Clinical Characteristics and Antipsychotic Medication Use in a Pediatric Population Diagnosed With Tourette Syndrome

POSTER NUMBER: 264

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BACKGROUND

- Most (eg, >85%) individuals with Tourette syndrome (TS) will have ≥1 comorbid psychiatric condition during their lifetime,[1] but real-world data on psychiatric comorbidities at time of TS diagnosis are limited
- Patients with TS and comorbid conditions are likely to be treated with antipsychotics (dopamine D2 receptor antagonists/partial agonists [D2RAs]), which are linked to adverse effects (eg, weight gain, lipid abnormalities, hyperglycemia) that can negatively impact quality of life and treatment adherence[2-7]

OBJECTIVES

- To describe the demographics and clinical characteristics of children and adolescents newly diagnosed with TS
- To assess antipsychotic medication discontinuation rates for the treatment of TS

METHODS

- Data (10-year identification period) were analyzed retrospectively using an electronic health records database (TriNetX Dataworks-USA Network) that contains information for >119 million individuals
- Demographics and clinical characteristics were analyzed for pediatric patients newly diagnosed with TS with a health care encounter with International Classification of Diseases (ICD), 9th Revision, Clinical Modification diagnosis code 307.23 or ICD, 10th Revision, Clinical Modification code F952 and no previous encounters with diagnosis code for TS within 18-month period prior to index date (ie, newly diagnosed)
  - Included patients were also required to have ≥1 provider encounter with any diagnosis code during a baseline period (18 months prior to index [TS diagnosis] date) and during an 18-month post-index period, thereby selecting for patients with multiple encounters in the medical system
- The D2RA-exposed cohort was defined by the following criteria:
  - TS diagnosis (ICD-9-CM: 307.23/ICD-10-CM:F952)
  - Exposure to a D2RA medication (aripiprazole, haloperidol, olanzapine, pimozide, quetiapine, risperidone, or ziprasidone), with date of first D2RA medication record serving as index date
  - Age 6 to 17 years at index date and ≥1 provider encounter during a baseline period (≥18 months prior to index date) and an 18-month follow-up period
  - Individuals were exact-matched to a non–D2RA-exposed TS cohort based on age group, index year, region, and sex (data not shown)
- Monthly D2RA medication use was estimated based on records during and prior to a particular month (eg, Days 31-91 postindex for "Month 3")

RESULTS

- 12,015 children and adolescents with TS were included in the newly diagnosed cohort (**Table**)
  - Most were male (71.5%); of those with available data, 32.7% were considered overweight or obese
  - The most common comorbid psychiatric conditions, among those examined, were attention-deficit hyperactivity disorder (ADHD) and anxiety (**Table**)

RESULTS

- For the D2RA-exposed cohort, 1684 matched individuals were identified with a new D2RA medication record (**Table**)
  - Median age was 13 years, 73.9% were male, and 57.0% had comorbid ADHD
  - Most common D2RAs identified at index were risperidone (42.0%), aripiprazole (33.1%), and haloperidol (7.6%)

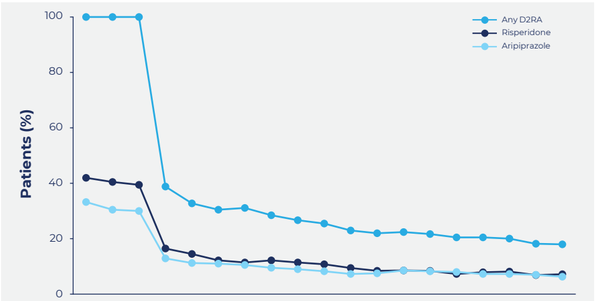
Table. Demographic and Baseline Characteristics in Children and Adolescents With TS

