

Valbenazine Treatment of Tardive Dyskinesia in Patients with Intellectual Disability: A Case Series

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INTRODUCTION

- Intellectual disability (ID) is characterized by cognitive and adaptive impairments that often present with comorbid medical, psychiatric, or behavioral conditions¹
- To manage psychiatric conditions, patients with ID are frequently treated with antipsychotics; additionally, many patients with ID may be treated with antipsychotics even in the absence of a comorbid psychiatric disorder (e.g., for the treatment of ID-associated challenging behaviors)^{2,3}
- All patients exposed to antipsychotics are at risk for developing tardive dyskinesia (TD), a persistent movement disorder that can affect the face, mouth, trunk, limbs, and/or extremities⁴
- Valbenazine is a novel and highly selective vesicular monoamine transporter 2 (VMAT2) inhibitor approved for the treatment of TD in adults⁵
- Patients with both ID and TD represent a unique patient population; the objective of the current study was to describe the clinical characteristics and treatment outcomes of ID patients who received once-daily valbenazine for TD

METHODS

- A retrospective chart review was conducted of patients with mild-to-severe ID who received valbenazine for the treatment of TD

RESULTS

- Four representative cases are presented, focusing on clinical history (**Table 1**), as well as TD symptoms and TD-related functional impairment before and after valbenazine initiation (**Table 2**)
- The four patients are illustrative of at least 15 recent cases seen at this facility with similar results

CASE 1

- 31-year-old, nonverbal, wheelchair-bound male with severe ID was diagnosed with TD in January 2018 and initiated on valbenazine (once-daily 40 mg for one week, then escalated to once-daily 80 mg) (**Table 1**)
 - Patient history of multiple significant comorbid diagnoses, including attention-deficit/hyperactivity disorder and depression
 - Suspected prior exposure to antipsychotics (type unknown)
 - TD symptom duration unknown
- TD symptoms/TD-related functional impairment before valbenazine treatment included the following (**Table 2**):
 - Prominent tongue protrusion that led to difficulty swallowing/eating and multiple episodes of aspiration pneumonia
- After 3 months of valbenazine treatment, the following relevant improvements were noted:
 - Minimal tongue protrusions
 - Improved swallowing/eating; no new episodes of aspiration pneumonia
 - Increased eye contact and interaction with caregivers
 - Exact onset/timing of symptom improvement unknown
- Patient had sustained TD improvement with no reported adverse events on once-daily 80 mg valbenazine until August 2018, when he was discontinued due to lack of insurance and experienced a return of TD symptoms

CASE 2

- 59-year-old female with moderate ID was diagnosed with TD in April 2018 and initiated on valbenazine (started and maintained on once-daily 40 mg)
 - Patient history of multiple significant comorbid diagnoses, including anxiety, atypical psychosis, bipolar disorder, depression, impulse control disorder, and intermittent explosive disorder (**Table 1**)
 - Previous exposure to multiple antipsychotics, including haloperidol, olanzapine, quetiapine, and risperidone
 - TD symptom duration unknown
- TD symptoms/TD-related functional impairment before valbenazine treatment included the following (**Table 2**):
 - Facial grimacing and tongue protrusion that led to difficulty swallowing, eating, and speaking
 - Constant bilateral hand movements; repetitive bilateral foot tapping
 - Unable to ambulate independently
- After 2 weeks of valbenazine treatment, the following relevant improvements were noted:
 - Minimal facial grimacing and minimal tongue protrusion, leading to improved swallowing/eating and clearer speech
 - Hand movements absent; decreased bilateral foot tapping
 - Improved ambulation
 - Increased eye contact and interaction with caregivers; more cooperative with caregivers
 - Exact onset/timing of symptom improvement unknown
- Patient currently remains on once-daily 40 mg valbenazine with no reported adverse events

