JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY
Volume XX, Number XX, 2019

Pp. 1–4
DOI: 10.1089/cap.2019.0087

Metabolic Monitoring Rates of Youth Treated with Second-Generation Antipsychotics in Usual Care: Results of a Large US National Commercial Health Plan

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Abstract

Objectives: To examine metabolic monitoring rates in commercially insured children and adolescents treated with a second-generation antipsychotic (SGA) during calendar years (CYs) 2016 and 2017.

Methods: In this retrospective study, data were collected from a large national commercial health plan for the period covering January 1, 2016 to December 31, 2017. Commercially insured children and adolescents, aged 8–19 years with ≥2 SGA prescription claims during the CY, were identified for the CY2016 and CY2017 cohorts. The primary outcome of interest was the percentage of subjects with any glucose or lipid metabolism parameter monitoring. Other calculated metabolic testing rates included glucose, hemoglobin A1c (HbA1c), low-density lipoprotein cholesterol (LDL-C), other cholesterol (including triglycerides), and combined glucose and lipid metabolism testing (≥1 test for blood glucose or HbA1c and ≥1 test for LDL-C or other cholesterol).

Results: In CY2016 and CY2017, 1502 and 1239 subjects, respectively, were identified for this study. The most common psychiatric diagnoses in CY2016 and CY2017 were major depressive disorder (57.1%, 56.5%, respectively), anxiety disorders (42.9%, 47.5%), attention-deficit/hyperactivity disorder (41.6%, 45.8%), and bipolar disorder (24.1%, 25.9%). The rate of any metabolic testing was 53.5% in CY2016 and 51.3% in CY2017. Glucose testing (50.3%, 46.9%, respectively) was most common in both CYs, followed by LDL-C testing (31.2%, 28.5%). Rates of combined glucose and lipid metabolism testing were 30.7% in CY2016 and 26.9% in CY2017.

Conclusions: Given the known potential for adverse cardiometabolic effects, rates of metabolic monitoring associated with SGA use in children and adolescents urgently need to be improved. There is a critical need for understanding barriers to routine monitoring, particularly of lipids, and developing interventions to enhance metabolic monitoring.

Keywords: antipsychotics, metabolic monitoring, quality

Introduction

The known metabolic risks associated with second-generation antipsychotic (SGA) use in children and adolescents (Galling et al. 2016) and downstream effects on cardiometabolic outcomes (De Hert et al. 2011) warrant routine monitoring of metabolic parameters, such as glucose, hemoglobin A1c (HbA1c), and lipids (ADA et al. 2004; Correll 2008). Baseline screening measures for all patients receiving antipsychotic treatment are recommended to be obtained at the initiation of an antipsychotic, with follow-up monitoring at 3 months; thereafter, glucose should be monitored annually and lipids at 5-year intervals, unless clinically indicated to be done more frequently (ADA et al. 2004). As part of the ongoing metformin for overweight and obese

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Funding: Dr. M.P.D.'s work on this topic is supported through a PCORI award 1406-19276. Dr. S.C.'s work on this topic is supported through AHRQ award 1R01HS026001 and PCORI award IHS-1409-23194. There was no other support (i.e., grant, funding source, or commercial interest) for this study. The data used for this study were supplied by Humana, Inc.

children with bipolar spectrum disorders treated with SGA (MOBILITY) study (PCS-1406-19276; ClinicalTrials.gov identifier: NCT02515773), a randomized, large, simple pragmatic clinical trial examining metformin as standard of care for overweight and obese youth (8–19 year old) with past or present bipolar-spectrum illness who require treatment with SGAs, rates of metabolic monitoring are being evaluated as part of the battery of outcome measures. Interim findings suggest suboptimal baseline monitoring of subjects (66.9% any lab, 66.1% glucose, 61.0% triglycerides, and 60.4% cholesterol), although higher than previously published studies that have reported rates of glucose (15%–50%) and lipid (13%) screenings in youth initiating SGA treatment (Morrato et al. 2010; Raebel et al. 2014). Although the MOBILITY trial is intended to reflect ''real-world'' clinical practice through its pragmatic study design, there is likely additional attention to laboratory tests compared with usual care because of the study's emphasis on metabolic monitoring.

