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Trends in the Prescribing of Psychotropic Medications to Preschoolers

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Abstract
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Abstract

Context: Recent reports on the use of psychotropic medications for preschool-aged children with behavioral and emotional disorders warrant further examination of trends in the type and extent of drug therapy and sociodemographic correlates.

Outline

Graphics

Objectives: To determine the prevalence of psychotropic medication use in preschool-aged youths and to show utilization trends across a 5-year span.

Design: Ambulatory care prescription records from 2 state Medicaid programs and a salaried group-model health maintenance organization (HMO) were used to perform a population-based analysis of three 1-year cross-sectional data sets (for the years 1991, 1993, and 1995).

Setting and Participants: From 1991 to 1995, the number of enrollees aged 2 through 4 years in a Midwestern state Medicaid (MWM) program ranged from 146,369 to 158,060; in a mid-Atlantic state Medicaid (MAM) program, from 34,842 to 54,237; and in an HMO setting in the Northwest, from 19,107 to 19,322.

Main Outcome Measures: Total, age-specific, and gender-specific utilization prevalences per 1000 enrollees for 3 major psychotropic drug classes (stimulants, antidepressants, and neuroleptics) and 2 leading psychotherapeutic medications (methylphenidate and clonidine); rates of increased use of these drugs from 1991 to 1995, compared across the 3 sites.

Results: The 1995 rank order of total prevalence in preschoolers (per 1000) in the MWM program was: stimulants (12.3), 90% of which represents methylphenidate (11.1); antidepressants (3.2); clonidine (2.3); and neuroleptics (0.9). A similar rank order was observed for the MAM program, while the HMO had nearly 3 times more clonidine than antidepressant use (1.9 vs 0.7). Sizable increases in prevalence were noted between 1991 and 1995 across the 3 sites for clonidine, stimulants, and antidepressants, while neuroleptic use increased only slightly. Methylphenidate prevalence in 2 through 4-year-olds increased at each site: MWM, 3-fold; MAM, 1.7-fold; and HMO, 3.1-fold. Decreases occurred in the relative proportions of previously dominant psychotherapeutic agents in the stimulant and antidepressant classes, while increases occurred for newer, less established agents.

Conclusions: In all 3 data sources, psychotropic medications prescribed for preschoolers increased dramatically between 1991 and 1995. The predominance of medications with off-label (unlabeled) indications calls for prospective community-based, multidimensional outcome studies.

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The prevalence of psychotropic medication treatment for children and adolescents with emotional and behavioral disorders has significantly increased in the United States during the last few decades, particularly in the last 15 years. Specifically, the 5 through 14-year-old age group has experienced a great increase in stimulant treatment for attention-deficit/hyperactivity disorder (ADHD), and the 15 through 19-year-old age group has had sizable increases in the use of antidepressant medications. 1-2

Approved and unapproved indications for psychotropic medications in young children are not extensive. These include: short-term use of analgesics and sedatives/hypnotics for pain relief; hydroxyzine for situational anxiety associated with medical, presurgical, and dental procedures; tricyclic antidepressants for nocturnal enuresis (6-year-olds and older); and amphetamines for ADHD in those 3 years old and older. 3 Accordingly, the prevalence of psychotropic medication treatment for children younger than 5 years old has not received much professional attention until recently. 4-6

Concern about this age group relates to off-label (unlabeled) use, ie, for treatment indications with little or no proven efficacy and lacking product package insert labeling information approved by the US Food and Drug Administration (FDA). 7 One psychiatric newsletter, citing FDA-compiled marketing data, reported that 3000 prescriptions for fluoxetine hydrochloride were written for children aged younger than 1 year in 1994. 8 In a 1998 professional meeting report, 5 pediatric researchers noted that 57% of 223 Michigan Medicaid enrollees aged younger than 4 years with a diagnosis of ADHD received at least 1 psychotropic medication to treat this condition during a 15-month period in 1995-1996. Of the treatments, methylphenidate and clonidine were prescribed most often.

Although the use of psychotropic medication in preschool-aged children compared with older youths is relatively small, the reports cited argue for additional assessment to more systematically estimate its use. Consequently, 3 large, computerized data sources were used to estimate total, age-specific, and gender-specific psychotropic medication prevalence for 2 through 4-year-olds; to compare prevalence in the youngest age group with that in older children and adolescents; and to show utilization trends in the 5-year span from 1991-1995.

