

False-Positive Methadone Drug Screens During Quetiapine Treatment

To the Editor: Quetiapine is a widely used antipsychotic and mood stabilizing compound. So far, false-positive methadone urine drug screens during quetiapine therapy have been described for 3 adults¹ and 12 adolescents.² Here, we report a case series of 10 inpatients, 4 men and 6 women from 22 to 48 years old, suffering from mood or psychotic disorders who tested positive for methadone. Since such false-positive methadone screenings may seriously affect the therapeutic relationship, this potential interaction is highly relevant for clinicians.

Case series. Urine drug screens were performed with the COBAS Integra Methadone II test kit (kinetic interaction of microparticles in solution [KIMS] methodology) by Roche. All serum quetiapine levels were measured in steady-state conditions. In none of our 10 patients who tested positive for methadone was this finding expected, and the patients believably denied intake of this drug. The urine of 4 patients was investigated with gas chromatography–mass spectrometry, which indicated negative results for methadone. All 10 patients received quetiapine, 4 of them in the extended release form. Doses varied between 200 and 800 mg/d. Data were gathered between January 2008 and June 2009.

Two of the 10 patients received quetiapine monotherapy. One of these patients tested negative for methadone in the urine drug screen at a serum quetiapine level of 51 ng/mL (150 mg/d of quetiapine) and then positive 2 weeks later at a quetiapine level of 80 ng/mL (200 mg/d). The other patient receiving monotherapy tested negative for methadone before quetiapine treatment was initiated and then positive at a serum level of 339 ng/mL (200 mg/d of quetiapine extended release).

In a further patient taking extended release quetiapine, a negative screening was obtained at a serum quetiapine level of 28 ng/mL, turning positive at 87 ng/mL. Positive methadone screens were also obtained at serum quetiapine levels of 64 ng/mL and 83 ng/mL, respectively, for 2 patients taking immediate release quetiapine. The patient with a serum level of 83 ng/mL, who was receiving 800 mg/d of quetiapine, later showed both positive and negative screening results at the lower dose of 600 mg/d.

On the basis of these 5 patients' serum quetiapine levels, one could assume a threshold of about 60 ng/mL to yield a false-positive methadone test. In Cherwinski et al,² 125 mg/d of quetiapine (no serum level was indicated) was sufficient to yield a false-positive methadone test. A systematic look at 142 methadone urine drug screens from 129 inpatients of our hospital in an 18-month period (January 2008–June 2009) revealed 4 positive methadone tests. Quetiapine was the only drug these 4 patients had in common. For 4 other patients from this group with negative drug screens, serum quetiapine levels have been determined: 87 ng/mL for immediate release quetiapine (1,100 mg/d) and 95, 271, and 391 ng/mL for extended release quetiapine (no trough level; doses were 500, 800, and 600 mg/d, respectively). This shows that in not every case does quetiapine have an effect on methadone screens.

Drugs that have been shown to cross-react with methadone³ feature a tricyclic structure with a sulfur and a nitrogen atom in the middle ring, which is common to both quetiapine and methadone. Therefore, it is plausible that this structural similarity between quetiapine and methadone could underlie cross-reactivity in the methadone drug screen.

In summary, this report strongly suggests that positive methadone drug screenings be confirmed by a second method such as high-performance liquid chromatography or liquid chromatography–mass spectrometry, especially in patients treated with quetiapine.

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