



False positive ecstasy (MDMA) urine drug screening test results due to bupropion use: A case report

Selin ACAR ŞAHAN^{1*}, Barış KARADAŞ¹, Semra AYDIN AKFIRAT², Nihat AYDEMİR², Saliha AKSUN³, Yusuf KAPLAN⁴

¹ Izmir Katip Celebi University School of Medicine, Department of Pharmacology, Izmir, Turkey

² Kaanmed Health Care Services (Toksilab), Istanbul, Turkey

³ Izmir Katip Celebi University School of Medicine, Department of Medical Biochemistry, Izmir, Turkey

⁴ Izmir University of Economics, Faculty of Medicine, Izmir, Turkey

*Corresponding author

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ABSTRACT

Abstract

This case report is about a false positive ecstasy (MDMA) result in the urine substance abuse screening analysis of a person using the antidepressant drugs bupropion and sertraline with a therapeutic indication. Urine drug and stimulant screening analysis of a 25-year-old male patient who is history of bupropion (300 mg/day) and sertraline (100 mg/day) use, followed in the Amatem polyclinic due to the probation law, was performed with Syva® Emit® II Plus kits and immunoassay method. In order to confirm the ecstasy test, which was positive in the screening analysis, the substance analysis was repeated on the same sample with the gas chromatography sequential mass spectrometry (GC-MS) method and ecstasy was not detected in the confirmation analysis. At the same time, the presence of bupropion and sertraline patient declared to use, was confirmed with the LC-MS-Iontrap device. In conclusion, with this case example, we wanted to highlight the potential interaction of bupropion with the Syva® Emit® II Plus urine ecstasy screening tests, which could lead to false positive results. When positive ecstasy values are detected in the urine samples analyzed with the immunoassay method in patients using bupropion, the final decision should be made after a confirmatory analysis.

Keywords: N-methyl-3, 4-methylenedioxy-amphetamine, MDMA, ecstasy, false positive reactions, Enzyme Multiplied Immunoassay Technique, bupropion

Bupropion kullanımına bağlı hatalı pozitif ecstasy (MDMA) idrar uyuşturucu tarama testi sonuçları: Bir olgu sunumu

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Öz

Bu olgu raporu, terapötik endikasyonla antidepresan etkili ilaçlar olan bupropion ve sertralin kullanan bir kişide yapılan idrarda madde kötüye kullanım tarama analizinde yanlış pozitif sonuçlanmış ekstazi (MDMA) sonucu ile ilgilidir. Denetimli serbestlik yasası nedeniyle Amatem polikliniğinde izlenen, öyküsünde bupropion (300 mg/gün) ve sertralin (100 mg/gün) kullanımı olan 25 yaşında erkek hastanın idrar uyuşturucu ve uyarıcı madde tarama analizi Syva® Emit® II Plus kitleri ile immunoassay yöntemi ile yapılmıştır. Tarama analizinde pozitif olarak sonuçlanan ekstazi testinin doğrulanması için aynı numunede madde analizi gaz kromatografi ardışık kütle spektrometre (GC-MS) yöntemi ile tekrar yapılmış ve doğrulama analizinde ekstazi saptanmamıştır. Aynı zamanda hastanın kullandığını beyan ettiği bupropion ve sertralin varlığı LC-MS-Iontrap cihazı ile doğrulanmıştır. Sonuç olarak, bu olgu örneği ile, bupropionun, Syva® Emit® II Plus idrar ekstazi tarama testleri ile yanlış pozitif sonuçlara yol açabilen potansiyel etkileşimi vurgulanmak istenmiştir. Bupropion kullanan hastalarda immunoassay yöntemi ile analiz edilen idrar örneklerinde pozitif ekstazi değerleri saptandığında, nihai kararın mutlaka bir doğrulama analizinden sonra verilmesi gereklidir.

