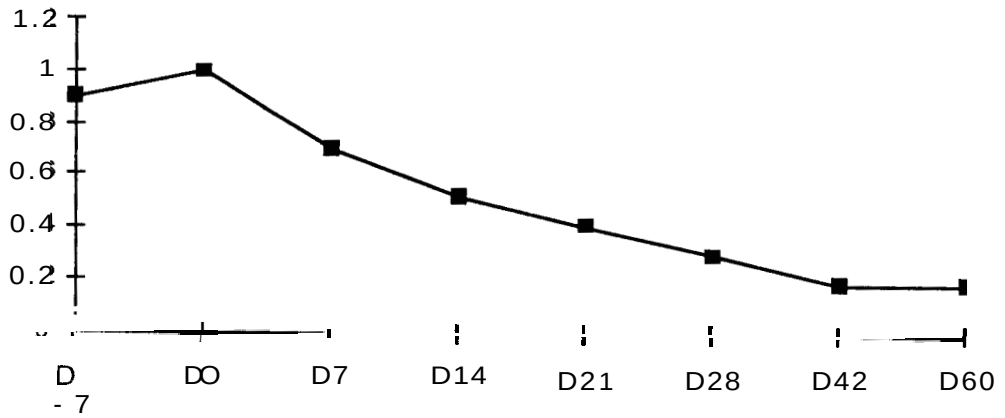
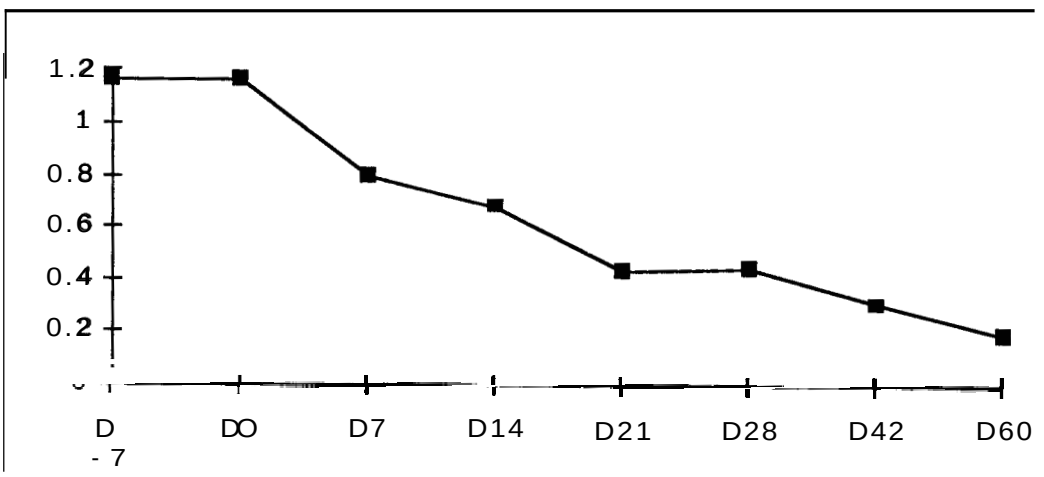


Fig.9: Change of diurnal variation of mood score during the study.



Side effects	Number of patients*
Nausea	7
Palpilations	2
Insomnia	1
Increased weight	3
Dizziness	1
Itching	1
Manic symptoms	1

Discussion

The findings in this study of sertraline for Egyptian depressed patients, are in support of what has been found by other previous studies, (designed for non-Egyptian patients) as those by Doogan and Caillard (1988), Cohn et al.(1990) and Doogan (1991). This indicates that the drug has good efficacy with no apparent inter-racial difference, as the case with some anti-depressants (Vessell, 1972).

The anti-depressant effect in the present study has been observed from as early as the first week of treatment, giving the drug the advantage of fair rapidity of onset. Such an early improvement has been noted significantly in the item of HAM-D scale concerning "psychological symptoms of depression" (mood, diurnal variation, helplessness and worthlessness), "insomnia", "behaviour" and some "somatic symptoms". All of these items showed significant improvement by D14, denoting that such types of symptoms in the context of a depressive disorder may show an earlier response to sertraline than others. However, by the end of the study period, the improvement was significant in most of the items of HAM-D scale. The full therapeutic effect, as with most classical anti-depressants take few weeks to be reached. At the same time, significant reduction has been found also in total anxiety scores from the early assessment visits, meaning that the drug is effective in controlling the anxiety symptoms accompanying depressive disorders, thus, it might be a "preferred" drug for patients with mixed anxiety-depression syndrome. The reported side effects were "minimal", with good tolerability explaining the near absence of drop-outs secondary to adverse drug effect, which is another advantage allowing the drug to be used for wide varieties of depressed patients including elderly people. Patients with cardiovascular troubles as well as those who need to be alert would benefit as the drug has no sedating effect, a factor which is highly important in improving the patient's compliance to treatment.

Conclusion

The use of Sertraline on a population of depressed Egyptian patients was shown to be an effective and well tolerated treatment with a low incidence of side effects. The advantage of rapid onset of antidepressant action (as features of depression had significantly improved on day 14) and few number of side effects reported helped to improve patient compliance.

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