



ToxTalks:

A Bulletin for Healthcare Professionals Who Manage Poisoned Patients

Blue Ridge Poison Center

| University of Virginia Health

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Bupropion



Overview

Bupropion is a medication that is FDA-approved for adult depression, seasonal affective disorder, and smoking cessation. Off-label, non-FDA-approved uses include anti-depressant-induced sexual dysfunction, attention-deficit/hyperactivity disorder (ADHD), depression associated with bipolar disorder, and obesity.

Pharmacology

Bupropion is a substituted cathinone and shares structural similarities to synthetic cathinones (e.g., illicit “Bath Salts”) and amphetamines. The mechanisms of bupropion and one of its active metabolites, hydroxybupropion, are reuptake inhibition of dopamine and, to a lesser extent, norepinephrine. Unlike other antidepressant medications, it has little to no effect on serotonin reuptake (at therapeutic doses). The elimination half-life of bupropion is approximately 21 hours at therapeutic doses, though the half-lives of certain active metabolites are greater than 24 hours. Absorption is complete and plasma concentrations peak within several hours after ingestion, however, clinical effects are often delayed and prolonged, especially with the extended-release formulations which are more commonly prescribed.

Available Forms

Bupropion is available as a tablet in immediate, sustained, and extended-release formulations. Brand names in the U.S. are *Aplenzin*, *Forfivo XL*, *Wellbutrin*, and *Zyban*. Generic forms are also available. A bupropion/dextromethorphan combination medication was recently released under the brand name *Auvelity*.

Clinical Effects

Given a similar chemical structure and mechanism, bupropion overdose shares many of the adverse effects of stimulants and in overdose can appear similar to a sympathomimetic toxidrome with tachycardia, hypertension, diaphoresis, agitation, tremor, and hallucinations. Similarly, if abused and insufflated, patients may report euphoria or a “high” similar to other stimulants. Other adverse effects that may be noted include anxiety, abdominal pain, nausea, anorexia, and insomnia.

Continued next page

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Bupropion has additional adverse effects that in overdose are common or warrant specific discussion, primarily seizures. Seizures may occur with therapeutic dosing of bupropion and are more common in certain at-risk populations, including those with an existing seizure disorder, previous traumatic brain injury, or eating disorder. Risk of seizures appears to be dose-dependent and unfortunately increases drastically with doses above the recommended daily maximum of 450 mg. In many cases, this might mean a patient only has to ingest one extra dose to be at risk for seizure activity. Seizures are very common in overdose and are typically self-limited, but may progress to status epilepticus. Another concerning adverse effect is cardiotoxicity. QRS complex prolongation may occur in large overdoses and QTc prolongation has also been less commonly reported. These may contribute to dysrhythmias, hypotension, and cardiovascular collapse. The QRS prolongation is not secondary to sodium channel blockade (as in several other medication-related QRS prolongations), but due to inhibition of gap junctional intracellular communication resulting in reduced cardiac coupling. Importantly, seizures and cardiotoxicity may present in a delayed fashion, up to 24 hours post-ingestion.

Treatment

Management of bupropion overdose starts with assessment of the patient's vitals, neurologic, and cardiovascular status. Administration of activated charcoal may be reasonable if given within one hour to patients with appropriate mental status. An ECG should be obtained, and continuous vital sign monitoring should be performed. There is no specific antidote for bupropion but several supportive measures may be required. First-line treatment of agitation or seizures is with benzodiazepines, though other GABA-A agonists may be used. If a prolonged QRS is present it is reasonable to treat with sodium bicarbonate, however, it is important to note that with bupropion's unique mechanism, this may not be effective. If severe cardiotoxicity is present, intra-lipid emulsion may be considered. Further aggressive medical measures that have been employed in case reports and have included extracorporeal membrane oxygenation (ECMO). Patients should be monitored for at least 8 hours with immediate-release formulations and 24 hours with extended-release formulations. Consultation with a poison center and/or medical toxicologist is recommended in all cases.

Summary

Bupropion is a common medication with frequent dosing errors or overdoses reported to poison centers. As little as one extra dose may place patients at risk

for serious adverse events, primarily seizures. The majority of patients with dosing errors or small overdoses recover well, however, there is potential for severe outcomes or death. Patients that overdose on extended-release formulations require 24-hour monitoring regardless of the presence of symptoms.