Increased Health Care Utilization in Children/Adolescents With Tourette Syndrome Treated With Dopamine D2 Receptor Antagonists: An Electronic Health Records Database Analysis

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BACKGROUND

- Tourette syndrome (TS) is a neurodevelopmental disorder characterized by motor and vocal tics of varying frequency, intensity, and complexity that begin in childhood and have a duration of ≥1 year[1,2]
- The dopamine D2 receptor antagonists/partial agonists (D2RAs) aripiprazole, haloperidol, and pimozide are indicated in the United States for treatment of TS; however, these medications are associated with multiple adverse effects (eg, weight gain, lipid abnormalities, hyperglycemia, hyperprolactinemia) that can limit long-term use[2-5]
- Data on health care resource utilization (HCRU) for children and adolescents with TS prescribed D2RAs are lacking

OBJECTIVE

- To compare HCRU in D2RA-exposed versus D2RA-nonexposed children and adolescents with TS

METHODS

- Data were analyzed from an electronic health records database (TriNetX Dataworks-USA Network) containing information for >119 million unique individuals
- The D2RA-exposed cohort was indexed on first record for a D2RA (2011-2021) with TS diagnosis (ICD-9-CM diagnosis: 307.23 or ICD-10-CM: F952) during a baseline period (18 months before and including index date), and the non-D2RA cohort was indexed on a randomly selected record with TS diagnosis (2011-2021)
- Additional criteria were age 6 to 17 years at index date and ≥1 provider encounter during baseline and during a follow-up period (18 months after index)
- Individuals in each cohort were 1:1 matched based on age group, index year, region, and sex
- Incidence rates (per 100 patient-years; allowing multiple events per patient) and incidence rate ratios (IRRs) for all-cause and TS-related HCRU (emergency, inpatient, and outpatient health care encounters) were calculated for the 18-month follow-up period
- All-cause HCRU was defined as health care encounters in any of the following settings: emergency, inpatient (hospital, non-acute, or short stay), and outpatient (ambulatory, home health, observation, pre-admission, or virtual)
  - TS-related HCRU was defined as health care encounters (noted above) with a TS diagnosis code (ICD-9-CM diagnosis: 307.23 or ICD-10-CM: F952)

RESULTS

- 1684 individuals aged 6 to 17 years with TS were included in the matched D2RA and non-D2RA cohorts (**Table**)
  - In the D2RA cohort, the first-month (index) D2RAs identified were risperidone (42.0%), aripiprazole (33.1%), haloperidol (7.6%), quetiapine (7.4%), pimozide (6.7%), olanzapine (3.4%), and ziprasidone (2.1%)

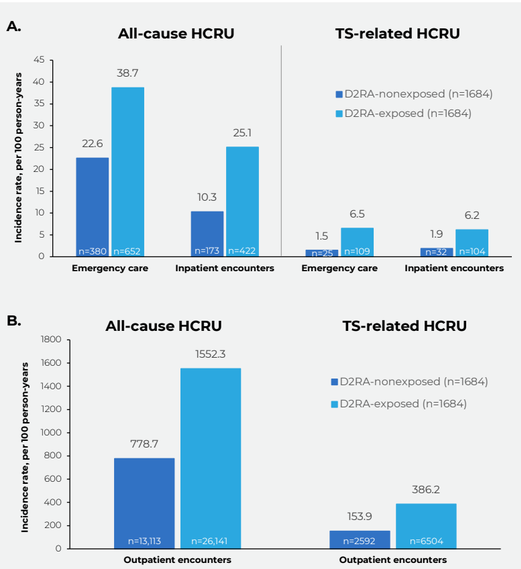
Table. Patient Demographic* and Baseline Characteristics† After Matching

Parameter	D2RA-Exposed Cohort (n=1684)	D2RA-Nonexposed Cohort (n=1684)
Age		
Median, y	13	13
6-11 y, n (%)	576 (34.2)	576 (34.2)
12-17 y, n (%)	1108 (65.8)	1108 (65.8)
Male, n (%)	1245 (73.9)	1245 (73.9)
Race, n (%)		
White	1290 (76.6)	1225 (72.7)
Black	87 (5.2)	105 (6.2)
Asian	27 (1.6)	29 (1.7)
Other	15 (0.9)	11 (0.6)
Missing	265 (15.7)	314 (18.6)
BMI category,‡ n (%)		
Underweight/normal weight§	706 (41.9)	610 (36.2)
Overweight/obesity¶	388 (23.0)	286 (17.0)
Missing	590 (35.0)	788 (46.8)
Neuropsychiatric comorbidities, n (%)		
Anxiety	998 (59.3)	680 (40.4)
ADHD	960 (57.0)	637 (37.8)
OCD	432 (25.7)	242 (14.4)
Depression/mood disorder	276 (16.4)	111 (6.6)
Autism spectrum disorder	256 (15.2)	135 (8.0)
Sleep disorder	200 (11.9)	137 (8.1)
Headache/migraine	147 (8.7)	150 (8.9)
Suicidality/suicide attempt	134 (8.0)	24 (1.4)
Abnormal involuntary movements	81 (4.8)	82 (4.9)
Non-D2RA TS-related medications, n (%)		
Guanfacine	669 (39.7)	386 (22.9)
Clonidine	422 (25.1)	194 (11.5)
Topiramate	147 (8.7)	75 (4.5)
Botulinum toxin A	2 (0.1)	2 (0.1)
Other medications, n (%)		
Antidepressant	922 (54.8)	346 (20.5)
ADHD medication	621 (36.9)	331 (19.7)
Antianxiety#	340 (20.2)	122 (7.2)
Antiseizure**	222 (13.2)	81 (4.8)

