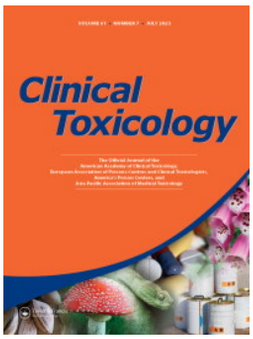

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CLINICAL RESEARCH

Clinical and electrocardiographic factors associated with adverse cardiovascular events in bupropion exposures

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ABSTRACT

Introduction: Bupropion toxicity can cause cardiogenic shock, ventricular dysrhythmias, and death. Clinical and electrocardiographic factors associated with adverse cardiovascular events in bupropion toxicity have not been well-studied. This study aimed to identify factors associated with adverse cardiovascular events in adult patients with isolated bupropion exposures.

Methods: This retrospective cohort study queried the National Poison Data System from 2019 through 2020. We included patients 20 years or older with acute or acute-on-chronic single-agent bupropion exposures evaluated in a healthcare facility. Exclusion criteria were confirmed non-exposure, withdrawal as a reason for exposure, lack of follow-up, documentation that exposure was probably not responsible for the effects, and missing data. The primary outcome was adverse cardiovascular events, defined as the presence of any of the following: vasopressor use, ventricular dysrhythmia, myocardial injury, or cardiac arrest. Independent variables were age, the intentionality of exposure, seizures, tachycardia, QRS widening, and QTc prolongation. Multivariable logistic regression was performed to test for independent associations between independent variables and adverse cardiovascular events.

Results: Of 4,640 patients included in the final analysis (56.7% female, 56.5% suspected suicidal intent), 68 (1.47%) experienced an adverse cardiovascular event. Age (odds ratio 1.03; 95% confidence intervals 1.02–1.05), single seizure (odds ratio 9.18; 95% confidence intervals 4.24–19.9) and complicated seizures (odds ratio 38.9; 95% confidence intervals 19.3–78.1), QRS widening (odds ratio 3.01; 95% confidence intervals 1.62–5.59), and QTc prolongation (odds ratio 1.76; 95% confidence intervals 1.00–3.10) were independently associated with adverse cardiovascular events. No patients with unintentional exposure experienced adverse cardiovascular events, prohibiting intentionality from inclusion in the regression model. In the post hoc subgroup analysis of intentional exposures, age, single and complicated seizures, and QRS widening remained independently associated with adverse cardiovascular events.

Conclusions: Increasing age, seizures, QRS widening, and QTc prolongation were associated with adverse cardiovascular events in bupropion exposures. Adverse cardiovascular events did not occur in unintentional exposures. Further research is needed to develop screening tools and treatments for bupropion cardiotoxicity.

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Bupropion; cardiotoxicity; adverse events; QRS; QTc; seizures; shock; dysrhythmias

Introduction

Bupropion is the antidepressant most frequently involved in fatalities according to data from the National Poison Data System (NPDS), and both exposures and severe outcomes related to bupropion have continued to increase each year since 2012 [1]. Bupropion is pharmacologically distinct among antidepressants due to its chemical properties as a synthetic cathinone and its inhibitory effects on the reuptake of dopamine and norepinephrine. While bupropion overdose is commonly associated with seizures, there are cases of cardiotoxicity described in the literature, manifesting as ventricular dysrhythmias, shock, and death [2–8]. Compared to selective serotonin reuptake inhibitors, bupropion ingestion is more likely to result in vasopressor use, cardiac arrest, and death [9].

Adverse cardiovascular events have been studied in the setting of drug overdose and defined as the presence of any of the following: ventricular dysrhythmias, shock (hypotension requiring vasopressors), myocardial injury/infarction, or cardiac arrest [10]. The incidence of adverse cardiovascular events in drug overdose, in general, is approximately 5.8% [11]. Clinical and electrocardiographic risk factors for adverse

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cardiovascular events have been previously described in the overdose population overall [10,12], but bupropion overdoses represent a unique, high-risk group that has not been well-studied.