CASE 3

- 63-year-old female with mild ID was diagnosed with TD in June 2017 and initiated on valbenazine (once-daily 40 mg for one week, then escalated to once-daily 80 mg) (**Table 1**)
- Patient history of multiple significant comorbid diagnoses, including schizoaffective disorder, bipolar type
 - Known prior long-term exposure to antipsychotics (type unknown)
 - TD symptom duration of at least 4 years
- TD symptoms/TD-related functional impairment before valbenazine treatment included the following (**Table 2**):
 - Prominent tongue protrusion, lip smacking, and chewing movements of the jaw that led to difficulty speaking
 - Constant bilateral arm/hand/finger movements
 - Instability during ambulation; some wheelchair assistance required
- After 2 months of valbenazine treatment, the following relevant improvements were noted:
 - Minimal tongue protrusions and very minimal lip and jaw movements; clearer speech
 - Minimal arm/hand/finger movements
 - Improved stability during ambulation; wheelchair no longer needed, and less assistance required for some activities of daily living (ADLs) (e.g., personal hygiene, putting on makeup)
 - Increased social interaction and involvement in activities outside the home
 - Exact onset/timing of symptom improvement unknown
- Patient currently remains on once-daily 80 mg valbenazine with no reported adverse events

CASE 4

- 28-year-old male with moderate ID and TD (date of TD diagnosis unknown) was initiated in February 2018 on valbenazine (once-daily 40 mg for one week, then escalated to once-daily 80 mg) (**Table 1**)
- Patient history of multiple significant comorbid diagnoses, including autism spectrum disorder, excoriation disorder, and schizoaffective disorder, bipolar type
 - Previous exposure to quetiapine
 - TD symptom duration unknown
- TD symptoms/TD-related functional impairment before valbenazine treatment included the following (**Table 2**):
 - Intermittent chewing movement of jaw
 - Constant bilateral hand/arm movements (e.g., opening and closing of hands/fingers; finger tapping)
 - Repetitive bilateral foot tapping
 - Truncal rocking
- After 2 months of valbenazine treatment, the following relevant improvements were noted:
 - No abnormal jaw movements
 - Minimal to no arm/hand/finger movements or foot tapping; no truncal movements
 - Care staff can take him out in the community; less resistant to caregiver assistance with ADLs
 - Increased participation in activities
- Patient currently remains on once-daily 80 mg valbenazine with no reported adverse events

Table 1. Summary of ID Patients Treated with Valbenazine for TD

	ID Severity	Significant Comorbid Diagnoses	Medications ^a	
			Antipsychotic	Other
CASE 1 (M, 31 yr)	Severe cognitive and physical impairment; nonverbal, wheelchair-bound, caregiver-dependent for ADLs	Psychiatric: ADHD, depression Other: Asthma, cerebral palsy, furunculosis, hypersensitivity, osteoporosis	Prior: Suspected prior exposure (type NA) Current: None	Prior: Citalopram, clonazepam Current: Citalopram, clonazepam, valbenazine
CASE 2 (F, 59 yr)	Moderate cognitive impairment; caregiver-dependent for most ADLs	Psychiatric: Anxiety, atypical psychosis, bipolar disorder, depression, impulse control disorder, intermittent explosive disorder Other: GERD, hyperlipidemia, hypothyroidism, polycythemia vera, tachycardia	Prior: Haloperidol, olanzapine, quetiapine, risperidone Current: None	Prior: Benzotropine, clonazepam, clonidine, donepezil, escitalopram, hydroxyzine, lamotrigine, levothyroxine, lorazepam, memantine, mirtazapine, pantoprazole, promethazine Current: Clonidine, donepezil, escitalopram, memantine, mirtazapine, N-acetylcysteine, levothyroxine, pantoprazole, valbenazine
CASE 3 (F, 63 yr)	Mild cognitive impairment; caregiver-dependent for some ADLs	Psychiatric: Schizoaffective disorder, bipolar type Other: Diabetes (Type 2), fibromyalgia, GERD, hyperlipidemia, hypertension, hypothyroidism, insomnia, neuropathy	Prior: Long-term prior exposure (type NA) Current: Asenapine	Prior: Benzotropine, fluoxetine, gabapentin, levothyroxine, memantine, metformin, N-acetylcysteine, pantoprazole, simvastatin, topiramate Current: Fluoxetine, levothyroxine, memantine, metformin, N-acetylcysteine, pantoprazole, simvastatin, valbenazine
CASE 4 (M, 28 yr)	Moderate cognitive and physical impairment; caregiver-dependent for mobility and most ADLs	Psychiatric: ASD, excoriation disorder, schizoaffective disorder, bipolar type Other: Hypertension, hypothyroidism, GERD	Prior: Quetiapine Current: Clozapine	Prior: Clonazepam, famotidine, lamotrigine, liothyronine, lithium, N-acetylcysteine, pindolol, valproate Current: Clozapine, famotidine, lamotrigine, liothyronine, lithium, lorazepam, N-acetylcysteine, ondansetron, pindolol, quetiapine, valbenazine, valproate, ziprasidone

