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Selected Topics: Toxicology

INTRAVENTRICULAR CONDUCTION DELAY AFTER BUPROPION OVERDOSE

Steven C. Curry, MD,*†‡ John S. Kashani, DO,*† Frank LoVecchio, DO,*† and William Holubek, MD*†

*Department of Medical Toxicology, Banner Good Samaritan Medical Center, Phoenix, Arizona, †Department of Emergency Medicine, Maricopa Medical Center, Phoenix, Arizona, and ‡Department of Medicine, University of Arizona College of Medicine, Phoenix, Arizona

Reprint Address: Steven Curry, MD, Department of Medical Toxicology, Banner Good Samaritan Regional Medical Center, 925 East McDowell Road, Second Floor, Phoenix, AZ 85006

□ **Abstract—Bupropion overdose mainly is characterized by tachycardia, agitation, and seizures. The few reports of QRS complex widening after bupropion overdose that have been published in peer-reviewed literature are notable for failure to have confirmed elevated plasma bupropion concentrations or failure to have excluded other causes of QRS widening. We describe two patients in whom bupropion overdose was confirmed with elevated plasma bupropion concentrations and in whom other cardiotoxic ingestions were excluded with comprehensive analytical toxicology testing. Our findings are in keeping with ex vivo studies in which bupropion antagonizes cardiac voltage-gated sodium channels. Bupropion overdose should be considered in the differential diagnosis of unexpected QRS widening. © 2005 Elsevier Inc.**

□ **Keywords—bupropion; overdose; intraventricular conduction delay; sodium chemicals**

INTRODUCTION

Bupropion is a monocyclic antidepressant that is structurally similar to amphetamine and diethylpropion and is thought to act mainly as an inhibitor of dopamine and norepinephrine uptake (1–3). Symptomatic bupropion overdose is characterized mainly by sinus tachycardia, agitation, and generalized seizures (1,4,5).

Widening of the QRS complex on the electrocardiogram (EKG) has uncommonly been reported after bupropion overdose. With the exception of one meeting abstract (6), no reports associating bupropion overdose with QRS prolongation contain information needed to exclude co-ingestants that may have prolonged QRS duration, or confirmed bupropion toxicity with elevated plasma bupropion concentrations. We report two cases of bupropion overdose with widening of QRS intervals in which plasma levels confirmed bupropion ingestion, and extensive comprehensive urine drug screening excluded other cardiotoxic ingestions. These data are in keeping with an ability of bupropion and metabolites to antagonize cardiac voltage-gated sodium channels at toxic concentrations.

CASE REPORTS

Case 1

A 30-year-old man with a history of a bipolar disorder, but in otherwise good health, stated he ingested a "full prescription bottle" containing bupropion (dose unknown) on the morning of admission. He was not taking other medication. He was found about 2 h later to be awake and alert, but disoriented. He was immediately

Currently, Dr. Holubek works in the Department of Emergency Medicine, Maimonides Medical Center, Brooklyn, New York.

