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Journal of Pharmacology & Clinical Toxicology

Case Report

Opioid False-positive in Urine Drug Screening due to Levomepromazine Cross-Reactivity

Nuno Rodrigues-Silva* and Ânegla Venâncio

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

***Corresponding author**

Nuno Rodrigues-Silva, Vila Nova de Gaia/Espinho Healthcare Center, Rua da Conceição Fernandes 4400, Vila Nova de Gaia, Portugal, Tel: +351938378600; Email: nuno.rodrigues.silva@chvng.min-saude.pt

Submitted: 16 February 2015

Accepted: 26 March 2015

Published: 30 March 2015

ISSN: 2333-7079

Keywords

- False-positives
- Cross reactivity
- Opioids
- Levomepromazine
- Urine drug screening

Abstract

In urine screening, false-positives are often reported for several drugs. This may lead to clinical misdiagnosis and has negative consequences for the patient on personal and social grounds, if they are not identified. False-positives for opiates are rare, but we report a case where a high-dose of levomepromazine was involved.

INTRODUCTION

In urine screening, false-positives are often reported for several drugs. This may lead to clinical misdiagnosis and has negative consequences for the patient on personal and social grounds, if they are not identified. False-positives for opiates are rare [1], but we report a case where levomepromazine waslikelyinvolved. 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 [2]. The biological half-life ranges from 16.5 to 77.9 hours, it undergoes extensive hepatic metabolism to several metabolites, which are excreted through the urine and feces, and only a small fraction as unchanged levomepromazine [3,4]. The present case reports a patient with a Bipolar disorder diagnosis admitted to a psychiatric inpatient facility at a general hospital in Portugal. Our main aim is to report for the first time a false-positive for opiates in urine drug screening probably induced by levomepromazine and raise awareness regarding this fact for future clinical practice.

CASE PRESENTATION

A 27-year old man was conducted to the psychiatric emergency unit due to behavioral disturbance over the past week. The patient was very hostile and agitated, with irritable mood, pressure of speech, flight of ideas and delusions. At the time of hospitalization, intramuscular (IM) haloperidol 10 mg, diazepam 10 mg and later chlorpromazine 50 mg were administered. Blood analyses were performed including complete blood count (CBC) and complete blood chemistry with electrolytes. A rapid urine drug toxicology screen (TOX/See by BIO-RAD) was positive only for cannabinoids. He had no insight over his situation and refused treatment or hospitalization and therefore was involuntarily committed to our psychiatric inpatient unit. This was his first psychiatric episode. In the past he had abused cannabinoids, cocaine and heroin. Apparently, he had been abstinent for the past 2 years, except for cannabinoids, which he still abused. Regarding his medical history he had asthma but he did not t need any medication in the last year. He did not take other medication and family history was unremarkable.

The following therapeutic regimen was initiated: risperidone 4mg/d*per os*(PO), lorazepam 10 m/d PO, levomepromazine 75mg/d PO. However the patient remained agitated. Levomepromazine was progressively adjusted to 300mg/d and behavioral disturbance improved. Biperiden 4mg/d PO was also started. During hospitalization there was a suspicion that the patient was consuming drugs. His wife claimed that he repeatedly asked her for drugs and some visitors he received were presumed drug users. In this context, a urine drug screen (Tox/See by BIO-RAD) was performed on day 7 and it was positive for cannabinoids and opiates, apparently confirming our suspicion. Confronting the patient with this fact, he reacted promptly, and denied drug use. Two days after, another test was done, with the same result. In the next days, a few other urine drug tests were performed (the last one on day 15). The results were always super imposable, 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 drawn after the last urine drug screening was performed. The blood was tested for the presence of opioids at the National Forensic Institute. There, samples are first analyzed with an

immune-enzymatic assay and there after gas chromatography/mass spectrometry (GC/MS) was performed to exclude false positives. In this case, the immune-enzymatic assay, using Enzyme Linked Sorbent Immunoassay (ELISA) was positive for opiates but Gas Chromatography/Mass Spectrometry was negative. As his clinical status was improving, levomepromazine was reduced to 25mg 3 per day (on day 19). 5 days later he was psycho pathologically stabilized and returned to his premorbid functioning state. At this time, and before discharge, the urine drug screen (TOX/See BIO-RAD) was repeated and was negative for opiates. New psychoactive substances were not tested.

The manufacturer, BIORAD, 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 reported to cross-react for opioids [5].

DISCUSSION

Urine drug screening tests provide only preliminary analytical test results and a more specific alternative analytical method must be used in order to confirm a 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 this case. Several psychoactive drugs have been reported to cross-react in urine drug screening, such as sertraline, venlafaxine, trazodone, quetiapine [1] and even some phenothiazines [6,7]. However, none of these were cross-reacted for opioids. False-positives for opioids are quite scarce in the literature, exception made for several quinolones, rifampin and poppy seeds, but with different urine drug screening tests [8].

We describe a case report in which levomepromazine is the most likely agent implicated in opiate cross-reactivity due to the following reasons: [5] the urine drug test was negative for opiates before drug administration [8]. 6 days after the therapeutic regimen was initiated, the urine drug test was positive for opiates [1] all drugs in the patient's therapeutic regimen but levomepromazine had been tested by the manufacturer and didn't cross react for opiates. In addition, other drugs remained the same during hospitalization [7] during positive urine drug tests, a blood analyses using GC/MS was negative for morphine and methadone [6] repeated urine drug screen tests were systematically positive for opiates, except when levomepromazine was reduced to 75mg/d, and no other changes to his medication were made. This provides evidence that a false-positive for opiates occurred due to a drug previously not reported in the literature.

Levomepromazine is probably implicated as assessed through the Adverse Drug Reaction probability scale [9]. To date, this is the first report demonstrating that levomepromazine, particularly at higher dosages, is probably implicated in cross-reactivity for opioids and could lead to false-positive results in urine drug screening (TOX/See BIO-RAD). However, we could not determine at this time if this is due to the parent compound levomepromazine or its metabolites, a combination of parent and metabolite. 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 report also stresses the need to be aware of a possible false-positive test, whenever the patient denies drug use, even when there is no data reporting that in the available literature and to perform a confirmatory test through a more precise method such as GC/MS.

ACKNOWLEDGEMENTS

List here any individuals who contributed in the work and grant details.

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Cite this article

Rodrigues-Silva N, Venâncio Â (2015) Opioid False-positive in Urine Drug Screening due to Levomepromazine Cross-Reactivity. J Pharmacol Clin Toxicol 3(3):1050.