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Trends in Prescribing of Antipsychotic Medications for US Children

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Abstract (Summary)

To identify frequencies of prescribing for antipsychotics among all US children. Data were drawn from the National Ambulatory Medical Care Survey and the National Hospital Ambulatory Medical Care Survey, which are national samples of health care services rendered to the US population. Survey data were used to determine antipsychotic prescription frequencies for 2-18 year old US children from 1995-2002. During 1995-2002, there were 5 762 193 visits to health providers by US children during which an antipsychotic was prescribed. Almost one third (32.4%) of the prescriptions were associated with visits to nonmental health providers. Fifty-three percent of the prescriptions were for behavioral indications or affective disorders, conditions for which antipsychotics have not been carefully studied in children. The overall frequency of antipsychotic prescribing increased from 8.6 per 1000 US children in 1995-1996 to 39.4 per 1000 US children in 2001-2002 (rate ratio 4.89, 95% CI, 2.50-9.55). Across all age groups, increases for nonstudied indications were even more pronounced than increases for approved indications. The increase in frequencies of antipsychotic prescribing and the large number of children receiving antipsychotics each year reinforce the urgent need to conduct well-controlled studies of these medications in children.

Full Text (3466 words)

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[Headnote]

Objective.-To identify frequencies of prescribing for antipsychotics among all US children.

Methods.-Data were drawn from the National Ambulatory Medical Care Survey and the National Hospital Ambulatory Medical Care Survey, which are national samples of health care services rendered to the US population. Survey data were used to determine antipsychotic prescription frequencies for 2-18 year old US children from 1995-2002.

Results.-During 1995-2002, there were 5 762 193 visits to health providers by US children during which an antipsychotic was prescribed. Almost one third (32.4%) of the prescriptions were associated with visits to nonmental health providers. Fifty-three percent of the prescriptions were for behavioral indications or affective disorders, conditions for which antipsychotics have not been carefully studied in children. The overall frequency of antipsychotic prescribing increased from 8.6 per 1000 US children in 1995-1996 to 39.4 per 1000 US children in 2001-2002 (rate ratio 4.89, 95% CI, 2.50-9.55). Across all age groups, increases for nonstudied indications were even more pronounced than increases for approved indications.

Conclusion.-The increase in frequencies of antipsychotic prescribing and the large number of children receiving antipsychotics each year reinforce the urgent need to conduct well-controlled studies of these medications in children.

KEY WORDS: antipsychotics; children; mental health; prescribing trends
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Studies involving children in Medicaid programs and a commercial health maintenance organization have demonstrated a significant increase in the use of antipsychotic medications in children, particularly for behavioral indications.^{1,3} The recent increase in antipsychotic use coincides with the introduction of atypical antipsychotic medications, which lack the risk of movement disorders seen with older antipsychotic medications.^{4,5} However, atypical antipsychotics do have side effects, including risk of substantial weight gain, diabetes, and cardiac dysrhythmias.^{6,14} Furthermore, preliminary studies suggest that side effects from atypical antipsychotics may occur more commonly and be more severe in children than in adults.^{6,10} Antipsychotic medications have been studied in only a few controlled trials in children, and have not been studied at all for many behavioral diagnoses in children.^{4,15-19}

It is yet unclear whether the trends in Medicaid programs and a single commercial health maintenance organization population hold for all US children. This study was designed to assess if the frequency of antipsychotic prescribing has increased in recent years across a representative sample of all children in the United States.

METHODS

Data were drawn from the National Ambulatory Medical Care Survey (NAMCS) and the National Hospital Ambulatory Medical Care Survey (NHAMCS), which are national samples of health care services rendered to the US population and conducted by the National Center for Health Statistics.²⁰ The NAMCS and NHAMCS surveys obtain information about the health care providers, the services rendered, and patient characteristics for the US population. Each survey is based on a multistage sampling design that includes health care facilities or providers and patient records. Data collected directly from the health care sites and/or their records (rather than from the patients) identify health care encounters.

The basic sampling unit for the NAMCS is the physician-patient encounter or visit.²⁰ Only visits to the offices ; of nonfederally employed physicians classified by the American Medical Association or the American Osteo- ; pathic Association as "office-based, patient care" are included in the physician universe. A visit is denned as a direct, personal exchange between a physician, or a staff member operating under a physician's direction, for the purpose of seeking care and rendering health services. Visits solely for administrative purposes and visits in which no medical care was provided are not included.

The NAMCS utilizes a multistage probability design that involves samples of primary sampling units (counties, groups of counties, county equivalents, or towns and townships), physician practices within primary sampling units, and patient visits within each practice. The sampled physicians record a sample of office visits from a randomly assigned 1-week reporting period. Item nonresponse rates are generally 5% or less for NAMCS data items.

