Sertraline maintenance treatment reduced relapse and dropouts in post-traumatic stress disorder


QUESTION: In patients who have post-traumatic stress disorder (PTSD) and have responded to continuation sertraline treatment, does maintenance sertraline treatment reduce relapse?

Design
Randomised (unclear allocation concealment)*, blinded (unclear)* placebo controlled trial with 28 weeks of follow up.

Setting
24 centres in the US.

Patients
96 patients who were 21 to 69 years of age (mean age 43y, 70% women); met the Diagnostic and Statistical Manual of Mental Disorders, 3rd 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 ≥ 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/day (mean dose 137 mg/d) (n=46), or placebo (n=50). Concomitant psychotropic therapy (except for chloral hydrate on ≤ 2 nights/wk) or cognitive behaviour 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 people completing the study, and adverse events. Patients who relapsed met 5 criteria on 2 consecutive visits: CGI improvement score ≥ 3; ≥ 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 non-completion, and acute exacerbation rates than did placebo (table). No adverse events with a rate ≥ 10% occurred in the sertraline group; dizziness was the only adverse event with a rate ≥ 10% in the placebo group (4.3% for sertraline v 18% for placebo, p=0.05).

Conclusion
In patients who had post-traumatic stress disorder and had responded to sertraline, maintenance sertraline reduced relapse and dropouts.

*See glossary.

COMMENTARY

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 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 randomised 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.

However, several methodological issues call for cautious interpretation of the results. The patients represent only a small proportion of those who entered the research programme. 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, 153 completed the open-label trial. Davidson et al then randomised 96 of these patients in the current trial, and only 48 completed the study.

This RCT is of much better quality than many previous studies of PTSD treatment. Notwithstanding these issues, the results convincingly favour 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.

Jonathan I Bisson, DM, MRCPsych
University Hospital of Wales
Cardiff, UK

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