Treatment-Resistant Depression

The Importance of Identifying and Treating Co-occurring Personality Disorders

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KEYWORDS

• Depression • Treatment-resistant depression • Personality traits
• Personality disorder • Borderline personality disorder

KEY POINTS

- Treatment-resistant depression (TRD) is common and produces significant burden to individuals and society. Comprehensive and individualized approaches are needed to address this complex clinical situation.
- Diagnostic reevaluation is indicated in cases of TRD to determine the numerous factors that could be playing a role in the treatment resistance.
- Diagnostic reevaluation in the setting of TRD should include assessment for personality disorders, because these are common contributors to treatment resistance and are often not adequately addressed.
- There are validated psychotherapeutic interventions that have proved effective in treating personality disorders to help patients improve both self-functioning and interpersonal functioning.

INTRODUCTION

Treatment-resistant depression (TRD) is a significant burden to individual patients and society because many individuals with depression do not achieve or sustain remission, despite multiple pharmacologic interventions and treatment settings. Review of the literature reveals many approaches to addressing TRD, including augmentation of antidepressants with atypical antipsychotics and other medications, aerobic exercise, manual-based psychotherapies, and a variety of neurostimulation strategies.[1] Despite this variety of treatment approaches, TRD remains a common and burdensome condition, and each case of TRD requires a thoughtful and individualized treatment approach with attention to the biological, psychological, medical, social, cultural, and spiritual factors involved.

Disclosure: The author has no disclosures.
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Psychiatr Clin N Am ■ (2018) ■–■
https://doi.org/10.1016/j.psc.2018.01.003 psych.theclinics.com
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Reevaluating the Diagnosis in Treatment-Resistant Depression

TRD often has multiple contributing factors that need to be identified so that they can be addressed with a comprehensive and individualized treatment plan. Reevaluating the clinical diagnoses to help clarify the contributing causes of treatment resistance is an essential component in the assessment of patients with TRD. Common causes of treatment resistance can include misdiagnosis of bipolar depression as unipolar depression, co-occurring substance use disorders, untreated medical conditions, cognitive impairments, trauma disorders, and co-occurring personality disorders. Considering all of these factors in a methodical and thoughtful way is essential in the diagnostic assessment of patients with TRD (**Fig. 1**).

Many psychiatrists have observed treatment resistance resulting from cases in which bipolar depression or mixed states of bipolar disorder have not been recognized and the symptoms have been treated as a unipolar depression. In these cases, the medication regimen often has included antidepressants indicated to treat major depressive disorder but not bipolar disorder. Antidepressants in the setting of bipolar disorder are often ineffective and can potentially exacerbate the symptoms of the bipolar illness and lead to agitation, restlessness, and increased anxiety. Considering the possibility of an underlying bipolar disorder in these cases is often the key to achieving a more effective pharmacologic approach.

In other cases of TRD, there is an underlying substance use disorder (eg, alcohol abuse), untreated or undertreated medical condition (eg, hypothyroidism, cardiovascular disease), underlying cognitive impairment (eg, mild cognitive impairment, dementia), or underlying trauma disorder (eg, posttraumatic stress disorder) complicating or confounding the successful treatment of the depressive episode. Careful history taking, physical examination, urine drug screens, basic medical screening laboratory tests, neurocognitive testing, and brain imaging can often be useful in identifying these contributors of treatment resistance so that appropriate interventions for these complicating factors can be recommended.

In addition to the aforementioned contributors to TRD, co-occurring personality disorders, including a poorly integrated or disrupted sense of self, can contribute significantly to treatment resistance and enduring depressive symptoms. For example, in an avoidant personality disorder there can be low self-esteem, feelings of inferiority, excessive feelings of shame or inadequacy, preoccupation with and sensitivity to criticism or rejection, avoidance of social activity, lack of energy for engaging in life, and a deficit in the capacity to feel pleasure. As another example, in borderline personality disorder (BPD) there can be a poorly developed or unstable self-image; excessive self-criticism; chronic feelings of emptiness; mood instability; frequent feelings of being down and hopeless; feelings of low self-worth; and thoughts of suicide, including

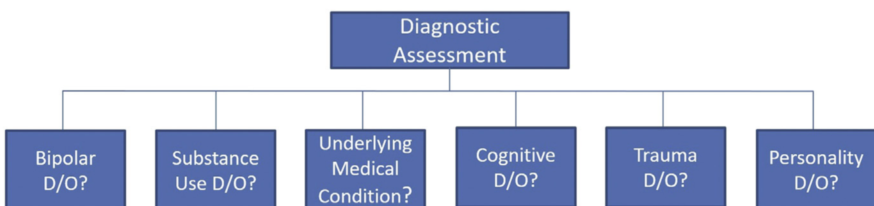

Fig. 1. Diagnostic assessment in TRD. D/O, disorder.

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