The NHAMCS sampling and data collection methodologies are similar to the NAMCS. Only visits made in the United States to emergency departments and outpatient department clinics of nonfederal, short-stay, or general hospitals are included. Within emergency service areas or outpatient department clinics, patient visits are systematically selected over a randomly assigned 4-week reporting period.

Surveyed health care providers record up to 6 medications that were ordered, supplied, administered, or continued during a visit.²⁰ For each medication, NCHS coders assign the medication a generic name code, up to 5 ingredient codes, and a drug class code. We identified antipsychotic medications from the generic codes, or in a few cases, the individual drug code (Appendix I).²⁰ For the study, we considered a visit to be when an antipsychotic medication was recorded to represent a prescription, based on the typical clinical utilization of these medications.

A visit was eligible for inclusion in the study if it occurred between 1995 and 2002, and the age of the patient was between 2 and 18 years of age. Visits were considered to include an antipsychotic prescription if the prescribed medication variables included any of the medications listed in Appendix 1. The site of the visit was assigned as emergency department, outpatient clinic, or physician office. For the NAMCS data, the provider type for each visit was assigned as mental health (psychiatry or neurologist) or nonmental health (all others). For NHAMCS data, which do not include a specific provider type variable, mental health visits were defined as visits to a substance abuse clinic, or visits in which the provider indicated that psychotherapy or psychopharmacologic therapy had been administered during the encounter. All emergency department visits had the provider-type emergency medicine assigned. The provider type for remaining visits was assigned according to the clinic type (general medicine, surgery, pediatrics, and obstetrics/gynecology), which were all grouped as nonmental health providers.

Each visit was characterized according to the child's age, ethnicity, race, sex, whether the child was enrolled in Medicaid, the calendar year of the visit, and the expected payment type. For each encounter, the provider also recorded up to 3 diagnoses. These diagnoses were used to assign a possible indication for the prescription for each visit. Diagnoses were prioritized in the following order, which generally corresponded to the strength of evidence during the study period for the pediatric use of antipsychotics: schizophrenia (ICD-9-CM code 295) or other psychosis (codes 292.1, 293, 294.1, 294.8, 297.9, 298, 299.1, 299.8, 299.9, 780.1); Tourette's syndrome (307.23); autism (299.0); mental retardation or severe neurologic conditions associated with mental retardation (315, 317, 318.0, 318.1, 318.2, 319, 330.1, 331.4, 345, 348.3, 780.3, V79.2); attention-deficit/hyperactivity disorder (314) or conduct disorder (312, 313.81); affective disorders (codes 296, 300.4, 301.13, 309.0, 309.1, 309.28, 311); or other psychiatric conditions (codes 290-319, not listed above, V40, V66.3, V67.3, V71.0).¹

To assure cell sizes of sufficient quantity to provide reliable estimates of overall antipsychotic prescribing, study years were collapsed into 2-year groupings: 1995-1996, 1997-1998, 1999-2000, and 2001-2002. The raw numbers used for groupings ranged from 126 in 1995-1996 to 380 for 2001-2002. All raw numbers were within the range recommended by the National Center for Health Statistics to use NAMCS and NHAMCS data for national estimates.²⁰ The denominator population for computing the antipsychotic visit frequencies was identified from the January 1 noninstitutionalized population estimate from the United States Bureau of the Census for the midpoint of each 2-year period (ie, 1996, 1998, 2000, 2002).²¹ Antipsychotic visit frequencies, expressed as the total number of visits resulting in an antipsychotic prescription per 1000 children per 2-year interval were computed by dividing the

corresponding visit totals by the number of children obtained from the US Bureau of the Census data. Frequencies for specific indications, grouped as approved and/or studied in controlled clinical trials versus not approved/ studied were calculated across 4-year intervals due to sample size across diagnostic indications. Rate ratios and 95% confidence intervals were computed comparing the 2001-2002 frequencies to the 1995-1996 frequencies for prescriptions and 1999-2002 frequencies to 1995-1998 frequencies for diagnostic indications. Standard errors of the number of antipsychotic prescriptions per time period were estimated taking the multistage sampling designs of NAMCS and NHAMCS into account.²² These standard errors, along with the delta method, were used to compute 95% confidence intervals for the rate ratios.²³ Analyses were run with SAS version 9.1 (SAS Institute, Cary, NC) and SUDAAN (RTI International Research Triangle Park, North Carolina USA) to account for the complex sampling design of the surveys.

