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Phenibut, the Appearance of Another Potentially Dangerous Product in the United States

To the Editor:

Since the advent of the Internet, many quasi-legal substances with significant toxicity and abuse potential have found their way into the hands of consumers across the US. In recent years, multiple reports of abuse and withdrawal syndromes related to Internet-purchased synthetic cannabinoids and synthetic cathinones known as "bath salts" have become prevalent.[1] We report a patient who reportedly suffered toxicity after using a novel substance named phenibut (β-phenyl-γ-aminobutyric acid).

A 25-year-old man with a history of ethanol dependence and depression was found by his roommate to be unconscious and minimally responsive. For the prior 4 days the patient reportedly had been ingesting Internet-purchased phenibut at a dose of 1.5 grams twice daily.

Initial vital signs in the Emergency Department were: blood pressure 110/50 mm Hg, pulse 69 beats per minute, temperature 36.2°C, and respirations 14 breaths per minute with a pulse oximetry of 100% on room air. Physical examination revealed a significantly depressed level of consciousness. To painful stimuli he would moan, open eyes slightly, and move all extremities equally. His pupils were of normal size and reactive. An electrocardiogram was normal, and routine laboratory testing (complete blood count, chemistry, coagulation studies) was normal except for slight hypernatremia (149 mmol/L) and hyperchloremia (108 mmol/L). Serum acetaminophen, salicylate, and ethanol were not detected. A computed tomography brain scan and chest radiograph were unremarkable. Further confirmatory serum testing was not available for phenibut through our hospital's associated national laboratory clinic.

Over the next 7 hours the patient slowly returned to a normal level of consciousness. He denied additional ingestions beyond therapeutic doses of his venlafaxine and mirtazapine. Telephone follow-up 1 week later revealed the patient remained asymptomatic after ceasing further phenibut use.

Although withdrawal from phenibut has been reported in the English literature,[2,3] we are not aware of any other published cases involving toxicity from either excessive or "therapeutic" doses. Phenibut was first synthesized in Russia in the 1960s, where it remains in use for anxiolysis as well as preoperative sedation and alcohol withdrawal. Phenibut is a $GABA_B$ agonist[4] that is structurally similar to the widely prescribed $GABA_B$ agonist baclofen, differing by only a single chlorine molecule. Given its mechanism of action, one would expect a sedative/hypnotic presentation as demonstrated in our patient.

Little is published about the pharmacokinetics of phenibut, and it is unclear in our case why toxicity manifested on the 4th day of use. Suggested daily doses range from 500 to 2000 mg; our patient's consumption exceeded maximal suggested dose by 1000 mg daily. In addition to central sedation caused by phenibut, it is plausible our patient could have had potentiation or interaction with his neuroleptics, leading to increased sedation. Potentiation of other medications with concomitant phenibut use has been demonstrated in animal models.[5]

In order to determine if our case was the sentinel case reported to poison control centers in California, we searched and subsequently found that 3 additional cases of phenibut toxicity (2 with "normal" use and one from withdrawal) had been reported within the previous 6 months. This raises serious concerns because phenibut has pharmacological activity found only in prescription medications in the US and is easily obtainable. A simple Internet search utilizing Google with the search phrase "buy phenibut" yielded 20 different retail sites, including vendors Walmart and EBay. Phenibut-related problems are beginning to increase in the US and physicians should be aware of its presence and adverse effects.

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