

Sertraline maintenance treatment reduced relapse and dropouts in posttraumatic stress disorder

Davidson J, Pearlstein T, Londborg P, et al. Efficacy of sertraline in preventing relapse of posttraumatic stress disorder: results of a 28-week double-blind, placebo-controlled study. *Am J Psychiatry*. 2001 Dec;158:1974-81.

QUESTION

In patients who have posttraumatic stress disorder (PTSD) and have responded to continuation sertraline treatment, does maintenance sertraline treatment reduce relapse?

DESIGN

Randomized (unclear allocation concealment*), blinded (unclear),* placebo-controlled trial with 28-week follow-up.

SETTING

24 centers in the United States.

PATIENTS

96 patients who were 21 to 69 years of age (mean age 43 y, 70% women); met the *Diagnostic and Statistical Manual of Mental Disorders, 3d edition, Revised* criteria for PTSD; had PTSD symptoms for > 6 months (mean duration 13 y) and a total severity score ≥ 50 on the Clinician-Administered PTSD Scale (CAPS) part 2; and met responder criteria (Clinical Global Impression [CGI] improvement score ≤ 2 and $\geq 30\%$ improvement in total severity score on CAPS part 2) after 24 weeks of sertraline. Exclusion criteria included bipolar disorder, schizophrenia, organic mental disorder, primary diagnosis of major depression or anxiety, and substance abuse. Follow-up was 88%.

INTERVENTION

Patients were allocated to sertraline, 50 to 200 mg/d (mean dose 137 mg/d) ($n = 46$), or placebo ($n = 50$). Concomitant psychotropic therapy (except for chloral hydrate on ≤ 2 nights/wk) or cognitive behavior therapy was not permitted. Other forms of psychotherapy could not begin or end during the study period.

MAIN OUTCOME MEASURES

Relapse, dropout because of clinical deterioration, acute exacerbation, number of persons completing the study, and adverse events. Patients who relapsed met 3 criteria on 2 consecutive visits: CGI improvement score ≥ 3 ; $\geq 30\%$ increase and increase of ≥ 15 points on CAPS, part 2; and substantial deterioration of patients' clinical condition as judged by the investigator.

MAIN RESULTS

Analysis was by intention to treat. Sertraline led to lower relapse, study noncompletion, and acute exacerbation rates than did placebo (Table). No adverse events with a rate $\geq 10\%$ occurred in the sertraline group; dizziness was the only adverse event with a rate $\geq 10\%$ in the placebo group (4.3% for sertraline vs 18% for placebo, $P = 0.05$).

CONCLUSION

In patients who had posttraumatic stress disorder and had responded to sertraline, maintenance sertraline reduced relapse and dropouts.

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*See Glossary.

Sertraline vs placebo for sertraline responders with posttraumatic stress disorder†

Outcomes at 28 wk	Sertraline	Placebo	RRR (95% CI)	NNT (CI)
Relapse	5.3%	26%	80% (27 to 95)	5 (3 to 19)
Relapse or discontinuation because of clinical deterioration	16%	46%	65% (27 to 85)	3 (2 to 10)
Acute exacerbation	16%	52%	70% (37 to 86)	3 (2 to 7)
Did not complete study	39%	60%	35% (1.7 to 58)	5 (3 to 135)

†Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

Davidson and colleagues report the first published randomized controlled trial (RCT) of maintenance treatment for PTSD. The idea of applying the standard treatment for depression to PTSD by continuing treatment with an antidepressant for 6 months after response (1) appears to be challenged.

This RCT is of much better quality than many previous studies of PTSD treatment. However, several methodologic issues call for cautious interpretation of the results. The patients represent only a small proportion of those who entered the research program. All patients completed a 12-week acute-phase RCT comparing sertraline with placebo plus a 24-week open-label sertraline-continuation study. Of the 380 patients who entered the acute-phase trial, 155 completed the open-label trial. Davidson and colleagues then randomized 96 of these patients in the current trial, and only 48 completed the study.

Twice as many men were in the placebo group as in the sertraline group. This difference is of concern because none of the 9 men in the sertraline group relapsed, whereas 5 of the 18 men in the placebo group did. Another potential issue is that 38 patients (40%) met the criteria for a secondary depressive disorder. The authors did not state how many of these patients were in each group, but they did state that the

presence of depressive disorder did not influence relapse rates. Perhaps more important is the failure to report how many patients were originally randomized to sertraline in the acute-phase RCT. The result is that some patients had already taken sertraline for 36 weeks and others for 24 weeks before study entry.

Notwithstanding these issues, the results convincingly favor sertraline maintenance. Most relapses occurred between 3 and 8 weeks after stopping sertraline, which supports the authors' conclusion that loss of prophylactic efficacy was more likely to explain the difference than was a discontinuation syndrome. If these results prove correct, it could be strongly argued that patients with chronic PTSD who respond to sertraline should not have it discontinued within a year, particularly because it appears to be well tolerated. Future research may identify subgroups that are more likely to need longer maintenance treatment than others. In this study, patients who responded most quickly in the acute-phase trial were those least likely to relapse on discontinuation.

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Reference

1. Loonen AJ, Peer PG, Zwanikken GJ. *Pharm Weekbl Sci*. 1991;13:167-75.