

GLP-1s May Interact With Psychiatry Medication

— Psychiatrists call for greater awareness of potential interaction

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During an appointment with her psychiatrist, a 50-year-old woman with bipolar disorder reported new symptoms of tremor in both hands, slurred speech, and blurred vision.

She was taking lithium, but 3 weeks prior, she had also started treatment with the dual GIP/GLP-1 receptor agonist tirzepatide (Zepbound), Jay Davis, MD, of the University of Colorado Anschutz Medical Campus in Aurora, and colleagues wrote in a [case report in the *Journal of Clinical Psychopharmacology*](#).

Labs showed her serum lithium level had increased from 0.7 to 1.2 mmol/L; a lithium dose reduction resolved her symptoms, suggesting a probable drug interaction, the researchers reported.

While this interaction has been reported before -- it's the fourth reported case of tirzepatide-associated lithium toxicity, they said -- it's still not well understood, Davis said.

"The favored mechanism for this medication interaction – increased fractional reabsorption due to decreased oral intake – raises interesting questions about whether and how these medications might be prescribed safely together," Davis told *MedPage Today*.

"There's reason to believe incretin mimics like tirzepatide will be increasingly prescribed to patient populations receiving lithium," he added. Awareness of this potential interaction is growing, but "we as a medical community still have work to do in growing that awareness further and deepening our understanding of it."

Jorge Almeida, MD, PhD, director of the bipolar disorder center at the University of Texas at Austin, who was not involved in the report, said it adds to a "small but growing set of cases" suggesting these medications may raise lithium levels, even in patients on a fixed dose with normal kidney function.

"A single case can't prove cause-and-effect, but the timeline and the resolution after the lithium dose was reduced make it hard to dismiss," Almeida told *MedPage Today*.

"The practical message is early monitoring, not avoidance," he said. "These medications may be valuable for people with bipolar disorder, who have high rates of obesity and type 2 diabetes. If a patient on lithium is starting one, I'd check a lithium level and kidney function within the first few weeks, and again after any dose changes."

Patients should know the early warning signs of toxicity and "call their prescriber rather than stopping either medication on their own," he added.

Despite its limitations, lithium remains "a cornerstone of management in patients with bipolar disorder," the case report authors wrote. Incretin mimetics "appear poised to benefit individuals with bipolar disorder due to their impressive efficacy in treating type 2 diabetes and obesity." Thus, further caution is warranted about potential drug interactions, they said.

In this case, the patient had started on lithium and titrated up from 300 mg extended release, through 450 twice daily, and finally consolidated to 900 mg nightly about 5 weeks later. She had an appointment with her primary care provider, where her labs showed no electrolyte abnormalities, normal renal function, and a serum lithium level of 0.7 mmol/L. Over the next month, she reported improved mood stability, and no adverse side effects, the authors wrote.

She was then prescribed tirzepatide in a dose of 2.5 mg subcutaneously once a week for chronic weight management. At her psychiatry appointment 3 weeks later, she had a noticeable tremor in both hands, slurred speech, and reported blurred vision. The symptoms were new, and had been ongoing for 2 days.

The trough serum lithium level taken the next day was 1.2 mmol/L. She hadn't changed her dose, how she was taking her lithium, or started any other drugs in the meantime, but said she had been eating smaller meals, achieved earlier satiety, and had some bloating since starting tirzepatide.

The patient was advised to reduce the lithium dose to 450 mg nightly, and her symptoms subsided soon after. A trough serum lithium level taken 17 days later was 0.4 mmol/L.

She had lost 5 pounds during the 3 weeks she was on tirzepatide, but she decided with her doctor not to restart treatment because of the apparent risk of interaction with lithium. She was gradually re-titrated up to 900 mg of lithium nightly.

Disclosures

Neither the authors nor Almeida reported any disclosures.

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