

Prophylactic Benzodiazepine Use in Bupropion Overdose

Seth Carroll^{1,2}, Raman Kaur^{1,2}, Rachel Pina^{1,2}, Elizabeth Grossart², Christopher Edwards¹, Steven Dudley^{1,2}

¹ University of Arizona College of Pharmacy, ² Arizona Poison & Drug Information Center



Pharmacy



BACKGROUND

- Bupropion is a norepinephrine/dopamine reuptake inhibitor (NDRI) commonly prescribed for depression, bipolar, and anxiety disorder.¹
- Patients taking bupropion are at an increased risk for suicidal ideation and often utilize their own medications to overdose.
- Seizures occur in up to 37% of bupropion overdoses.²
- Benzodiazepines are an effective treatment to manage seizures and considered first-line treatment for the management of drug-induced seizures.³
- Seizures can progress to status epilepticus and are associated with a variety of complications including respiratory changes, physical injuries, psychiatric disorders, cognitive impairment, sleep disorders and even death.
- Benzodiazepines are suspected to work for this indication because of their effects at GABA receptors enhancing GABA-mediated synaptic inhibition. This leads to an increase in chloride through the ion channels, resulting in central nervous system depression. Therefore, administering benzodiazepines prophylactically should prevent seizure onset.

OBJECTIVE

This study aims to determine if prophylactic benzodiazepine administration prevents seizures in bupropion overdoses.

METHODS

Study Design

This retrospective observational study was approved by the University of Arizona Institution Review Board and included Arizona Poison and Drug Information Center (AZPDIC) cases from May 1, 2017, to April 30, 2022.

Data Collection

Data was initially collected when a call was made to AZPDIC by a person or healthcare provider. ToxSentry Query Builder was used to extract the cases that fit the inclusion criteria. Cases were reviewed by the authors to determine eligibility and collect data.

Data Analysis

Statistics were performed using an unpaired t-test in GraphPad Prism version 9.5.0.

