Destruction by Designer Benzodiazepines: A Case Report

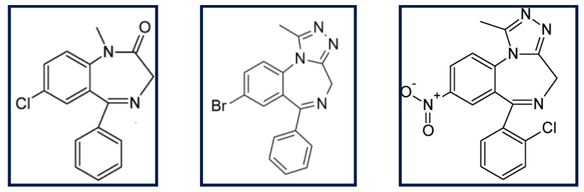
HCA Florida Brandon Hospital

Sumyyah Yousufi, DO, MBA & Abbas Sina, MD (No disclosures)
HCA Florida Brandon Hospital, Addiction Medicine, Brandon, FL

INTRODUCTION

Designer Benzodiazepines (DBZD) are substances that possess the same core structure as FDA-approved Benzodiazepines (BZD), but have alterations made to functional groups yielding an entirely new BZD that is not licensed for therapeutic use.

Figure 1: Examples of functional group alterations in DBZD



Traditional BZD Bromazolam Clonazolam

Widely available for purchase online labeled as "research chemicals"
DBZD specific pharmacological properties and their use related risks are not well studied or understood.

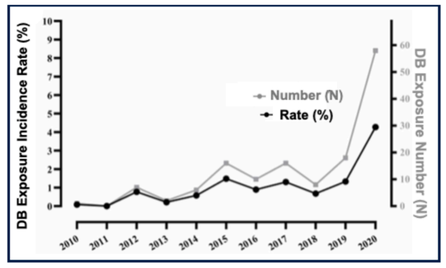
CASE REPORT

A 41 year-old male presented to a treatment center for DBZD dependence and withdrawal leading to multiple hospitalizations for severe withdrawals and five separate admissions that are outlined below with respective treatment approach and discharge plan.

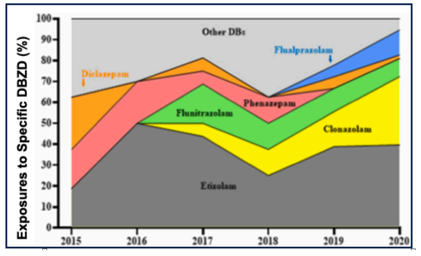
- **First admission:** Clonazepam taper initiated upon entering treatment. He was ultimately discharged to a sober living with Levetiracetam, and 3mg Clonazepam with plan to continue an outpatient taper with his psychiatrist.
- **Second Admission**: Returned to using 8 mg of Clonazolam. Unable to tolerate taper due to debilitating anxiety, as a result, he was maintained on 2mg daily of Clonazepam until discharge to a sober living.
- **Third Admission**: returned to use but now using 12 mg Clonazolam. He subsequently developed hallucinations, warranting hospital admission. Treatment entailed tapering off of all BZD prior to discharge to sober living.
- **Fourth Admission**: returned to use but due to Clonazepam shortage, began using Bromazolam. The patient was started on Clonazepam. After extensive discussion, decision was made to once again trial an outpatient taper with Clonazepam.
- **Fifth Admission**: Overdosed on Bromazolam. He remains in treatment at this time. Due to multiple relapses in a short time period, the possibility of long term supervised treatment was discussed but not finalized.

DISCUSSION

- Modifications are made to the core structure of the benzodiazepine, yielding an entirely new BZD that is not covered by the national legislation and thus allows suppliers to market the drug without any legal sanctions or penalties.
- Initial studies suggest DBZD characteristically have higher potencies and shorter half-lives, resulting in more severe withdrawal symptoms. [1] In turn, making the treatment of DBZD withdrawal more difficult.
- Between January 2014 and December 2017, yearly single exposures increased by 330%, from 26 in 2014 to 112 in 2017.[1]
- Clonazolam possess a shorter half life, but is almost 10 fold more potent than 1 mg of Lorazepam.[5]
- In the US between 2020 and October 2022, Bromazolam was detected in over 250 toxicology cases, 236 post-mortem, and 14 cases of driving impairment.
- Rates of use have increased, in the U.S. as well as Europe, as illustrated in Graph 1 and 2.



Graph 1: Incidence rate and number of DBZDs exposures reported to Dutch Poisons Information Center (DPIC) from 2010-2020



Graph 2: Exposures to to the most prevalent DBZD's reported to the DPIC between 2015 and 2020

- Major challenges regarding diagnosing and treating DBZD use include:
  - The limited information on the pharmacology and toxicity of these substances, variations in the dosage, onset and duration of effects, and the concomitant use of these substances with other drugs can result in unpredictable risks to patients.
  - Thus making treatment difficult.
- Standard urine drug screens do not detect DBZD or the metabolites of DBZD

DISCUSSION

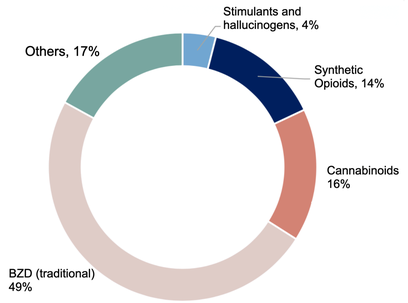


Figure 2: Various classes of designer drugs and their association with fatalities between 2020-2021

CONCLUSION

- Clinicians should understand there is a substantial amount yet to discover about DBZDs.
- Public health interventions should be aimed at decreasing DBZD availability, increasing awareness of the dangers associated with DBZD use.
- Further research regarding pharmacology and analytical development is vital for exploring pharmaceutical therapies as well as more efficient and timely diagnosis and treatment.

REFERENCES

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Graph 1 & 2, https://doi.org/10.1016/j.drugalcdep.2021.109244 Figure 2: https://www.unodc.org/documents/scientific/NPS_threats_IV_web.pdf