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Depression Series (Part 2): My Antidepressant Doesn't Work. What Can My Psychiatrist Do?

By Michael G. Rayel, MD

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Maria has been increasingly depressed for the past few years. She has tried at least four newer antidepressants but so far, she doesn't seem to respond. Unable to work, she's now feeling helpless and hopeless. Likewise, her family is discouraged. Frustrated and baffled by Maria's lack of progress, the family doctor refers her to a psychiatrist.

What can the psychiatrist do to help Maria?

The psychiatrist has several options in dealing with a treatment-resistant or refractory depression. First, Maria's psychiatrist can optimize the dose of her antidepressant. Maria has been taking low doses of antidepressants. In spite of her lack of response, the medication dosage has not been increased. To obtain a clinical response, her psychiatrist should increase the dose every two to three weeks. The antidepressant can be adjusted up to the maximum allowable dose if no or only partial response is observed.

Second, her psychiatrist can choose to augment the effect of her antidepressant with another medication such as lithium, triiodothyronine (T3), or buspirone. Among augmenters, lithium and triiodothyronine have the best support from the literature. Despite lithium's efficacy, some doctors avoid this drug because it requires regular blood monitoring and has unfavorable side effect profile such as acne, tremors, and thyroid and renal dysfunction.

Recently, studies have shown atypical neuroleptics such as olanzapine and risperidone to be good augmenters. In my opinion, further studies are necessary to establish these two drugs as standard augmenters. Indeed, research studies and clinical experience have found augmentation strategy to be effective.

Third, combination strategy is worthwhile to try. Maria's psychiatrist can add another antidepressant to boost the effect of her current antidepressant. For instance, trazodone can be added to an SSRI

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(serotonin reuptake inhibitor e.g. citalopram). Literature suggests that combining two drugs with different mechanisms of action and drugs that involve several brain chemicals has resulted in clinical improvement. In this scenario, one antidepressant plus another antidepressant is equal to three, or four or even ten, not two.

Fourth, the psychiatrist can switch from one antidepressant to another. Previous studies have shown that when making a switch, a drug should be replaced by a drug from a different class e.g. from SSRI to SNRI (serotonin and norepinephrine reuptake inhibitor e.g. venlafaxine), or from TCA (tricyclic agent e.g. nortriptyline) to SSRI. But recent studies show that switching drugs within the same class (e.g. SSRI to another SSRI) is just as effective.

Fifth, Maria's psychiatrist can also treat other ongoing symptoms or drug-related problems that further complicate her depression. If she is anxious and agitated, then her psychiatrist should prescribe an anxiety drug (e.g. lorazepam) or if Maria is psychotic then adding an antipsychotic drug should

help. Moreover, medication side effects (such as insomnia, dryness of mouth, constipation, etc.) that negatively affect Maria's compliance to the drug should be addressed promptly.

Lastly, if despite above measures Maria doesn't respond to antidepressants, then electroconvulsive therapy should be entertained. Of course, this procedure should be done with her consent.

In summary, Maria's psychiatrist can optimize the dose, augment or combine treatment, switch the medication, treat side effects and ongoing symptoms, or use electroconvulsive therapy for treatment-resistant or refractory depression.

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Depression Series: Why Don't I Respond to Medications? (Part 1)

By Michael G. Rayel, MD

Maria has been feeling depressed for at least two and a half years. About three years ago, her husband of 20 years left her for another woman. Devastated, she became despondent and tearful almost daily.

Eventually, her depression got worse associated with inability to function. Her appetite, energy, concentration, and sleep became impaired. She also felt hopeless and suicidal. Her psychiatrist put her on a starting dose of antidepressant. She responded initially but after a few days, she felt just like before taking the medication.

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For the past two years, Maria has tried four types of antidepressants. She has taken the usual adult doses of these drugs. Although she somewhat improves, she has virtually remained the same — depressed and disabled.

Maria seems to be taking the medications regularly. But why is she not responding to her antidepressants?

Maria is just one of the many depressed individuals who don't feel "normal" despite treatment. Depression is a treatable disease but how come some people don't do well on medications?

There are many reasons why depressed patients like Maria don't improve on antidepressants.

First, is the diagnosis correct?

Depression can be caused by many clinical entities. Sometimes, knowing the right diagnosis is a challenge. Medical disorders, medications such as beta-blockers and benzodiazepines (e.g. clonazepam), and various psychiatric disorders can cause depression and they all require different treatment. If your doctor fails to identify and treat the true cause of your depression, you will remain depressed despite the use of antidepressant.

Second, are there co-morbid disorders?

Depression can exist along with other psychiatric disorders such as anxiety disorder, alcohol or drug problems, personality disorder, dementia, and psychosis. Depression will persist if these co-morbid disorders are not treated. For instance, depressive disorder with psychosis cannot be adequately treated just with antidepressant alone. You need an antipsychotic drug added to an antidepressant to treat the illness.

Third, is there an ongoing neurological or medical disorder that precipitates, aggravates, or complicates depression?

Hypothyroidism, hyperthyroidism, vitamin B-12 deficiency, pancreatic cancer, brain tumor, Parkinson's

disease, and stroke can all cause depression. If any of these disorders are present, antidepressants are less likely to help. The goal in these situations is to treat the underlying medical condition. A 65 year-old lady came to see me complaining of severe depression. On evaluation, she disclosed that she had been on three types of antidepressants for the past four years with minimal response. I checked her recent laboratory results which showed an abnormal thyroid! No wonder, she was not responding to the medication.

Fourth, are there ongoing psychosocial issues?

Financial problems, family conflict, work-related stress can all precipitate and complicate depression. Despite adequate medication treatment, some individuals will remain depressed especially if such problems are not addressed by the therapist or psychiatrist. Is there any way you can reduce the

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stressors? Please do so the earliest you can.

The treatment of depression is frequently straightforward. Occasionally however, various factors complicate it. For antidepressant to be effective, a psychiatrist should ensure that the diagnosis is correct, that co-morbid psychiatric disorders and medical problems are treated, and that psychosocial issues are adequately addressed.

Maria's doctor should explore further the real problem and provide the most appropriate intervention.

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