We performed a retrospective cohort study using NPDS to identify clinical and electrocardiographic risk factors for adverse cardiovascular events among adults with bupropion exposures. We hypothesized that increased age, the intentionality of exposure, tachycardia, seizures, QRS widening, and QTc prolongation would be associated with adverse cardiovascular events.

Methods

Study design

This is a retrospective cohort study utilizing data from NPDS maintained by America's Poison Centers. National Poison Data System is a national database of de-identified case records entered by trained poison center specialists during clinical care. This database is utilized in public health surveillance and toxicology research [13,14]. This study was found to be exempt from further review by the sponsoring institution's institutional review board.

Study population

We included adult (defined in NPDS as 20 years or older) cases of acute or acute-on-chronic single-agent bupropion exposures evaluated in a healthcare facility from January 1, 2019 to December 31, 2020. This study period was chosen because 2019 was the first year that QRS and QTc interval widening/prolongation were included as distinct clinical effects in NPDS. Bupropion exposures were determined by generic or product codes. Evaluation in a healthcare facility was determined by coding of management site as "Patient already in (en route to) healthcare facility when poison center called" or "Patient was referred by poison center to a healthcare facility," and the level of healthcare facility care documented as "Admitted to critical care unit," "Admitted to noncritical care unit," "Admitted to a psychiatric facility," or "Treated/evaluated and released." We excluded cases with a medical outcome of "Confirmed non-exposure" or reason for exposure as "Withdrawal" from bupropion rather than exposure, cases that were not followed or unable to be followed, and cases with documentation that "The exposure was probably not responsible for the effect(s)." We also excluded cases with missing data on independent variables.

Outcome definition

The primary outcome was the previously described composite outcome of adverse cardiovascular events. Bupropion cardiotoxicity is not well defined, but the authors believed that the components of adverse cardiovascular events could be reasonably interpreted as signs of cardiotoxicity, and using a previously described outcome allowed for comparison to previous studies. Adverse cardiovascular events were defined as the presence of any of the following clinical effects or therapies marked as "Related to the exposure" in NPDS:

1. ventricular dysrhythmia, coded as "V. tachycardia/V. fibrillation" or "Torsade de Pointes;"
2. treatment with vasopressors "Performed" or "Recommended and Performed;"
3. myocardial injury, coded as "Troponin elevation" or;
4. cardiac arrest, coded as "Cardiac Arrest," "Asystole," or "Pulseless Electrical Activity;" or "V. tachycardia/V. fibrillation" in a patient with an outcome of "Death."

Statistical analysis

Clinical characteristics, including demographic information, adverse cardiovascular events, and the individual components of adverse cardiovascular events, were reported with descriptive statistics (medians with interquartile ranges and frequencies with proportions). Missing data were assumed to be missing at random and removed with listwise deletion. National Poison Data System assigns medical outcomes based on the degree of severity of clinical effects of the exposure, including no effect; minor, moderate, or major effects; and death. These outcomes were included as part of demographic data but were not included in further statistical analyses [1].

Based on prior literature and clinical experience, age [10], intentionality [15], tachycardia [4,5], seizures [2,4], QRS widening [4,5,16,17], and QTc prolongation [10,12,18] were chosen *a priori* as candidate risk factors for adverse cardiovascular events.

Intentionality was derived from the coding of the reason for exposure. Misuse/abuse and suspected suicide were considered intentional. Adverse reactions and unintentional exposures were considered unintentional. Malicious exposures were considered intentional. Cases with reason documented "Unknown reason" or "Unknown" were considered unknown intentionality. QRS widening, QTc prolongation, seizures, and tachycardia were considered present if documented as "Related" to exposure. As defined in NPDS coding, QRS widening is a QRS greater than 100 milliseconds, and QTc prolongation is a QTc greater than 430 milliseconds in an adult male or 450 milliseconds in an adult female [1]. Exact QRS and QTc values are not recorded in NPDS. Seizures were categorized into single ("Single seizure" in NPDS) or complicated ("Multiple discrete seizures" or "Status epilepticus").

