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Unusual False-Positive Case of Urinary Screening for Buprenorphine

Giuseppe Lippi,[1]* Araelsis Romero,[1] Gianfranco Cervellin,[2] and Mariella Mercadanti[1]
[1]*U.O. Diagnostica Ematochimica, Azienda Ospedaliero-Universitaria di Parma, Parma, Italy*
[2]*U.O. Pronto Soccorso e Medicina d'Urgenza, Azienda Ospedaliero-Universitaria di Parma, Parma, Italy*

Buprenorphine is a centrally acting analgesic drug that is administered for the management of opioid dependence and as an analgesic drug for the treatment of chronic pain. The growing use of this substance has determined an increased need for laboratory testing for either detection and confirmation of the illicit use or monitoring compliance as a substitution therapy for opioid dependence. We describe here the case of urinary sample adulteration with exogenous buprenorphine (6,952 ng/ml), which has led to a false-positive immunoassay test result (14.9 ng/ml) on a subsequent sample due to a phenomenon of instrumental carry-over. This unusual case confirms the importance to take into account adulteration when screening urines for buprenorphine in patients undergoing substitution therapy for opioid dependence, routinely perform a confirmation assay on positive samples, and rule out instrumental carry-over. J. Clin. Lab. Anal. 25:244–245, 2011. © 2011 Wiley-Liss, Inc.

Key words: adulteration; buprenorphine; norbuprenorphine; screening; analytical errors

INTRODUCTION

Buprenorphine, a derivative of thebaine, is a centrally acting analgesic drug. It acts as a partial agonist of the μ-opioid receptors, and as a strong competitive antagonist of the κ-opioid receptors. Due to these characteristics, the higher potency (i.e. 25–50 times) and the longer duration of action as compared with morphine, it is widely used, administered sublingually, for the management of opioid dependence, as an alternative to methadone, and it is also administered transdermally, intramuscularly, and sublingually as an analgesic drug for the treatment of chronic pain. The drug has a highly variable half-life (i.e. from 3 to 44 hr), in part depending on the administration route, is extensively metabolised by N-dealkylation to the active metabolite norbuprenorphine primarily through cytochrome P450 (CYP) 3A4, and is predominantly eliminated in the feces, with approximately 10–30% excreted in urine (1).

The growing use of this substance has contextually determined an increased need for laboratory testing for either detection and confirmation of the illicit use, or monitoring compliance as a substitution therapy for opioid dependence (i.e. for identifying patients straying from therapy). Two different approaches are traditionally used for urine drug testing: The immunoassays, which are quick, sensitive, and relatively inexpensive but have sub-optimal specificity (e.g. they detect classes of drugs without distinguishing among individual drugs within that class and are more susceptible to analytical interferences) and gas or liquid chromatography (GC, LC) with or without mass spectrometric (MS) detection, which is a more expensive and time-consuming approach, but still represents the gold standard for confirming a positive result on immunoassay. Although confirmation methods are thereby needed for the accurate detection of buprenorphine and its metabolites (i.e. namely norbuprenorphine), rapid and sensitive immunoassays are widely used and validated for buprenorphine screening and monitoring (2).

CASE DESCRIPTION

We describe here the case of urinary sample adulteration with exogenous buprenorphine, which has led to a false-positive immunoassay test result on a subsequent sample due to a phenomenon of instrumental carry-over.

*Correspondence to: Giuseppe Lippi, U.O. Diagnostica Ematochimica, Azienda Ospedaliero-Universitaria di Parma, Via Gramsci 14, 43126 Parma, Italy. E-mail: glippi@ao.pr.it, ulippi@tin.it

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While performing a routine analytical session for urinary buprenorphine screening on the V-Twin® Drug Testing Immunoassay System (Siemens, Milano, Italy), which uses a buprenorphine antibody with significant cross reactivity to norbuprenorphine and minimal cross-reactivity to the associated glucuronides, an urinary sample (sample A) with a value exceeding the upper limit of linearity of the assay (i.e. >40 ng/ml) was detected. The subsequent urinary sample (Sample B) also tested positive for buprenorphine, at a concentration of 14.9 ng/ml. Sample A was then reanalyzed after serial dilutions with buffer, yielding a final buprenorphine concentration of 6,952 ng/ml. Sample B was also reanalyzed alone, and tested negative for buprenorphine (the low limit of detection of the assay is 0.7 ng/ml). The further analysis of urinary norbuprenorphine by a high-pressure LC (HPLC) system with fluorimetric detection (Varian 920-LC, EUREKA srl, Ancona, Italy) was negative for the presence of the metabolite norbuprenorphine in both Samples A and B. Buprenorphine testing in HPLC is not routinely performed, since it is not required by the current national legislation.

To troubleshoot the cause of the false positivity encountered with the commercial screening immunoassay, sample A was reanalyzed (undiluted), immediately followed by a cup containing saline. A strong positivity was confirmed on Sample A, whereas a value of 13.4 g/l was obtained on saline, which is thereby highly suggestive for a phenomenon of instrumental carry-over due to the extremely high concentration of the analyte in the preceding sample.

DISCUSSION

This case report confirms the challenge of urine drug screening (3), and paves way to some analytical and clinical considerations. First, adulteration of the specimen (i.e. exogenous contamination from buprenorphine tablets dissolved by the patient in the urine sample) should always be suspected when screening urines for buprenorphine in patients undergoing substitution therapy for opioid dependence. Then, routine performance of confirmatory techniques (e.g. HPLC) for urinary norbuprenorphine might be advisable to rule out potential adulteration of urine samples that have tested positive for buprenorphine with a screening method. Finally, instrumental carry-over should exclude out when obtaining positive results in a urine sample that immediately follows a previous specimen with an extremely high concentration of buprenorphine.

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