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Case Report

Co-occurring Addiction of Synthetic Benzodiazepine Clonazolam and Propylhexedrine presenting as Acute Brief Psychosis

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- Clonazolam
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Abstract

We report the case of a 25-year-old man who developed acute neuropsychiatric sequelae after consuming a designer benzodiazepine (Clonazalam) with concurrent ingestion of over-the-counter (OTC) nasal decongestant Benzedrex (Propylhexedrine). The psychiatric and medical symptoms of extreme aggression, paranoia, visual hallucinations, and anterograde amnesia subsided within 24 hours of admission. The report highlights the fact that synthetic and OTC drugs abuse, including amphetamine-type stimulants and new psychoactive substances are drastically increasing. Moreover, with the growing number of new products, which are freely available on the internet, it is likely that drug users will innovate with unique formulations and experiment with combination of old and new drugs of abuse. Hence, the medical personnel should be educated and mindful of uncommon cases of co-occurring multiple drug use and be alert for unexpected responses to therapeutic interventions and to a rapid change in patient presentation.

ABBREVIATIONS

OTC: Over-the-counter; ED: Emergency Department; LSD: Lysergic Acid Diethylamide

INTRODUCTION

Drug use is a growing national issue, compounded with an ominous new trend of increased recreational use of new psychoactive substance - synthetic or designer benzodiazepines. In the last few years, the number of designer substances with potentially harmful effects have increased drastically and become readily available through over the counter (OTC) and online vendors [1,2]. Today more than 50 different synthetic benzodiazepine are available on the illegal internet market, with some of the first designer benzodiazepines being diclazepam, flubromazepam and pyrazolam, and more recently clonazolam, deschloroetizolam, flubromazolam, nifoxipam and cinazepam [3]. Such availability enhances risk of complications like over-doses and psychosis as a result of intoxication. These new designer benzodiazepines drugs have the classic benzodiazepine properties that are attractive to the recreational drug abusers-they are sedative, hypnotic, anxiolytic, and muscle relaxant. Despite similarities in structure to prescription benzodiazepines, none have been tested for safety or efficacy in humans and are not regulated by law and lack oversight in their manufacturing processes [4]. Clonazolam has a fast onset of action of 20-60 minutes with duration of 8-14 hours. Its capsule, tablet, pellet, blotter and powder form is now widely available online, and is advertised under the brand name Clonazolam or Clonitrazolam. It is reputed to be highly potent, and concerns have been raised that Clonazolam may pose moderately higher risks than other synthetic benzodiazepines due to their ability to produce strong sedation and amnesia at oral doses of 0.5 mg [2].

In this report, we focus on the concurrent use of nasal decongestant Propylhexedrine (Benzedrex) with Clonazolam. In contrast to the new designer drugs, Propylhexedrine use disorder is documented in several case reports since 1970 mentioning negative effects of abuse, including pulmonary hypertension, myocardial infarction, psychosis, ventricular arrhythmias, shock and death. The OTC nasal decongestant Propylhexedrine is a strong alpha-adrenergic sympatho-mimetic that delivers 0.4-0.5 mg of the drug in each 800 mL of air and was made as a substitute for the widely abused amphetamine sulfate (Benzedrine) inhaler, which is no longer in the market. This drug is considered a "last resort" to stimulant users when they are unable to acquire amphetamine or other controlled stimulants. Users disassemble the inhaler and extract the cotton plug from the inhaler which is saturated with 250mg of propylhexedrine. The cotton plug is either swallowed or soaked in water to make a solution for intravenous injection or ingested orally [5].

CASE PRESENTATION

A 25-year-old man with a history of polysubstance use

disorder and on prescribed medications (Baclofen, Bisoprolol Fumarate, Nortriptyline, Amlodipine) presented to the Emergency Department (ED) after his mother recognized his aggressive and odd behavior. Upon first responder arrival, he was noted to be confused and aggressive. On arrival to the ED, blood pressure was 160/95 mmHg, pulse rate 106 beats/min, respiratory rate 19 breaths/min, temperature 98.6 C, and oxygen saturation 97%. Physical examination was notable for equally round and reactive mid-range pupils. He was severely agitated, anxious, and reported of visual hallucinations and anterograde amnesia. He was assessed by the Psychiatrist and admitted to the medical inpatient unit for stabilization.