Univariate analysis was conducted to evaluate the association between the candidate risk factors and adverse cardiovascular events. Chi-squared (or Fisher's exact tests in cases of sparse data) and Mann–Whitney *U* tests were used to test associations for categorical and continuous independent variables, respectively. We then estimated a multivariable logistic regression model with adverse cardiovascular events as the dependent variable and the aforementioned candidate risk factors as the independent variables.

Statistical analysis was performed with R Studio 7.1 (Boston, MA) and Stata 16.0 (College Station, TX). All statistical tests were two-sided, and the alpha was set at < 0.05. Results were reported as frequencies with percentages,

medians with interquartile range, or as odds ratios (OR) with 95% confidence intervals (CI).

Results

Eleven thousand, eight hundred and sixty-eight adult single-agent bupropion exposures were documented during 2019 and 2020. Eleven thousand and nine were acute or acute-on-chronic exposures. Five thousand and ten were evaluated in a healthcare facility. Four patients were excluded for confirmed non-exposure, 245 were excluded due to lack of follow-up, 92 were excluded because the overall clinical effects were judged as unlikely related to exposure, three patients were excluded for withdrawal listed as the reason for exposure, and 26 patients were excluded for missing data on age, the only independent variable with missing data, leaving 4640 patients in the final analysis (Figure 1).

The median patient age was 34 (interquartile range: 26–46) years. Two thousand, six hundred and thirty-one (56.7%) patients were female. Five hundred and twenty (11.2%) patients had a major effect, and 13 (0.28%) died. The most common reason for exposure was suspected suicide (2,620, 56.5%). Additional clinical characteristics are described in Table 1.

Sixty-eight (1.47%) patients experienced an adverse cardiovascular event (Table 2). Sixty-three (1.36%) received vasopressors, eight patients (0.17%) developed ventricular dysrhythmia, 12 patients (0.26%) experienced cardiac arrest, and three (0.06%) developed myocardial injury.

In the univariate analysis, intentionality, tachycardia, single and complicated seizures, QRS widening, and QTc prolongation were all associated with adverse cardiovascular events ($P < 0.001$), while age was not ($P = 0.13$) (Table 3). Intentionality was unable to be included in the multivariable logistic regression model because there were zero occurrences of adverse cardiovascular events in the unintentional group. The following variables were independently associated with adverse cardiovascular events in the model: age (OR 1.03; 95% CI 1.02 – 1.05), single seizures (OR 9.18; 95% CI 4.24 – 19.9), complicated seizures (OR 38.9; 95% CI 19.3 – 78.1), QRS widening (OR 3.01; 95% CI 1.62 – 5.59), and QTc prolongation (OR 1.76; 95% CI 1.00 – 3.10). Tachycardia was not found to be associated with adverse cardiovascular events (Table 4).

We conducted a *post hoc* subgroup analysis of intentional exposures, given the findings above related to intentionality.