Nonetheless, it is important to evaluate the practice of metabolic monitoring of children and adolescents treated with SGAs on a broader, population health scale. With this consideration in mind, this study was conducted to establish a better understanding of recent rates of metabolic monitoring among a generalizable sample of commercially insured youths receiving treatment with an SGA. This study is part of a quality improvement initiative at a large, national health plan. Based on the available literature, we hypothesized that real-world cardiometabolic monitoring rates would be insufficient in high-risk youth with mental health diagnoses who receive an SGA.

Methods

This was a retrospective study examining the rates of metabolic monitoring in commercially insured children and adolescents treated with SGA during calendar years (CYs) 2016 and 2017. The study protocol was reviewed and approved by the Advarra Institutional Review Board.

Data source

Data were collected from a large national commercial health plan for the time period covering January 1, 2016 through December 31, 2017. Study data included enrollment information, medical claims, pharmacy claims, and laboratory claims. Enrollment data were used to determine date of benefit enrollment and termination, as well as certain demographic characteristics (age, gender, geographic region). Medical claims data included *International Classification of Diseases, Tenth Revision, Clinical Modification* (ICD-10-CM) codes associated with medical encounters, which were used to identify psychiatric and medical conditions. Pharmacy claims data included prescription fill dates, National Drug Code (NDC) numbers, and Generic Product Identifier (GPI) codes. All medical and pharmacy claims included in the study were fully adjudicated and paid.

Study population

Commercially insured children and adolescents, aged 8 through 19 years as of January 1 of the respective CY, and with two or more SGA prescription claims during the CY, were identified for the CY2016 ($n=1800$) and CY2017 ($n=1327$) cohorts. Patients were then excluded from research if they were enrolled in a group health plan contractually (CY 2016: $n=298$, 16.6%; CY2017: $n=88$, 6.6%).

Measures

In addition to demographic characteristics, psychiatric and specific metabolic/endocrine conditions were identified for each subject in each CY cohort using medical claims during that respective CY. Mental, behavioral, and neurodevelopmental diagnoses were determined for each subject for CY2016 and CY2017 using ICD-10-CM diagnostic codes F01-F99. Metabolic/endocrine diagnoses were determined using the following ICD-10-CM diagnostic codes: drug-induced diabetes (E09), type 2 diabetes mellitus (T2DM; E11), overweight and obesity (E66), hypercholesterolemia (E78.0X), hyperglyceridemia (E78.1), mixed hyperlipidemia (E78.2), other hyperlipidemia (E78.4), unspecified hyperlipidemia (E78.5), and metabolic syndrome (E88.81). Psychiatric and medical diagnoses were not mutually exclusive to allow for the reporting of comorbid conditions.

Specific SGA and metformin use was determined for each subject for CY2016 and CY2017 using drug-specific NDC and GPI codes. SGA use was not mutually exclusive to allow for the reporting of concurrent use or use of more than one SGA through the course of the respective CY.

The primary rate of interest was the percentage of subjects with any metabolic monitoring. Other rates that were calculated included percentage of subjects with (1) glucose testing; (2) HbA1c testing; (3) low-density lipoprotein cholesterol (LDL-C) testing; (4) other cholesterol testing, and (5) at least one test for blood glucose or HBA1c and at least one test for LDL-C or other cholesterol. The relevant Current Procedural Terminology (CPT) and Logical Observation Identifiers Names and Codes (LOINC) codes for each type of testing were obtained from HEDIS technical specifications for the Metabolic Monitoring for Children and Adolescents on Antipsychotics (APM) measurement (NCQA 2018).

Analyses

Descriptive statistics were used to characterize demographic and diagnostic attributes of each CY cohort, as well as to report rates of various monitoring.

Results

Altogether, 1502 subjects were identified in CY2016 and 1239 in CY2017. Table 1 shows a summary of demographic and clinical (diagnostic and medication use) information. Roughly 10%–11% of subjects in both CYs did not have a psychiatric diagnosis identified.

In CY2016, the rate of any metabolic testing was 53.5% ($n=803$). The percentage of subjects in CY2016 with glucose testing was 50.3% ($n=755$), HbA1c testing 16.0% ($n=240$), LDL-C testing 31.2% ($n=469$), other cholesterol testing 22.0% ($n=330$), and combined testing was 30.7% ($n=461$). In CY2017, the rate of any metabolic testing was 51.3% ($n=636$). The percentage of subjects in CY2017 with glucose testing was 46.9% ($n=581$), HbA1c testing 15.4% ($n=191$), LDL-C testing 28.5% ($n=353$), other cholesterol testing 19.2% ($n=238$), and combined testing was 26.9% ($n=333$).

