Acute intoxication following massive bupropion sniffing: A case report

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Abstract

Bupropion intranasal misuse potential should be considered in the suspect of sympathomimetic syndrome for illicit drug or medication intoxication. A 31-year-old man was admitted for intranasal misuse of 30 crushed tablets of bupropion with adrenergic mild presentation. Lorazepam infusion was started with complete clinical resolution. Further forensic investigations detected a bupropion serum and urine concentration levels at 18 hours from intake of 1905.26 ng/mL and 2001.57 ng/mL, respectively. This case of intranasal bupropion misuse shared only some features with oral overdose, despite a plasma concentration five times higher than the lowest toxic level. Nasal bupropion snorting in chronic users could have lower toxicity compared to other snorted stimulants but symptomatic treatment remains the gold standard for preventing complications. Bupropion misuse might rapidly become a concerning issue and monitoring by healthcare professionals is needed.

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Introduction

Despite being an under-recognized phenomenon, prescription and Over The Counter (OTC) medication misuse (a practice known with the term "pharming") is rapidly becoming an issue of world-wide concern.[1]

Bupropion is an atypical antidepressant with medical indication for major or seasonal depressive disorder and smoking cessation,[2] in addition to off-label uses for Attention Deficit Hyperactivity Disorder (ADHD), obesity, binge-eating disorder and some Substance Use Disorder (SUD) (e.g. cocaine and methamphetamine).[3] Bupropion acts by blocking dopamine, norepinephrine and to a lesser extent serotonin reuptake. It also acts as an antagonist on many nicotine receptors.[4] Its chemical structure is similar to cathinone, a natural stimulant extracted from *Catha edulis*, and therefore it is comprised within the pharmacological class of substituted cathinones along with other synthetic compounds (e.g. amphetamines and 'bath salts').[5] Bupropion has a narrow therapeutic window, leading to severe cases of overdose with possible fatal complication such as seizures[6] and heart failure.[7]

Despite the belief of bupropion having a lesser addictive potential compared to cocaine or amphetamines,[5] issues about its non-medical use have been raised for years[1] especially among young adults[8] and inmates in correctional facilities.[9] Its recreational snorting misuse has been reported since 2002,[10] whereas overdose ingestion is more associated with suicidal attempts.[11] Intravenous (IV) bupropion abuse has also been reported[12] sometimes leading to serious complications.[13]

We hereby present a case of nasal sniffing of a huge amount of bupropion crushed tablets, requiring benzodiazepine (BZD) infusion without the development of any major complication.

Case Report

In April 2021, a 31-year-old man was referred to the Emergency Department 2 hours after sniffing 30 crushed bupropion tablets "for playful purpose".

His medical history was positive for ADHD treated with psy-

chotherapy and bupropion (unknown formulation dosage) besides a previously diagnosed cocaine use disorder.

Mental confusion, hypertension, deep tendon hyperreflexia and dry mouth were present at medical examination while electrocardiogram (ECG) at arrival showed sinus tachycardia with a 484 msec corrected QT interval (QTc) prolongation (Figure 1). No QRS complex alteration was present. The above-mentioned findings were compatible with the suspected intoxication.

A toxicology consultation was requested and Poison Control Centre (PCC) suggested cardiac monitoring in addition to IV rehydration. Given the risk of hyper-activation status, possible seizures and serotonin syndrome due to the hypothetical high amount of absorbed bupropion, lorazepam (4 mg IV) was administered.

Subsequent electroencephalogram (EEG) and CT-scan ruled out any evidence of neurologic impairment (epileptic patterns, parenchymal lesions and blood extravasation) due to acute bupropion intoxication. A toxicological urine screening was performed with resulting positivity only for BZD, whereas only mild leukocytosis was detected at blood test (15.23 x10^3/uL with normal range 3.5-9.5).

Clinical signs and symptoms of intoxication normalized after 27 hours of observation without any complication. The patient decided to self-discharge after a psychiatric consultation, being therefore referred to his psychotherapist. To certify the reported intake of bupropion, blood and urine samples were taken 18 hours after the event in order to perform a second-level investigation with gas chromatography-mass spectrometry (GC-MS). Bupropion serum and urine concentration levels were 1905.26 and 2001.57 ng/mL, respectively (Figure 2).

Urine toxicological screening and clinical monitoring of vital signs throughout hospitalization are summarized in Table 1.

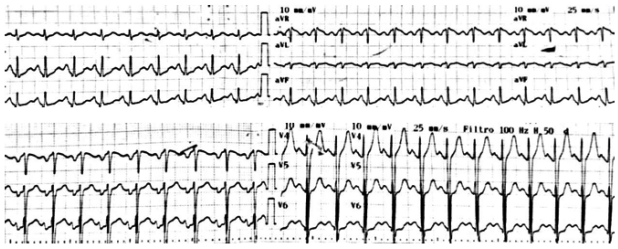

Figure 1. Sinus tachycardia with 125 beats per minute heart rate and nonspecific alterations of ventricular repolarization.QTc prolongation (484 msec).