*Age, sex, and race reported at index. †BMI category, neuropsychiatric comorbidities, and medication records during the baseline period (18 months before and including index). ‡Based on BMI Z score (calculated per age and sex using US Centers for Disease Control and Prevention growth charts). §BMI Z score <1.0. ¶BMI Z score ≥1.0. #Benzodiazepine (excluding clonazepam) or buspirone. **Did not include topiramate.
ADHD = attention-deficit/hyperactivity disorder; BMI = body mass index; D2RA = dopamine D2 receptor antagonist/partial agonist; OCD = obsessive-compulsive disorder; TS = Tourette syndrome.

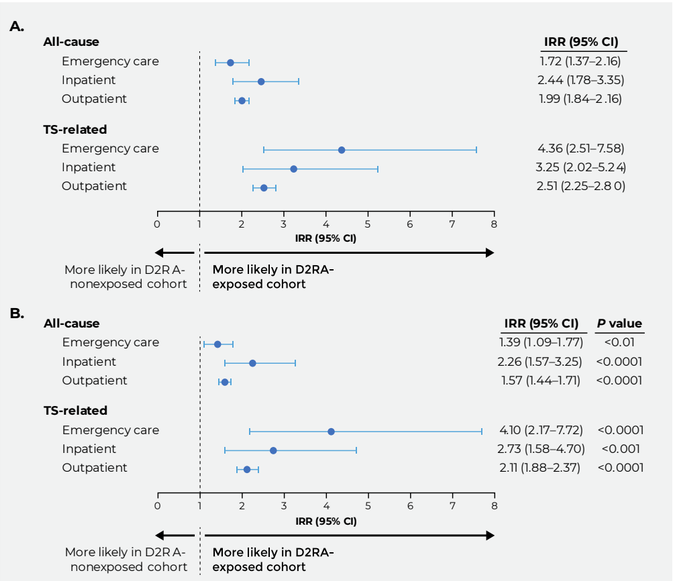
- The D2RA-exposed TS cohort had a higher rate of all-cause HCRU compared with the non-D2RA exposed TS cohort during the 18-month follow-up period (**Figures 1A and 1B**), with 1.7-fold higher emergency care, 2.4-fold higher inpatient encounters, and 2.0-fold higher outpatient encounters (**Figure 2A**)
  - The D2RA-exposed TS cohort also had a higher rate of TS-related HCRU compared with the non-D2RA exposed TS cohort (**Figures 1A and 1B**), with 4.4-fold higher emergency care, 3.3-fold higher inpatient encounters, and 2.5-fold higher outpatient encounters (**Figure 2A**)
- Similar results were observed after multivariable adjustment for demographics and clinical characteristics, with significantly greater increase (IRR) in the D2RA-exposed versus non-D2RA cohort for all-cause and TS-related emergency, inpatient, and outpatient health care encounters (IRR range, 1.4-4.1; *P*<0.01 for all; **Figure 2B**)

Figure 1. All Cause and TS-Related (A) Emergency and Inpatient and (B) Outpatient Health Care Resource Utilization During an 18-Month Follow-Up Period in Children and Adolescents With TS



D2RA = dopamine D2 receptor antagonist/partial agonist; HCRU = health care resource utilization; TS = Tourette syndrome.

Figure 2. Health Care Resource Utilization in Children and Adolescents With TS During an 18-Month Follow-Up Period (A) Before and (B) After Multivariable Adjustment



D2RA = dopamine D2 receptor antagonist/partial agonist; IRR = incidence rate ratio; TS = Tourette syndrome.

CONCLUSIONS

- Data suggest high HCRU burden in children and adolescents with TS treated with D2RAs
  - Exposure (versus nonexposure) to D2RAs in individuals with TS appeared to be associated with higher rates of HCRU, particularly TS-related emergency and inpatient health care encounters
  - Although the exact reason(s) for each HCRU encounter were not determined, higher HCRU in the D2RA-exposed cohort could have been related to drug-related adverse effects, TS severity, or a combination of both
- Further research to disentangle roles of medication class versus TS severity are warranted

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DISCLOSURES:

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