RESULTS

Figure 1: Patients Included

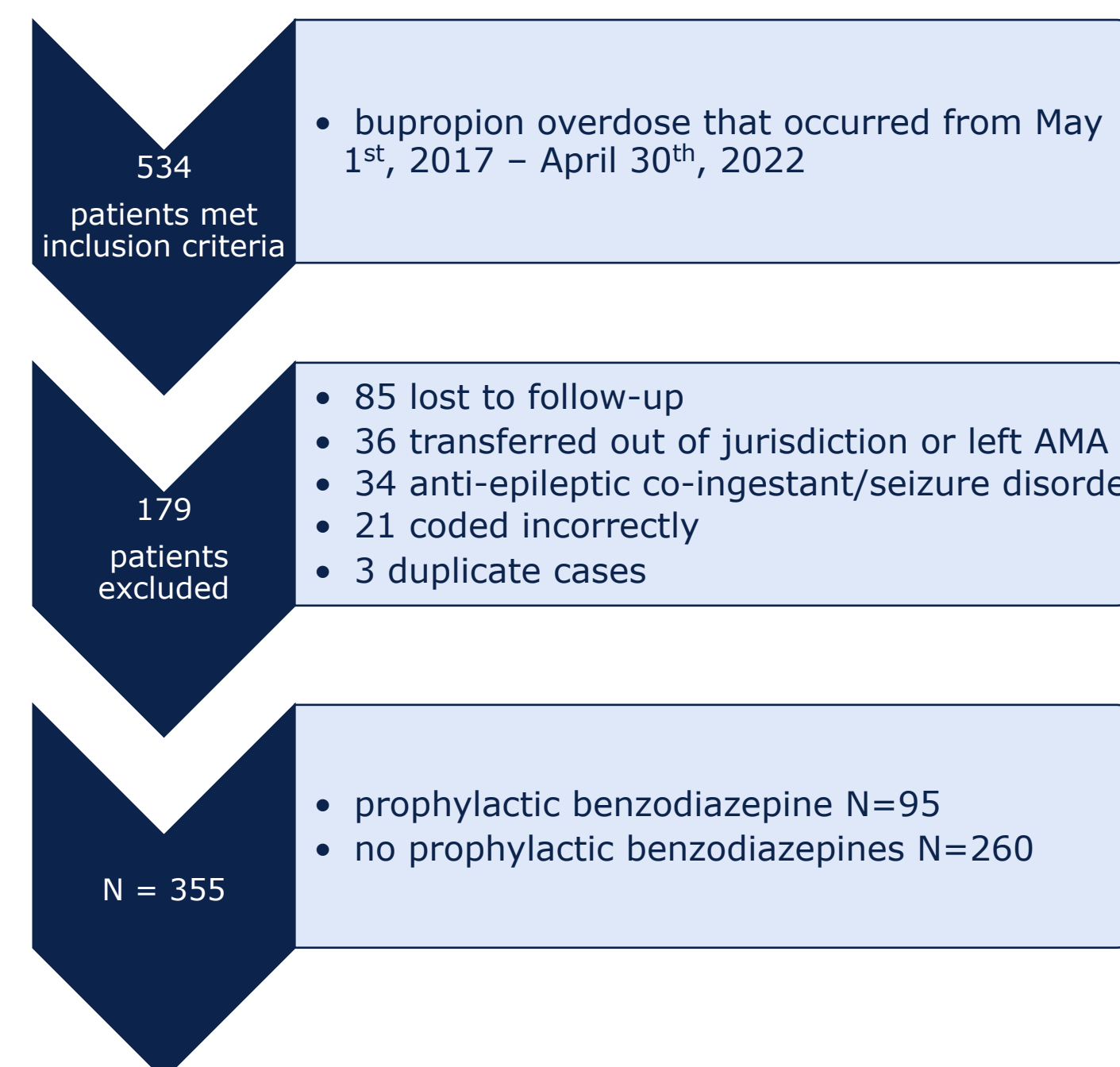
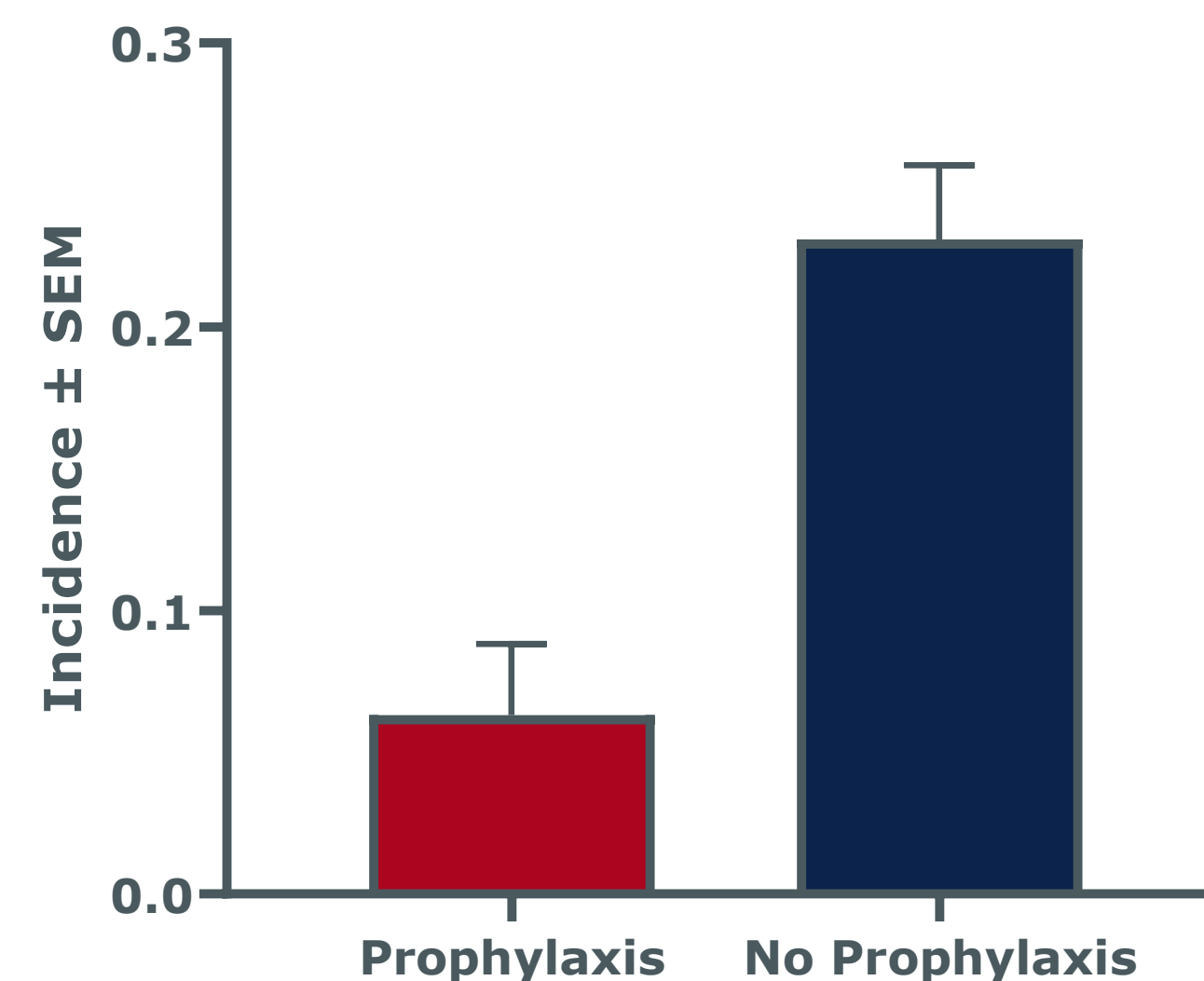


