
LETTER TO EDITOR

NOTA CLÍNICA

BUPROPION MISUSE BY NASAL INSUFFLATION WITH A FATAL OUTCOME: CASE REPORT AND REVIEW

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ABSTRACT

Introduction. Bupropion is the only FDA - approved synthetic cathinone, with increasing popularity in clinical practice due to its wide range of action, and lack of sexual side effects. However, its stimulant effect similar to amphetamines has growing the concern regarding its recreational use.

Aims and Methods. In this manuscript we report a case of bupropion misuse via nasal insufflation with a fatal outcome and preform a brief review of the recreational use of bupropion.

Results. We report the case of a man in his fifties, with long-term abuse of bupropion mainly via nasal insufflation, who suddenly deceased about two weeks after he was discharged for a type 2 acute myocardial infarction secondary to bupropion overdose.

Throughout the last decades, several studies have reported an increasing misuse of bupropion by non-oral routes, especially through nasal insufflation, and intravenous use, particularly in patients with a previous history of substance abuse, adolescents or in correctional settings.

Despite most patients having mild to moderate side effects, devastating consequences, such refractory seizures or refractory cardiogenic shock may occur in overdose, demanding a timely recognition and rapid approach to prevent these major outcomes.

In case of an overdose, there is no specific antidote available or curative treatment approved, its management is focused on treatment of symptoms.

Conclusions. Bupropion is an effective antidepressant, nevertheless it has a potential for recreational use, especially in high-risk groups. This paper alerts all physicians for the emerging problem involving bupropion misuse, and it adds some insights into its timely recognition and management.

Keywords. Bupropion; Drug misuse; Insufflation; Drug overdose; Toxicity

Dear editor,

Bupropion is an atypical antidepressant approved in 1985 by US Food and Drug Administration (FDA) for a major depressive disorder treatment¹, that currently plays a crucial role in the management of several mental disorders²⁻⁴.

Bupropion is the only FDA - approved synthetic cathinone, chemically considered as derivative of phenethylamines⁵, which acts by norepinephrine-dopamine-nicotine reuptake inhibition. This mechanism of action gives it an attractive profile due to the lack of sexual side effects, commonly reported with other antidepressants¹. However, its stimulant effect, similar to amphetamines, increases the concern regarding its recreational use⁵.

This drug is only approved by oral route and there are 3 formulations available: immediate release (IR), sustained release (SR) and extended release (XL), the last two to obtain stable plasmatic levels of bupropion with minimum side effects¹.

Tachycardia, seizures, agitation/irritable, hallucinations/delusions and tremor are the most frequently reported adverse effects of bupropion abuse⁶, however it has a narrow therapeutic window that can lead to delayed onset of symptoms with extended-release formulations, and major or fatal outcomes, though less common, may occur in overdose⁷.

In this manuscript we report a case of bupropion misuse via nasal insufflation with a fatal outcome and preform a brief review of recreational use of bupropion, aiming to raise awareness about this emerging problem, which remains often underdiagnosed, despite having serious clinical implications.

CASE REPORT

We report the case of a man in his fifties, who spent most of his life living abroad, until he returned to Portugal, where he lived with poor economic and social support, maintaining, despite that, psychiatry outpatient follow-up.

He had a history of severe head trauma and secondary personality and behavioral disorder, associated with abuse of alcohol and cannabis in the past.

He described three previous psychiatric hospitalizations abroad for major depressive episodes, which led to the introduction of bupropion XR 300 mg/daily several years ago, which he has never stopped, even after returning to Portugal.

The patient reported a family history of depression, but denied other familiar psychiatric conditions, including history of substance abuse, self-injury or suicide attempts.

Recently, he was admitted to the emergency room presenting with psychomotor agitation and dyspnea after the intake of 2100 mg of bupropion, mainly by nasal insufflation of crushed tablets.

At presentation, the patient was very agitated, with sinus tachycardia, and increasing elevation of high-sensitivity cardiac troponin T (182 > 326 ng/L). Therefore, he was evaluated by Cardiology, and he was hospitalized with a type 2 acute myocardial infarction (AMI) secondary to bupropion overdose.

