

Opioid false-positivity in urine drug screening: levomepromazine cross-reactivity

Nuno Rodrigues-Silva & Ângela Venâncio

To cite this article: Nuno Rodrigues-Silva & Ângela Venâncio (2017) Opioid false-positivity in urine drug screening: levomepromazine cross-reactivity, *Psychiatry and Clinical Psychopharmacology*, 27:1, 93-95, DOI: [10.1080/24750573.2017.1293254](https://doi.org/10.1080/24750573.2017.1293254)

To link to this article: <https://doi.org/10.1080/24750573.2017.1293254>



© 2017 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group



Published online: 31 Mar 2017.



Submit your article to this journal [↗](#)



Article views: 977



View related articles [↗](#)



View Crossmark data [↗](#)



Citing articles: 1 View citing articles [↗](#)

CASE REPORT



Opioid false-positivity in urine drug screening: levomepromazine cross-reactivity

Nuno Rodrigues-Silva and Ângela Venâncio

Department of Psychiatry and Mental Health, Vila Nova de Gaia Healthcare Center, Vila Nova de Gaia, Portugal

ABSTRACT

Urine drug screening false-positives are reported for several drugs, which may lead to clinical misdiagnosis and have negative consequences for the patient on personal and social grounds, if not identified. False-positives for opiates are rare, but we report a case where high-dose levomepromazine was very likely involved.

ARTICLE HISTORY

Received 11 March 2015
Accepted 22 November 2016

KEYWORDS

False-positives; cross-reactivity; opioids; levomepromazine; urine drug screening

Introduction

Urine drug screening represents a useful ancillary test in differential diagnosis of substance-induced psychiatric disorders and for monitoring purposes of patients with a record of drug abuse. However, due to the relevance and potential impact of misinformation, screening results should be accurate, with low rates of false-positives. Despite its accuracy in most cases, several substances cross-react with urine drug screening tests, generating false-positive results [1]. This can have a profound impact in the patient and families, so one should be aware of all agents which have the potential to cross-react and for which specific substance of abuse. This would avoid misinterpretation of data and subsequent misleading clinical decisions and unfair burden to the patient.



Case description

A 27-year-old man presented to the psychiatric emergency unit due to behavioral disturbances over the last week. The patient was very hostile and agitated, with irritable mood, pressure of speech, flight of ideas, and delusions. At that time intramuscular (IM) haloperidol 10 mg, diazepam 10 mg and later chlorpromazine 50 mg were administered. Blood analyses were performed and were unremarkable, including complete blood count (CBC) and blood chemistry with electrolytes. A rapid urine drug toxicology screen (TOX/see BIO-RAD) was positive only for cannabinoids. He had no insight for his situation and refused treatment or hospitalization and therefore was involuntarily committed to our psychiatric inpatient unit.

This was Mr B's first psychiatric episode. In the past he abused drugs, cocaine, and heroin. Apparently, he had been abstinent for the past 2 years, except for cannabinoids, which he was still abusing. Regarding his medical history, he had bronchial asthma but did not need any medications during the past year. He had no other medications and family history was unremarkable.

The following therapeutic regimen was initiated: risperidone 4 mg/day PO, lorazepam 10 mg/day PO, and levomepromazine 75 mg/day PO. However, the patient remained agitated. Levomepromazine was progressively adjusted to 300 mg/day and behavioral disturbance improved. Biperiden 4 mg/day PO was also initiated. During hospitalization, there was a suspicion the patient was consuming drugs. His wife told that he repeatedly asked her for drugs and some of his visitors were presumably drug users. In this context, a urine drug screen (TOX/see BIO-RAD) was performed on day 7 and it was positive for cannabinoids and opiates, apparently confirming our suspicion. Upon confronting the patient with this fact, he reacted promptly, denying that he was abusing drugs. Two days after, another test was done, with the same results. Again, the patient denied completely that possibility. In the next days, a few other urine drug tests were performed (the last one on day 15). The results were always superimposable, as well as the patient's attitude.

Based on his unmovable stand and to the possibility that it could be a false-positive result for opiates, a blood sample was withdrawn after the last urine drug screen was performed, and tested for the presence of opioids, outside our institution, at the National

CONTACT Nuno Rodrigues-Silva  ruxnux@gmail.com  Department of Psychiatry and Mental Health, Vila Nova de Gaia Healthcare Center, Vila Nova de Gaia, Portugal

© 2017 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group
This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Forensic Institute. There, samples were first analysed with an immunoenzymatic assay and, if tested positive, gas chromatography–mass spectrometry (GC-MS)) was performed to exclude false-positives. In this case, the immunoenzymatic assay was positive for opiates but the GC-MS test was negative. As his clinical status was improving, levomepromazine was reduced to 25 mg three times a day (on day 19). Five days later he was clinically stabilized and returned to his pre-morbid functioning state. At this time, and before the discharge, the urine drug screen (TOX/see BIO-RAD) was repeated and was negative for opiates.