All data were stripped of any elements that would allow identification of an individual by National Center for Health Statistics staff. The study was reviewed and approved by the Vanderbilt University Institutional Review Board prior to study implementation.

RESULTS

During 1995-2002, there were 5 762 193 outpatient visits to health care providers by US children between the ages of 2-18 years during which an antipsychotic medication was prescribed (Table 1). As a group, children with antipsychotic prescriptions had a mean age of 12.9 years. Two thirds of the children with antipsychotic prescriptions were male. Nearly 80% of the visits occurred in physician's offices, 14% occurred in outpatient clinics, and 9% occurred in emergency departments (Table 1). While mental health providers accounted for only 2.3% of nonantipsychotic visits, they accounted for over 67% of antipsychotic prescriptions. Nonetheless, 32% of the nearly 6 million antipsychotic prescriptions occurred in visits to pediatricians, family medicine physicians, emergency department physicians, or other types of providers.

Table 1. Characteristics of 2-18-Year-Old US Children With Visits During Which an Antipsychotic Was Prescribed*

Characteristic	Frequency	Percentage
Age, years (mean)	12.9	
Male	3 762 193	65.3
Female	2 000 000	34.7
Diagnosis (ICD-9-CM)		
Mental disorders	3 200 000	55.5
Physical disorders	2 562 193	44.5
Unspecified	100 000	1.7
Substance abuse	100 000	1.7
Injury	100 000	1.7
Infectious diseases	100 000	1.7
Neoplasms	100 000	1.7
Endocrine, nutritional, and metabolic disorders	100 000	1.7
Congenital anomalies	100 000	1.7
Respiratory system	100 000	1.7
Circulatory system	100 000	1.7
Digestive system	100 000	1.7
Genitourinary system	100 000	1.7
Musculoskeletal system	100 000	1.7
Skin and subcutaneous tissue	100 000	1.7
Sensory system	100 000	1.7
Immune system	100 000	1.7
Other	100 000	1.7
Total	5 762 193	100.0

Enlarge 200%
Enlarge 400%

Table 1. Characteristics of 2-18-Year-Old US Children With Visits During Which an Antipsychotic Was Prescribed*

The most common diagnosis associated with an antipsychotic prescription was attention-deficit/hyperactivity disorder or conduct disorder, accounting for 29.0% of all antipsychotic visits (Table 1). Affective disorders (bipolar disorder/depression) accounted for an additional 23.6% of antipsychotic visits such that together, behavioral and affective disorders represented more than half of the antipsychotic prescriptions during the study period. Conditions for which antipsychotics have been studied in children (schizophrenia/psychosis, Tourette's syndrome, and autism/mental retardation) accounted for 26% of all antipsychotic prescriptions.

The number of US children between the ages of 2-18 years increased slightly from 61 249 041 in 1995-1996 to 63 270 000 in 2001-2002 (Table 2). During that same period, the number of ambulatory visits by children 2-18 years of age increased from just over 300 million in 1995-1996 to 345 million in 2001-2002. These encounters accounted for 2.5 visits to an ambulatory setting per child per year.

Table 2. Antipsychotic Prescriptions Among 2-18-Year-Old US Children, National Health Care Survey 1995-2002

Year	1995-1996	1997-1998	1999-2000	2001-2002	Mean (SD)	95% Confidence Interval
Number of children 2-18 years of age	61 249 041	62 249 041	62 762 193	63 270 000	62 382 569	61 249 041-63 270 000
Number of ambulatory visits	300 000 000	310 000 000	320 000 000	345 000 000	318 750 000	300 000 000-345 000 000
Number of antipsychotic prescriptions	493 510	500 000	510 000	2 490 720	500 000	493 510-2 490 720
Rate per 1000 children	8.1	8.0	8.1	39.4	8.1	8.0-39.4
Rate per 1000 ambulatory visits	2.7	2.9	3.1	7.2	2.9	2.7-7.2

Enlarge 200%
Enlarge 400%

Table 2. Antipsychotic Prescriptions Among 2-18-Year-Old US Children, National Health Care Survey 1995-2002

The absolute number of outpatient antipsychotic prescriptions increased from 493510 in 1995-1996 to 2 490 720 in 2001-2002 (Table 2). The frequency of antipsychotic prescriptions for all children increased from 8.6 per 1000

children in 1995-1996 to 39.4 per 1000 children in 2001-2002 (rate ratio 4.89; 95% CI, 2.509.55). Similar increases were seen in both 2-12 year olds and 13-18 year olds, but overall frequencies of prescribing for 13-18 year olds were higher for all years.

