Schizoaffective Exacerbation in a Roux-en-Y Gastric Bypass Patient Maintained on Clozapine

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Although clozapine is the treatment of choice for treatment-resistant schizophrenia, weight gain may undermine compliance in this population.[1,2] Over the last few years, Roux-en-Y gastric bypass (RYGB) has emerged as a popular procedure for the treatment of obesity.[3] RYGB can change several pharmacokinetic factors. Some changes happen instantly, such as those in the absorption surface area, acidity, and intestinal metabolism of medications. Other factors such as fat storage and the volume of distribution may change later.[4] More recent studies[5,6] focused on RYGB postsurgical changes with antidepressants. However, to the best of our knowledge, there are no published reports regarding changes with clozapine, with the exception of 1 in vitro modeling study[7] that postulated a decrease in clozapine blood levels following RYGB.

Case Report

A 31-year-old man with a diagnosis of schizoaffective disorder and a history of multiple inpatient hospitalizations was maintained on clozapine 325 mg daily in divided doses, lithium 1,200 mg daily, and venlafaxine 225 mg daily and functioned well in society for 3 years. After gaining weight over the last few years—he now weighed over 300 lb—and subsequently developing severe sleep apnea, he decided to undergo RYGB. One week prior to surgery, his clozapine level was 451 ng/dL and lithium level was 0.8 ng/dL, but no levels were obtained thereafter. Within 1 month following RYGB, according to his family, his paranoia and delusions reemerged, and he consequently became nonadherent with medications, resulting in a psychiatric hospitalization at 3 months postsurgery. During his hospitalization, he refused to be restarted on clozapine and was treated with both paliperidone intramuscular 234 mg every 4 weeks and aripiprazole 30 mg daily. He was discharged from the hospital after 6 weeks.

Discussion

RYGB is known to have multiple effects on pharmacokinetics, thus altering the body's response to medications.[4] It can result in a reduction of gastric acidity, protein binding, surface area, and absorption.[4] With a further decrease in weight and body fat, volume of distribution of the medication changes, consequently altering the medication activity.[4] The maximal plasma concentration of sertraline was reported to be significantly smaller in subjects who had undergone RYGB than in matched subjects who had not.[8]

The effect of RYGB on several psychotropics has been studied and reported to vary considerably from drug to drug. Most studies[5,6] report a decrease in blood levels of most selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors and recommend close follow-up of patients on these medications to avoid relapse of symptoms. On the other hand, published case reports[9–11] show an increase in lithium blood level but no apparent changes with haloperidol.

Our patient had a therapeutic clozapine level 1 week before surgery, and he was compliant and clinically stable for 3 years prior. Although the absence of blood clozapine level measures following RYGB for comparison can be considered a limitation, his previous compliance with medications for 3 years and worsening with discontinuation raises concerns about likely pharmacokinetic changes affecting the clozapine level and resulting in clinical decompensation.

Clozapine deserves important consideration, as it remains the medication of choice in the treatment-resistant population and is notorious for weight gain. Surprisingly, there are no human studies that examined the effect of RYGB on clozapine levels, with only 1 in vitro study[6] suggesting that its level can decrease significantly after the surgery. This potential level reduction is serious, as it can result in symptomatic relapse, leading to prolonged hospitalizations and possibly functional impairment. Our report is the first to describe such decompensation. Close clinical follow-up and frequent monitoring of clozapine blood levels and medication dose adjustments are warranted following RYGB.

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