Paroxetine plus cognitive behavioural therapy reduced the number of panic attacks in panic disorder


Objective
To evaluate the effectiveness and tolerability of paroxetine plus cognitive behavioural therapy (CBT) in patients with panic disorder.

Design
Randomised, double-blind, placebo-controlled trial with 14-week follow-up.

Setting
7 Danish centres.

Patients
120 patients between the ages of 18 and 70 years (mean age 37 y, 76% women) with a diagnosis of panic disorder according to the Diagnostic and Statistical Manual of Mental Disorders, Third Edition Revised (DSM-III-R), with or without agoraphobia, with ≥ 3 full panic attacks in the 4 weeks before study entry, and with a score of ≤ 14 on the 17-item version of the Hamilton Depression Scale were included. The exclusion criteria were primary diagnosis of major depression or generalised anxiety disorder or schizophrenia; organic brain disease; alcohol or drug abuse; or concomitant treatment with psychotherapies, monoamine oxidase inhibitors, anticoagulants, or benzodiazepines. 89% completed the study.

Intervention
All patients received "standardised" CBT. After 3 weeks of placebo, 120 patients were allocated to either paroxetine or placebo for 12 weeks. The dosage of paroxetine was increased from 10 to 20 mg/d during the first 2 weeks; from week 3 onward, the dosage was either 20 or 40 mg/d; and for 4 weeks onward, the dosage could be increased to 60 mg/d based on efficacy and tolerability. 12 weeks of treatment were followed by 2 weeks of placebo.

Main Outcome Measures
Frequency of panic attacks (assessed at 3-week intervals) and of adverse effects.

Main Results
12 weeks of paroxetine treatment led to more patients who had at least a 50% reduction from baseline in the number of panic attacks at 6, 9, and 12 weeks of follow-up than did placebo (82% vs 50% of responders at 12 weeks, P = 0.001). This absolute risk improvement of 32% means that 3 patients would need to treated for 12 weeks for 1 patient to have at least a 50% reduction in the number of panic attacks, 95% CI 2 to 7; the relative risk improvement was 64%, CI 24% to 129%. At 12 weeks, 36% of patients in the paroxetine group compared with 16% of patients in the placebo group had the number of panic attacks reduced to 1 or 0 (P = 0.024). Only 4 patients who received paroxetine were withdrawn because of adverse effects. Sudden discontinuation of medication after 12 weeks was well tolerated, although patients who received paroxetine had more adverse events (35%) than did patients who received placebo (15%) (P = 0.01).

Conclusion
More patients with panic disorders had a reduced number of panic attacks with paroxetine plus an unspecified form of cognitive behavioural therapy than with placebo plus behavioural cognitive therapy.

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*Numbers calculated from data in article.

Commentary
This study adds to the evidence that certain classes of antidepressant drugs, notably tricyclic antidepressants, selective serotonin re-uptake inhibitors, and high-potency benzodiazepines, are effective in the treatment of panic disorder with or without agoraphobia.

Few direct comparisons of antidepressants in panic disorder have been done, although clozapine is probably superior to imipramine (1). In this study, 36% of patients who received paroxetine had the number of panic attacks reduced to 1 or 0, and a high proportion (82%) of patients treated with paroxetine showed a ≥ 50% decrease in scores on the Hamilton Anxiety Scale, a change commensurate with significant clinical improvement. On the other hand, many patients (64%) continued to have some panic attacks, which may explain why almost half received the maximum dosage of 60 mg daily.

CBT is also effective in the treatment of panic disorder, and it was superior to imipramine in 1 controlled study (1). Although patients in the present study received "standardised cognitive therapy," the lack of detail about the CBT makes it difficult to determine their combined effects. When CBT is effective, treatment gains appear to be maintained after the end of therapy, which is not usually true for drug treatment (2). Therefore, in the study by Oehrberg and colleagues, it is important to know the course of the panic disorder after discontinuation of paroxetine therapy.

Antidepressant drugs undoubtedly are useful in the treatment of panic disorder, whether or not they are administered with CBT (1, 2). Selective serotonin re-uptake inhibitors have a distinct side-effect profile and are tolerated better in some patients than tricyclic antidepressants; however, gradual dose escalation is probably the key to low drop-out rates with both of these drugs (1, 2).

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References
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