Antipsychotics for treating adult depression linked with higher mortality

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Rutgers researchers, together with colleagues at Columbia University, have reported an increased mortality risk in adults with depression who initiated augmentation with newer antipsychotic medications compared to a control group that initiated augmentation with a second

antidepressant.

The study was published in the journal *PLOS ONE*.

Although antidepressants are the first-line pharmacological treatment for depression, many people do not respond to the first course of treatment. Subsequent treatment options include switching to another antidepressant followed by various augmentation strategies, including augmentation with a second antidepressant and augmentation with newer antipsychotics, such as aripiprazole, quetiapine and olanzapine.

"Antipsychotics have well-recognized and often serious adverse effects, including a more than 50 percent increased mortality risk in older adults with dementia," said lead author Tobias Gerhard, an associate professor at Rutgers Ernest Mario School of Pharmacy. "It had been previously unknown whether this mortality risk applies to non-elderly adults using newer antipsychotics as augmentation treatment for depression. The clinical trials that led to the approval of various newer antipsychotics for depression were just too small and too short to be informative for this question."

The researchers looked at data of 39,582 Medicaid beneficiaries ages 25 to 64 from 2001 to 2010, linked to the National Death Index. After a period of treatment with a single antidepressant, study patients initiated either augmentation with a newer antipsychotic or with a second antidepressant. The researchers found a 45 percent relative increase in mortality risk for those initiating a newer antipsychotic, which for the study cohort translated to one additional death for every 265 people taking the antipsychotic for one year.

"Our results require replication, ideally with a publicly financed pragmatic randomized controlled trial. However, in the meantime, our study suggests that physicians should consider prescribing antipsychotics

to adults with depression carefully, as the potential health risks are substantial and the benefits are quite modest and controversially debated," said Gerhard. "Of particular relevance for our results is a finding from our previous work. It is well-known that most antidepressants take about four to six weeks to be fully effective. However, contrary to the drug label and treatment guidelines many patients in the United States initiate antipsychotic treatment for depression without having completed an adequate prior trial with a single antidepressant. Our results emphasize the importance of considering newer antipsychotics only after non-response to less risky, evidence-based treatment options has been established."

More information: *PLOS ONE* (2020). journals.plos.org/plosone/arti… journal.pone.0239206

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