

Tardive Dyskinesia in Individuals With Intellectual or Developmental Disability

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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 comorbid psychiatric conditions, individuals with ID are frequently treated with antipsychotics; additionally, many individuals 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 behavior)²
- All individuals exposed to antipsychotics are at risk for developing tardive dyskinesia (TD), a persistent and potentially disabling involuntary movement disorder that can affect the face, mouth, trunk, limbs, and/or extremities³
- TD symptoms can be highly disruptive for the affected individuals and their caregivers, causing embarrassment, isolation, increased behavioral disturbances, and reduction in daily functioning and quality of life
- Valbenazine (INGREZZA®) is a novel vesicular monoamine transporter 2 (VMAT2) inhibitor approved to treat TD in adults
- The efficacy and safety of valbenazine was demonstrated in 2 long-term, phase 3 studies (KINECT 3 extension [NCT02274558] and KINECT 4 [NCT02405091])^{4,5} and a rollover study (NCT02736955)⁶; however, individuals with ID were not included in these trials, as subjects were required to have the capacity to provide informed consent to participate

CASE PRESENTATIONS

- Five cases are presented, focusing on clinical history as well as TD symptoms and TD-related functional impairment before and after valbenazine initiation; these cases are representative of approximately 80-90 individuals with ID and TD at this facility who have been treated to date with similar results
- All 5 individuals had multiple comorbid psychiatric, behavioral, and other medical conditions, and a history of antipsychotic exposure (**Table 1**)
- Abnormal movements were observed affecting the tongue/mouth/jaw, upper extremities, lower extremities, and trunk, which resulted in diminished ability to speak, ambulate, and perform activities of daily living (**Table 2**)
- Once-daily valbenazine resulted in marked improvements in TD symptoms within a few weeks of starting treatment, resulting in improvements in daily functioning, demeanor, and social and caregiver interactions (**Table 2**)
- All 5 individuals remained stable after initiation of valbenazine treatment with no adverse events and no TD-related changes to concomitant medications (antipsychotic medications were changed concurrently with valbenazine initiation in 2 individuals due to parkinsonism and persistent psychosis)

Table 1. Summary of ID Patients Treated with Valbenazine for TD				
Case Number (gender, age)	ID Severity	Significant Comorbid Diagnoses	Medications ^a	
			Antipsychotic	Other
CASE 1 (M, 63 yr)	Moderate cognitive impairment; nonverbal, caregiver-dependent for most ADLs	Psychiatric: major depressive disorder Other: arthritis, anemia, GERD, hyperlipidemia, Parkinson's disease	Prior: quetiapine Current: quetiapine	Prior: atorvastatin, benztropine, carbidopa-levodopa-entacapone, donepezil, duloxetine, escitalopram, memantine, omeprazole, pregabalin, tramadol Current: atorvastatin, benztropine, carbidopa-levodopa, donepezil, duloxetine, escitalopram, memantine, omeprazole, pregabalin, tramadol, valbenazine
CASE 2 (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, overactive bladder, neuropathy	Prior: olanzapine, risperidone Current: asenapine	Prior: benztropine, fluoxetine, gabapentin, levothyroxine, memantine, metformin, mirabegron, N-acetylcysteine, pantoprazole, simvastatin, topiramate Current: fluoxetine, levothyroxine, memantine, metformin, N-acetylcysteine, oxybutynin, pantoprazole, simvastatin, valbenazine
CASE 3 (M, 28 yr)	Moderate cognitive and physical impairment; caregiver-dependent for mobility and most ADLs	Psychiatric: excoriation disorder, schizoaffective disorder (bipolar type) Other: ASD, hypertension, hypothyroidism, GERD, seizures	Prior: quetiapine Current: clozapine	Prior: clonazepam, famotidine, lamotrigine, liothyronine, N-acetylcysteine, pindolol, valproate Current: famotidine, lacosamide, lamotrigine, levothyroxine, lithium, N-acetylcysteine, pindolol, valbenazine, valproate
CASE 4 (M, 61 yr)	Moderate cognitive impairment; caregiver-dependent for some ADLs	Psychiatric: depressive disorder, impulse control disorder, OCD, schizophrenia (paranoid type) Other: diabetes (type 2), enuresis, hyperlipidemia, hypertension, hypothyroidism, GERD, glaucoma, tachycardia	Prior: chlorpromazine, clozapine, haloperidol, quetiapine, risperidone, thioridazine Current: clozapine	Prior: atorvastatin, bethanechol, escitalopram, famotidine, lisinopril, memantine, N-acetylcysteine, naltrexone Current: atorvastatin, doxazosin, escitalopram, famotidine, glycopyrrolate, latanoprost, levothyroxine, memantine, N-acetylcysteine, pindolol, valbenazine
CASE 5 (M, 45 yr)	Mild cognitive impairment	Psychiatric: schizophrenia (paranoid type) Other: COPD, hepatitis C, seizures	Prior: aripiprazole, brexpiprazole, haloperidol, olanzapine, quetiapine, risperidone, ziprasidone Current: clozapine	Prior: benztropine, buspirone, carbamazepine, citalopram, fluoxetine Current: duloxetine, gabapentin, valbenazine
^a Related to significant comorbid diagnoses. AD/HD, attention-deficit/hyperactivity disorder; ADLs, activities of daily living; ASD, autism spectrum disorder; COPD, chronic obstructive pulmonary disease; F, female; GERD, gastroesophageal reflux disease; ID, intellectual disability; M, male; OCD, obsessive-compulsive disorder; TD, tardive dyskinesia; yr, years.				

