Changing trends in diet pill use, from weight loss agent to recreational drug

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The prevalence of obesity and obesity-related conditions in the United States is increasing. Many weight-loss products and dietary supplements are used in an attempt to combat this epidemic, but little evidence exists of their efficacy and safety.

We present a case report of a middle-age woman who developed severe psychotic symptoms while taking phentermine hydrochloride (HCl), a psychostimulant similar to amphetamine that is used as a weight-loss agent and for recreational purposes. Phentermine has been associated with mood and psychotic symptoms and has a tendency to cause psychological dependence and tolerance.

To investigate the risks and potential effects of using this drug, we searched OVID and PubMed databases using the search string "phentermine + psychosis." We conclude that there is a need for awareness about early detection and treatment of reversible psychotic and mood symptoms caused by what might appear to be harmless weight-loss and energy pills.

Obesity epidemic, wide-ranging weight-loss efforts

There has been a dramatic increase in obesity in the United States in the past 20 years: More than one-third of adults and approximately 17% of children and adolescents are obese. Obesity-related conditions, such as heart disease, stroke, and type 2 diabetes mellitus, are leading causes of preventable death.[1] Weight monitoring, a healthy lifestyle, surgical intervention, traditional herbs, and diet-pill supplements are some of the modalities used to address this epidemic.

Most so-called supplements for weight loss are exempt from FDA regulation. They do not undergo rigorous testing for safety. Furthermore, many contain controlled substances; some supplements are anti-seizure medications or other prescription drugs; and some are drugs not approved in the United States.[2] Since the 1930s, such drugs as dinitrophenol, ephedrine, amphetamine, fenfluramine, and phentermine have flooded the market with the promise of quick weight loss.[3,4]

Phentermine, a contraction of "phenyltertiary-butylamine," and its various types (***Table, e4***) is a psychostimulant of the phenethylamine class, with a pharmacologic profile similar to that of amphetamine. It is known to yield false-positive immunoassay screening results for amphetamines.

Medically, phentermine is used as an appetite suppressant because of its activity on dopaminergic and adrenergic systems. It is a Schedule-IV drug, by prescription only. When used illicitly, it is associated with acute-onset psychosis and mood changes.[5-13]

continued

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Table

Phentermine and its branded formulations

Generic compound	Brand names and formulations
Phentermine HCl Dosages: 15 mg, 30 mg, and 37.5 mg Phentermine HCl, 37.5 mg = phentermine resin, 30 mg Phentermine HCl, 30 mg = phentermine resin, 24 mg Phentermine HCl, 15 mg = phentermine resin, 12 mg	**Adipex-P** Available as 37.5-mg pill **Suprenza** Orally disintegrating tablet Dosages include 15-mg, and 30-mg pill **Qsymia** Previously known as Qnexa Combination of phentermine and extended-release topiramate Limited distribution in the United States Dosage forms: 3.75 mg/23 mg ER; 7.5 mg/46 mg ER; 11.25 mg/69 mg ER; 15 mg/92 mg ER **Fen-Phen** Combination of fenfluramine and phentermine Withdrawn from the U.S. market in September 1997 because of reports of potentially fatal valvular heart disease and pulmonary hypertension, secondary to fenfluramine

ER: extended release; HCl: hydrochloride

Clinical Point

Medically, phentermine is used as an appetite suppressant because of its activity on dopaminergic and adrenergic systems

CASE REPORT

Acute psychotic break

Ms. B, age 37, with a history of postpartum depression, arrives at the emergency room reporting auditory hallucinations of her son and boyfriend; vivid visual hallucinations; and persecutory ideas toward her boyfriend, whom she believes had kidnapped her son. She also complains of insomnia and intermittent confusion for the past week.

Speech is pressured, fast, and difficult to comprehend at times; affect is labile and irritable. Ms. B denies suicidal ideation and is oriented to time, place, and person.

A urine drug screen is positive for amphetamine.

Pre-admission medications include alprazolam, 1 mg as needed, and zolpidem, 10 mg at bedtime, prescribed by Ms. B's primary care physician for anxiety and insomnia. She discontinued these medications 3 weeks ago because of increased drowsiness at work. She denies other substance use and is unable to account for the positive urine drug screen.

Her medical history, physical examination, and a CT scan of the head are unremarkable. The components of a comprehensive metabolic panel and complete blood count are within normal limits.

After admission, in-depth assessment reveals that Ms. B has been taking phentermine, 37.5 mg (under the brand name Adipex-P), once daily since age 16 for weight loss. She recently discontinued the drug, abruptly, for 1 month, then resumed taking it at an unspecified higher dosage 1 week before she came to the emergency room, for what she said was recreational use and to meet the demands of her job, which required shift work and long hours.

Over the next few days in the hospital, Ms. B's symptoms resolve as the drug is eliminated from her body. Speech becomes comprehensible and sleep improves. Affective distress diminishes considerably after admission; slight mood lability persists. She no longer reports perceptual disturbances or distress secondary to intrusive thoughts.

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Ms. B is discharged 1 week after admission, with instructions to follow up at a dual-diagnosis outpatient program.

Pharmacologic profile

Phentermine acts through sympathomimetic pathways by increasing brain noradrenaline and dopamine. The drug has no effect on serotonin.[4,5] Phentermine can lead to elevated blood pressure and heart rate, palpitations, restlessness, and insomnia, and can suppress appetite. Increased sympathomimetic activity has been implicated in the ability of phentermine to induce psychotic symptoms.

The literature. Our PubMed search of "phentermine + psychosis" produced 13 results, including 6 case reports of phentermine use. Five citations were more than 4 decades old[5-12]; only 1 could be considered recent (2011).[13]

Patients in these reports developed psychotic or manic features after chronic or acute phentermine use, mainly for weight reduction. The most recent article[13] mentioned 4 patients who were abusing diet pills recreationally (including "for lethargy"). As with Ms. B, in all 4 of those patients, phentermine precipitated the primary pathology (mania in bipolar disorder; depression in postpartum depression and substance abuse) or revealed underlying illness.

Changing landscape of use and abuse

There has been a trend observed in the pattern of diet pill use: Initially marketed as an appetite suppressant, these pills are now being abused across ethnic, racial, and socioeconomic groups, by males and females.[14] There is also a scarcity of useful guidance for clinicians.

Not only are diet pills used by people with an eating disorder; their recreational use is an emerging problem. If reports[12,13] continue to reveal that phentermine is a substance of abuse and has catastrophic effects on the user's psyche, the need for stronger warnings and guidelines might be warranted to allow consumers to make an informed choice about using the drug.

Drug Brand Names

Alprazolam • Xanax
Fenfluramine • Pondimin
Phentermine HCl • Adipex-P, Fen-Phen, Qsymia, Suprenza
Topiramate • Topamax, Trokendi XR
Zolpidem • Ambien

Call for awareness

The case we presented here exemplifies the importance of tighter regulation of both over-the-counter and prescription stimulant analogs. There is a need for awareness among practitioners about early detection and treatment of reversible psychotic and mood symptoms secondary to what might be promoted as, or appear to be, "harmless" weight loss and energy pills.

Clinical Point

Not only are diet pills used by people with an eating disorder; their recreational use is an emerging problem

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