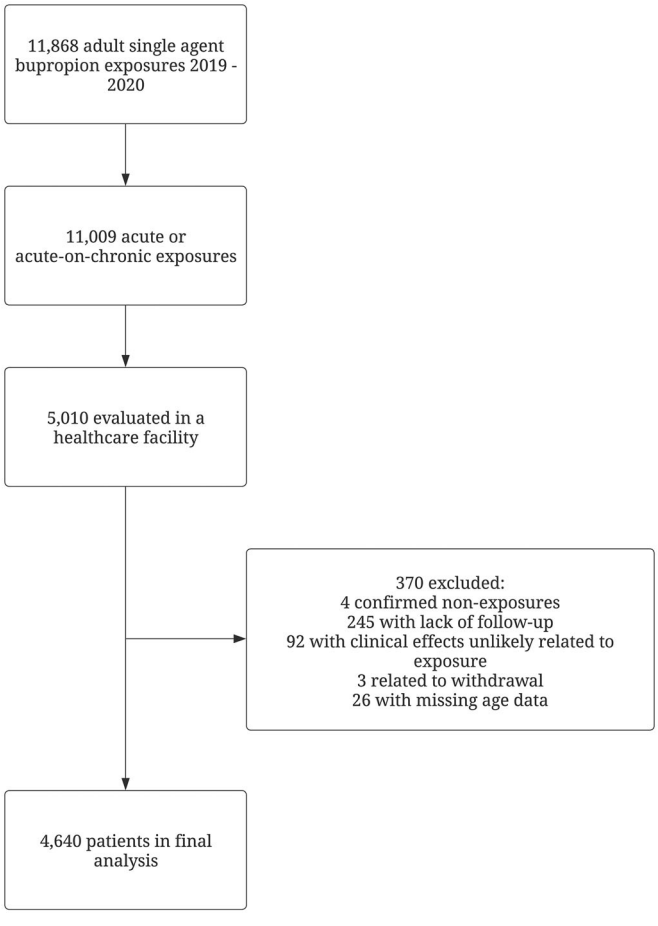

Figure 1. Study inclusion flow chart.

Table 1. Study sample clinical characteristics.

Characteristic	Category	*n*
Age (years), median (IQR)[a]		34 (26–46)
Gender	Female	2631 (56.7%)
	Male	2007 (43.3%)
	Other	2 (0.04%)
Exposure route[b]	Ingestion	4410 (95.0%)
	Nasal inhalation	216 (4.66%)
	Parenteral	34 (0.73%)
	Vaginal	1 (0.02%)
	Unknown	4 (0.09%)
	Other	
Chronicity	Acute	2082 (44.9%)
	Acute-on-chronic	2558 (55.1%)
Intention	Intentional	3293 (71.0%)
	Abuse	344 (7.41%)
	Misuse	222 (4.78%)
	Suspected suicide	2620 (56.5%)
	Intentional, unknown	106 (2.28%)
	Malicious	1 (0.02%)
	Unintentional	1303 (28.1)
	Environmental	2 (0.04)
	General	64 (1.38)
	Misuse	18 (0.39)
	Therapeutic error	1166 (25.1%)
	Adverse reaction	48 (1.03%)
	Unintentional, unknown	5 (0.11%)
	Unknown	44 (0.95%)
Medical Outcome	No effect	870 (18.8%)
	Minor effect	1112 (24.0%)
	Moderate effect	2125 (45.8%)
	Major effect	520 (11.2%)
	Death	13 (0.28%)
Tachycardia	Related	2100 (42.3%)
	Unknown if related	68 (1.47%)
	Not related	7 (0.15%)
Seizures	Any seizure	828 (17.8%)
	Single seizure	539 (11.6%)
	Multiple discrete seizures	274 (5.91%)
	Status epilepticus	15 (0.32%)
QRS widening	Related	230 (4.96%)
	Unknown if related	40 (0.86%)
	Not related	13 (0.28%)
QTc prolongation	Related	539 (11.6%)
	Unknown if related	42 (0.91%)
	Not related	6 (0.13%)

[a]Interquartile range.
[b]Total exposure routes is > 100%, as some patients had multiple routes of exposure.

Table 2. Individual components of adverse cardiovascular events ($n = 68$)[a].

Criteria	*n* (% study sample)	% adverse cardiovascular events
Vasopressor use	63 (1.36%)	93
Ventricular dysrhythmia	8 (0.17%)	12
Ventricular tachycardia/ventricular fibrillation	8 (0.17%)	12
Torsade de pointes	0 (0%)	0
Cardiac arrest	12 (0.26%)	18
Asystole	11 (0.24%)	16
Pulseless electrical activity	6 (0.13%)	9
Ventricular tachycardia/ventricular fibrillation	6 (0.13%)	9
Cardiac arrest, not otherwise specified	0 (0%)	0
Myocardial injury	3 (0.06%)	4

[a]Adverse cardiovascular event criteria are not mutually exclusive, total $N > 68$).

Table 3. Univariate analysis.