Table 2. TD Symptoms and Daily Functioning in ID Patients Before and After Treatment with Valbenazine		
Case Number (gender, age)	TD Symptoms/TD-Related Functional Impairment ^a	
	Before Valbenazine	After Valbenazine (80 mg)
CASE 1 (M, 63 yr)	<ul style="list-style-type: none">• Constant tongue protrusion and intermittent chewing movements of jaw; severe drooling and difficulty swallowing• Excessive, pronounced blinking• Bilateral shoulder/hand/finger movement• Constant left foot tapping• Instability during standing and ambulating; wheelchair assistance required and caregiver assistance needed with some ADLs	<ul style="list-style-type: none">• No tongue protrusion or chewing movements of jaw; able to close mouth; reduced drooling and improved swallowing• Reduced frequency and less pronounced blinking• Minimal shoulder/hand/finger movement• No foot tapping• Improved stability during standing and ambulating; able to ambulate with walker and less caregiver assistance needed with ADLs
CASE 2 (F, 63 yr)	<ul style="list-style-type: none">• Repetitive tongue thrusting; lip smacking; chewing movements of mouth/jaw; unclear speech• Constant bilateral arm/hand/finger movements• Instability during ambulation; some wheelchair assistance required	<ul style="list-style-type: none">• Minimal tongue thrusting and lip/mouth/jaw movements; clearer speech• Minimal arm/hand/finger movements• Improved stability during ambulation; less assistance required for some ADLs
CASE 3 (M, 28 yr)	<ul style="list-style-type: none">• Intermittent chewing movement of jaw• Constant bilateral arm/hand/finger movements• Repetitive bilateral foot tapping• Truncal rocking	<ul style="list-style-type: none">• No jaw movements• Minimal to no arm/hand/finger movements• Minimal to no foot tapping• No truncal rocking
CASE 4 (M, 61 yr)	<ul style="list-style-type: none">• Intermittent tongue thrusting, chewing motion of jaw, and facial grimacing• Intermittent nodding/forward movement of head/neck• Frequent eye blinking• Constant bilateral hand movement	<ul style="list-style-type: none">• No tongue thrusting or chewing motion of jaw, and minimal facial grimacing• Minimal head/neck movement• Normal eye blinking• No hand movement
CASE 5 (M, 45 yr)	<ul style="list-style-type: none">• Intermittent lip puckering, jaw movements, and facial grimacing; unclear speech• Constant bilateral shoulder/hand/finger movement• Repetitive bilateral foot tapping• Truncal rocking• Instability during ambulation; wheelchair assistance and caregiver assistance with some ADLs required	<ul style="list-style-type: none">• Very minimal lip/jaw movements and no facial grimacing; clearer speech• Minimal shoulder/hand/finger movement• Minimal foot tapping• Minimal truncal rocking• Improved stability during ambulation; able to ambulate independently with a cane and less assistance required for ADLs
^a For nonverbal or minimally verbal patients, based on caregiver reports and observations during follow-up visits. ADLs, activities of daily living; F, female; ID, intellectual disability; M, male; TD, tardive dyskinesia; yr, years.		

CONCLUSIONS

- Given the extent of antipsychotic usage in ID patients, it is recommended that this population be routinely screened for TD and treated appropriately
- In this case series, 5 individuals with ID and TD received once-daily valbenazine and experienced marked improvement in their TD symptoms and daily functioning, resulting in increased quality of life for the affected individuals and their caregivers
- Improvements were observed in abnormal movements affecting the face, tongue, jaw, upper extremities, and/or lower extremities, resulting in improved ability to eat/swallow, ambulate, and speak

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