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Anahtar sözcükler: N-metil-3, 4-metilendioksi-amfetamin, MDMA, ekstazi, yalancı pozitif reaksiyonlar, enzim çoğaltılmış immünoassay tekniği, bupropion

¹ selin.acar@ikc.edu.tr

¹ <https://orcid.org/0000-0003-4083-8660>

² bariskaradas@gmail.com

² <https://orcid.org/0000-0001-9347-2565>

³ doktorsemra@hotmail.com

³ <https://orcid.org/0000-0002-3112-0852>

⁴ nihataydemir06@gmail.com

⁴ <https://orcid.org/0009-0004-6334-0931>

⁵ salihaaksun@yahoo.com

⁵ <https://orcid.org/0000-0002-7991-1645>

⁶ seawise@gmail.com

⁶ <https://orcid.org/0000-0003-0369-7934>

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Introduction

N-methyl-3,4-methylenedioxy-amphetamine or 3,4-methylenedioxymethamphetamine (MDMA, ecstasy) is an amphetamine derivative that is abused for stimulating and hallucinogenic purposes. Ecstasy increases the net release of monoamine neurotransmitters and inhibits presynaptic re-uptake of serotonin¹. In Europe, the prevalence of ecstasy use was 0.61% (0.51-0.83%) in 2018². Ecstasy can be detected in urine with various immunochemical methods such as CEDIA (Cloned enzyme donor immunoassay), DRI (Diagnostic Reagents Incorporated) enzyme immunoassay, EMIT (Enzyme mediated immunological technique) and FPIA (Fluorescence polarization immunoassay). Several prescription drugs such as ephedrine, pseudoephedrine and phenylpropanolamine may interfere with EMIT II Plus immunoassay tests and cause false positive ecstasy results³. Forensic threshold values are used when reporting urine drug abuse analysis. This value is 500 ng/mL for ecstasy. In this report, we describe a case who had a positive urine drug screen for ecstasy while being treated with bupropion and sertraline.

Case

25 years old male patient was admitted to our Amatem Outpatient Clinic (Illicit Drug Addiction Treatment Center) and received treatment for drug abuse. He was also taking bupropion 300 mg/day and sertraline 100 mg/day for the treatment of depression. Two-level control samples are studied before each ecstasy test. The high-level control value is 500 (400-600) ng/ml with a CV of 2.9%. Low-level control value is 360.0 (288.0-432.0) ng/ml, with a CV of 3.26%. Method performance evaluations for all drug and stimulant analyses are conducted every three months to assess repeatability and accuracy. During the performance evaluation, a sample pool prepared from patient samples in urine matrix is used for repeatability assessment. Intra-assay CV: 5.1%, Inter-assay CV: 4.2%. Ecstasy calibration is performed at five points using calibrators at concentrations of 1000, 750.0, 500.0, 250.0, and 0 ng/ml. The LOQ value for the ecstasy test is 5.0 ng/ml. The urine analysis with Syva® Emit® II Plus immunoassay (SIEMENS Dimension®) gave a positive result for ecstasy (772.0 ng/mL, cut-off value was 500.0 ng/mL). He denied that he had used any illicit drugs. The sample was analyzed with GC-MS for confirmation and the result was negative for ecstasy (<35.0 ng/mL). The presence of bupropion, sertraline and their metabolites in patient's urine was confirmed as qualitatively in LC-MS-Iontrap.

In 2009, using the Emit II method (Dimension, Siemens), in 2012 and 2013, using the Cedia immunochemical method (Thermo Scientific, USA) with the Olimpos automated analyzer at our hospital, tests for amphetamines, ecstasy, cocaine, marijuana, opiates, benzodiazepines, and barbiturates in the patient's urine were found to be negative. In the analysis conducted in 2015, the urine sample was tested using the EMIT immunochemical method (Siemens, Germany) with the Dimension automated analyzer (USA), and ecstasy was detected at a level of 772.0 ng/mL, reported as positive. The patient objected to the ecstasy result and he stated that he used bupropion and sertraline at the same time. The same urine sample underwent re-examination utilizing Gas Chromatography-Mass Spectrometry (GC-MS). After chromatographic separation and sequential mass measurement by GC MS method, it was determined that the ecstasy analyte was not found in the urine sample. In the following year, another urine sample from the same patient was tested in our laboratory, and ecstasy and other screened substances were found to be negative.

