

June 1993

Letters to the Editor

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Recommended Citation

(1993) "Letters to the Editor," *Jefferson Journal of Psychiatry*. Vol. 11 : Iss. 2 , Article 12.

DOI: <https://doi.org/10.29046/JJP.011.2.015>

Available at: <https://jdc.jefferson.edu/jeffjpsychiatry/vol11/iss2/12>

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Letters to the Editor

SERTRALINE DOSING IN DEPRESSED INPATIENTS

To the Editor:

In a retrospective chart review of all psychiatric inpatients, at the University of Texas Harris County Psychiatric Center, 24 patients were started on sertraline for treatment of their depressive symptoms. The primary question to be answered by this case study was the dose at which the majority of inpatients respond to sertraline in a clinical setting. There are no known reports concerning the dose at which most inpatients respond.

Patients were not included in this study unless sertraline was prescribed as recommended by the manufacturer (Pfizer), i.e., an initial dose of 50 mg with a weekly increase of 50 mg if clinically indicated, up to a maximum of 200 mg. There were 24 patients (18 women, 6 men) with a mean age of 35.2 years (range 17–58). Twenty patients had a diagnosis of major depressive disorder, 10 of whom had concomitant psychotic symptoms. Three patients had a diagnosis of schizophrenia or schizoaffective disorder, and another had bipolar disorder, depressed phase. In addition to each patient receiving sertraline, 16 of the patients received neuroleptics and 20 were treated with benzodiazepines.

Of the 24 patients, 21 were treated with sertraline for greater than 5 days. Of these 21, 10 (48%) responded at the initial 50 mg daily dose, 8 (38%) at 100 mg daily, 2 (10%) at 150 mg daily, and 1 (5%) at 200 mg daily. A response was defined as a significant improvement in the depression such that the patient could be discharged from the hospital. No rating scales were used. One patient was taken off sertraline after 1 day and another after 5 days for worsening medical or psychiatric problems, which were not felt to be related to sertraline. A third patient had sertraline discontinued on day 5 for urinary and fecal incontinence, which was felt to be a side effect. Of the 21 patients who were discharged on sertraline, 3 complained of side effects which included mild dizziness, mild to moderate nausea and occasional dry mouth. Fifteen charts had documentation indicating no side effects; 3 charts had no documentation regarding side effects.

In this retrospective review, 48% of depressed inpatients responded at the initial 50 mg daily dose, and 86% responded at 100 mg or less. Thompson et al in a controlled dose escalation study reported 59% of depressed outpatients responded at the initial 50 mg sertraline dose (1). Doogan and Caillard (2) in a similar design reported that 78% of depressed outpatients improved on a mean sertraline dose of less than 100 mg daily. Optimum dose is best evaluated in a fixed dose trial, since dose escalation studies usually favor higher doses as most effective. To date, there have been no controlled fixed dose trials with sertraline. Our current results using a dose escalating regimen must be viewed with caution for this reason as well as others. The retrospective nature of this review as well as the mixed diagnostic groups, concomitant medication use, variable length of hospitalization and lack of standardized assessment of depressive symptoms are clear limitations of this report. Further, the apparent high response rate in our subjects and relatively benign side effect profile may be due to limited chart documentation of optimal benefits and drawbacks of medication. Nonetheless, this anecdotal

report may provide some clinical guide until well controlled, fixed dose prospective studies are reported.

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TARDIVE DYSKINESIA AND CLOZAPINE

To The Editor:

We wish to report a case of tardive dyskinesia that has shown a rapid and dramatic response to Clozapine without incident of serious side effects.

Case Report: A.S. is an 80 year-old, widowed, white female who had carried a diagnosis of chronic schizophrenia since 1964 and had since then taken Trilafon, 8 mg b.i.d. with satisfactory therapeutic results.

As early as 5 years prior to admission, A.S. was seen to have problems with “blinking of her eyes.” Examination showed a left facial hemispasm that would persist for several seconds duration, sometimes up to 30 seconds. This was accompanied by a fine twitching about both eyelids and both sides of her mouth. Approximately 3 months prior to admission, she was seen in clinic for uncontrollable eye blinking that had worsened in the preceding 7 months. No signs of lip smacking, tongue rolling, or pill rolling movements were noticed by her doctor. Her family had noticed a slight tremor bilaterally in her upper extremities in addition to her facial movements. A preliminary diagnosis of tardive dyskinesia was established and her Trilafon was subsequently reduced to 4 mg b.i.d.. She was seen again three weeks later without subsequent improvement, and her medications were discontinued. Her family reported that her auditory hallucinations then markedly worsened, and her thought became extremely incoherent. One month later, she was again re-examined and found to have worsening of her eye blinking and facial grimacing. She was then admitted to a psychiatric unit for evaluation and alternative psychotropic therapy.

