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RESEARCH NOTES

Hepatotoxicity upon using niacin to pass a drug test: A case report

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ABSTRACT

Objectives: To report a case of hepatotoxicity when niacin was used by a patient with HIV to pass a drug test.

Methods: Niacin is a soluble pyridine derivative widely used in the management of dyslipidemia. Common adverse effects include flushing, nausea, gastrointestinal discomfort, and hepatotoxicity. The use of niacin for nonmedical purposes has been increasing in prevalence in recent years, particularly in attempts to alter or mask results of urine drug tests. Although there is no scientific evidence that niacin can alter a urine drug screen result, easily retrievable information exists on the Internet touting niacin as a potential way to prevent detection of tetrahydrocannabinol (THC). The following report describes a case of hepatotoxicity in an HIV-infected adult who reported using niacin to mask THC in urine drug screen results.

Results: The patient developed marked elevations in his liver enzymes (aspartate aminotransferase greater than 25 times the upper limit of normal and alanine aminotransferase greater than 3 times the upper limit of normal) that resolved after discontinuation of the drug. Because of the patient's self-reported use and discontinuation of niacin, the Naranjo Adverse Drug Reaction Probability Scale demonstrated a "definite" relationship between the development of hepatotoxicity and the ingestion of over-the-counter sustained-release niacin. The patient did not develop further clinical abnormalities proposed to be secondary to niacin toxicity in previously published case reports, including glucose abnormalities, coagulopathies, metabolic acidosis, QTc prolongation, and myalgias.

Conclusion: Health care providers should be aware of this nonmedical use of niacin to alter or mask a drug test, especially when discerning the cause of hepatotoxicity. In addition, pharmacists in the community setting should be aware of this use of niacin when encountering patients purchasing over-the-counter niacin, particularly in patients who may be more likely to use illicit substances.

Niacin (nicotinic acid, vitamin B3) is a soluble pyridine derivative with well-established clinical uses, including the treatment of dyslipidemia, pellagra, and use as a nutritional supplement.[1] Formulations include immediate release, sustained release (SR), and extended release, which are readily available over the counter or by prescription.

The efficacy of niacin for the treatment of dyslipidemia is questionable, and its use is often limited because of intolerability.[1] The most commonly reported adverse effects include flushing, nausea, gastrointestinal discomfort, and hepatotoxicity.[2] Niacin undergoes metabolism in the liver by conjugation and amidation pathways. Conjugation of niacin with glycine involves a low-affinity, high-capacity system that forms nicotinuric acid. Nicotinuric acid plays a role in the release of prostaglandin and causes flushing. The amidation pathway is a high-affinity, low-capacity system with multiple reactions that convert niacin to nicotinamide adenine dinucleotide, which inhibits beta-oxidation and causes mitochondrial dysfunction, leading to liver cell apoptosis, inflammation, and a rise in liver enzymes.[1] Immediate-release products quickly saturate the amidation pathway, with most of the drug undergoing conjugation, resulting in an increased incidence of flushing. Conversely, slowly absorbed preparations such as the SR formulation are metabolized primarily by amidation, resulting

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in an increased incidence of hepatotoxicity. Although clinicians tend to avoid prescribing the SR formulation because of its potential for hepatotoxicity, the SR formulation is still readily available without a prescription. Furthermore, niacin hepatotoxicity appears to be dose-dependent and is most common with doses exceeding 2-3 g/day.[3]

The severity of hepatotoxicity related to niacin use can vary, from mild elevations in serum enzyme levels to acute liver failure. The Drug-Induced Liver Injury Network has developed a 5-point scale for grading the severity of liver injury. The scale is based on jaundice, hospitalization, signs of hepatic or other organ failure (elevated liver enzymes, coagulopathy, ascites, encephalopathy), and ultimate patient outcome, with scores ranging from mild to fatal.[4]