Characteristics	Newly Diagnosed Cohort (N=12,015)	D2RA-Exposed Cohort (n=1684)
Median age (Q1, Q3), y	11 (9, 14)	13 (11, 15)
Age group, n (%)		
6-11 y	6267 (52.2)	576 (34.2%)
12-17 y	5748 (47.8)	1108 (65.8%)
Male, n (%)	8594 (71.5)	1245 (73.9%)
Race, n (%)		
White	9026 (75.1)	1290 (76.6)
Black	814 (6.8)	87 (5.2)
Other	297 (2.5)	42 (2.5)
Missing	1878 (15.6)	265 (15.7)
BMI category, n (%)*		
Underweight	319 (2.7)	54 (3.2)
Healthy weight	3980 (33.1)	652 (38.7)
Overweight	932 (7.8)	171 (10.2)
Obesity	1161 (9.7)	217 (12.9)
Missing	5623 (46.8)	590 (35.0)
Metabolic syndrome, n (%)†		
Unknown	10,335 (86.0)	1347 (80.0)
Mild	1565 (13.0)	318 (18.9)
Moderate	115 (1.0)	19 (1.1)
Neuropsychiatric comorbidities, n (%)		
Anxiety	4594 (38.2)	998 (59.3)
ADHD	4663 (38.8)	960 (57.0)
OCD	1485 (12.4)	432 (25.7)
Depression/mood disorder	892 (7.4)	276 (16.4)
Autism spectrum disorder	1228 (10.2)	256 (15.2)
D2RA TS-related medications, n (%)‡		
Risperidone	656 (5.5)	707 (42.0)
Aripiprazole	485 (4.0)	557 (33.1)
Haloperidol	121 (1.0)	128 (7.6)
Quetiapine	163 (1.4)	125 (7.4)
Pimozide	94 (0.8)	112 (6.7)
Olanzapine	77 (0.6)	57 (3.4)
Ziprasidone	63 (0.5)	36 (2.1)
Non-D2RA TS-related medications, n (%)		
Guanfacine	2658 (22.1)	669 (39.7)
Clonidine	1391 (11.6)	422 (25.1)
Topiramate	478 (4.0)	147 (8.7)
Botulinum toxin A	6 (0.05)	2 (0.1)
Other medications, n (%)		
Antidepressant	2568 (21.4)	922 (54.8)
ADHD medication	2472 (20.6)	621 (36.9)
Antianxiety§	1065 (8.9)	340 (20.2)

*Underweight (BMI z-score <−1.6); normal weight (BMI z-score −1.6 to <1.0); overweight (BMI z-score 1.0 to <1.6); and obese (BMI z-score ≥1.6). †Metabolic syndrome conditions defined as: abdominal obesity (ie, any BMI result indicating obesity), hypertension, any triglyceride result(s) ≥100 mg/dL, any HDL-C result(s) ≤50 mg/dL, and prediabetes, diabetes, or any fasting glucose result(s) ≥110 mg/dL. Mild defined as 1 to 2 metabolic syndrome conditions; moderate defined as 3 to 5 metabolic syndrome conditions. ‡>1 D2RA medication at index may have been identified for a patient. §Benzodiazepines and buspirone.
ADHD = attention-deficit hyperactivity disorder; BMI = body mass index; D2RA = dopamine D2 receptor antagonist/partial agonist; HDL-C = high-density lipoprotein-cholesterol; OCD = obsessive-compulsive disorder; Q = quartile; TS = Tourette syndrome.

- In the DRA-exposed cohort (n=1684), evidence of D2RA use progressively decreased over time, most dramatically, between Months 2 and 3 (**Figure 1**)
  - During Month 3 postindex, only 38.8% of individuals had evidence of D2RA use (**Figure 1**)
  - During Months 12 and 18 postindex, overall D2RA use further decreased to 22.4% and 17.9%, respectively (**Figure 1**)

Figure 1. Percentage of Patients With TS With Medication Records for Any D2RAs and for the 2 Most Common D2RAs Identified at Index*

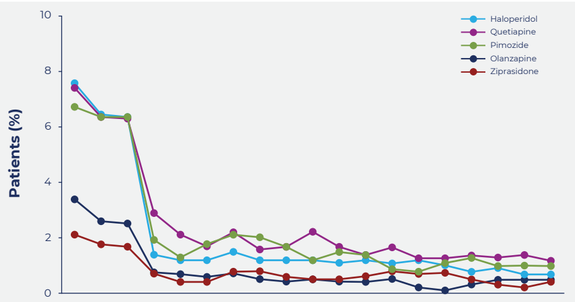


Patients, %	Index	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12	M13	M14	M15	M16	M17	M18
Any D2RA	100.0	100.0	100.0	38.8	32.6	30.4	30.8	28.4	26.7	25.4	22.8	21.8	22.4	21.7	20.4	20.5	20.0	18.1	17.9
Risperidone	42.0	40.3	39.3	16.5	14.4	12.2	11.5	12.1	11.5	10.6	9.5	8.3	8.5	8.3	7.2	7.9	8.1	6.6	7.2
Aripiprazole	33.1	30.4	29.8	13.0	11.1	10.9	10.5	9.4	8.9	8.2	7.1	7.4	8.3	8.1	7.8	7.1	7.2	7.0	6.1

*D2RA-exposed cohort (n=1684); index date was date of first D2RA medication record.
D2RA = dopamine D2 receptor antagonist/partial agonist; M = month; TS = Tourette syndrome.