Discussion

The calculated rates of laboratory monitoring in both CYs indicate that slightly more than half the children and adolescents receiving SGA treatment are receiving at least one form of metabolic testing. However, rates of monitoring are lower when considering combined testing for glucose and lipid parameters. These findings support the fact that there is an opportunity to improve ''real-world'' metabolic monitoring practices. Since approximately

Table 1. Demographic and Clinical Characteristics of 2016 and 2017 Cohorts

Characteristic	*CY2016* (n = *1502*)	*CY2017* (n = *1239*)
Age (years), mean (SD)	14.8 (±3.03)	14.7 (±3.13)
Gender (girls), *n* (%)	650 (43.3)	536 (43.3)
Geographic region, *n* (%)		
South	969 (64.5)	802 (64.7)
Midwest	412 (27.4)	367 (29.6)
West	115 (7.7)	64 (5.2)
Northeast	<10 (<0.7)	<10 (<0.9)
Psychiatric diagnosis (ICD-10-CM), *n* (%)[a]	1326 (88.3)	1118 (90.2)
Anxiety disorders (F41)	645 (42.9)	589 (47.5)
ADHD (F90)	625 (41.6)	568 (45.8)
MDD, single (F32)	457 (30.4)	378 (30.5)
MDD, recurrent (F33)	401 (26.7)	322 (26.0)
Bipolar disorder (F31)	362 (24.1)	321 (25.9)
Stress reaction, PTSD, adjustment disorder (F43)	265 (17.6)	210 (16.9)
Unspecified mood disorder (F39)	261 (17.4)	213 (17.2)
Pervasive developmental disorders (F84)	260 (17.3)	240 (19.4)
Conduct disorders (F91)	241 (16.0)	208 (16.8)
Persistent mood disorders (F34)	228 (15.2)	166 (13.4)
Metabolic-related diagnosis, *n* (%)		
Overweight/obesity	99 (6.6)	72 (5.8)
Any diabetes	11 (0.7)	<10 (<0.9)
Any dyslipidemia	48 (3.2)	39 (3.1)
Metabolic syndrome	10 (0.7)	<10 (<0.9)
No. of unique SGAs per subject, *n* (%)[b]		
1	1231 (82.0)	1002 (80.9)
2	225 (15.0)	198 (16.0)
3+	46 (3.1)	39 (3.1)
Specific SGA use, *n* (%)[a]		
Aripiprazole	599 (39.9)	533 (43.0)
Risperidone	464 (30.9)	363 (29.3)
Quetiapine	443 (29.5)	349 (28.2)
Olanzapine	154 (10.3)	117 (9.4)
Ziprasidone	92 (6.1)	71 (5.7)
Lurasidone	35 (2.3)	40 (3.2)
Other	44 (2.9)	48 (3.9)
Metformin use, *n* (%)	36 (2.4)	32 (2.6)

[a]Not mutually exclusive.
[b]Does not necessarily mean concurrent use.
ADHD, attention-deficit hyperactivity disorder; CY, calendar year; ICD-10-CM, *International Classification of Diseases, Tenth Revision, Clinical Modification*; MDD, major depressive disorder; PTSD, posttraumatic stress disorder; SD, standard deviation; SGA, second-generation antipsychotic.

half of the subjects in this study received glucose testing each CY, it is indeed achievable to raise lipid testing rates, and thus combined testing rates. Given the high potential for the cardiometabolic adverse effects of antipsychotics, as well as their negative long-term effects in this vulnerable age group (De Hert et al. 2011; Galling et al. 2016), a 100% screening rate is the desirable target.

Glucose testing was most common, which is consistent with findings from previous studies (Morrato et al. 2010; Edelsohn et al. 2015). Edelsohn et al. (2015) reported glucose testing in 50% of Medicaid youth who were prescribed antipsychotics in 2012, which was considerably higher than the 28% lipid testing rate. Similarly, glucose screening (32%) was higher than lipid testing (13%) in Medicaid youth initiating SGA treatment between 2004 and 2006 (Morrato et al. 2010). Relative to glucose testing, the lower rates of lipid testing may reflect a variety of issues, such as the emphasis on the acute weight gain associated with SGAs and the short-term potential for subsequent T2DM, rather than the long-term effects of elevated lipids. The rates of combined testing in this study are generally consistent with national benchmarks for HEDIS APM measurements (NCQA 2019), which have ranged from 30%–37% in the commercial sector. It should be noted that compared to the HEDIS APM specifications, this study used a different age range and focused solely on the SGA class (NCQA 2019). Our rates of glucose and lipid monitoring in 8–19-year-olds were either higher than or comparable to those reported in other age ranges such as ≤17 years, 6–17 years, and 2–18 years old (Morrato et al. 2010; Raebel et al. 2014; Edelsohn et al. 2015). Age may influence rates of metabolic monitoring (Raebel et al. 2014), with older youth receiving more monitoring. Undoubtedly, the relationship of age and metabolic monitoring rates needs to be further examined.