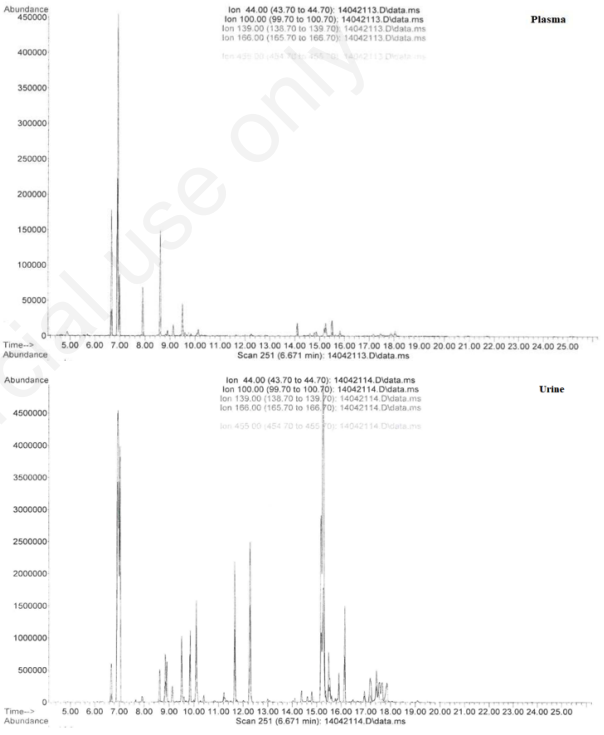

Figure 2. Bupropion serum and urine concentration levels at 18-hours from the event.

Discussion

This case of intranasal bupropion misuse shared only some of the most common clinical features of a classical bupropion ingestion overdose (considering comparable amounts of medication).[14] Therapeutic daily doses for bupropion are usually up to 300 mg/day[15] reaching peak concentration after 1.5 hours and 3-5 hours for immediate or modified-release formulations, respectively.[16] Half-life is about 21 hours in chronic users and it can be even longer for the presence of active metabolites.[14] Therapeutic window is considered between 5 to 100 ng/mL.[17] Although our patient's bupropion dose formulation was unknown, only 150 mg and 300 mg modified/sustained formulations are available on the

Table 1. Patients vitals and laboratory screening during hospitalization.

Vitals	Day 1 12:42 pm	Day 1 01:41 pm	Day 1 02:24 pm	Day 1 02:26 pm	Day 1 09:46 pm	Day 2 10:06 am	Day 2 14:41 pm
HR (bpm)	140		88	120	95	90	85
RR			20	16			16
BP (sys mmHg)	158	130	133	133	122	120	130
BP (dia mmHg)	116	60	72	72	82	70	79
BT (C°)	36		36	36.9	36	36	36.7
Pain (VAS)				1			0
GCS			15	15	15	15	15
SpO2 (% AA)	97		97	99	98	98	96
Semi-quantitative screening (urine)	Day 2 09:54 am	Amphetamine	Benzodiazepines+	Cannabinoids	Cocaine	Methadone	Opioids

Italian market, making the possible total intranasal intake ranging from 4,5 g to 9 g. Second-level forensic investigation assessed an 18-hour blood bupropion level of 1905,26 ng/ml, estimating this way an approximate 6 g intake consistent with the number of tablets stated by our patient (anecdotal computation given the different oral versus nasal route of administration).

Considering that decontamination would not be effective after intranasal misuse, this case suggests that this administration route might have less or slower absorption compared to an almost 100% absorption by enteral route[4], differently from what happens with other typical snorted stimulants (e.g. cocaine) that have faster intranasal intoxication in contrast to its ingestion.[18] Furthermore, neurologic complications are usually more likely above 450 mg dosing.[6] This case may imply that chronic abusers may not be as sensitive to average toxic levels as naïve or therapeutic use patients, as was also reported on a case of 2.1 g snorting without seizures occurrence.[19] Another interesting aspect that could be considered is the different amount of active metabolites after nasal overdose compared to ingestion, due to lesser intestinal/hepatic metabolism.[20] This could possibly explain a milder clinical presentation despite high dosages.

In spite of the known bupropion cross reactivity for amphetamines,[21] only iatrogenic BZD were found in the patient's initial urine screening, requiring further investigations as to confirm the reported source of intoxication. High levels of the original compound were indeed assessed even after 18 hours from misuse. This stresses the idea that expectancy for urinary cross reactivity at standard screenings can underestimate the real incidence of bupropion abusers and it should be taken with a grain of salt.

As previously reported by other authors,[22] leukocytosis can be found in case of oral bupropion overdose. Our case, despite the different route of exposition, was consistent with this aspect.

Eventually, in this case report we would like to underline the chance that bupropion nasal exposure toxicokinetic may differ from classical enteral intoxication. Still, symptomatic treatment of mild presentations with BZD remains the gold standard for preventing complications such as seizures and life-threatening arrhythmias.

Because of its "cathinone-like" properties, bupropion results among the most frequent antidepressants prone to pharming and this highlights the need for a more vigilant monitoring by healthcare professionals both in prescribing and selling medications, especially as long as specific categories are involved (e.g. unfamiliar patients or past SUD patients) and urine screenings may not always detect the misused substance. Prompt PCC consultation enables health providers to effectively manage intoxications deriving from unordinary administration routes for medication misuse.

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