Figure 2: Seizure Incidence



Seizures occurred in 6.3% of the patients that received prophylactic benzodiazepines compared to 23.0% of patients that did not receive prophylactic benzodiazepines, resulting in a risk reduction of $16.8 \pm 4.6\%$ ($p=0.0003$) [95% CI 0.07731 to 0.2579].

DISCUSSION

Prevention of seizures in bupropion overdose may prevent complications leading to increased morbidity.

The results of the study suggest that the use of benzodiazepines prophylactically in patients who overdose on bupropion is effective in reducing the incidence of seizures. This is indicated by the significantly lower seizure rate in the benzodiazepine prophylaxis group (6.3%) compared to the no prophylaxis group (23%) representing a risk reduction of $16.8 \pm 4.6\%$.

In contrast to previous studies, this study evaluates prophylactic administration of benzodiazepines in bupropion overdose and the effect on seizure incidence. The administration of the benzodiazepines were for other symptoms of bupropion overdose (tachycardia, tremor, restlessness, anxiety, agitation) which resulted in a decreased incidence of seizures. These effects were isolated by excluding patients with a past medical history of seizure disorder or co-ingestions of antiepileptic medications.

Prospective studies should be considered to confirm the findings of this study. The study does have limitations, including possible inaccuracies to the chart as the information was initially collected telephonically.

CONCLUSION

In conclusion, the results of this study support the usage of prophylactic benzodiazepines to prevent seizures in patients who are suspected to have overdosed on bupropion.

REFERENCES

- IBM Watson Health. Bupropion hydrochloride: Adverse effects & FDA Uses. IBM Micromedex Drugdex [Electronic version]. Retrieved January 27, 2022, from <https://www.micromedexsolutions.com/>
- Offerman S, Gosen J, Thomas S. H., Padilla-Jones A., Ruha A.M., & Levine M. Bupropion associated seizures following acute overdose: who develops late seizures. *Clinical Toxicology*. 2020; 58(12): 1306–1312. <https://doi.org/10.1080/15563650.2020.1742919>
- Chen, H. Y., Albertson, T. E., & Olson, K. R. Treatment of drug-induced seizures. *British Journal of Clinical Pharmacology*. 2016; 81(3): 412–419. <https://doi.org/10.1111/bcp.12720>

LOGISTICAL INFORMATION

- For questions regarding this project please contact Seth Carroll at SethCarroll@arizona.edu
- IRB approval was received on 9/6/2022 with a study ID of STUDY00001803