*Two of the above authors (DW, CP) hold stock in Pfizer Pharmaceuticals.

Examination upon admission revealed persistent abnormal involuntary movements. These consisted of exaggerated eye blinking bilaterally, unusual extreme grimacing, jaw clenching, occurring at a frequency of approximately once per second, and various lingual movements. A pill rolling tremor was also noted in the absence of other truncal and upper/lower limb extremity movements. A DISCUS assessment at that time revealed a score of 25.

On day 6 of admission, she was started on clozapine, 25 mg b.i.d. The dose was subsequently raised to 25 mg t.i.d. on day 7. Her signs of tardive dyskinesia showed a subsequent dramatic and rapid improvement in response to this medication. She was evaluated with the DISCUS on day 11 which revealed a score of 16. Throughout the remainder of her stay, facial movements persisted, although to a lesser degree than upon admission, and she was subsequently discharged on day 12 on clozapine, 25 mg b.i.d.

On follow-up 4 weeks later, she was seen to have continuing involuntary movements. A DISCUS assessment revealed a score of 13, with grimacing and blinking remaining severe. Auditory hallucinations continued, but to a lesser degree. Throughout her Clozapine trial, weekly hematologic monitoring revealed no signs of neutropenia.

Discussion: Current estimates of the prevalence of TD among patients taking neuroleptic drugs is thought to be 20%; however, rates vary among patient populations, certain subgroups of elderly exceeding 50% (1,2,3). Conventional neuroleptics have all been implicated in causing drug-induced movement disorders (1,3,4), which are thought to result from altered dopaminergic activity within the basal ganglia (5).

This patient demonstrated a rapid and dramatic response to clozapine, her DISCUS score dropping from 25 to 16 within 11 days, and to 13 within one month. Most of the immediate improvement was seen in reduction of oral and lingual movements; unfortunately, facial and eye movements continued to remain severe. There was no worsening in any of the DISCUS scale items at one month compared to her initial exam.

Lieberman, et al. (3) suggests several possible explanations for the effectiveness of clozapine in patients with TD. There may exist a suppressive (masking) effect, such as that seen with "classical" neuroleptics. However, there may be a gradual improvement in reversible TD in the absence of an agent that promotes TD. There may also exist a specific therapeutic effect in which clozapine actively reduces symptoms of TD. This patient's rapid response suggests that she benefited from an acute suppressive effect; however, either of the two remaining mechanisms may still account for patient's long term improvement with clozapine. Data from clinical trials suggest that approximately 43% of patients with TD, particularly those with dystonic features, show improvement (50% or greater reduction in TD symptoms) after treatment with clozapine.

Currently, no satisfactory treatment exists for irreversible tardive dyskinesia, although some cases do appear to be reversible if detected early enough. Therefore, current treatment is focused on prevention, the physician having an obligation to decrease the dosage of neuroleptic therapy without compromising psychiatric benefit. For those patients who do develop TD, several therapeutic strategies have been proposed, but have subsequently proved to be disappointing (1). Reduction or discontinuation of neuroleptic therapy is usually recommended, but difficult due to breakthrough of psychiatric symptoms (1,2); prolonged therapy usually aggravates TD to the point where it may eventually become life-threatening for the patient.

Perhaps all patients capable of tolerating clozapine, who show probable or definite signs of TD, should routinely receive a trial of clozapine. Serious side effects may contribute to a physicians reluctance to initiate clozapine therapy with such patients; however, routine

hematologic monitoring has virtually eliminated fatalities associated with agranulocytosis. Moreover, in the absence of an adequate treatment for TD, patients are often caught in an unfortunate clinical situation in which both decreases and increases in neuroleptic therapy aggravate TD in the short and long term, respectively. With continued use and increases in patient reporting, clozapine may emerge as the gold standard in neuroleptic therapy for the prevention and/or treatment of TD.

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