Tianeptine Sodium: A Nootropic With Potentially Lethal Consequences

To the Editor: In recent years, "nootropics" have become increasingly popular drugs and supplements accessible from internet resources and used to enhance mood and cognitive functioning, often without medical consultation.[1] Some nootropics, eg, tianeptine sodium, are medications prescribed in other countries but have not received US Food and Drug Administration approval for use in the United States. The international sale of nootropic agents is growing; estimated sales approach 1 billion US dollars annually.[2] We describe a patient whose use of tianeptine led to unintended life-threatening consequences.

Case report. A 42-year-old man displayed shallow and variable breathing; he was unresponsive to his wife's attempts at arousal. In the ambulance, he was administered naloxone 0.8 mg intravenously, to which he responded with arousal and improved respiration. A second dose was administered, resulting in improved alertness and spontaneous respirations. He was admitted to the hospital and treated for aspiration pneumonia; his toxicology screen was positive for opioids and benzodiazepines.

He reported taking tianeptine for chronic back pain but acknowledged using more than he customarily would. He had done so unwittingly in combination with his usual alprazolam dose. He indicated, and his wife corroborated, that he had not intended to end his life but to manage pain.

He endorsed dysphoria related to back pain but denied neurovegetative symptoms of depression. He also denied a history of anxiety or mania and was able to reality test.

He said no doctor would give him anything for pain due to a remote history of illicit substance use. He discovered tianeptine sodium from internet blogs, advocating its usefulness for pain. He was able to inexpensively acquire it online (eg, from Amazon).

Subjectively, he maintained that tianeptine induced euphoria and a "sense of calm." "You take one scoop of the powder whenever you just feel bad," he said. However, the effects of tianeptine were short-lived. He reported tolerance, needing larger doses over time to achieve the same desired effects. Believing it was harmless, he had taken an inordinately large amount of tianeptine, prompting this hospitalization.

He was receptive to education, acknowledging the life-threatening potential of tianeptine use; he no longer intended to use it. He was discharged home in stable condition. Outpatient psychiatric and chemical dependency–based treatment were arranged to reinforce abstinence and relapse prevention and address pain-related distress.

This case illustrates the misuse and abuse potential of tianeptine sodium, an atypical antidepressant structurally similar to tricyclic antidepressants, marketed for use in Europe and Asia. It acts by serotonergic augmentation but without marked anticholinergic effects.[3] Tianeptine sodium is not associated with cognitive, psychomotor, or cardiovascular effects encountered with tricyclic overdose as manifest in the present case.

Additionally, tianeptine has demonstrated opioid agonist influences,[4] enhancing its appeal and potential for misuse. A review of the literature suggested that there is an abuse potential associated with tianeptine,[5] consequently, it has been classified as a controlled substance in several countries. With the implementation of prescription monitoring programs and regulatory measures to prevent opioid misuse within the United States, those seeking opioids may resort to internet sites to surreptitiously acquire (and use) tianeptine or related compounds.

Internet blogs[6,7] discuss the extramedical (ie, recreational) use of tianeptine and management of withdrawal. Tianeptine is available in tablet, capsule, and powder form and is accessible from online commercial sources under the rubric of nootropics. Ingestion of amounts (250–1,000 mg) exceeding the recommended daily antidepressant dose (37.5 mg) has been advocated on internet blogs[6,7] to achieve opioid-like effects. Although tianeptine has not been demonstrated to cause tolerance in rodent models,[8] anecdotal reports from internet blogs[6,7] seem to suggest that higher doses are necessary to acquire euphoric effects over time, as illustrated in this case.

Additionally, animal models suggest that tianeptine does not produce respiratory depression, at least at doses comparable to those employed for clinical purposes.[9] Nonetheless, tianeptine seems to have induced respiratory depression in this patient, which is supported by the naloxone reversal, perhaps because our patient was using vastly higher doses than are recommended clinically. The concurrent use of alprazolam with tianeptine may have resulted in synergistic effects that contributed to his respiratory depression. Overdose of tianeptine has resulted in 2 deaths,[10,11] but only 1 of those was directly related to tianeptine toxicity.[9] Cases[12,13] of tianeptine overdose were reversible with naloxone, as in the present case.

Extramedical tianeptine use is potentially associated with severe health risks. Clinicians should entertain the possibility that use of such agents acquired from internet resources can confound the clinical presentation and complicate management of their patient's condition.

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