Independent variable	No adverse cardiovascular events ($n = 4572$)	Adverse cardiovascular events ($n = 68$)	
	n (%)		*P* value
Age (years), median (IQR)	34 (26–45)	37.5 (26–51)	0.13
Intention			
Intentional	3,226 (70.1)	67 (98.5)	<0.001
Unintentional	1,303 (28.5)	0 (0)	
Unknown	43 (0.9)	1 (1.5)	
Tachycardia	2,055 (44.9)	45 (66.2)	<0.001
Seizures	773 (16.9)	55 (80.9)	<0.001
Single	523 (11.4)	16 (23.5)	
Complicated	250 (5.5)	39 (57.4)	
QRS widening	210 (4.6)	20 (29.4)	<0.001
QTc prolongation	512 (11.2)	27 (39.7)	<0.001

Table 4. Logistic regression model for adverse cardiovascular events.

Main analysis		
Characteristic	Odds ratio	95% Confidence interval
Age (years)	1.03	1.02 – 1.05
Tachycardia	1.11	0.61 – 2.01
Seizures		
Single	9.18	4.24 – 19.9
Complicated	38.9	19.3 – 78.1
QRS widening	3.01	1.62 – 5.59
QTc prolongation	1.76	1.00 – 3.10

Intentional exposures subgroup analysis		
Characteristic	Odds ratio	95% Confidence interval
Age (years)	1.04	1.02 – 1.06
Tachycardia	1.01	0.56 – 1.82
Seizures		
Single	6.41	3.01 – 13.7
Complicated	25.8	13.0 – 50.9
QRS widening	2.9	1.56 – 5.39
QTc prolongation	1.66	0.94 – 2.90

As in the main logistic regression model, age, single and complicated seizures, and QRS widening were independently associated with adverse cardiovascular events but with slightly modified effect sizes compared to the original model (Table 4). QTc prolongation was not independently associated with adverse cardiovascular events in the intentional exposures subgroup.

Four patients were documented as developing ventricular dysrhythmia but not documented as tachycardic. While it is possible these patients developed ventricular fibrillation and never had a documented elevated heart rate, we considered coding error as a possibility. Therefore, we performed a *post hoc* sensitivity analysis re-classifying those four patients as tachycardic for the logistic regression model in the main analysis. Again, tachycardia was not independently associated with adverse cardiovascular events (OR 1.55; 95% CI 0.85 – 2.92) (Supplemental Table 1).

Discussion

Our study identified several independent risk factors for adverse cardiovascular events in bupropion exposures. Adverse cardiovascular events were relatively rare in our sample of single-agent bupropion overdoses (1.47%) compared to 5.8% found in previous studies of drug overdose in general [11]. We attribute this in part to our study design and the limitations of NPDS data—discussed in detail in the "Strengths and limitations" section—rather than a suggestion that bupropion is not as dangerous as previously thought, especially given the 11.2% prevalence of major effects. The contribution of bupropion to adverse cardiovascular events in the setting of poly-exposures should be a focus of future research.

Vasopressor use was more common than ventricular dysrhythmias (63 versus eight cases), suggesting that bupropion cardiotoxicity may induce hypotension independent of ventricular dysrhythmias. This is a novel finding in the literature of bupropion cardiotoxicity, in which existing case reports of ventricular dysrhythmias outnumber those of shock. While hypotension may be multifactorial, previously reported cases involving both hypotension and biventricular systolic failure on echocardiogram implicate a component of cardiogenic shock [7,8]. The exact mechanism remains unknown. Catecholamine depletion may play a role similar to cocaine, which also inhibits dopamine reuptake, or amphetamine, which effluxes catecholamines *via* reverse transport through

plasma membrane transporters [19,20]. Alternatively, there may be a direct myocardial depressant effect related to the inhibition of cardiac gap junctions, similar to that seen in sodium channel blockade [17,21]. Further research should focus on the underlying pathophysiology of bupropion-induced cardiogenic shock to inform treatment strategies.