METHODS

Data Sources

Three large data sets were assembled from 2 types of health care systems. The first 2 are outpatient data sets from 2 geographically distinct Medicaid populations, 1 in a Midwestern state and 1 in a mid-Atlantic state. The third set of data comes from a group-model health maintenance organization (HMO) serving a predominantly employed population in the northwest region of the United States. The total enrollments for those younger than age 20 years in 1991 and 1995, respectively, are as follows: Midwestern Medicaid (MWM), 669,164 and 687,722; mid-Atlantic Medicaid (MAM), 165,502 and 248,466; and group-model HMO (HMO), 131,038 and 131,860. These populations included both continuous and noncontinuous enrollees for each study year. The Medicaid youth populations were almost entirely eligible under Aid to Families with Dependent Children, and a small proportion qualified because of disability status (Supplemental Security Income) or foster care status. Nonwhites were overrepresented in the Medicaid populations and were underrepresented among HMO enrollees according to general statistical profiles of the settings. 9

Study Measures

Psychotropic medication prevalence was defined for each study year as the frequency of persons with 1 or more HMO pharmacy records or Medicaid prescription claims for a psychotropic medication class, subclass, or specific medication per 1000 enrolled youths. Time trends were assessed across the 5-year span with data from 3 cross-sectional annual analyses (1991, 1993, and 1995).

For age-specific prevalence, children were grouped into 4 age strata (aged 2-4, 5-9, 10-14, and 15-19 years) according to US census categories. Data analyses focused on children aged 2 through 4 years. We were unable to investigate psychotropic medication use in infants 1 year old or younger in the 2 Medicaid populations because year of birth is recorded in a 2-digit field. Thus, "95" could refer to someone born in 1895 or 1995. We were unable, therefore, to distinguish those 1 year old and younger from 100- and 101-year-olds. We do present data on methylphenidate use in infants 1 year old or younger from the HMO program, as 4-digit years of birth were available. From 1991-1995, the number of enrollees aged 2 through 4 years ranged from 146,369 to 158,060 in the MWM program; from 34,842 to 54,237 in the MAM program, and from 19,107 to 19,322 in the HMO.

A separate analysis was performed to examine medication use among preschool-aged children by year of age. Gender-specific prevalence provided separate prevalence rates for boys and for girls.

Psychotropic Medications

Three psychotropic medication classes were examined: stimulants (methylphenidate, other stimulants), antidepressants (selective serotonin reuptake inhibitors [SSRIs], tricyclic antidepressants [TCAs], and other antidepressants), and neuroleptics. Selection was based on the frequent use of stimulants and antidepressants and the public health significance of the use of neuroleptics in the very young. In addition, 2 specific medications (methylphenidate and clonidine) were examined because their use alone or as a combined treatment has increased substantially since the early 1990s. All the drugs were identified using a data dictionary encompassing the national drug codes for each of the 3 study years. The study was given an exempt classification by the institutional review board-expedited review.

RESULTS

Total Psychotropic Medication Prevalence

The rank order of psychotropic medication prevalence in 1995 for the MWM program shows that, per 1000 enrollees, stimulants (12.3) were the leading treatment among those 2 through 4 years old, followed by antidepressants (3.2), clonidine (2.3), and neuroleptics (0.9) (Table 1). Within classes, methylphenidate prevalence (11.1 per 1000 enrollees) represented 90% of the stimulant treatment, while TCA prevalence (2.4 per 1000 enrollees) led the antidepressant class. A similar ranking of medication prevalence in 1995 was observed for the MAM program, while preschool-aged children in the HMO had nearly 3 times more clonidine use than antidepressant use (Table 1).

Table. Annual Prevalence Rate per 1000 2 Through 4-Year-Old Children for Selected Psychotropic Medications in 3 Health Care Sites (1991, 1993, 1995)*

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Pronounced differences in psychotropic prevalence across the 3 sites are apparent from Table 1. Stimulant and antidepressant use in 1995 was considerably less among preschoolers in the MAM program and HMO than among those in the MWM program. Enrollees in the MWM program and in the HMO led in the use of clonidine, whereas its use in the MAM program was one-half to two-thirds that of the other sites. Neuroleptic use per 1000 enrollees in either Medicaid program (0.9 in the MWM program, and 0.5 in the MAM program) was more common than in the HMO (0.2).

