Adding antipsychotic medication to antidepressant may help older adults with treatment-resistant depression.

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Introduction

For older adults with clinical depression that has not responded to standard treatments, adding the drug aripiprazole to an antidepressant they're already taking is more effective than switching from one antidepressant to another. Aripiprazole originally was approved by the FDA in 2002 as a treatment for schizophrenia but also has been used in lower doses as an add-on treatment for clinical depression in younger patients who do not respond to antidepressants alone. Many people with clinical depression don't respond to medications used to treat the condition. Consequently, some doctors switch such patients to different antidepressants in the pursuit of finding one that works, while other physicians may prescribe another class of drugs to see if a combination of medications helps. Both strategies have been recommended by experts as options for older adults with treatment-resistant depression [1]. However, the new study was designed to help determine which strategy is most effective. Augmenting an antidepressant with aripiprazole helped 30% of patients with treatment-resistant depression, compared to only 20% who were switched to another solo antidepressant, results of the study show.

Often, unless a patient responds to the first treatment prescribed for depression, physicians follow a pattern in which they try one treatment after another until they land on an effective medication," It would be beneficial to have an evidence-based strategy we can rely on to help patients feel better as quickly as possible [2]. We found that adding aripiprazole led to higher rates of depression remission and greater improvements in psychological well-being-which means how positive and satisfied patients felt-and this is good news. However, even that approach helped only about 30% of people in the study with treatment-resistant depression, underscoring the need to find and develop more effective treatments that can help more people. Treatment-resistant depression is no more or less common in older people than younger people, but because it seems to accelerate cognitive decline, identifying more effective ways to treat it is very important. Studied 742 people, ages 60 and older, with treatment-resistant depression, meaning their depression had not responded to at least two different antidepressant medications.

The researchers evaluated strategies commonly used in clinical practice to help alleviate treatment-resistant depression in older patients and designed the study to have two distinct phases. In the first phase, 619 patients, each of whom was taking an antidepressant such as Prozac, Lexapro or Zoloft, were randomly divided into three groups. In the first group, patients remained on whatever antidepressant drug each already was taking but also received the drug aripiprazole. A second group also continued taking antidepressants but added bupropion, and a third group tapered off of the antidepressant each had been taking and switched to bupropion entirely. Over the course of 10 weeks, the participants received biweekly phone calls or in-person visits with study clinicians. At these visits, the medications were adjusted according to the individual patient's response and side effects. The researchers found that the group that experienced the best overall outcomes was the one in which patients continued with their original antidepressants but added aripiprazole [3]. The researchers also anticipated that some people in the study wouldn't respond to the various treatments, so they added a second phase that included 248 participants. In this phase, patients taking antidepressants such as Prozac, Lexapro and Zoloft were treated with lithium or nortriptyline - medications that were widely used before those other, newer antidepressants were approved more than two decades ago. Rates of alleviating depression in the study's second phase were low, about 15%. And there was no clear winner when augmentation with lithium was compared with switching to nortriptyline.

Those older drugs also are a bit more complicated to use than newer treatments," "Lithium, for example, requires blood testing to ensure its safety, and it's recommended that patients taking nortriptyline receive electrocardiograms periodically to monitor the heart's electrical activity. Since neither lithium nor nortriptyline were promising against treatment-resistant depression in older adults, those medications are unlikely to be helpful in most cases. But even the best treatment strategy-adding aripiprazole to an antidepressant-was not markedly successful for many older patients with treatment-resistant depression [4]. Any given treatment is likely to help only a subset of people, and ideally, we would like to know, in advance, who is most likely to be helped, but we still don't know how to determine that.

Overall antidepressants are highly helpful for the majority of people suffering from clinical depression. At least half of

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all people with depression feel much better after they begin taking the first medication they try. And almost half of the remainder not helped by a first drug improve when switched to a second drug, but that leaves a sizeable group with clinical depression that does not respond to two treatments. The problem is particularly difficult in older adults, many of whom already are taking several medications for other conditions such as high blood pressure, cardiac issues or diabetes [5]. So switching to new antidepressants every few weeks or adding other psychiatric drugs can be complicated. In addition, because depression and anxiety in older adults may accelerate cognitive decline, there's an urgency to find more effective treatment strategies.

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