False-Positive Phencyclidine Drug Screenings During Psychopharmacologic Treatment

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Phencyclidine (phenylcyclohexylpiperidine; PCP), also called "Angel Dust," is a noncompetitive antagonist of *N*-methyl-D-aspartate (NMDA) receptors and a drug of abuse that can cause symptoms similar to those experienced by patients with schizophrenia.[1] False-positive drug screenings have been reported for several drugs and can be caused by a variety of agents.[2,3] In particular, false PCP-positive urine drug screenings have been reported to be caused by venlafaxine, lamotrigine, tramadol, ibuprofen, imipramine, diphenhydramine, and dextromethorphan.[4–9]

METHOD

We systematically looked at all psychiatric inpatients with PCP-positive urine drug screenings treated in our department between 2008 and 2013 (40 patients; see Table 1). Drug screenings were performed during clinical routine for intensive care patients or for suspected drug use. The PCP urine drug screenings were performed with the Cobas c502 test system by Roche/Hitachi (25 ng/mL cutoff; Roche Diagnostics GmbH, Mannheim, Germany), based on the kinetic interaction of microparticles in a solution (KIMS) technique.

RESULTS

Only 1 of the 40 patients with a PCP-positive urine test confirmed PCP consumption. All other patients plausibly denied intake of PCP. Ten patients admitted to taking other—also illegal—drugs, 7 claimed to have been drug-free for many years, and 22 denied having ever taken illegal drugs. Among the 39 cases assumed to be false-positive, 14 patients received venlafaxine (112.5–375 mg/d), which has been reported to be associated with false-positive screening results.[4,7,8] However, the most frequent medication (16 patients) in our cohort was chlorprothixene (30–335 mg/d), which has not been reported so far to have the potential to cause false-positive PCP drug screenings. Four patients received lamotrigine (100–275 mg/d). One patient received imipramine (175 mg/d), and 4 received the chemically very similar trimipramine (100–600 mg/d). One patient received tramadol (375 mg/d), another clomipramine extended release 150 mg/d plus clomipramine immediate release 25 mg/d, and 1 a combination of olanzapine (10 mg/d) with citalopram (20 mg/d).

In 1 case (patient 16), chlorprothixene was given only once at a dose of 100 mg during the night before a positive drug test was performed. The test had been negative for PCP 2 days before and was repeated because it was positive for opioids and cannabis. Repeated testings in the chlorprothixene-obtaining patients were done in 10 cases, and all revealed negative results without chlorprothixene, making a role of other drugs improbable. One of the 16 chlorprothixene-treated patients was also given ibuprofen (400 mg/d) and trimipramine (50 mg/d), but the test became negative after discontinuation of chlorprothixene. No other chlorprothixene-treated patients received any of the other possibly cross-reacting drugs mentioned above as comedication. We did not suspect any of the other psychiatric and nonpsychiatric comedications (see Table 1) in our patients as being able to cause false-positive PCP drug screenings because the mentioned drugs could sufficiently explain the result and the other comedication was not regularly combined with a positive screening result. One chlorprothixene- and 1 venlafaxine-treated patient received monotherapy. In the latter patient (patient 19 in Table 1), the PCP screening became negative after discontinuation of venlafaxine for 2 days and became positive again 5 days after the pause. In contrast to chlorprothixene, repeated testings in venlafaxine-treated patients revealed negative results with unchanged, lower, or even higher doses of venlafaxine in 7 of the 14 cases, while only in 1 of the 16 chlorprothixene cases (patient 6) did we find a negative result in spite of chlorprothixene treatment. Thus, we conclude that chlorprothixene has a stronger and more persistent cross-reacting ability than venlafaxine.

DISCUSSION

Our report indicates a very high percentage of false-positive PCP drug screenings for numerous medications using a commercially available test system based on the KIMS technique. With the KIMS technique, false-positive drug screenings were observed for PCP with the Online KIMS assay by Roche,[10] but also for methadone.[3] Cross-reactivity has also been observed with several other PCP screening assays, such as the enzymes multiplied immunoassay technique (EMIT) II, the Abbott AxSYM phencyclidine immunoassay,[4] and the Syva RapidTest d.a.u. 9 Test Panel.[8] A comparison between EMIT II and KIMS immunoassay techniques showed that both have a low sensitivity and specificity for PCP compared to the detection of other drugs.[10]

A limitation of our findings is the lack of confirmation of our PCP screening results as false-positive by a second independent method such as high-performance liquid chromatography or liquid chromatography–mass spectrometry. However, self-reports in our patient group with regard to other drugs of abuse were consistent with drug screening results, and in some of the above described cases the temporal course of positive PCP screening is clearly indicative of a relationship with our psychotropic medication and not a possible drug abuse prior to admission.

Table 1. Medication of All Phencyclidine (PCP)-Positive Patients[a]