Time Trends in Psychotropic Medication Prevalence Across a 5-Year Span

The rate of psychotropic medication prescribed for preschoolers in the MWM program increased substantially from 1991-1995. The increase was greatest for clonidine (28.2-fold), stimulants (3.0-fold), and antidepressants (2.2-fold). By contrast, neuroleptic use did not increase substantially during this time. Comparisons of psychotropic medication between sites showed that trends were similar in all 3 sites, with minor deviations for neuroleptics and antidepressants in the population enrolled in the HMO (Table 1). Specifically, the methylphenidate prevalence increase by site was: MWM, 3-fold; MAM, 1.7-fold; and HMO, 3.1-fold. Increases were more dramatic when the base prevalence was low. For example, methylphenidate use in the HMO was the lowest of the 3 sites, but its rise from 1.3 per 1000 enrollees in 1991 to 4.0 per 1000 in 1995 represented the largest methylphenidate increase (3.1-fold) across the 3 sites (Table 1).

Age-Specific Methylphenidate Medication Prevalence

Methylphenidate use according to age group in children and adolescents in the MWM program was most prominent for those aged 5 through 14 years (Figure 1). By comparison, children 2 through 4 years old were treated at approximately one tenth the rate of their 5 through 14-year-old counterparts. The time trend analysis revealed that those in all 4 age groups experienced increases in the use of methylphenidate during the 5-year period. The largest

methylphenidate increase (311%) was among 15 through 19-year-olds, whereas the 2 through 4-year-olds, like the 5-through 14-year-olds, had a smaller but still substantial increase (169% to 176%). The increase in prevalence within the preschool-aged group was greater for older children in the MWM program (from 6.9 to 20.8 per 1000 4-year-olds vs 1.1 to 3.5 per 1000 2-year-olds). The age-specific trends by year of age for those in the MAM program and HMO were consistent with those in the MWM program (Figure 1). There was no methylphenidate use in infants 1 year old or younger in the HMO population.

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Figure 1. Methylphenidate Prevalence per 1000 Enrollees Across a 5-Year Span (1991-1995)Trends in age-specific methylphenidate prevalence per 1000 enrollees by age for the Midwestern state Medicaid population. Left, Enrollees aged 2 through 19 years. Right, Enrollees aged 2 through 4 years.

Gender-Specific Methylphenidate Medication Prevalence

There was a greater proportional increase in preschool-aged girls receiving methylphenidate from 1991 through 1995; in the HMO, the male-to-female ratio decreased from 7:1 to 4:1 during this time. A similar but less dramatic trend was evident in the MAM program (4:1 in 1991 to 3:1 in 1995). By contrast, the gender ratio for methylphenidate treatment in the MWM program was stable over these years (3:1 in 1991 and in 1995).

Changes in Drug Utilization and Off-Label Use

Changes in the use of older agents with a well-established efficacy profile were observed. For example, despite a general increase in total stimulant use, methylphenidate use in the MAM program decreased proportionally by 7% from 1991 to 1995, while the use of other stimulant medications rose from 15% to 27% of total stimulant use among preschoolers. In all 3 sites, TCAs were the mainstay of the antidepressant category in 1991, and their prevalence remained relatively stable through 1995. By contrast, the use of SSRI antidepressants increased dramatically at the Medicaid sites, although by 1995 these drugs comprised only a small proportion of antidepressants used in the HMO (Figure 2). Thus, antidepressant use increased, particularly through off-label use, in the preschool-aged group.

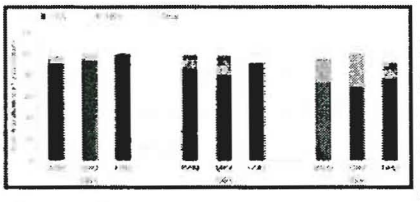

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Figure 2. Distribution of Antidepressant Subclasses Among Preschoolers in 3 Health Care Sites in 1991, 1993, and 1995Trends in the percent distribution of antidepressant subclasses among preschoolers in 3 health care sites. MWM indicates a Midwestern state Medicaid program; MAM, a mid-Atlantic state Medicaid program; HMO, health maintenance organization; TCA, tricyclic antidepressant; and SSRI, selective serotonin reuptake inhibitor. The proportions exceed 100% because more than 1 class may have been used in the same individual.

