Delirium, thrombocytopenia, insomnia, and mild liver damage associated with MAOI withdrawal

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Eur J Clin Pharmacol (2009) 65:1269–1270
DOI 10.1007/s00228-009-0711-y

LETTER TO THE EDITORS

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Received: 24 June 2009 / Accepted: 21 July 2009 / Published online: 5 August 2009

Dear Sir,

Monoamine oxidase inhibitors (MAOIs) are effective second-line treatment options for depression [1, 2]. A recent study showed that tranylcypromine (TCP), a nonselective and irreversible MAOI, remains commonly used in standard psychiatric clinics [3]. The risk of hypertensive crisis due to drug−food interactions when MAOIs are prescribed is widely known. Less well appreciated is the fact that MAOIs can cause addiction and that a particular patient population may be at high risk. Here we present a case of TCP dependence that brings together all signs and symptoms so far described after TCP withdrawal, including delirium, thrombocytopenia, insomnia, and mild liver damage.

Case

A 30-year-old woman diagnosed with major depressive disorder and borderline personality disorder and with past history of alcohol, marihuana, amphetamine, and cocaine abuse, presented to the emergency room. For the preceding 1−2 years, she had been treated with TCP and titrated to 60 mg a day, along with chlorpromazine 350 mg at night for "sleep." Two months after the initiation of TCP, she steadily increased her dose to 170 mg a day. In order to maintain her TCP intake, the patient visited multiple physicians in search for prescriptions. Three days prior to admission, she ran out of TCP and gradually became agitated, irritable, and paranoid. When she presented to the emergency room, she was confused, unable to recognize her mother, and oriented to person only. She was described as responding to internal stimuli and laughing inappropriately. On physical examination, she had a mild tachycardia, a severe tremor, and extensive bruising involving upper and lower extremities. Laboratory evaluation revealed a thrombocytopenia of 72,000/μl.

On further inpatient evaluation, her cognitive status improved. By the second day, her platelets had decreased to 55,000/μl, and on the third day, these cells dropped further to 25,000/μl. During her third day of hospitalization, her partial thromboplastin time (PTT) extended to 40.9 s and her liver function tests showed an aspartate transaminase (AST) of 106 IU/l. A liver ultrasound revealed fatty-acid infiltrates. On day 6, her platelets returned to normal limits. Nine days after admission, the patient was able to sleep 6 h without any medication, and her tremor was completely resolved.

Discussion

This abrupt change in behavior and cognition coincides with previously reported cases of delirium after acute withdrawal from TCP [4–6]. It has been proposed that delirium and paranoia could result from acute removal of the sympathomimetic component of MAOIs on presynaptic receptors [7]. Under normal conditions, this presynaptic effect aims to diminish the release of catecholamines. It is likely that when MAOIs are suddenly stopped, norepinephrine and dopamine acutely increase in the synapse, rendering patients susceptible to psychosis and delirium [6, 7].

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Thrombocytopenia has also been previously described after a sudden removal of TCP [4, 5, 8]. Even though the reason for the thrombocytopenia in unclear, this has been explained as a sympathomimetic effect secondary to TCP withdrawal that results in spleen venous pooling and also as a consequence of the long-term inhibition of MAO in platelets which, in turn, may lead to a reduced life span of these cells [9].

The AST increase, PPT extension, as well as the fatty-acid infiltrate could have originated from MAOI abuse [4, 10]. This possibility is further supported by the AST and PTT normalization after being off TCP for several consecutive days. On the other hand, insomnia could be associated to a rebound from rapid eye movement sleep suppression, as it has been previously observed when MAOIs are abruptly stopped [11].

The combination of a past history of substance abuse and a diagnosis of either borderline or histrionic personality disorder seems to render patients at higher risk of developing MAOI dependence [11–17], perhaps because these medications are either structurally similar to amphetamines [6, 17] or are, like selegiline, metabolized into excitatory compounds [18].

Clinicians are exhorted to ponder the addictive potential of MAOIs when prescribing these drugs.

Acknowledgements AB receives support from FRM France, CONACYT #74641 and The Young Minds in Psychiatry Award.

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