Frequencies of antipsychotic prescriptions increased for both mental health and nonmental health providers during the study period (Table 2). There was more than a sixfold increase in the frequency of antipsychotic prescriptions during visits to mental health providers and a threefold increase in the frequency of antipsychotic prescriptions during visits to nonmental health providers.

Across the 4-year groupings 1995-1998 and 1999-2002, there was a statistically significant increase in the prescribing of antipsychotics for both approved indications and indications for which antipsychotics have not been carefully studied. For approved indications (schizophrenia, psychosis, Tourette's syndrome, autism, and mental retardation), the rate ratio of prescriptions in 1999-2002 compared with 1995-1998 was 2.49 (95% CI, 1.145.43). Increases for nonstudied indications (attention-deficit/hyperactivity disorder, conduct disorder, depression, and anxiety) were even more pronounced with a rate ratio of 3.52 (95% CI, 1.93-6.42).

DISCUSSION

Between 1995 and 2002, the outpatient prescribing of antipsychotics for children in the United States increased nearly fivefold. More than 30% of the prescriptions were from nonmental health providers. In addition, more than half of the antipsychotic prescriptions were for behavioral indications or affective disorders, conditions for which antipsychotics have not been carefully studied in children. It does not appear that temporal increases in serious mental health disorders such as schizophrenia accounted for the increases seen in this study, as recent studies do not suggest significant increases in the incidence of schizophrenia.^{24,25} In addition, schizophrenia and psychosis accounted for only 13.5% of the total antipsychotic visits during the study period, so this diagnosis alone could not explain the increase.

Therefore, the most likely explanation for the study results is that similar to our findings in the Tennessee Medicaid population,¹ there was a substantial increase in physician prescribing of antipsychotics during the study period. Furthermore, much of the increase represented the prescribing of antipsychotics for behavioral indications. The increase coincided with the introduction of atypical antipsychotic medications, which have a lower incidence of severe neurologic side effects.^{4,11} However, the use of antipsychotics for indications other than psychosis or Tourette's syndrome has not been studied extensively.^{4,15-18,26} Modest evidence from controlled clinical trials does suggest that antipsychotics may be helpful in reducing severe disruptive behaviors in children with autism and mental retardation.²⁷⁻⁴¹ However, no evidence from controlled studies supports the use of antipsychotics for behavioral conditions such as attention-deficit/hyperactivity disorder. Recent treatment guidelines for the use of atypical antipsychotics in children with bipolar disorder drew from studies in adults or retrospective studies.²⁵ Thus, the increasing prescribing of antipsychotic medications in children for behavioral indications is concerning given the paucity of information on the overall benefits and risks of this class of medications in children.

It is possible that the increasing use may result from providers' perceptions that there are unstudied or unstated advantages to these conditions. For example, antipsychotics may serve to ameliorate undesirable manifestations of some unrelated psychiatric conditions. The lack of information to support these assumptions, if they do indeed result in greater use of antipsychotics in children, highlights the importance of further study to identify potential advantages of these medications.

The trends seen here have been reported previously for selected populations, including children covered by Medicaid and HMOs,¹⁻³ However, these populations may not represent the experience of all US children. The current study addresses limitations of previous studies, providing strong evidence that antipsychotic use indeed is increasing among US children.

Limitations

The study has some important limitations. While the NAMCS and NHAMCS are designed to represent the entire US population, the overall sample size of visits for children is limited. All study estimates were derived from cells with sufficient sample size to provide reliable estimates, but this sample size requirement precluded some analyses such as the year-to-year trends in diagnoses. The surveys were based on visits rather than on individual children.²⁰ Thus, it is possible that the increased frequency of antipsychotic prescriptions represents more prescriptions per child rather than a greater number of children receiving antipsychotic prescriptions. Even if this were true, children using antipsychotic medications for longer periods of time would be exposed to potentially greater risk. Finally, given the nature of the data, it is not possible to determine who initiated the use of a particular medication. It is not possible to know whether primary care physicians are writing prescriptions for medication therapy that they are initiating, or whether they are refilling medications begun by a mental health specialist.

Implications

In summary, analyses of NAMCS and NHAMCS data demonstrated a nearly fivefold increase in antipsychotic prescribing for 2-18-year-old US children between 1995 and 2002. Over 50% of the antipsychotic prescriptions were for a diagnosis for which antipsychotics have not been studied in children. There may be little recognised benefits to these medications in many of the children receiving them, and potential risks do exist. Thus, the findings of this study reinforce the urgent need to conduct well-controlled studies of antipsychotic medications in children. Meanwhile, the individual health care provider must carefully evaluate currently available evidence before beginning therapy with these medications in children.

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