Increased age was associated with adverse cardiovascular events in our study, although the effect size was modest (OR 1.03 per year increase in age), and no cutoff could safely exclude adverse cardiovascular events, as the youngest patent with cardiac arrest in our sample was 20 years old. In fact, of the 12 cases of cardiac arrest, six were younger than the sample median age of 34 years. This is congruent with prior case reports of adverse cardiovascular events in adolescents [8,22,23] and should alert clinicians to the fact that bupropion cardiotoxicity can lead to cardiovascular collapse even in young patients, who are unlikely to have extensive comorbidities.

No unintentional exposures in this study resulted in adverse cardiovascular events. Cardiotoxicity in pediatric exploratory ingestions has been reported [23,24], but the vast majority of cases have occurred in intentional or presumed intentional ingestions. Our findings support the hypothesis that doses involved in cases of cardiotoxicity are highly unlikely to be attained in unintentional adult exposures.

Although a common manifestation of bupropion toxicity and a predictor of seizures [6,25], tachycardia was not found to be an independent risk factor for adverse cardiovascular events. One-third of patients with adverse cardiovascular events were not documented to be tachycardic; again, this may be related to the depletion of catecholamines or a direct effect of cardiotoxicity. The sensitivity analysis re-classifying all patients with ventricular dysrhythmias to also have tachycardia did not identify an independent association between tachycardia and adverse cardiovascular events, making this finding less likely attributable to coding errors. Although most cases of severe bupropion toxicity feature tachycardia, several published cases have described bupropion cardiotoxicity without pronounced tachycardia [3,5,7]. Clinicians should, therefore, not discount the possibility of cardiotoxicity based solely on the absence of tachycardia.

Seizures were strongly associated with adverse cardiovascular events in both the main analysis and the intentional exposure subgroup. The effect size was much greater in cases of multiple seizures or status epilepticus, but even single seizures were independently associated with adverse cardiovascular events. This retrospective study cannot differentiate whether ongoing or untreated seizures contribute to the development of adverse cardiovascular events or if they are simply a marker of severity, and thus we cannot at this time recommend more aggressive or prophylactic treatment with benzodiazepines than would otherwise be performed. Most prior case reports of cardiotoxicity also feature seizures [2,4,7,8]. Our study demonstrates that patients without seizures are significantly less likely to experience adverse cardiovascular events. Future research should explore the possibility of a causal relationship, but in the meantime, seizures should be treated supportively.

Bupropion is believed to inhibit both cardiac potassium channels and myocardial gap junctions, based on the Caillier et al. [17] study involving guinea pig hearts, although another investigation using human connexin proteins did not find bupropion to be a gap junction uncoupler [26]. QRS widening and QTc prolongation, both described in bupropion toxicity and independently associated with adverse cardiovascular events in our study, are important risk factors, as they can be pharmacologically intervened upon. These interval abnormalities on the electrocardiogram are classically associated with ventricular dysrhythmias [10,21,27–30], but in this cohort, they were associated with adverse cardiovascular events even in the absence of ventricular dysrhythmias, which made up only eight cases of adverse cardiovascular events.

While QTc prolongation was independently associated with adverse cardiovascular events in our study, this finding bordered on statistical significance, and the association disappeared in the intentional exposure subgroup analysis. Given that adverse cardiovascular events only occurred in intentional exposures, QTc seems less likely to be a clinically meaningful predictor of adverse cardiovascular events in bupropion exposure. The diminished association compared to prior literature supports the hypothesis that potassium channel inhibition may not be a major contributor to bupropion cardiotoxicity [10,12,31]. This discrepancy may be due in part to the definition of QTc prolongation in NPDS being lower than prior literature on adverse cardiovascular events that utilized a threshold of 500 milliseconds. Other QT-related measures such as QT dispersion are not recorded in NPDS and were not studied. Whether electrolyte replacement or empiric magnesium sulfate administration affect rates of adverse cardiovascular events cannot be definitively elucidated in this study and requires further research, but these treatments may reduce rates of ventricular dysrhythmia by preventing further predisposition to R on T phenomenon and Torsade de Pointes [32,33].

