

Alprazolam problems: A prolonged withdrawal delirium in an older woman with chronic benzodiazepine use

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Background

- Age-related changes in the body affect the sensitivity to and metabolism of benzodiazepines (BZD) in an unpredictable manner.
- We present a case of an older adult with long-term alprazolam use and subsequent complicated withdrawal.

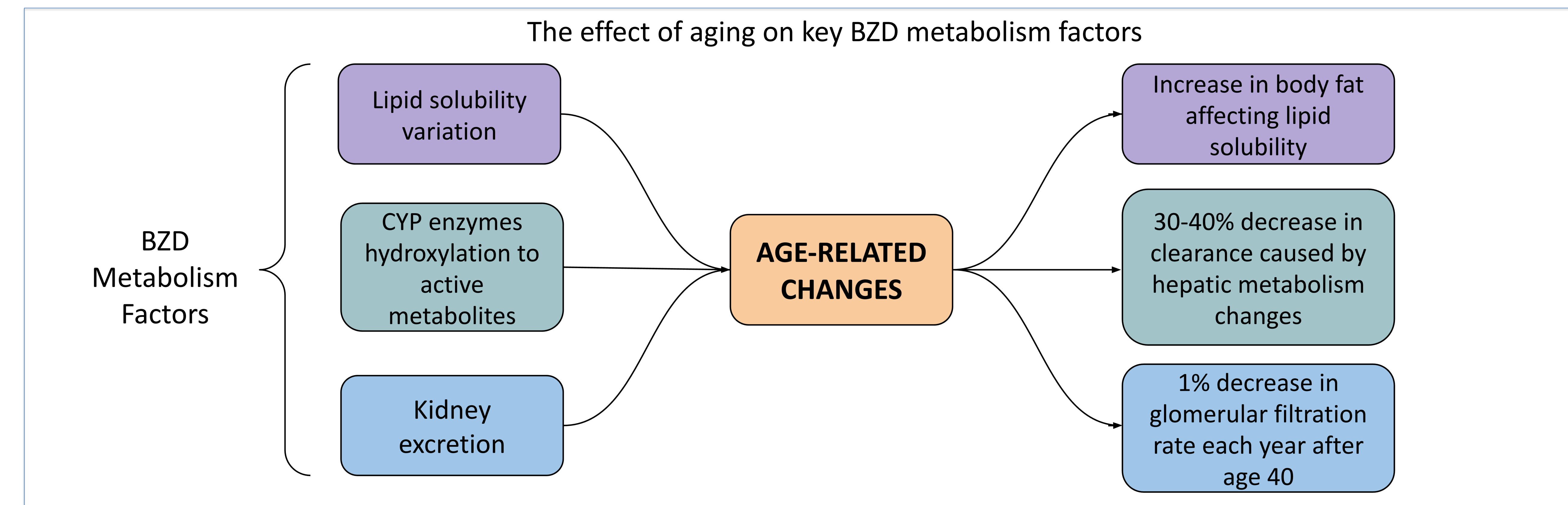
Case

- A 72-year-old female with a medical history of hypertension, metastatic lung cancer, and a reported past psychiatric history of “anxiety and bipolar disorder” managed for several years on alprazolam 1mg twice daily presented to the emergency department (ED) after a physical altercation with her grandson resulting in a facial hematoma.
- ED workup was significant only for elevated AST and ALT, and the patient was admitted to medicine for safe discharge planning.
- On hospital day 3, the patient was found to be increasingly confused, agitated, and showing signs of hyperactive delirium, complicated by possible dementia at baseline.
- Collateral information revealed the patient was admitted to an outside hospital 2 weeks prior following an intentional alprazolam overdose and was now without alprazolam for at least 1 week.
- Her delirium symptoms improved with only low dose chlordiazepoxide (5-10 mg) once daily over 3 days.
- Given the collateral and her response to chlordiazepoxide, her delirium was attributed to prolonged benzodiazepine withdrawal.

Discussion

- In the United States, more than 10% of women and 6% of men aged 65 to 80 years filled at least one BZD prescription in a 1-year period, with nearly one-third of patients receiving BZDs for longer than 120 days in a year.
- Because cessation of chronic use of short-acting BZDs would be expected to precipitate withdrawal in as early as 24-48 hours, it is likely that age-related metabolic factors (see figure) likely played a role in this patient’s presentation.
- Age-related metabolic factors can cause unpredictable changes to the volume of distribution, half-life, and elimination of BZD medications.
- Taper recommended for individuals taking BZDs >3 weeks.
- Recommended taper schedule for older adults: 25% reduction every 2 weeks, followed by 12.5% reduction every 2 weeks.

| Benzodiazepine | Half Life (hours) | CYP | Metabolism Mechanism | Elimination |
|----------------------------|-------------------|-----------------|--------------------------------|-------------|
| Chlordiazepoxide (Librium) | 5-30 | CYP3A4 | Hydroxylation, glucuronidation | Renal |
| Diazepam (Valium) | 30-100 | CYP3A4, CYP2C19 | Hydroxylation, glucuronidation | Renal |
| Alprazolam (Xanax) | 6.3-26.9 | CYP3A4, CYP3A5 | Hydroxylation, glucuronidation | Renal |
| Clonazepam (Klonopin) | 18-50 | none | Acetylation, glucuronidation | Renal |
| Lorazepam (Ativan) | 10-20 | none | Glucuronidation | Renal |



Conclusion

- This case illustrates that the adage “start low, go slow” pertains to not only medication titration but also medication cessation and withdrawal syndrome management.
- When managing benzodiazepine withdrawal in the elderly, age-related pharmacokinetic changes and medical comorbidities must all be considered by the CL psychiatrist in order to avoid adverse outcomes.

References

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