Clinical Characteristics of Tetrabenazine-Induced Parkinsonism

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CONCLUSIONS

In this cohort, TBZ was used to treat a variety of hyperkinetic movement disorders.

DIP occurred in 27.9% of the group (n=17) – though this is not a true prevalence estimate based on the study methods

We intended to include only patients whose active treatment status was known rather than assuming lack of onset of DIP since last known follow-up, or assuming TBZ dose.

TBZ-induced parkinsonism was most common in patients with tardive dyskinesia, though this was not statistically significant (p=0.249, Fisher’s exact test).

Likely due to small sample size

Age at onset of DIP or onset of TBZ therapy did not differentiate those with DIP from those without DIP.

Mean dosage of TBZ and duration of therapy at the onset of DIP also was not significantly different in DIP vs. non-DIP groups.

Latency to onset of DIP ranged from 1-216 months of TBZ therapy, but on average occurred 50 months after TBZ therapy was begun

DIP may occur earlier in the course of TBZ therapy in the TD group (3 of 9 cases had onset within first 6 months of therapy, whereas onset was 10mos or later in other diseases).

Based on factors analyzed in this study, predictors of TBZ are unclear; individual factors (such as pharmacogenomics) may therefore also be relevant

Clinicians should maintain a high index of suspicion of DIP in individuals treated with TBZ, regardless of disease state, throughout therapy, and throughout the dosing range.

Bradykinesia and gait changes are the most common initial manifestations of DIP, followed by rigidity and tremor.

DaTscans can be useful in differentiating DIP from those who have co-existing idiopathic PD or other neurodegenerative parkinsonisms.

In this cohort, levodopa was most commonly used for management of DIP, and less commonly amantadine and dopamine agonists. Three responded to decrease in TBZ dose alone.

Patients responded well to all management options fairly equally with improvement and/or stability in parkinsonian symptoms, with most described as having “mild” symptoms by clinician.

Limitations of this study include:

Retrospective analysis

Non-uniform description parkinsonism features

Dificulty ascertaining whether parkinsonism in an HD patient is related to disease manifestations or DIP

Small sample size

CYP2D6 metabolizer status unavailable on all subjects

Prospective, long-term data regarding parkinsonism in patients treated with TBZ are needed.

REFERENCES


METHODS

Retrospective chart review of cross-sectional population of tertiary Movement Disorders center

Inclusion criteria:

Treated with TBZ over 1 month with follow up within past year

Development of parkinsonism (tremor, rigidity, bradykinesia or postural instability) attributable to TBZ use

Exclusion criteria:

Medication noncompliance

Lost to follow up for over a year or deceased

Unknown TBZ start date

By chart review, we collected indication for TBA, total duration of TBZ treatment, presence of DIP and date of diagnosis, latency to onset of DIP. TBZ dose at time of diagnosis and at last follow-up, symptoms of DIP, treatment of DIP and response, and any DaTscans results.

Information was extracted to a database for analysis. Statistical methods included 2-tailed Fisher’s exact test to compare incidence of DIP across disease states, ANOVA to compare mean duration of DIP, TBZ dose at time of diagnosis and at last follow-up, symptoms of DIP, treatment of DIP and response, and any DaTscans results.

RESULTS

In this cohort, TBZ was used to treat a variety of hyperkinetic movement disorders.

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