Depressive recurrence on antidepressant treatment (DRAT): 4 next-step options

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"Poop-out" and "tachyphylaxis" are terms used to describe loss of antidepressant response after initial benefit, but both descriptors are problematic. Poop-out carries a mildly offensive aura that conveys a lack of seriousness about the patient's suffering. Tachyphylaxis is a pharmacologic term describing rapid or acute reduction in response to a drug after administration; it is not appropriate for antidepressant loss of response, which typically occurs months to years after treatment initiation.[1]

Depressive recurrence on antidepressant treatment (DRAT) is a better term to describe recurrence of a major depressive episode despite sustained treatment with an antidepressant that had induced remission. Maintenance studies of antidepressant treatment indicate DRAT occurs in approximately 10% of patients at 6 months and 20% at 2 years.[2]

Despite this high prevalence, there is little clinical trial data on which to base treatment decisions for patients who experience DRAT. There are 4 options:

1. Raise the dose. In small studies, doubling the dose of fluoxetine or duloxetine led to regaining response in approximately 60% of patients.[3] However, these studies lacked a placebo comparison arm, so the specific benefit derived from the dose increase is unknown. Improvement with a dose increase is somewhat at odds with the known mechanism of action of selective serotonin reuptake inhibitors (SSRIs), which are thought to have a flat dose-response curve. That is, once an SSRI blocks approximately 80% of the serotonin transporters, further dose increases produce minimal further blockade and, presumably, little clinical benefit via this mechanism.[4]

2. Switch medication. No studies have examined switching antidepressants after DRAT. Switching to a medication with a different mechanism may be justified based on the results of treatment-resistant depression (TRD) trials, in which patients who failed to respond to an initial medication—typically an SSRI—improved after switching to an antidepressant from a different class. However, the biology of DRAT may differ from that of SSRI nonresponse. Unlike many patients with TRD, patients who experience DRAT while taking an SSRI have demonstrated previous response to serotonergic modulation.

3. Augmentation. Similar to switching, this approach has not been studied specifically for DRAT. This approach is derived from trials in which patients who did not attain response after treatment with a single antidepressant had a second medication added. Again, the biology of these patients may differ from those with DRAT, who at one point did remit with antidepressant treatment.

4. Psychotherapy. This addition is a low-risk option for patients who previously have not received evidence-based psychotherapy for depression.

Clinicians have scant evidence on which to base their decisions for this common and important problem. Dose increase after DRAT represents the best supported, simplest, and perhaps least costly next step in treatment.

In DRAT patients, consider raising the antidepressant dose, switching or augmenting medication, or psychotherapy

References

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