Discussion

Several studies, case-reports and the Syva® Emit® II Plus test label (SIEMENS Dimension®) suggest that bupropion may cause false positive results in the urine amphetamine and/or ecstasy tests⁴⁻¹¹. This effect varies according to the bupropion dose and the selected threshold values of ecstasy or amphetamine which determined the test result is positive or negative. According to Syva Emit II plus Ecstasy kit prospectus¹²; some structurally related compounds like bupropion can produce a positive MDMA result equivalent to the 300 ng/mL and 500 ng/mL MDMA cutoff. Nixon et al. reported that, after the patient was treated with bupropion 300mg/day for 3 weeks, urine EMIT II monoclonal immunoassay of the patient became positive for amphetamines, whereas it was negative for methamphetamine and amphetamine by liquid chromatography⁴. Following the analysis of bupropion and its three major metabolites in monoclonal EMIT II immunoassay, it was reported that all four compounds showed cross reactivity to some extent⁴. In another case report by Vidal et al., following the use of sustained-release formulation of bupropion 150 mg/day for 14 days and 300 mg/day for 7 days, urine CEDIA analysis of the patient was positive for amphetamines/ecstasy. Subsequently, although amphetamine, methamphetamine, or amphetamine derivatives were not detected by GC/MS, bupropion was detected by GC/MS and LC/MS in urine⁶. Öztürk et al. reported a positive urine toxicology assay

(repeated twice) for amphetamine and ecstasy in a patient who received risperidone 2 mg/day, mirtazapine 45 mg/day, venlafaxine 150 mg/day, quetiapine 550 mg/day, hydroxyzine 50 mg/day, bupropion 150 mg/day and acamprosate 1998 mg/day. One week after bupropion was discontinued, the urine analysis was negative for amphetamine and ecstasy⁸. In a retrospective study conducted with the patients presented to the emergency department in USA, it was reported that, bupropion had been prescribed to 41% (53/128) of patients whose samples were positive in urine amphetamine screening with Syva EMIT II Plus but were not confirmed by GC⁹. In a study by Marin et al., 100 false-positive EMIT II immunoassay specimens for amphetamine and/or ecstasy were analyzed in the Agilent 6230 time-of-flight (TOF) mass spectrometer to identify compounds that may cause false positive results in immunoassay tests in urine and bupropion was detected in 28 of these specimens¹⁰. In a retrospective study aimed to evaluate true positive and false positive rates of urine drug screen panels, 174 (2%) of 8825 specimens tested with Syva EMIT II Plus reagents were positive for MDMA, all of which subsequently were confirmed to be false positive by LC-MS-MS. These false positive specimens were tested using LC-MS-MS for the presence of bupropion and/or trazodone; two specimens contained bupropion only, one specimen contained both bupropion and trazodone¹¹.

In the literature, there is no publication related to the use of sertraline that can cause false positivity in MDMA screening with the urine immunochemical analysis method. In addition, Syva Emit II plus Ecstasy kit prospectus¹² indicated that, sertraline added drug free urine sample 125 µg/mL gave negative MDMA result for either 300 or 500 ng/mL ecstasy cutoff. However, it is indicated in the Syva Emit II plus Ecstasy kit prospectus that bupropion, a compound structurally related to MDMA, can give a positive MDMA result equivalent to the 300 ng/mL and 500 ng/mL MDMA cutoffs¹². The performance of the ecstasy test during the period of examination of the sample related to the case presented in the study was determined to be acceptable through repeatability and accuracy measurements. The performance evidence of the ecstasy test parameter, with a LOQ value of 5.0 ng/ml and intra-assay and inter-assay CV values of 5.1% and 4.2%, respectively, was found to be below the total acceptable error limits. Therefore, the cause of false positive ecstasy in the urine during concomitant use of bupropion and sertraline in this case was associated with the use of bupropion. However, the patient's urine was not analyzed before and after

bupropion medication, which is a limitation of our study.

Conclusion

Bupropion may interfere with Syva® Emit® II Plus urine ecstasy tests and cause false positive results. To make a definitive conclusion, more cases and further studies are required. The most important limitation of this case report was the lack of a negative Syva® Emit® II Plus urine ecstasy test following the cessation of bupropion (dechallenge). For the correct interpretation of urine drug analysis; taking a detailed over-the counter and prescription medication history of the patient is significantly important and further confirmation of the sample with advanced analytical methods such as GC-MS or LC-MS-MS is necessary.

Compliance with Ethical Standards:

We would like to extend our sincere thanks to Toksilab and MVZ Labor Dessau GmbH undertaking the analyses. This case report was presented as an oral presentation at the 2nd Regional Tiaft Meeting in Turkey in 2016.

S.A.A. and N.A. worked for the Toksilab. No conflict of interest was declared by the other authors.

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