The manufacturer, BIO-RAD, was contacted regarding information on the cross-reactivity profile of several substances. An extensive list of tested drugs was shared but levomepromazine was not included. The other drugs that the patient was taking were searched and were not previously reported to cross-react for opioids [2]. In addition, we did not find information in the literature regarding cross-reactivity with opioids.

Discussion

Urine drug screening tests provide only preliminary analytical test results and a more specific alternative biochemical method must be used in order to confirm a test result. The preferred method for confirmation and established by the Substance Abuse and Mental Health Services Administration (SAMHSA) is GC-MS, which was used in the case we report here. Several psychoactive drugs have been reported to cross-react in urine drug screening, like sertraline, venlafaxine, trazodone, quetiapine [3], and even some phenothiazines [4,5]. However, none of these drugs cross-reacted with opioids. False-positives for opioids are quite rare in the literature, with an exception for quinolones, but with different urine drug screening tests [6].

Levomepromazine is an aliphatic phenothiazine, low-potency first-generation antipsychotic (about half as potent as chlorpromazine) but with strong sedative effects. It is commonly used in psychiatric emergency wards to treat acute psychosis or mania and to reduce high levels of agitation and aggressiveness [7]. The biological half-life ranges from 16.5 to 77.9 h, it undergoes extensive hepatic metabolism yielding several metabolites, which are excreted through the urine and feces, and only a small fraction was unchanged levomepromazine [8,9].

We find levomepromazine the most likely agent implicated in opiate cross-reactivity due to the following reasons: [1] the urine drug test was negative for opiates before drug administration [2], 6 days after the therapeutic regimen was initiated, the urine drug test was positive for opiates [6], all other drugs in the patient's therapeutic regimen but

levomepromazine had been tested by the manufacturer and did not cross-react with opiates [4], during positive urine drug tests, a blood analysis using GC-MS was negative for opiates [3], repeated urine drug screen tests were systematically positive for opiates, except for when levomepromazine was reduced to 75 mg/day, and no other changes to his medications were made. This provides evidence that a false-positive for opiates occurred due to drugs previously not reported in the literature.

Levomepromazine is probably implicated according to Adverse Drug Reaction Probability Scale [7]. To date, this is the first report showing that levomepromazine, at higher dosages, is probably implicated in cross-reactivity with opioids and could lead to false-positive results in urine drug screen (TOX/see BIO-RAD). However, we may not ascertain at this time if this is due to parent levomepromazine, its metabolites, a combination of parent and metabolite or a combination of all medications the patient was taking. Levomepromazine has also shown strong analgesic properties. One may speculate if structural similarity with analgesics might be responsible for cross-reactivity with opiate urine drug screens. This case report also stresses the need to be aware of a possible false-positive test, whenever the patient denies drug use, even when there are no data reporting that in the available literature and necessity to perform a confirmatory test through a more precise method such as GC-MS. Further studies are needed to clearly determine if levomepromazine cross-reacts with opiates in this specific urine drug screening test, as such information is of value for clinical practice.

Disclosure statement

No potential conflict of interest was reported by the author.

References

- [1] Jaffee WB, Trucco E, Levy S, et al. Is this urine really negative? A systematic review of tampering methods in urine drug screening and testing. *J Subst Abuse Treat.* 2007;33(1):33–42.
- [2] BIO-RAD. TOX/seeTM cross-reactivity table by trade name, provided by the manufacturer.
- [3] Melanson SE, Lee-Lewandrowski E, Griggs DA, et al. Reduced interference by phenothiazines in amphetamine drug of abuse immunoassays. *Arch Pathol Lab Med.* 2006;130(12):1834–1838.
- [4] Smith-Kielland A, Olsen KM, Christophersen AS. False-positive results with Emit II amphetamine/methamphetamine assay in users of common psychotropic drugs. *Clin Chem.* 1995;41(6 Pt 1):951–952.
- [5] Dahl SG, Strandjord RE, Sigfusson S. Pharmacokinetics and relative bioavailability of levomepromazine after repeated administration of tablets and syrup. *Eur J Clin Pharmacol.* 1977;11(4):305–310.

- [6] Brahm NC, Yeager LL, Fox MD, et al. Commonly prescribed medications and potential false-positive urine drug screens. *Am J Health Syst Pharm.* [2010](#);67(16):1344–1350.
- [7] Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther.* [1981](#);30(2):239–245.
- [8] Hals PA, Dahl SG. Metabolism of levomepromazine in man. *Eur J Drug Metab Pharmacokinet.* [1995](#);20(1): 61–71.
- [9] van der Zwaan S, Blankespoor RJ, Wolters AM, et al. Additional use of methotrimeprazine for treating refractory agitation in pediatric patients. *Intensive Care Med.* [2012](#);38(1):175–176.