Treatment-resistant depression

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The term "resistant" does not usually bode well in the healthcare setting. "Antimicrobial resistant," "resistant to care," "chemotherapy resistant cancer"—all of these may prompt specific focused interventions or programs, often involving multi-disciplinary team approaches, and creative, out-of-the box solutions, to attempt achievement of positive outcomes for the patients involved.

Treatment-resistant depression is no different. It is a diagnosis that is often dreaded by patients, caregivers, and providers alike. It is responsible for increased hospitalizations, increased outpatient provider visits, greater use of psychotropic medications, and an average six times greater total healthcare cost incurrence compared to non-treatment-resistant depressed patients.[1] Yet, the definition of treatment-resistant depression (TRD) remains somewhat controversial. In its simplest form, TRD can be defined as lack of significant improvement after two adequate trials of two different antidepressants from two different pharmacologic classes.[2] However, the definition can quickly become quite complicated. According to Berlim, one can find more than 10 different definitions of TRD throughout the published literature.[3] In addition, various authors have proposed staging systems for further description and characterization of TRD.[4,5,6,7,8] Still others have argued that perhaps many instances of TRD actually represent undiagnosed bipolar disorder,[9] nonadherence with therapy, and/or inadequate dose or duration of antidepressant therapy.[10]

The published literature focusing on treatment approaches for the management of TRD remains somewhat muddled due to the varying methods for defining TRD and how these definitions are employed in intervention studies. Despite the confusion and difficulty to extract conclusions on the data, some progress is being made in the treatment of TRD. This issue highlights some of that progress. Articles highlighting the use of lithium and second-generation antipsychotics for treatment of TRD provide a solid review of these important treatment options. Additional pieces discussing emerging therapies in TRD and the pharmacogenomic foundations upon which future TRD treatment decisions may be made highlight the directions in which we are heading. A toolbox summarizing pharmacologic treatment options and their advantages and disadvantages in TRD is also included and may serve as an excellent reference when working with this patient population.

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