COMMENT

Several prominent trends characterized the use of psychotropic medications in preschoolers during the early to mid 1990s. Overall, there were large increases for all study medications (except the neuroleptics) and considerable variation according to gender, age, geographic region, and health care system. These findings are remarkable in light of the limited knowledge base that underlies psychotropic medication use in very young children. 10 Controlled clinical studies to evaluate the efficacy and safety of psychotropic medications for preschoolers are rare. 3 Efficacy data are essentially lacking for clonidine and the SSRIs and methylphenidate's adverse effects for preschool children are more pronounced

than for older youths. 11 Consequently, the vast majority of psychotropic medications prescribed for preschoolers are being used off-label. 7 Specific study findings are discussed below according to 3 major outcomes: prevalence findings for specific medications; age- and gender-specific data; and geographic and health care system variations.

Prevalence Findings

Stimulant treatment in preschoolers increased approximately 3-fold during the early 1990s. The prominence of stimulant and clonidine use is consistent with Michigan Medicaid use patterns for children younger than 4 years with an ADHD diagnosis. 5 The data show greater US methylphenidate prevalence for children younger than age 5 years than was reported in a prevalence study in Western Australia (0.26% to 0.64% vs approximately 0.1%). 12 Hypothesized reasons for the overall increased stimulant use include: (1) a larger pool of eligible youths because of expanded diagnostic criteria for ADHD since 1980 13; (2) more girls being treated for ADHD as evidenced by the narrowing of the gender ratio even among preschoolers; (3) greater acceptance of biological treatments for a behavioral disorder; and (4) the expanded role of school and preschool health personnel in identifying medical needs. 14

Methylphenidate accounted for the vast majority of stimulant use (eg, 90% of the 1995 stimulant use in the MWM program). There was a modest but consistent decrease in the proportion of methylphenidate use relative to other stimulants across the 3 time periods. Generalizing from the efficacy and adverse effect experience of stimulants in older youths to preschoolers is often not valid, 11 at least partly because of preschoolers' developmental immaturity.

Clonidine had the most dramatic increases, although its use in 1995 was only 15% to 35% of the prevalence rate of stimulants. Clonidine use is particularly notable because its increased prescribing is occurring without the benefit of rigorous data to support it as a safe and effective treatment for attentional disorders. Cardiovascular adverse effects including bradycardia, atrioventricular block, and syncope with exercise have been reported in children treated with clonidine in combination with other medications for the treatment of ADHD and its comorbidities. 15-16 Problems with abrupt withdrawal producing noradrenergic overdrive have been reported. Its use to combat the insomnia associated either with ADHD itself or secondary to the stimulant treatment of ADHD is new and largely uncharted, 17-18 and its increased use for ADHD since 1991 helps explain the increased clonidine poisonings in children taking either their own medications or that of siblings. 19-20

The combined use of clonidine and methylphenidate has been associated with questions of safety 16, 21 and has been debated. 22 Unfortunately, the present data do not distinguish single vs concomitant medication use, information vital to understanding how these agents are being used in children. Such an analysis is better undertaken in a continuously enrolled cohort so that censored data do not create artifactual findings. We are currently conducting a continuously enrolled retrospective cohort study.

Antidepressants were the second most commonly prescribed psychotropic class of drugs for preschoolers, and their use increased substantially from 1991-1995. Tricyclic antidepressants still represent the bulk of early childhood antidepressant use, although the growth in use of SSRIs was strong in those enrolled in both Medicaid programs but very modest in those in the HMO. The proportional decrease in use of TCAs was largely explained by the recent increase in use of SSRIs, a trend we have previously shown for older youths 2 and one that has been documented in adults. 23 The use of TCAs for enuresis is common among 5 through 13-year-olds, 24 but its use in the preschool group is puzzling. It is also likely that some use of imipramine and desipramine was related to the treatment of ADHD in preschoolers. 25

Neuroleptic use was infrequent and relatively stable across the study period. The neuroleptic prevalence rate in this preschool data showed rates one-tenth to one-half the annual prevalence among 5 through 19-year-olds in Rome from 1986 through 1991. 26 Both the neuroleptic and antidepressant findings bring new information on population-based prevalence and provide some benchmarks to chart the use of these agents in ambulatory settings. Additional clinical interpretation, however, awaits prospective outcome studies.