The intent of recommended metabolic monitoring is to facilitate early detection of changes in metabolic status, thereby allowing for potential modifications to pharmacotherapy to reduce risk of harm to the patient. The importance of such monitoring is paramount to the execution of a successful treatment plan that involves the use of an antipsychotic and that has a favorable benefit-risk profile for the patient. Thus, a comprehensive and collaborative approach is needed. First, we need to improve our understanding of the root causes of the suboptimal metabolic monitoring rates. Specifically, it remains unclear whether clinicians fail to order metabolic blood tests, patients do not complete ordered blood tests, and/or patients and clinicians are unaware of the risks associated with poor monitoring. To be effective, interventions aimed to improve metabolic monitoring will need to account for and target where process breakdown(s) in metabolic monitoring are occurring. Second, developing, testing, and implementing novel strategies to improve metabolic monitoring for patients taking SGA medications are critically needed. As part of an ongoing quality improvement initiative, a partnership with all stakeholders—patients, providers, policymakers, and payers—to develop a targeted, cost-effective, and widely implementable solution is of interest to produce meaningful change in rates of metabolic monitoring. For example, the implementation of required baseline metabolic monitoring for off-label use in children and younger adolescents may be an appropriate utilization management strategy to reinforce the importance of metabolic monitoring to providers and patients (Olin et al. 2019). This, in turn, may improve the safety and tolerability of SGAs, leading to better adherence and fewer exacerbations of psychiatric and behavioral disorders.

Conclusion

Rates of metabolic monitoring associated with SGA use in children and adolescents are suboptimal and must be improved. Understanding barriers to routine metabolic monitoring, particularly of lipids, and the development of interventions designed to enhance monitoring are needed.

Clinical Significance

Routine metabolic monitoring in children and adolescents prescribed SGAs is an important clinical practice that enables timely intervention to minimize risk of metabolic dysregulation and to ensure optimal cardiometabolic and psychiatric outcomes.

Disclosures

J.D.H., L.H., and N.C.P are employees of Humana Healthcare Research, Inc., a wholly owned subsidiary of Humana, Inc.; T.P., M.R., and S.T. are employees of Humana, Inc.; C.C.K., L.R.P.D., J.A.W., and S.C. have no disclosures to report.

C.U.C. has been a consultant and/or an advisor to and has received honoraria from: Alkermes, Allergan, Angelini, Boehringer-Ingelheim, Gerson Lehrman Group, Indivior, IntraCellular Therapies, Janssen/J&J, LB Pharma, Lundbeck, MedAvante-ProPhase, Medscape, Merck, Neurocrine, Noven, Otsuka, Pfizer, Rovi, Servier, Sumitomo Dainippon, Sunovion, Supernus, Takeda, and Teva. He has provided expert testimony for Bristol-Myers Squibb, Janssen, and Otsuka. He served on a Data Safety Monitoring Board for Boehringer-Ingelheim, Lundbeck, Rovi, Supernus, and Teva. He received royalties from UpToDate and grant support from Janssen and Takeda. He is also a shareholder of LB Pharma.

M.P.D. has received grant or research support from National Institute of Mental Health, the National Institute of Diabetes and Digestive and Kidney Diseases, the Patient-Centered Outcomes Research Institute, Janssen, Johnson and Johnson, Supernus, Sunovion, Otsuka, Pfizer, Lundbeck, and Acadia. She has served on the advisory board of Sunovion, Neuronetics, Akili, Supernus, Lundbeck, and Johnson and Johnson. She has served as a consultant to Johnson and Johnson, Neuronetics, and Sunovion. She has received honoraria from American Academy of Child and Adolescent Psychiatry Institute, CMEology, CME institute, Medscape, Sunovion, and Otsuka for presentations.

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