QRS widening independently predicting adverse cardiovascular events is a novel finding in bupropion cardiotoxicity, with previous conflicting results described in studies on tricyclic antidepressant overdoses and drug overdose in general [10,34–36]. This finding is likely related to the aforementioned unique cardiotoxic properties of bupropion. The optimal treatment of QRS widening in bupropion overdose remains an area of ambiguity. The first-line treatment for xenobiotic-induced QRS widening is hypertonic sodium bicarbonate [37,38], which narrows the QRS, increases the maximum velocity of depolarization, terminates ventricular dysrhythmias, and improves hypotension in sodium channel blockade [21,39]. Whether sodium bicarbonate therapy is effective in bupropion toxicity and gap junction inhibition is not well described. There are case reports of QRS widening and ventricular dysrhythmias that did not respond to hypertonic sodium bicarbonate therapy [5,22,40]. Because hypertonic sodium bicarbonate may worsen QTc prolongation *via* iatrogenic hypokalemia and increase the risk of adverse

cardiovascular events without clear evidence of benefit in bupropion cardiotoxicity, the role of this treatment should be the focus of future studies [41]. Lipid emulsion therapy is another potential treatment in refractory dysrhythmias, critical illness, or cardiac arrest; cases of apparently successful use exist, but larger studies are less encouraging [42,43]. QRS widening is independently associated with adverse cardiovascular events, and therefore finding a safe and effective treatment is of the utmost importance.

Strengths and limitations

Because NPDS data are obtained voluntarily from callers, data collection may be incomplete. For example, there was one death without documented cardiac arrest; whether this discrepancy reflects the withdrawal of care in certain cases versus incomplete data recording is not readily discernible, although this single case is unlikely to affect the study results.

We included only single-agent exposures in order to isolate the effects of bupropion, but this excluded poly-exposures in which bupropion played a meaningful clinical role. Similarly, our definition of adverse cardiovascular events included only clinical characteristics documented as "Related" and did not include deaths without recorded cardiac arrest. The aforementioned design features likely contributed to the lower-than-expected prevalence of adverse cardiovascular events. Our definition of clinical characteristics as present only if marked "Related" strengthens the associations found in this study by excluding ambiguous outcomes that the treating team and/or documenting specialist did not feel were clearly related to bupropion exposure.

Due to the nature of NPDS data, few, if any, exposures are confirmed with serum drug testing, and thus it is possible that patients in this cohort were not truly exposed to bupropion, were exposed to other xenobiotics, or were exposed by routes other than the documented exposure routes. However, this reflects the reality of clinical practice in most settings, where confirmatory toxicological testing cannot be obtained in a clinically meaningful time period, and decisions are made based on available history and clinical information.

The patients in our study were evaluated in a healthcare facility, and the findings may not be generalizable to other settings. This study is also limited by its retrospective nature and can only identify associations, not causation. Several of the independent risk factors identified are potentially modifiable, but it is not known whether modifying these would reduce the risk of adverse cardiovascular events or if they are simply markers of the overall severity of exposure.

Conclusions

Adverse cardiovascular events were uncommon in this retrospective cohort study of adult isolated bupropion exposures. While previous case reports of cardiotoxicity have focused on ventricular dysrhythmias and cardiac conduction abnormalities, the prevalence of shock was nearly eight times greater than that of ventricular dysrhythmias. Patients of older age and those exhibiting seizures, QRS widening, or QTc prolongation are at greater risk for adverse cardiovascular events. In contrast to seizures, adverse cardiovascular events were not reported in any unintentional adult exposures. Further research is needed to develop appropriate screening tools and treatments for bupropion cardiotoxicity.

Disclosure statements

Michele Burns is the Pediatric Toxicology Section Editor at UpToDate. The remaining authors have no competing interests to declare.

National Poison Data System data do not reflect the entire universe of exposures to a particular substance as additional exposures may go unreported to the poison center; accordingly, National Poison Data System data should not be construed to represent the complete incidence of United States exposures to any substance(s). Exposures do not necessarily represent a poisoning or overdose and America's Poison Centers is not able to completely verify the accuracy of every report. Findings based on National Poison Data System do not necessarily reflect the opinions of America's Poison Centers".

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