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### **Authors**

Chuang, Tammy

Sweeney, Dana

Tsai, Monica

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## CLINICAL VIGNETTE

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# Withdrawal Symptoms of Commonly Prescribed Medications: The Importance of Medication Adherence

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Tammy Chuang, MD, Dana Sweeney, DO and Monica Tsai, MD

### *Introduction*

Many commonly prescribed medications can be associated with withdrawal symptoms with abrupt discontinuation following long term use. We describe a patient that highlights the importance of medication adherence with beta blockers, GABA analogs, and antidepressants.

### *Case Presentation*

A 62-year-old man with a complex past medical history including: hypertension, hyperlipidemia, prior polysubstance use disorder, Parkinson's disease, mood disorder, obstructive sleep apnea, chronic tobacco use, cervical radiculopathy, primary hyperparathyroidism and prior nephrolithiasis. He presented as a new patient to primary care requesting medication renewals. He recently moved to the area to participate in a halfway house sobriety program and ran out of most of his medications. His chronic medications included carbidopa-levodopa, fluoxetine, buspirone, trazodone, lisinopril, gabapentin, and metoprolol tartrate. Other than carbidopa-levodopa, he had been off all of his other medications for five days and he reported anxiety, stress, labile emotions, terrible nightmares, nausea and fatigue. He denied any recreational drug use in the past six months and reported that the halfway house performed frequent drug tests. He denied fever, chills, chest pain, shortness of breath, cough, dysuria, hematuria, flank pain, vomiting, or diarrhea.

His presenting vital signs included a temperature of 97.7 F, heart rate of 136 beats per minute, blood pressure of 119/87mmHg, and oxygen saturation of 98% on room air. On physical exam, he appeared anxious and diaphoretic. Cardiac exam was notable for tachycardia, otherwise the pulmonary, abdominal, and extremity exams were benign. His labs were notable for white blood cell count of 14.1, hemoglobin of 18.7, platelet of 262, creatinine of 1.54, BUN of 31, TSH of 0.758, blood glucose of 99, and unremarkable urinalysis.

### *Case Outcome*

His medications were promptly resumed. At his one week follow up, he reported that his symptoms started to improve within a day of resuming his medications and he felt back to his usual state of health over the following week. His vital signs normalized with blood pressure of 110/66 mmHg, and heart rate of 83 beats per minute. His labs also normalized with WBC of

8.24, hemoglobin of 16.2, platelet of 244, creatinine of 1.16, and BUN of 12. He was thankful to be feeling much better and that he planned to be more adherent with future medication renewals.

### *Discussion*

Metoprolol is a widely utilized beta-adrenergic antagonist frequently prescribed for many conditions: hypertension, heart failure, angina pectoris or arrhythmias.<sup>1</sup> When higher doses of beta blockers are abruptly stopped without a taper, acute withdrawal can occur due to rebound increased sympathetic activity. Symptoms can start within 24 hours of cessation and include tachycardia, nervousness, anxiety, agitation, diaphoresis as well as angina or myocardial infarction in patients with heart failure or coronary artery disease.<sup>2</sup> Gradual taper is recommended for beta blockers with shorter half-lives, such as short acting metoprolol tartrate. One recommended taper regimen reduces the daily dose of the beta blocker by 50% per week until reaching the lowest dose, then maintaining that dose for one week prior to full discontinuation.<sup>3</sup>

Gabapentin is a gamma-aminobutyric acid (GABA) analog that has various indications including use as an anticonvulsant and anti-spasmodic agent. The medication is also used in neuropathic pain, alcohol withdrawal, anxiety and depression.<sup>4</sup> Rapid cessation of gabapentin can lead to symptoms such as irritability, confusion, palpitations, agitation, dizziness, and diaphoresis.<sup>5</sup> Gabapentin should be tapered slowly over several weeks. One suggested taper schedule reduces the daily dose by 300 mg every 4 days.<sup>6</sup>

Buspirone is a partial agonist of 5HT1 receptors and therefore has no effect on benzodiazepine GABA receptors. As such, abrupt discontinuation of buspirone should not lead to benzodiazepine withdrawal symptoms and could not account for our patient's symptoms.<sup>7</sup>

This case reiterates the importance of recognizing antidepressant discontinuation syndrome, which can occur in about 20% of patients who abruptly stop antidepressants that they have been taking continuously for at least a month. Symptoms of antidepressant discontinuation syndrome can be remembered using the mnemonic FINISH: flu-like symptoms, insomnia, nausea, imbalance, sensory disturbance, and hyperarousal (such

as anxiety, irritability, aggression).<sup>8</sup> Discontinuation symptoms have been observed in all classes of antidepressants. In our case, abruptly stopping the serotonin modulator trazodone and to a lesser degree the selective serotonin-reuptake inhibitor (SSRI) fluoxetine, also may have contributed to his symptoms. Abrupt cessation of trazodone can cause headache, anxiety, nausea, and weakness. The recommendation is to taper trazodone gradually over two to four weeks prior to cessation.<sup>9</sup> The risk of withdrawal symptoms with SSRIs depends on the medication half-life. The longer half-life of fluoxetine may have a safety advantage over short-acting SSRIs such as paroxetine. As such, fluoxetine has the lowest risk of withdrawal symptoms amongst SSRIs.<sup>10</sup> Most SSRIs recommend tapering over two to four weeks prior to discontinuation. Given the long half-life of fluoxetine, tapering over one to two weeks may be sufficient.

### Conclusion

This case illustrates adverse withdrawal symptoms that may occur with the abrupt medication cessation. In this patient, the cessation of metoprolol, gabapentin, trazodone, and fluoxetine all likely all contributed to the constellation of symptoms, abnormal vital signs and laboratory values. Careful tapering of these medications after long term use is warranted if discontinuation is indicated.

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