American Association of Psychiatric Pharmacists (aapp.org)

What to Know About Treatment-Resistant Depression

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- About 60% of people starting medications for depression have to try more than one medication before their symptoms go away.[6] There are many treatment options, so it is important to be open when working with your doctor and make treatment decisions together.
- If you or someone you know is thinking about suicide or needs emotional support, call or text one of the following 24 hours a day, 7 days a week:
  - **Suicide & Crisis Lifeline:** Call or text 988
  - **National Suicide Prevention Lifeline**: 1-800-273-8255
  - **Crisis Text Line**: Text HELLO to 741741
  - **Veterans Crisis Line**: 1-800-273-8255; Press 1

What is treatment-resistant depression?

Treatment-resistant depression means different things to different people. Most often, it means a person has tried two or more antidepressants for several months each and still has depressive symptoms.[1] Some common antidepressants are: Zoloft®, Celexa®, Lexapro®, Prozac®, Cymbalta®, Effexor®.

Why do some people have treatment-resistant depression?[2,3]

- Family history of depression
- Genes that can lead to a poor response to medications
- Use of substances, such as alcohol or marijuana
- Side effects caused by medications
- Having illnesses that contribute to a depressed mood
- Ongoing home or life stressors

What medication changes can be made for treatment-resistant depression?

If an antidepressant already being used is not working, the first step is to make sure that it is at the right dose for a long enough time-period. The best dose for one person may be different than the best dose for another. A doctor should decide what the best dose is and when to try the next step. If symptoms do not get better after dose increases of one medication, the doctor may decide to:

- Switch to a different antidepressant
- Add on a second antidepressant
- Add on a medication used for other mental illnesses besides depression

Two medications approved by the Food and Drug Administration (FDA) for treatment-resistant depression are olanzapine/fluoxetine (Symbyax®) and intranasal esketamine (Spravato®).[4] Another option for treatment-resistant depression is ketamine. This is given by intravenous (IV) infusion in a clinic setting and improvement in symptoms can be seen in hours. Unfortunately, at this time it is not known how well this treatment works long-term.[5]

What are some other treatments that may help?

Talk therapy has been shown to work for depression, even in people who have not gotten better from medication in the past.[6] Therapy can provide tools for dealing with life stressors that medication cannot help. It has also been shown that the effects of therapy can last longer than the effects of medications. Most people do better on both talk therapy and medication than just one alone.[2,6]

Additionally, there are certain brain stimulation procedures for treatment-resistant depression that are performed by a physician in a clinic. Transcranial magnetic stimulation (TMS) is done when a person is awake while electroconvulsive therapy (ECT) and vagus nerve stimulation (VNS) are done when a person is under sedation.[2] These are used when many different medications have failed to help depression symptoms.

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What life routine changes can be made to help depression symptoms?

- Avoid illegal drugs, alcohol, and cigarettes. These can make depression worse by working against medication and changing emotions.
- Exercise can help to improve depression symptoms by increasing chemicals in the brain that improve mood.[1] Be sure to always check first with your doctor to see what exercise is appropriate for you.
- Be open about life changes. There are often physical causes of depressive symptoms, such as starting a new medication, hormonal changes, or poor sleep and diet.[7] Talking with a therapist, close friend, or relative and following up with your doctor may help uncover causes of depressive symptoms.
- Develop a daily routine. Studies have shown keeping busy can improve physical function, anxiety, and depressive symptoms.[8]

After making any changes, discuss with a doctor:

- If you have thoughts of suicide
- If medications for depression have been stopped for any reason
- If medication doses are missed
- If medications for depression have caused side effects
- If you have changed thoughts, mood, energy, or interest in activities

Go online to find more information about treatment-resistant depression and to view the references for this toolkit.

https://aapp.org/resource/patients

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