

Trends in the Prescribing of Psychotropic Medications to Preschoolers

Original Contribution

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FROM 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.

Objectives:

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

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 [**RITALIN**] and clonidine [**CATAPRES**]); 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 [**RITALIN**] (11.1); antidepressants (3.2); clonidine [**CATAPRES**] (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 [**CATAPRES**] than antidepressant use (1.9 vs 0.7). Sizable increases in prevalence were noted between 1991 and 1995 across the 3 sites for clonidine [**CATAPRES**], stimulants, and antidepressants, while neuroleptic use increased only slightly.

Methylphenidate [**RITALIN**] prevalence in 2 through 4-year-olds increased at each site: MWM, 3-fold; MAM, 1.7-fold; and HMO, 3.1-fold.

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.

THESE AUTHORS ALSO NOTE:

"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."

"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."

The prevalence of psychotropic medication treatment for children younger than 5 years old has not received much professional attention.

The concern for children younger than 5 years old is because of the off-label (unlabeled) use of these medications. Off-label use means use for "treatment indications with little or no proven efficacy."

A psychiatric newsletter reported that 3000 prescriptions for fluoxetine hydrochloride [**Prozac**] were written for children aged younger than 1 year in 1994.

In 1998 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. Treatment with methylphenidate [**RITALIN**] and clonidine [**CATAPRES**] were most common.

In this article, the authors used 3 large, computerized data sources to estimate total, age-specific, and gender-specific psychotropic medication prevalence for 2 through 4-year-olds; and to show utilization trends in the 5-year span from 1991-1995.

METHODS

Psychotropic medication prevalence trends were assessed for age-specific prevalence. Children were grouped into 4 age strata: 2-4, 5-9, 10-14, and 15-19 years. Data analyses focused on children aged 2 through 4 years.

The authors were unable to investigate psychotropic medication use in infants 1 year old or younger because their computers could not distinguish those 1 year old and younger from 100- and 101-year-olds.

Psychotropic Medications

Three psychotropic medication classes were examined:

- (1) stimulants
(methylphenidate [**RITALIN**], other stimulants)
- (2) antidepressants
(selective serotonin reuptake inhibitors [SSRIs], [**Prozac, Paxil**]
tricyclic antidepressants [TCAs], and other antidepressants)
- (3) neuroleptics

There is frequent use of stimulants and antidepressants and there is public health significance to the use of neuroleptics in the very young.

Two specific medications (methylphenidate [**RITALIN**] and clonidine [**CATAPRES**]) were examined because their use alone or as a combined treatment has increased substantially since the early 1990s.

RESULTS

Total Psychotropic Medication Prevalence

Psychotropic medication prevalence:

Stimulants were the leading treatment among those 2 through 4 years old, followed by antidepressants, clonidine [**CATAPRES**], and neuroleptics.

Methylphenidate [**RITALIN**] prevalence represented 90% of the stimulant treatment.

TCA prevalence led the antidepressant class.

The HMO assessed had nearly 3 times more clonidine [**CATAPRES**] use than antidepressant use.

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 [**CATAPRES**] (28.2-fold), stimulants (3.0-fold), and antidepressants (2.2-fold)."

Age-Specific Methylphenidate [**RITALIN**] Medication Prevalence

Methylphenidate [**RITALIN**] use was most prominent for those aged 5 through 14 years.

"The largest methylphenidate [**RITALIN**] 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%)."

Gender-Specific Methylphenidate [**RITALIN**] Medication Prevalence

"There was a greater proportional increase in preschool-aged girls receiving methylphenidate [**RITALIN**] from 1991 through 1995."

Changes in Drug Utilization and Off-Label Use

"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."

"Antidepressant use increased, particularly through off-label use, in the preschool-aged group."

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)."

"These findings are remarkable in light of the limited knowledge base that underlies psychotropic medication use in very young children."

"Controlled clinical studies to evaluate the efficacy and safety of psychotropic medications for preschoolers are rare."

"Efficacy data are essentially lacking for clonidine [**CATAPRES**] and the SSRIs [**Prozac, Paxil**] and methylphenidate's [**RITALIN**] adverse effects for preschool children are more pronounced than for older youths."

"The vast majority of psychotropic medications prescribed for preschoolers are being used off-label."

Prevalence Findings

"Stimulant treatment in preschoolers increased approximately 3 fold during the early 1990s."

This pattern of increased use is consistent with an ADHD diagnosis.

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.
- (2) more girls being treated for ADHD.
- (3) greater acceptance of biological treatments for a behavioral disorder.

Clonidine [**CATAPRES**] had the most dramatic increases of stimulant use. This 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 [**CATAPRES**] in combination with other medications for the treatment of ADHD and its comorbidities."