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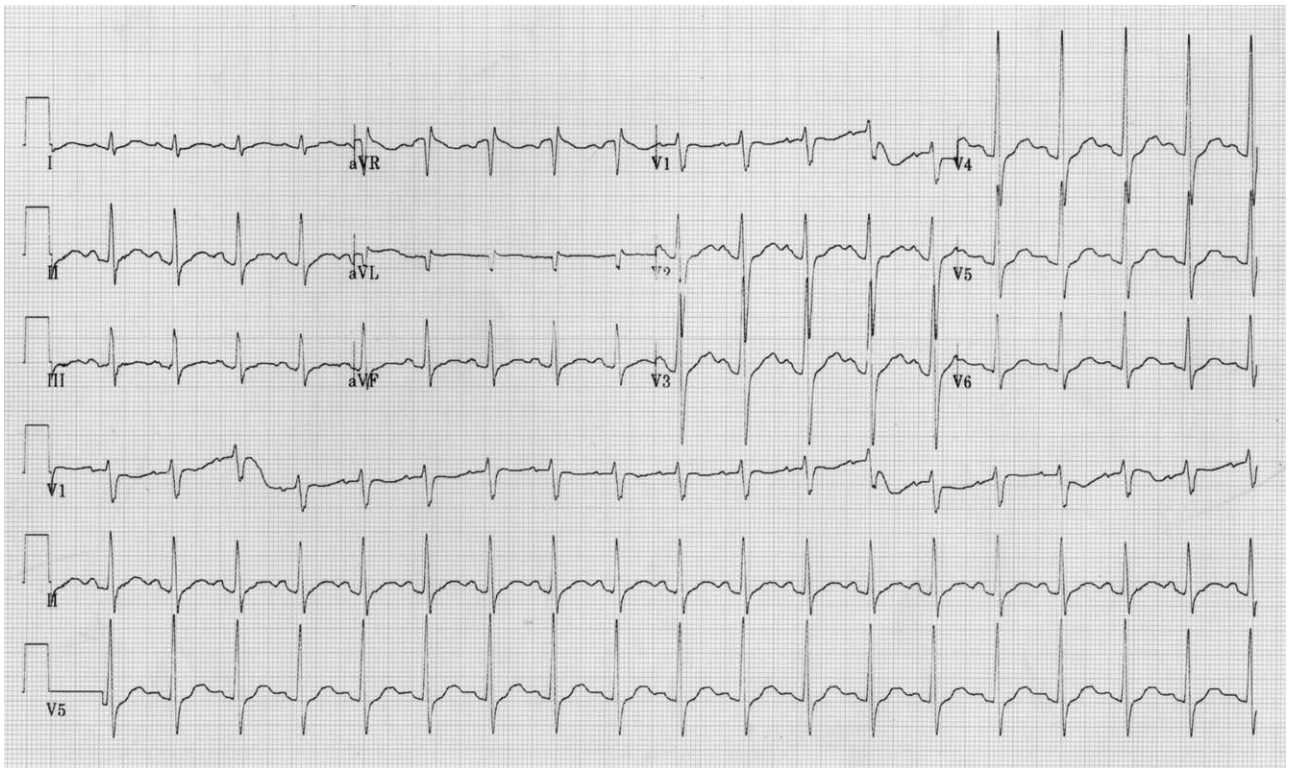

Figure 1. Patient 1: EKG 8.7 h after ingestion of bupropion. QRS interval 120 ms. The QRS interval narrowed to 90 ms by 71 h after ingestion.

taken to an outlying Emergency Department (ED) where he was described as being agitated with a blood pressure of 110/72 mm Hg; heart rate 138 beats per minute, and respirations of 22 per minute. No temperature was taken. A rhythm strip demonstrated sinus tachycardia with a QRS interval of 90 ms. The patient received 1 mg lorazepam i.v. and drank 50 g activated charcoal before being transferred to our facility.

On arrival in the intensive care unit (ICU) at our hospital, the patient was awake and alert, but only oriented to person and city. Vital signs showed heart rate 135 beats per minute, blood pressure 138/80 mm Hg, respiration 15 breaths per minute, and temperature 37.2°C (98.9°F). Pulse oximetry reported 99% saturation. Physical examinations of the head, eyes, ears, nose, throat, abdomen, extremities, skin, and chest were unremarkable. Auscultation of the heart revealed a regular rhythm without murmurs or gallops. Neurological examination demonstrated continuous choreoathetoid movements involving the face, extremities, and trunk. Pupils were mid-position and briskly reactive, and other cranial nerve testing was normal. Deep tendon reflexes were all 2+ and symmetrical. Babinski reflexes were absent, and sensation and motor function were grossly intact. No rigidity, tremor, or spasticity was noted.

Blood and urine specimens were obtained for analysis before we gave any medication. Laboratory studies on serum showed Na 143 mmol/L, K 3.8 mmol/L, Cl 107 mmol/L, CO_2 23 mmol/L, creatinine 0.9 mg/dL, BUN 16 mg/dL, creatine kinase 133 U/L, glucose 149 mg/dL, albumin 4.3 g/dL, calcium 9.4 mg/dL, aspartate aminotransferase (AST) 32 U/L, and alanine aminotransferase (ALT) 16 U/L. Acetaminophen, salicylate, and lithium were undetectable in serum. A complete blood count revealed WBC 10,000/μL, hemoglobin 14.6 g/dL; and platelets 177,000/μL. An EKG taken 8.7 h after ingestion showed sinus tachycardia with QRS duration of 120 ms (Figure 1).

A comprehensive urine drug screen obtained 3 h after ingestion was positive only for bupropion and lorazepam, which was given before transfer. This screen, which comprises immunoassays for common substances of abuse, urine volatiles, thin layer chromatography, and gas chromatography-mass spectrometry, can detect over 1000 drugs, including sodium channel blockers such as antidepressants, group IA and IB antidysrhythmics, phenothiazines, propoxyphene, carbamazepine, lamotrigine, cocaine, local anesthetics, antihistamines, central muscle relaxants, chloroquine, and hydroxychloroquine.

His clinical course was characterized by mild choreoathetosis, agitation, disorientation, hallucinations, and