^aRefer to significant comorbid diagnoses. ADHD, attention-deficit/hyperactivity disorder; ASD, autism spectrum disorder; F, female; GERD, gastroesophageal reflux disease; ID, intellectual disability; M, male; NA, not available; TD, tardive dyskinesia; yr, year.

Table 2. TD Symptoms and Daily Functioning in ID Patients Before and After Treatment with Valbenazine

	TD Symptoms/TD-Related Functional Impairment ^a	
	Before Valbenazine	After Valbenazine (80 mg) ^b
CASE 1 (M, 31 yr)	<ul style="list-style-type: none">Prominent tongue protrusionDifficulty swallowing/eatingMultiple episodes of aspiration pneumonia	<ul style="list-style-type: none">Minimal tongue protrusionImproved swallowing/eatingNo new episodes of aspiration pneumonia
CASE 2 (F, 59 yr)	<ul style="list-style-type: none">Facial grimacingTongue protrusion; difficulty swallowing/eating; unclear speechConstant bilateral hand movementsRepetitive bilateral foot tappingUnable to ambulate independently	<ul style="list-style-type: none">Minimal facial grimacingMinimal tongue protrusion; improved swallowing/eating; clearer speechHand movements absentDecreased bilateral foot tappingImproved ambulation
CASE 3 (F, 63 yr)	<ul style="list-style-type: none">Prominent tongue protrusion; unclear speechLip smacking; chewing movements of jawConstant bilateral arm/hand/finger movementsInstability during ambulation; some wheelchair assistance required	<ul style="list-style-type: none">Minimal tongue protrusion; clearer speechVery minimal lip/jaw movementsMinimal arm/hand/finger movementsImproved stability during ambulation; less assistance required for some ADLs
CASE 4 (M, 28 yr)	<ul style="list-style-type: none">Intermittent chewing movement of jawConstant bilateral arm/hand/finger movementsRepetitive bilateral foot tappingTruncal rocking	<ul style="list-style-type: none">No abnormal jaw movementsMinimal to no arm/hand/finger movementsMinimal to no foot tappingNo truncal movements

^aRefer to or minimally verbal patients; based on caregiver reports and observations during follow-up visits. ^bCase 1 discontinued 80 mg valbenazine in August 2018 due to lack of insurance; Case 2 received once-daily 40 mg valbenazine. ADLs, activities of daily living; F, female; ID, intellectual disability; M, male; TD, tardive dyskinesia; yr, year.

CONCLUSIONS

- Once-daily valbenazine treatment (40 mg or 80 mg) resulted in marked improvements in TD symptoms and daily functioning in four adult patients (aged 28–63 years) with mild-to-severe ID, all of whom had multiple comorbid conditions; these patients are illustrative of at least 15 others seen within the same facility with similar results
- Improvements were observed in abnormal movements affecting the face, tongue, jaw, upper extremities, and/or lower extremities, resulting in improved ability to eat/swallow (n=2), ambulate (n=2), and speak (n=2)
- Additionally, the improvement in TD symptoms and daily functioning were associated with noticeable improvement in patients' demeanor and social/caregiver interactions
- Given the extent of antipsychotic usage in ID patients, it is recommended that this population be routinely screened for TD and treated appropriately

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