Two weeks after the discharge, he was admitted to the psychiatric emergency department due to increasingly irritability and impulsive behavior at home. During the clinical evaluation, he admitted long-term abuse of bupropion mainly via nasal insufflation, claiming that this route gave him a chemical euphoria, and a brief "high" feeling. He confirmed that he has continued to abuse the remaining bupropion he had at home. He denied any current alcohol or illicit drug use and admitted having access to extra amounts of bupropion through the practice of visiting multiple physicians to obtain bupropion prescriptions.

At presentation in the psychiatric emergency department, he was awake and oriented in all domains and showed adequate self-care. He was noted to be unquiet and exhibited an anxious mood. The speech was well-organized, centered on long-term bupropion misuse, and his difficulty on abandon its drug addiction; however, overall, he was little motivated to stop bupropion. Psychotic symptoms were not present. No intention of self-harm or harm to others was noted. His physical examination was normal, and the complete blood count and metabolic panel were within normal limits. His blood alcohol level and urine toxicology screen were negative, although tests for bupropion were not available.

Psychiatric hospitalization was proposed for psychopathological stabilization and therapeutic adjustment, but

the patient refused it. A few days later, he was found in full cardiopulmonary arrest at home.

DISCUSSION

Throughout the last decades, several studies have reported an increasing misuse of bupropion by non-oral routes, especially through nasal insufflation⁸⁻¹¹, and intravenous use^{12,13}, particularly in patients with a previous history of substance abuse, adolescents or in correctional settings^{14,15}.

Users usually report euphoria, increased energy, and feeling "high", particularly after bupropion insufflation, which seems being dependent on its rapid absorption by nasopharyngeal mucosa and nasal bypass to the first-pass metabolism effect^{1,10}.

The major adverse effect of bupropion overdose most reported are seizures, which are dose-dependent. It has also been related with cardiotoxicity, often leading to prolongation of both QRS and QTc on electrocardiogram^{1,6}.

These consequences usually are self-limited and have an adequate response to supportive care, however devastating consequences as refractory seizures or refractory cardiogenic shock may occur in larger overdose^{16,17}.

Indeed, in case of overdose, there is no specific antidote available or curative treatment approved¹⁸. The treatment is focused on symptoms management^{1,18}, such as the use of benzodiazepines as the first-line treatment of bupropion-induced seizures. Active charcoal administration, gastrointestinal decontamination, gastric lavage, and bowel irrigation have been proposed to reduce bupropion absorption in selected cases.

Although, sodium bicarbonate is a well-known antidote for tricyclic antidepressant overdose, bupropion-induced QRS widening is often unresponsive to sodium bicarbonate, as this QRS prolongation it is not caused by sodium channel blockage¹⁹. Therefore, other measures, including intravenous lipid emulsion or extracorporeal membrane oxygenation, have been suggested to lead with life-threatening cardiovascular toxicity²⁰.

Looking at this case, we highlight the importance of providers being aware for the red flags that might suggest a recreational use of bupropion, such as previous history of substance abuse, *doctor shopping*, new-onset seizures of unknown cause, nonhealing skin ulcers, sudden deterioration of psychiatric condition or previous hospitalizations for bupropion toxicity^{11,14}.

Similarly, physicians should educate their patients and relatives about the risks regarding bupropion misuse, restrict the amounts provided, or evaluate the potential supervision of this medication by cohabitants^{6,14}. Once there is suspicion of bupropion misuse, providers should consider switching this antidepressant to another class⁶.

We recognize the access to autopsy data, including postmortem blood concentrations of bupropion levels, would be important to clarify the cause of the death. Nonetheless, looking at his recent episode of type 2 AMI secondary to bupropion overdose with continued abuse, leads us to consider that there is a link, even if indirect, between bupropion misuse and his fatal outcome. This can be supported by the fact the weeks to months following AMI have been recognized as a particularly vulnerable period, where the absolute rate of sudden cardiac death is increased²¹.

CONCLUSIONS

We may conclude that bupropion is a popular and effective antidepressant, nevertheless it has a potential for misuse, particularly in patients with a previous history of substance abuse, adolescents or in the correctional settings, with potential serious clinical and psychiatric consequences.

The recognition of this condition is often difficult and delayed, therefore all physicians should be especially cautious when they decide to prescribe this drug.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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