Problems with abrupt withdrawal from clonidine [**CATAPRES**] produce noradrenergic overdrive. Clonidine [**CATAPRES**] use to "combat the insomnia associated either with ADHD itself or secondary to the stimulant treatment of ADHD is new and largely uncharted, and its increased use for ADHD since 1991 helps explain the increased clonidine [**CATAPRES**] poisonings in children taking either their own medications or that of siblings."

The combined use of clonidine [**CATAPRES**] and methylphenidate [**RITALIN**] has been associated with questions of safety.

"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.

However, the recent decrease in use of TCAs is largely explained by the recent increase in use of SSRIs [**Prozac, Paxil**] for both older youths and adults.

Age- and Gender-Specific Prevalence Findings

"Preschoolers' use of methylphenidate [**RITALIN**] 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."

"Notable is the finding that the HMO prevalence rates, collectively, were substantially lower than those of the Medicaid programs."

The authors imply that the reason for greater psychotropic medication prevalence in Medicaid program populations as compared to HMO populations is because Medicaid coverage pays for these medications with an ADHD diagnosis. **[This suggests that our government is partly to blame for the problem of increasing psychotropic medication use in our children. Apparently, if the government, we the people, will pay for these drugs, medical doctors will prescribe them.]**

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."

"Unresolved questions involve the long-term safety of psychotropic medications, particularly in light of earlier ages of initiation and longer durations of treatment."

The possibility of adverse effects on the developing brain cannot be ruled out.

Subtle changes to the developing personality may occur as a result of a psychotropic drug's impact on brain neurotransmitters.

THIS ARTICLE WAS FOLLOWED BY THE FOLLOWING EDITORIAL:

Psychotropic Drug Use in Very Young Children

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Joseph T. Coyle, MD

The study by Zito and colleagues in this issue of THE JOURNAL on the use of psychotropic medications in very young children suggests that 1% to 1.5% of all children 2 to 4 years old are receiving stimulants, antidepressants, or antipsychotic medications.

The "prevalence of neuropsychopharmacologic interventions in this age group increased substantially during the last decade."

Several other recent studies "provide additional evidence that the prescription of psychotropic drugs to very young children has increased during the last decade."

One study shows a 3-fold increase in methylphenidate [**RITALIN**] prescriptions in Canada and a 10-fold increase in the prescription of selective serotonin reuptake inhibitors [**Prozac, Paxil**] in the United States for children 5 years old and younger between 1993 and 1997.

"It should be emphasized that most of the drugs prescribed involve off-label use because efficacy of psychotropic drugs has not been demonstrated in very young children."

In fact, methylphenidate [**RITALIN**], the most commonly prescribed drug in these studies, "carries a warning against its use in children younger than 6 years."

"Furthermore, the validity and reliability of the diagnoses of attention-deficit/hyperactivity disorder, mood disorders, and schizophrenia in very young children have not been demonstrated."

This author surveyed the editorial board (48 physicians) of the Journal of Child and Adolescent Psychopharmacology by facsimile about their prescribing of stimulants, clonidine [**CATAPRES**], antidepressants, and antipsychotics for 2- to 4-year-old children. Most responded either no use or very rare prescribing of these medications in this age group, and these are expert clinicians and clinical researchers who are likely to treat the most

difficult cases. **[This suggests that other, less knowledgeable physicians, are way over prescribing these medications.]**

There is virtually no clinical research on the consequences of pharmacologic treatment of behavioral disturbances of very young children.

“Early childhood is a time of tremendous change for the human brain. Visual processing, language, and motor skills are acquired during this sensitive period. The cortical synaptic density reaches its maximum at the age of 3 years and is substantially modified by pruning during the next 7 years. At the same time, the cerebral metabolic rate peaks between 3 and 4 years of age.”

“Studies in experimental animals indicate that the aminergic systems that are the target of action of these psychotropic medications play an important role in neurogenesis, neuron migration, axonal outgrowth, and synaptogenesis.”

“Perinatal treatment of rats with an antipsychotic drug results in a long-standing abnormality in dopamine receptor function and altered levels of dopamine and norepinephrine in adulthood. Thus, it would seem prudent to carry out much more extensive studies to determine the long-term consequences of the use of psychotropic drugs at this early stage of childhood.”

“Given that there is no empirical evidence to support psychotropic drug treatment in very young children and that there are valid concerns that such treatment could have deleterious effects on the developing brain, the reasons for these troubling changes in practice need to be identified.”

“Many state Medicaid programs now provide quite limited reimbursement for the evaluation of behavioral disorders in children and preclude more than 1 type of clinical evaluator per day. Thus, the multidisciplinary clinics of the past that brought together pediatric, psychiatric, behavioral, and family dynamic expertise for difficult cases have largely ceased to exist.”

Consequently, “it appears that behaviorally disturbed children are now increasingly subjected to quick and inexpensive pharmacologic fixes as opposed to informed, multimodal therapy associated with optimal outcomes.”

This “disturbing prescription practices suggest a growing crisis.”

Dan Murphy