Initial laboratory studies (complete blood count, comprehensive metabolic panel and lactate levels) drawn within minutes of ED arrival were within normal limits. Electrocardiogram demonstrated sinus tachycardia with a rate of 106 beats/min, with normal axis and conduction. Urine drug screening performed by immunoassay was positive for benzodiazepines and cannabinoids and negative for amphetamines, barbiturates, cocaine, opiates, and opioids. Serum ethanol, acetaminophen, and salicylate concentrations were undetectable.

The patient developed increasing agitation and aggressive behavior during his hospital stay, beginning on hospital day two, as he physically assaulted the staff. Acute agitation and psychotic symptoms were controlled with Lorazepam and Haloperidol respectively. Symptoms and his mental status improved significantly over the course of the day as medications were titrated and weaned. A Psychiatric evaluation revealed a significant history of anxiety disorder with an eight-year history of polysubstance use comprising of Hydrocodone, OxyContin, Lysergic acid diethylamide (LSD), Cocaine, Opiates, Amphetamines, Benzodiazepines, Marijuana, Nicotine and Pregablin. He denied use of phencyclidine PCP, bath salts, opiates, alcohol and cocaine within the previous month. The patient denied any suicidal ideations, but did experience significant visual hallucinations, anterograde amnesia, and paranoia. He reported ingesting 100 mg of Internet-bought Clonazolam over the course of two days in the prior week. In addition, he used 2 to 4 Benzedrex inhaler cottons (500 to 1000 mg) daily within the same week. After completing the detoxification with benzodiazepines, he was discharged to outpatient substance use counselling program.

DISCUSSION

According to recent reviews, benzodiazepines are the second most commonly used class of medications, after opioids [6]. The high availability and low prices of the alternative designer benzodiazepines through online vendors makes it easy for patients to self-medicate and develop addiction disorder. These new unscreened and unregulated designer benzodiazepines like Clonazolam are also concurrently taken with stimulants to decrease unpleasant effects, which can alter the clinical symptoms at presentation [4]. In this case, the patient ingested OTC Propylhexedrine — an old stimulant drug of last resort to abusers which has been on the market for decades. The unrestricted access to these new drug alternatives in multidrug users entails the risk of toxicity and death for users of designer benzodiazepines. As the number of drug overdose deaths continues to increase, novel drugs such as designer benzodiazipines, including Clonazolam, should be suspected as an offending agent, especially given its gaining popularity in the United States.

Our patient had purchased the Clonazolam over the internet in tablets of 0.5 mgs, and reported that he ingested 100 mg in an attempt to control his anxiety. Previous literature cases of Clonazolam toxicity or withdrawal are not published, and as such limited information on the acute toxicity, withdrawal and drug interaction are reported. In one study, new designer benzodiazepines metabolites were detected in 77 cases of which 7 were Clonazolam [3]. Through cross-reactivity, synthetic benzodiazepines may be detected in urine by commercial immunochemical tests with a concentration greater than 140 ng/mL [8]. In the case of our patient, routine drug screen and benzodiazepine screening panel in the emergency department, yielded a positive result for benzodiazepines. This case is limited by the inability to document levels of Clonazolam in our patient. Moreover, the mass spectrometric tests utilized for conformation did not analyze for all metabolites of the designer benzodiazepines. Additionally, other drugs were detected in our patient, thus making it difficult to assess the clinical effects of Clonazolam alone. The patient in study was observed to display progressive neuropsychiatric symptoms complicated with aggression and visual hallucinations that waxed and waned during his treatment, which could have been consistent with a benzodiazepine withdrawal, to a manifestation of pharmacodynamics interaction with Propylhexedrine, or to substance-induced delirium. Designer drugs, including Clonazolam, should be investigated in patients with a history of substance abuse presenting with a clinical progression of acute onset of neuropsychiatric symptoms. The acute onset of hallucinations and cognitive impairment in young healthy individuals without a history of psychotic disorder should alert the clinician to take detailed history of designer drugs of abuse.

We conclude that the radical online availability of designer Benzodiazepines and OTC drugs like Propylhexedrine, make it imperative for the providers to take history of the internet buying of drugs in all suspected cases. Given the emerging problem of new designer benzodiazepines, clinicians should be educated on the assessment and therapeutic intervention protocols. Individuals with designer drug toxicity and withdrawal, inclusive of Clonazolam, should be admitted for clinical assessment of hemodynamic instability and improvement of their altered mental status [9].

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