Age- and Gender-Specific Prevalence Findings

Preschoolers' use of methylphenidate showed increases similar to those of 5 through 14-year-olds, suggesting that

the expanded use of this medication for attentional disorders in US youths extends even to the very young. It is notable that the largest gains in use occurred among high school-aged students (15 through 19-year-olds), a trend that has been documented from county school survey data. 13

Geographic and Health Care System Variations

Disparities in psychotropic medication prevalence data between the 2 state Medicaid program populations are provocative and suggest numerous hypotheses. These include differences between the states in (1) policies for eligibility or access to continuing care; (2) the proportion of individuals with emotional or mental disorders that may be related to the proportion of youths receiving Supplemental Security Income and foster care in each state; (3) preschool health assessment and referral programs; (4) physician specialty training, particularly among psychiatrists and primary care providers, with resultant referral or practice differences; (5) the cultural values that underlie families' decisions to accept or reject medication for behavioral or mental disorders; and (6) racial/ethnic population differences that may affect cultural orientations and beliefs. Also notable is the finding that the HMO prevalence rates, collectively, were substantially lower than those of the Medicaid programs. In this instance, geography and clinical population factors confound the prevalence findings related to HMO vs Medicaid systems. The presence of less severely disabled youths in the HMO population is likely to explain a large part of the differences, but geographic and patient cultural factors need to be considered as well. Also, the rapid expansion of Supplemental Security Income benefits since 1990 resulted in more youths with ADHD being eligible for Medicaid coverage than in previous years. 27

Limitations

The study is limited in several ways. First, the findings may be generalizable to comparable Medicaid programs and to group-model HMO enrollees, but the extent to which they may apply to other treatment settings is unknown. Second, the cross-sectional nature of the data from the 3 study years do not permit a follow-up of the natural course of treatment. Until a continuously enrolled cohort is assembled, descriptive data on the natural course of treatment and prescription changes over time cannot be adequately assessed. However, noncontinuously enrolled individuals make up the bulk of the Medicaid membership. Thus, capturing these annual data snapshots of both noncontinuous and continuous enrollees is useful for clinical description. Third, no diagnostic codes were linked to the medications in this analysis, thus limiting information about why certain medications were selected. Fourth, computerized data sources use a limited number of variables to describe the clinical patterns in the usual practice settings. However, they have the advantage of describing the usual practice setting without the artificiality and the interference that prospective studies impose on physicians' decisions about medication and patients' decisions about treatment. Compared with data from specialty clinic samples, data from community treatment settings provide a far more accurate assessment of medication practices, therapy variations, and treatment. Adding outcome assessments would allow the effectiveness of the treatments to be evaluated.

Clinical Research Recommendations

Because children's responses to medications are not necessarily similar to those of adults, systematic and careful outcome research specifically needs to be done for them. 7 Two types of studies would help provide more systematic information on psychotropic drug therapy in children. First, epidemiologic (naturalistic) studies could describe youth treatment in major medical settings (eg, traditional preferred provider organizations, Medicaid, salaried medical group-model HMOs, and other managed care organizations) to document types of treatments, diagnosis, severity, and time in treatment and to evaluate clinical outcomes. Outcome measures could include symptom control; social, day care, and preschool functioning; parent satisfaction; reasons for initiation and discontinuation; and adverse drug events. 28 Second, randomized, double-blind, controlled clinical trials are needed for off-label indications to evaluate dosages, efficacy, and safety of single and multiple agents shown to be commonly used or widely recommended. For disorders that occur very infrequently or questionable combinations of drug therapy with unknown risks, a case registry approach may be useful.

Future studies using large databases for clinical descriptive information should require that the year of birth be stored as a 4-digit number to avoid misclassification of elders as youths. Finally, youths in Medicaid programs should be subdivided by type of eligibility (eg, low income [formerly Aid to Families with Dependent Children, now called

Temporary Assistance for Needy Families], Supplemental Security Income, or foster care) so that the total treatment prevalence, which includes children with known disabilities and major social stressors, will not be unfairly compared with that of less impaired youths in non-Medicaid populations. 27

Unresolved questions involve the long-term safety of psychotropic medications, particularly in light of earlier ages of initiation and longer durations of treatment. While it is reassuring that anecdotal reports have rarely documented these problems, the possibility of adverse effects on the developing brain cannot be ruled out. 29 Active surveillance mechanisms for ascertaining subtle changes that the developing personality may undergo as a result of a psychotropic drug's impact on brain neurotransmitters should be developed.

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