- Risperidone and aripiprazole use was 82.9% and 81.7% lower, respectively, during Month 18 compared with index (**Figure 1**)
- Other D2RA use exhibited a similar trend over time (**Figure 2**)

Figure 2. Percentage of Patients With TS With Medication Records for Less Common D2RAs Identified at Index*



Patients, %	Index	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12	M13	M14	M15	M16	M17	M18
Haloperidol	7.6	6.5	6.4	1.4	1.2	1.2	1.5	1.2	1.2	1.2	1.2	1.1	1.2	1.1	1.2	1.0	0.8	0.9	0.7	0.7
Quetiapine	7.4	6.4	6.3	2.9	2.1	1.7	2.2	1.6	1.7	2.2	1.7	1.4	1.7	1.3	1.3	1.4	1.3	1.4	1.2
Pimozide	6.7	6.4	6.4	1.9	1.3	1.8	2.1	2.0	1.7	1.2	1.5	1.4	0.9	0.8	1.1	1.3	1.0	1.0	1.0
Olanzapine	3.4	2.6	2.5	0.8	0.7	0.6	0.7	0.5	0.4	0.5	0.4	0.4	0.5	0.2	0.1	0.3	0.5	0.5	0.5
Ziprasidone	2.1	1.8	1.7	0.7	0.4	0.4	0.8	0.8	0.6	0.5	0.5	0.6	0.8	0.7	0.7	0.5	0.3	0.2	0.4

*D2RA-exposed cohort (n=1684); index date was date of first D2RA medication record.
D2RA = dopamine D2 receptor antagonist/partial agonist; M = month; TS = Tourette syndrome.

CONCLUSIONS

- Common psychiatric comorbidities of TS in this cohort were ADHD, anxiety, obsessive-compulsive disorder, depression/mood disorder, and autism spectrum disorder
- Evidence of D2RA use decreased considerably during the 18 months following initiation
  - Up to 61.2% and 82.1% of individuals no longer had a D2RA medication record by Months 3 and 18, respectively, suggestive of treatment discontinuation
  - A similar profile in discontinuation rates over time was observed across the D2RAs analyzed
  - Reasons for discontinuation were not studied, but may reflect issues with tolerability, safety, perceived efficacy, access to care, and/or initiation of an additional medication with potential drug-drug interactions
- Although reasons for discontinuation of D2RA treatment could not be determined, and stratification by comorbid conditions/concomitant medication use was not conducted, results demonstrate that adherence to D2RA treatment is poor and reinforce the need for alternative safe and effective long-term TS treatment options

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ACKNOWLEDGMENTS:
This study was funded by Emalex Biosciences, Inc. Editorial and medical writing assistance were provided under the direction of the authors by Mary Beth Moncrief, PhD, Synchrony Medical Communications, LLC, West Chester, PA. Funding for this assistance was provided by Emalex Biosciences, Inc., Chicago, IL.

DISCLOSURES:
KKT has been a clinical trial site investigator for Emalex Biosciences, Inc.; received travel support from Emalex Biosciences, Inc.; and received consulting fees from Jazz Pharmaceuticals. JPS, FMD, FM, and CAP are employees of Thermo Fisher Scientific, a company that received funding from Emalex Biosciences, Inc., to conduct the analyses. GBK, SDA, and FEM are employees of and have personal equity interest in Emalex Biosciences, Inc. SPW and TMC are employees of Paragon Biosciences, LLC, which has controlling equity interest in Emalex Biosciences, Inc.; additionally, they have personal equity interest in Emalex Biosciences, Inc. DLG is a clinical trial site investigator for Emalex Biosciences, Inc., Quince Therapeutics, and PTC Therapeutics, and has received consulting fees and/or travel support from Emalex Biosciences, Inc., PTC Therapeutics, and Vima Therapeutics. DAI has been a clinical investigator for Emalex Biosciences, Inc., and receives funding from Teva Branded Pharmaceutical Products, R&D, Inc.

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