Cardiotoxicity following bupropion overdose

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Authors' objectives
To determine whether an overdose of bupropion has been associated with cardiotoxicity.

Searching
MEDLINE (from 1966 to January 2002), EMBASE (from 1980 to January 2002), Current Contents (January 2002) and PubMed (January 2002) were searched. The keywords used in the search included 'bupropion', 'overdose (drug)', 'intoxication', 'poisoning' and 'acute ingestion'. The reference lists from identified studies and reviews were also examined. Only studies published in the English language were included.

Study selection
Study designs of evaluations included in the review
Studies of any design were eligible for inclusion. The included studies were retrospective case series (cases reported to six U.S. poison centres between 1989 and 1991) and case reports.

Specific interventions included in the review
Studies of bupropion overdose were eligible for inclusion. The included studies were of bupropion ingestion, either alone or in combination with other drugs such as acetaminophen, aspirin, caffeine, cannabinoids, amphetamines, paroxetine, possibly lithium, carbamazepine, thioridazine, diphenhydramine, possibly benzodiazepine, fluoxetine, flurazepam and ethanol.

Participants included in the review
Studies of adults or children who had taken an overdose were eligible for inclusion.

Outcomes assessed in the review
Studies that assessed toxicity were eligible for inclusion. The review reported cardiotoxicity, hypotension and other symptoms experienced by the patients.

How were decisions on the relevance of primary studies made?
Both authors independently scanned titles and abstracts according to the inclusion criteria.

Assessment of study quality
Validity was not formally assessed. The authors commented upon the potential for bias inherent in retrospective studies.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction. The tabulated information included the following: age and gender of the patient; amount of bupropion ingested; drugs that were ingested at the same time; time of arrival in the emergency department relative to ingestion; symptoms; treatment; and outcome. Unpublished data were not included.

Methods of synthesis
How were the studies combined?
The results from the case series and the case reports were described separately in a narrative synthesis. The percentage of patients in the case series was reported for patients ingesting bupropion alone and for those ingesting multiple drugs.

How were differences between studies investigated?
The authors do not state how differences between the studies were investigated.

**Results of the review**

One case series (102 patients) and 14 case reports (total of 14 patients) were included.

Overall, sinus tachycardia occurred in 40% of the cases.

Case series (102 cases).

Nineteen reports lacked adequate information and these cases were excluded. No deaths were reported.

The 58 patients ingesting bupropion alone were aged from 2 to 66 years. The mean toxic ingestion was 2.3 g bupropion. All 58 patients had an electrocardiogram (ECG) performed. Sinus tachycardia was found in 43%; no other arrhythmias or conduction defects were found. No patients developed hypotension.

Twenty-five patients ingested bupropion plus other drugs. The amount of bupropion ingested was not stated in the reports. The nine patients who ingested bupropion plus benzodiazepine were aged 30 to 62 years. All nine patients had an ECG performed. Three patients (33%) had sinus tachycardia and one patient developed hypotension; no other cardiac arrhythmias or conduction defects were reported.

Case reports (14 patients).

In 11 cases, no cardiotoxicity was reported. In three cases conduction defects, including a widened QRS interval and/or a prolonged QT interval, were reported. In two of these cases, bupropion was ingested in combination with other drugs (cannabinoids plus possibly amphetamines in one case and paroxetine in the second case). The ECG abnormalities resolved without any specific intervention.

**Authors' conclusions**

All patients who have taken a bupropion overdose should have an ECG on admission and should be monitored for conduction delays and/or cardiac arrhythmias.

**CRD commentary**

The review question was clear in terms of the participants, intervention and outcome. Several relevant databases were searched, the key terms used in the search were reported, and two authors selected the included studies. Limiting the search to English language publications may have resulted in the omission of other relevant studies; this raises, as the authors acknowledged, the possibility of publication bias. Validity was not formally assessed, but the authors did comment on the potential bias inherent in retrospective studies. No details were given of the methods used to extract the data, thus the adequacy of the methods used to reduce bias and errors cannot be judged.

A narrative review was appropriate given the small number of identified studies of case series or case report design. Some of the limitations of the review, including the small number of studies and the design of the identified studies, were discussed. Given the small number of cases included in the case series and case reports, and the limitations of such evidence, it does not seem possible to determine the incidence of cardiotoxicity resulting from bupropion overdose. The authors' conclusion that all patients should be monitored is supported by the evidence.

**Implications of the review for practice and research**

Practice: The authors state that all patients who have taken a bupropion overdose should have an ECG on admission and should be monitored for conduction delays and/or cardiac arrhythmias.

Research: The authors did not state any implications for further research.
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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.