Enhanced Metabolism of Buprenorphine in a Man Prescribed Prednisone for Crohn's Disease

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Buprenorphine/naloxone is a medication that is commonly used in the treatment of opioid use disorder. Here, we discuss an unusual case in which a man's prednisone therapy for Crohn's disease enhanced buprenorphine metabolism via upregulation of hepatic enzymes, ultimately leading to a false-negative urine drug screen.

Case Report

A 28-year-old man presented to the addiction clinic for treatment of opioid abuse. His history was significant for Crohn's disease with diverting loop ileostomy. He was diagnosed with opioid use disorder according to *DSM-5* criteria and started on sublingual buprenorphine/naloxone 8/2 mg 3 times daily. As part of his treatment regimen for opioid use disorder, the patient was required to undergo urine drug screening (UDS) on a weekly basis. Enzyme-linked immunosorbent assay (ELISA) and gas chromatography–mass spectrometry (GCMS) were used for drug detection. The cutoff for a positive result was 5 ng/mL for ELISA and 0.5 ng/mL for GCMS. The patient's first UDS was positive for a variety of substances including alcohol, amphetamines, benzodiazepines, cocaine, opiates, marijuana, buprenorphine, and norbuprenorphine (a metabolite of buprenorphine). Subsequent screening tests were only positive for buprenorphine/norbuprenorphine. Our patient experienced significant benefit from buprenorphine therapy and reported an improvement in his quality of life due to reduced fatigue and pain.

On the fourth week of buprenorphine treatment, the patient's UDS was negative for buprenorphine/norbuprenorphine. He reported taking buprenorphine as prescribed. A thorough chart review revealed that the patient was started on 40 mg of prednisone as therapy for an acute exacerbation of his Crohn's disease 13 days prior to the negative screen. After another 4 weeks of stable treatment, the patient's UDS was again negative for buprenorphine/norbuprenorphine. This time, chart review revealed the patient was started on 180-mg prednisone therapy for a Crohn's disease flare-up 3 days prior to the negative screen. Interestingly, the patient reported no increase in his cravings on either of these 2 occasions.

Discussion

Patients undergoing treatment with buprenorphine at addiction clinics who present with negative screens for buprenorphine are often suspected of improper intake or diversion, which is frequently the case. However, psychiatrists and primary care physicians must understand the pharmacodynamic factors that may potentially lead to false-negative UDS results.

It is well known that hepatic cytochrome enzymes play a key role in the metabolism of drugs, both illegal and legal. Many potential drugs of abuse, including cocaine, amphetamine, morphine, and tetrahydrocannabinol, are processed via cytochrome-mediated enzymatic pathways.[1] Similarly, buprenorphine and prednisone are both metabolized by the cytochrome P450 (CYP) enzyme CYP3A4.[2–4] Prednisone is also a potent inducer of CYP3A4, a characteristic that can enhance the metabolism of other CYP3A4 substrates.[3] We believe concurrent administration of prednisone and buprenorphine may have led to a false-negative UDS in this patient via CYP3A4 enzyme induction. Theoretically, CYP3A4 induction could have altered the UDS results for other illicit drugs. During the instances when our patient tested positive for street drugs, he was not taking prednisone.

Buprenorphine has an extremely low oral bioavailability, as it undergoes extensive presystemic metabolism. Sublingual administration bypasses gastric enzymes and the hepatic first-pass effect.[5] As a result, sublingual buprenorphine has become an efficient means of treating opioid use disorder. In patients with inflammatory bowel disease and enteric diversion, intestinal nutrient absorption becomes less efficient. This inflammation can also affect drug absorption, depending on the extent of disease. Sublingual administration of buprenorphine effectively bypasses this factor. Therefore, we do not believe this patient's Crohn's disease or diverting ileostomy played any role in his negative UDS, although this was an idea hypothesized by the patient.

Conclusion

Although diversion and improper intake are leading causes of negative UDS for buprenorphine/

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norbuprenorphine in the treatment of opioid use disorder, it is also important that clinicians consider other possible explanations. Pharmacodynamic factors and drug-drug interactions should always be part of a thorough differential diagnosis when evaluating buprenorphine treatment compliance in patients with opioid use disorder.

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