Mental health

Discontinuing antidepressants too early raises risk of relapse

Patients who had been taking antidepressants for at least 9 months and felt well enough to stop were more likely to relapse by 52 weeks if their treatment was discontinued compared with those who carried on with their current therapy, a UK primary care study has found.

A total of 150 general practices, in Bristol, London, Southampton and York, took part in the double-blind trial. Potential participants were identified by searching electronic health records.

Inclusion criteria were: age 18-74 years; ≥ 2 prior episodes of depression or duration of antidepressant treatment ≥ 2 years; adherence to a therapeutic dose of citalopram, fluoxetine, sertraline or mirtazapine for at least 9 months; and feeling well enough to consider stopping treatment.

Patients with ICD-10 depression identified by the computerised CIS-R were excluded from the study.

Of a total of 1,466 patients who underwent screening, 478 were included in the trial. The average age was 54 and 73% were women. Around half (238) were randomised to maintenance treatment and 240 were randomised to the discontinuation arm. For those in the discontinuation group, treatment was tapered over 2 months followed by placebo. During the 52-week follow-up period, participants were followed up at 6, 12, 26, 39 and 52 weeks and relapse was identified using a modified retrospective CIS-R.

By the end of the 52-week trial period, 92/238 (39%) patients in the maintenance group and 135/240 (56%) patients in the discontinuation group had relapsed. The hazard ratio was 2.06 (95% CI: 1.56-2.70).

Compared with those in the maintenance group, patients in the discontinuation group had more symptoms of depression and anxiety (measured with the PHQ-9 and GAD-7 respectively). Overall, 70% of those in the maintenance group adhered to the trial regimen compared with 52% in the discontinuation group.

The British Association for Psychopharmacology (BAP) guideline recommends that all patients should take antidepressants for at least 6-9 months after full remission. For those at increased risk of relapse the duration of treatment should be tailored to the relapse risk. Risk factors include previous depression episodes, residual symptoms, severe or prolonged depression, or a history of treatment resistance. Those at high risk (e.g. > 5 lifetime episodes and/or ≥ 2 episodes in the past few years) should continue treatment for at least 2 years and most should consider indefinite treatment.[1]

NICE also recommends a minimum of 2 years' treatment for those with two or more depressive episodes in the recent past which have been associated with functional impairment.[2]

The risk of relapse increases with the number of previous depressive episodes.[3] In the present study, 93% of participants had ≥ 3 previous episodes of depression and most had been taking antidepressants for a number of years. Clearly these were high-risk patients for the majority of whom the BAP would recommend consideration of indefinite treatment.

NICE recommends that people who are currently well but have experienced 3 or more previous episodes of depression should be offered mindfulness-based cognitive therapy for relapse prevention.[2]

It is of interest that 39% of the maintenance group relapsed and this cannot be entirely explained by non-adherence. Other possible reasons for recurrence include tolerance to the drug, loss of placebo effect or an increase in disease severity.[4] Relapses, both in those receiving and not receiving antidepressants, are often self-limiting[1] and it is a pity that the study did not compare severity and duration of depression relapses between the maintenance and discontinuation groups.

For patients who meet the trial inclusion criteria, many of whom will be at high risk of relapse, the study findings may facilitate an informed choice as to whether to continue maintenance antidepressant treatment. Of every 100 such patients, 39 will experience a relapse within 12 months regardless of their decision and an additional 17 will experience a relapse if they choose to discontinue their antidepressant. In other words, the absolute risk reduction gained from 12 months' maintenance treatment is 17 in 100 and the NNT is 6.

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