Fluoxetine may prevent relapse in post traumatic stress disorder


QUESTION: Is fluoxetine effective and tolerable for preventing relapse in post traumatic stress disorder (PTSD) for up to 6 months?

Design
Randomised controlled trial. Participants, clinicians and outcome assessors were blind to treatment allocation.

Setting
18 centres is Belgium, Bosnia, Croatia, Yugoslavia, Israel and South Africa; June 1998 to August 2000.

Participants
Participants were 131 people diagnosed with PTSD (DSM-IV criteria); 81% men; 90% Caucasian; 47% exposed to combat-related traumatic events; mean age 38 years; mean duration between trauma and start of trial 5 years. Exclusion criteria were serious comorbid illness; concomitant psychotherapy; suicide risk or serious risk to others; Axis I psychiatric disorder 5 years before traumatic episode or following the primary traumatic episode, or lifetime diagnosis of bipolar disorder, obsessive compulsive disorder or schizophrenia.

Intervention
After 12 weeks of acute treatment with fluoxetine, responders received 24 weeks of relapse prevention with fluoxetine or placebo. (Responders had a 50% or greater decrease in the 8-item Treatment Outcome PTSD (TOP-8) score from baseline.) The initial dose of fluoxetine was 20 mg/day, increased to a maximum of 80 mg/day. The mean final dose was 53 mg/day. Mean drug exposure was 157 days during the 6-month maintenance period.

Main outcome measures
Time to PTSD relapse was measured using the TOP-8 scale and the Clinical Global Impression of Severity scale (CGI-S). Safety was assessed using adverse effects, discontinuation due to adverse effects, measurement of vital signs and clinical laboratory tests.

Main results
Participants receiving fluoxetine maintenance were less likely to relapse compared with placebo (table) and had greater mean improvement on the TOP-8 scale. There were no significant differences in treatment emergent adverse effects.

Conclusions
Fluoxetine maintenance may prevent relapse in post traumatic stress disorder for up to 6 months.

Outcomes for people with post traumatic stress disorder receiving fluoxetine or placebo maintenance for up to 6 months

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Fluoxetine % (n=69)</th>
<th>Placebo % (n=62)</th>
<th>Number needed to treat to benefit 1 with fluoxetine</th>
<th>Relative risk reduction %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completed relapse prevention</td>
<td>82.6</td>
<td>66.1</td>
<td>6 (3 to 59)</td>
<td>25 (0 to 51)</td>
</tr>
<tr>
<td>Discontinued due to relapse</td>
<td>5.8</td>
<td>16.1</td>
<td>9 (5 to 208)</td>
<td>68 (31 to 105)</td>
</tr>
</tbody>
</table>

Note: 95% confidence intervals are in parentheses.

COMMENTARY
Pharmacotherapy research in PTSD is still evolving, with fewer than 25 published randomised controlled studies. This study supports the emerging consensus: SSRIs are an effective first-line treatment for chronic PTSD. Further, among responders, pharmacotherapy should be continued for at least 6 months. This work extends that of an earlier study reporting that sustained treatment with an SSRI (sertraline) may prevent PTSD relapse. Although reports are mixed, SSRIs may be effective in PTSD treatment across all three core PTSD symptom clusters: (1) re-experiencing; (2) intrusion and avoidance; (3) numbness and hyperarousal. Martenyi et al found no improvement in the intrusive symptom subscore. Improvement was on symptom domains measured by providers, which were stronger than patient-rated measures. This contrasts with a study of sertraline that found improvement in PTSD symptoms in patient self-rated scales, but not clinician administered scales.

PTSD seldom lives alone – depression, panic disorder, and psychosis are often comorbid conditions. Excluding severe depression and psychotic spectrum disorders, although useful in designing research trials, limits generalisability to clinical practice. High rates of trauma and PTSD have been observed in people with psychotic spectrum disorders. Most recent large trials of SSRIs in PTSD have been among women with chronic PTSD related to assaultive interpersonal violence or rape. Martenyi et al’s study is a welcome addition to the literature because the cohort is predominantly men, many with combat-related traumatic stress. Participants were drawn from several different countries. The finding that fluoxetine is effective in men with chronic, predominantly combat-related, PTSD contrasts with other reports. Gender differences in trauma, PTSD and treatment response warrant further research.

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