There are reports of niacin use for nonmedical purposes. L. Ron Hubbard, founder of the Church of Scientology, developed a detoxification program called "The Sweat Program" in 1977; it used niacin along with other treatments to decrease lipid-stored xenobiotics, defined as synthetic chemicals that are foreign to the body.[5] The Hubbard regimen has been proposed to remove illegal (e.g., marijuana) and legal drugs (e.g., codeine) from the body.[5] Niacin has also been used in attempts to alter or mask results of urine drug tests. A Colorado poison control center reviewed their niacin exposure cases from January to September 2006 and found that 8 callers used niacin to mask a drug screen (approximately 7.5% of niacin calls during the review period).[6] They also noted 10 calls regarding adverse reactions to niacin when the reason for exposure was not stated to be masking, although the circumstances "were suspicious for use related to masking drug screens."[6] A related editorial suggests that this number of cases from a single poison control center may suggest a high prevalence in the overall population.[7] Although there is no documented evidence that niacin can alter a urine drug screen result, easily retrievable information exists on the Internet documenting niacin as a potential way to prevent detection of tetrahydrocannabinol (THC). In fact, a report from the United States General Accounting Office reported concern over the volume of products and information advertised on the Internet to mask drug screens.[8]

The abundance of misinformation on the Internet, availability of niacin products on the nonprescription market, and potential for hepatotoxicity at high doses makes the misuse of niacin to mask drug screen results particularly concerning. The following report describes a case of hepatotoxicity when niacin was ingested to mask THC in urine drug screen results.

Case report

A 25-year-old African American male with a 6-year history of HIV infection was seen for a primary care appointment at our Veterans' Affairs (VA) health care system as part of transferring care from a different VA system (day 1). The patient had no other medical conditions. His only prescription medication was efavirenz/emtricitabine/tenofovir desoproxil for HIV, and he reported no over-the-counter medications or natural supplements. Routine laboratory parameters, including complete blood cell count (CBC), complete metabolic panel (CMP), and hepatitis serology were all within normal limits at the time of his transfer of care (Table 1). Four months later, the patient was scheduled for his first appointment with the HIV clinic at the new VA health care system. The HIV attending physician ordered multiple laboratory parameters, including complete blood cell count, CMP, HIV viral load, and T cell counts, which were obtained on day 112. His HIV viral load was slightly elevated at 209 copies/mL (goal: < 20 copies/mL), but the patient had previously reported inconsistently taking his antiretroviral medications since transferring care. The only other test results not within normal limits were the aspartate aminotransferase (AST) and the alanine aminotransferase (ALT), which were markedly elevated at 942 IU/L (normal range, 15-37 IU/L) and 158 IU/L (normal range, 13-61 IU/L), respectively. This patient experienced "mild" liver injury according to the Drug-Induced Liver Injury Network scoring system.

Upon initial assessment of the laboratory results, the attending physician and clinical pharmacist both suspected that the patient could be experiencing infectious acute hepatitis because the patient had denied use of any new medications, acetaminophen-containing medications, alcohol, or illicit substances. The HIV medications were an unlikely culprit because these medications are uncommonly associated with hepatotoxicity, and his prior liver enzymes had been normal while using the same medications. The possibility of a laboratory error was also considered. The patient returned for further laboratory testing 2 days later (day 114). These repeated tests revealed an AST of 954 IU/L and an ALT of 211 IU/L; serology test results for hepatitis A, B, and C were all negative, and all other laboratory parameters were within normal limits. With acute hepatitis being ruled out, and a laboratory error being unlikely as 2 consecutive tests were abnormal, the etiology of the increased AST and ALT was unclear. The HIV-attending physician ordered a computed tomography (CT) scan of the liver, which required referral to a different VA health care system and could not be accomplished immediately. When the elevated liver enzymes were first reported, the clinical pharmacist conducted a telephone interview in which the patient denied any clinical signs and symptoms that might suggest hepatotoxicity and again denied use of any new medications, acetaminophen-containing medications, alcohol, or illicit substances. The patient was advised not to drink any alcohol and to avoid all products with acetaminophen while waiting for the CT scan to be completed, which would likely have been within 2 weeks.

On day 131, the patient arrived for his first in-person visit to the HIV clinic. There were no abnormalities noted on physical examination. A repeated CMP was obtained during the clinic visit, which revealed an AST of 34 IU/L and an ALT of 35 IU/L (Table 1). After further questioning by the pharmacist and physician, the patient eventually admitted to using THC. He was seeking employment and had read on the Internet that taking high doses of niacin could mask the results of a urine drug screen. Although he did not know the exact strength or dose of niacin he had taken, he knew it was the SR formulation and reported taking "most of the bottle" over the course of a few days that corresponded to the same week of his AST/ALT elevations. He stopped taking the niacin after the initial telephone call from the clinical pharmacist. The patient was provided THC avoidance counseling and instructed not to use niacin again. The CT scan of the liver was canceled, and all subsequent laboratory parameters remained within normal limits after he discontinued niacin.