Bupropion poisoning with plasma levels in the lethal range

Intoxicación por bupropion con niveles plasmáticos en rango de letalidad

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Benzodiazepine and antidepressant poisoning is increasingly common due to the high number of prescriptions currently issued. Bupropion is a heterocyclic antidepressant that inhibits dopamine and norepinephrine reuptake but not serotonin. At high doses, it may cause tachycardia and hypertension.[1] In severe cases, it can induce seizures, QRS widening, QT prolongation, and torsades de pointes.[2-5] There is limited clinical information correlating its toxic effects with plasma levels.

A 50-year-old woman was found lying on the floor of her home with decreased level of consciousness. She was transferred to a secondary hospital, where flumazenil was administered for suspected benzodiazepine overdose. Immediately after, she developed a brief seizure lasting a few seconds, prompting transfer to our facility. Approximately four hours had elapsed since she was found, though the time of ingestion remained unknown. Her past medical history included depressive symptoms since adolescence, recent divorce (3 months prior), and ongoing pharmacologic treatment with duloxetine, diazepam, bupropion, lorazepam, and pregabalin.

Upon arrival to our emergency department, she experienced another brief tonic seizure with ocular deviation. Physical examination revealed blood pressure 76/55 mmHg, heart rate 77 bpm, respiratory rate 15 rpm, temperature 36°C, oxygen saturation 98%, and blood glucose 140 mg/dL. The patient appeared somnolent, pale, and had dry mucous membranes. Neurologic evaluation showed isocoric, reactive pupils, motor response and eye opening to painful stimulation, and incomprehensible verbal sounds (Glasgow Coma Scale score 10/15). Plantar reflexes were flexor bilaterally; the remainder of the exam was normal.

Electrocardiogram (ECG) revealed sinus rhythm at 77 bpm, axis –80°, flattened T waves in all leads, and a QTc of 468 ms. Head CT showed no abnormalities. Laboratory tests revealed pH 7.24, normal blood count and biochemistry, C-reactive protein (CRP) < 5, and creatine phosphokinase (CPK) 31 IU/L. Urine toxicology was positive only for benzodiazepines. Chest X-ray was normal.

Supportive care was initiated, including continuous ECG monitoring, 1,000 mL/24 h of 0.9% saline, and 1,000 mL/24 h of 0.3% glucose-saline solution. A total of 330 mEq of sodium bicarbonate was administered over several hours, improving venous pH to 7.31.

Given this clinical picture, an anticholinergic toxidrome was suspected due to the presence of dry mucous membranes, seizures, and neurological impairment. Because the patient was unable to maintain a secure airway, 4 mg of physostigmine (2 mg/5 mL vial) were administered, resulting in an improvement in the Glasgow Coma Scale score to 14/15, with some residual verbal confusion. An additional 2 mg dose of physostigmine was required 7 hours later to achieve full recovery. The patient remained under observation for 48 hours, reaching a Glasgow score of 15/15, and remained hemodynamically and respiratory stable, with adequate urine output. After resolution of the toxic episode, a psychiatric consultation was performed. Blood and urine samples were collected 12 hours after discovery and sent to the Canary Islands Delegation of the National Institute of Toxicology and Forensic Sciences. Using gas chromatography–mass spectrometry (GC/MS) and high-performance liquid chromatography with diode-array detection (HPLC-DAD), the substances listed in Table 1 were identified.

Therapeutic bupropion concentrations range from 0.025 to 0.1 mg/L, though higher levels may occur in special circumstances. Concentrations > 0.17 mg/L are associated with seizures,[5] and levels > 0.45 mg/L may be fatal, although recovery has been reported at higher values.[6] In this case, bupropion plasma concentration was 0.38 mg/L, near the lethal threshold.[6,7] Duloxetine, a serotonin–norepinephrine reuptake inhibitor, typically shows therapeutic levels between 0.02 and 0.11 mg/L; this patient had 0.30

Table 1. Detected substances

Drug	Blood Levels
Bupropion	0.38 mg/L
Duloxetine	0.30 mg/L
Diazepam	0.35 mg/L
Nordiazepam	0.23 mg/L
Oxazepam	0.003 mg/L
Lorazepam	0.1 mg/L
Acetylaminoantipyrine	1.01 mg/L
Pregabalin	4 mg/L

mg/L.[2-5] Other detected substances were within therapeutic ranges. Information regarding the ingested doses or timing was unavailable.

The literature contains few reports of bupropion poisoning, and only one describes serum levels.[1] In our case, toxic—potentially fatal—levels were confirmed, likely corresponding to the hours preceding sampling. Seizures may have been related to flumazenil administration and bupropion's proconvulsant effect. Observation time in our emergency department aligns with other studies, underscoring the importance of monitoring such cases in short-stay or observation units under supervision or teleconsultation by clinical toxicology experts.[2,9]

Treatment consisted of supportive care, close monitoring, and physostigmine, a safe and effective antidote for anticholinergic toxicity.[10] Its use should be considered in appropriate clinical settings, while being aware of possible complications. Some reports describe the use of intravenous lipid emulsion (ILE) therapy. In a series by Chhabra *et al.*, the Chicago Poison Center reviewed 1,274 bupropion poisoning cases (2009–2015): 14 deaths occurred, and ILE was used in 9 patients. Although survival improvement was not demonstrated, the authors advocate its use, as evidence—mainly case-based—suggests benefit given bupropion's lipophilicity.[2] According to Herrman et al., early administration may yield better outcomes than its use as rescue or last-line therapy in severe cases.[11] In our case, ILE was prepared for immediate use during the patient's observation but was ultimately unnecessary. Nevertheless, ILE therapy is not without risks. Collaboration among Emergency Departments, Clinical Toxicology Units, and Forensic Toxicology Laboratories is essential to enhance the clinical–toxicological understanding of complex poisoning cases.

Note of the editors: This is a BOWMAN-generated English translation of the officially indexed Spanish-language article, which should be cited as Rev Esp Urg Emerg. 2024;3:196-197. In this translated version, the editors have supervised the process; however, it cannot be ruled out that some errors resulting from the artificial intelligence translation process may have gone unnoticed.

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