Patient	Chlorprothixene	Venlafaxine	Lamotrigine	Imipramine	Trimipramine	Tramadol	Drugs Other Than PCP[b]	Comedication
1	30	…	…	…	…	…	Yes	L-dopa 125
2*	50	…	…	…	…	…	Yes	Mirtazapine 45, risperidone 2, bisoprolol 10
3	50	…	…	…	…	…	Yes	L-thyroxine 0.0625
4*	25	…	…	…	…	…	Yes	Mirtazapine 15, lorazepam 1
5*	300	…	…	…	…	…	In the past	Doxepin 100, L-thyroxine 0.05
6** >	50	…	…	…	…	…	In the past	Flupentixol 7
7*	160	…	…	…	…	…	Yes	Valproate 2,000, lorazepam 1, amitriptyline 100, flupentixol 5
8*	60	…	…	…	…	…	In the past	Perazine 50
9*	100	…	…	…	…	…	Never	Chlorprothixene monotherapy
10*	100	…	…	…	…	…	Yes	Haloperidol 5
11*	50	…	…	…	50	…	Never	Agomelatine 50, ibuprofen 400
12*	335	…	…	…	…	…	Never	Olanzapine 25, maprotiline 50, diazepam 17.5, pantoprazole 40, L-thyroxine 0.05
13	130	…	…	…	…	…	Never	Pantoprazole 40, prednisone 30
14	300	…	…	…	…	…	Never	L-thyroxine 0.1, escitalopram 30, azathioprine 100, budesonide 9, methylphenidate 45, zopiclone 7.5, pantoprazole 20
15	100	…	…	…	…	…	In the past	Lorazepam 2
16*	100	…	…	…	…	…	Never	Haloperidol 5, lorazepam 1, pantoprazole 40
17	…	300	…	…	…	…	Never	Amitriptyline 150
18** <	…	150	…	…	…	…	Never	Mirtazapine 60, doxepin 150, enalapril 20, urapidil 60, propranolol 160, bromazepam 12
19*	…	375	…	…	…	…	In the past	Venlafaxine monotherapy
20	…	225	…	…	…	…	Yes	Mirtazapine 30
21** <	…	300	…	…	…	…	Never	Amitriptyline 175
22** =	…	375	…	…	…	…	Never	Mirtazapine 30
23** =	…	225	…	…	…	…	Never	Mirtazapine 15, pregabalin 300
24** <	…	112.5	…	…	…	…	Never	Quetiapine 300, L-thyroxine 0.075
25** =	…	225	…	…	…	…	Never	Mirtazapine 45, valproate 1200
26*	…	300	…	…	…	…	Never	Quetiapine 200, mirtazapine 45, valproate 1,000, naloxone/oxycodone 10/5, allopurinol 100, metamizole 500, simvastatin 10, prednisone 7.5
27*	…	225	…	…	…	…	Yes	Mirtazapine 45, quetiapine 700, metoprolol 47.5
28** <	…	300	…	…	…	…	Yes	Mirtazapine 45, quetiapine 300, terbinafine 250, distigmine 5
29	…	375	275	…	…	…	In the past	Quetiapine 300
30	…	150	100	…	…	…	Never	Quetiapine 300
31	…	…	100	…	…	…	Never	Valproate 1,200, escitalopram 5
32	…	…	150	…	…	…	Never	Quetiapine 300, lorazepam 0.5, amitriptyline 100, metformin 1,000, ramipril 10, hydrochlorothiazide 12.5
33	…	…	…	175	…	…	In the past	Escitalopram 15, lithium carbonate 800, aripiprazole 5, pipamperone 40
34	…	…	…	…	100	…	Yes	Pipamperone 40
35	…	…	…	…	300	…	Never	Escitalopram 20, mirtazapine 7.5, diazepam 15
36	…	…	…	…	600	…	Never	Intoxication with trimipramine
37	…	…	…	…	…	1,200	Never	Diazepam 30, pantoprazole 40
38	…	…	…	…	…	…	Never	Olanzapine 10, escitalopram 20
39	…	…	…	…	…	…	Never	Clomipramine 175
40	…	…	…	…	…	…	Yes, PCP	Clomipramine 225, valproate 600

[a]Doses shown in mg/d.
[b]The state of actual or past drug abuse besides PCP according to the patients' statement; only patient 40 affirmed PCP intake.
*Repeated testings revealed negative drug screenings without the medication.
**Repeated testings revealed negative drug screenings with the same medication (> higher, = same, or < lower doses).
Symbol: … = medication not received by patient.

Our report adds chlorprothixene (and possibly also trimipramine) to the already described list of drugs. It also strongly confirms venlafaxine as a cross-reacting agent by adding at least 12 cases of false-positive PCP screenings under this medication to the so-far reported 5 cases.[4,7,8] No obvious similarity between chlorprothixene and PCP concerning the 2-dimensional chemical structure exists, as is also the case for venlafaxine.[8] We think this information is highly relevant for clinicians since certainty about PCP intake is necessary not only for diagnostic reasons as PCP may induce schizophrenia-like symptoms, but also because false-positive drug-screenings may affect the therapeutic relationship. Positive PCP drug screening tests should be confirmed by a second method such as high-performance liquid chromatography or liquid chromatography–mass spectrometry.

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Drug names: allopurinol (Lopurin, Zyloprim, and others), aripiprazole (Abilify), azathioprine (Azasan, Imuran, and others), bisoprolol (Zebeta and others), budesonide (Uceris), citalopram (Celexa and others), clomipramine (Anafranil and others), diazepam (Diastat, Valium, and others), diphenhydramine (Benadryl and others), doxepin (Silenor and others), enalapril (Vasotec and others), escitalopram (Lexapro and others), haloperidol (Haldol and others), ibuprofen (Ibu-tab and others), imipramine (Tofranil and others), lamotrigine (Lamictal and others), lithium (Lithobid and others), lorazepam (Ativan and others), metformin (Glucophage and others), methadone (Methadose and others), methylphenidate (Focalin, Daytrana, and others), metoprolol (Toprol, Lopressor, and others), mirtazapine (Remeron and others), olanzapine (Zyprexa), oxycodone (OxyContin, Roxicodone, and others), prednisone (Rayos and others), pregabalin (Lyrica and others), propranolol (Inderal, InnoPran, and others), quetiapine (Seroquel), ramipril (Altace and others), risperidone (Risperdal and others), simvastatin (Zocor and others), stramadol (Ultram, Ryzolt, and others), terbinafine (Lamisil and others), trimipramine (Surmontil and others), venlafaxine (Effexor and others).

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