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Psychotropic Utilization and Psychiatric Presentation of Hospitalized Very Young Children

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ABSTRACT

Background: **Despite the growth in use of psychotropics in preschoolers, little information is available about the clinical characteristics of very young children who receive psychotropics. No information, specific to young children, is available about the prescribing practices of physicians with the most extensive training in child psychopharmacology, i.e., child psychiatrists.**

Objective: **The aim of this study was to examine the prevalence and nature of psychotropics prescribed by child psychiatrists to very young children with severe functional impairment secondary to psychiatric pathology, and to examine the clinical context in which these psychotropics were prescribed.**

Methods: **The medical charts of 93 children, who were admitted consecutively to a psychiatric unit and who were less than 7 years old, were retrospectively reviewed.**

Results: **The children (mean age, 5.4 ± 1.1 years) had a high rate of exposure to abuse or trauma (64.5%). Functional impairment, as measured on the Clinical Global Assessment Scale (CGAS), was high (mean score, 14.4 ± 6.7). Most children (78.5%) received psychotropics during the admission. Children were prescribed antipsychotics (50.6%), psychostimulants (41.9%), and antidepressants (36.6%). Of those on psychotropics, the majority (68.5%) were on 2 or more psychotropics.**

Conclusions: **This naturalistic, retrospective study suggests that psychotropics are commonly prescribed to very young children with extremely severe psychopathology and who are in need of inpatient care. Clinical safety and efficacy trials of these agents in very young children are needed.**

INTRODUCTION

Recent studies have reported an increase in the use of psychotropics in preschoolers (Rappley et al. 1999; Zito et al. 2000). Moreover, concerns have been expressed in the professional literature and media about this growth because of the paucity of short-term and long-term efficacy, safety, and tolerability data of these agents in this young age group (Charatan 2000; Coyle 2000; Kalb 2000; Shute et al. 2000; Zito et al. 2000). There are only a handful of case reports on psychopharmacological interventions and even fewer randomized, controlled trials in very young children (Anderson et al. 1984; Harmon and Riggs

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1996). The controlled studies in this age group are limited to either autistic spectrum disorders or attention deficit hyperactivity disorder (ADHD) (Ghuman et al. 2001).

Zito et al. studied the issue of utilization of psychotropics in a population served by 2 Medicaid programs and an HMO (Health Maintenance Organization) (Zito et al. 2000). In the years spanning 1990–1995, they found that 1%–1.5% of all children who were 2–4 years old were receiving stimulants, antidepressants, or antipsychotic agents (Zito et al. 2000). Moreover, they also reported a 1.8–3.1-, a 1.3–2.2-, and a 1.2–1.5-fold increase in the use of stimulants, antidepressants, and antipsychotics from 1991–1995, respectively (Zito et al. 2000).

However, this study did not provide the clinical context in which these medications were written (such as characteristics of the children and their families, their presenting symptoms or diagnoses, the specialty of the prescribing physician, and history of trauma). As this study did not provide the diagnoses or the clinical presentation of the children, it is unclear why clinicians prescribed these agents. In addition, it did not distinguish single agent versus combination pharmacotherapy—which is important, given that limited data is available in this age group. Information on psychotherapeutic intervention in these children is also limited. This study spanned the years 1990–1995, and since then several newer medications (particularly atypical antipsychotics) have been introduced that are used in children and adolescents (Del Bello et al. 2002; Findling et al. 2000).

Since the publication of the study conducted by Zito et al. (2000), attempts have been made to study the clinical context in which psychotropics are prescribed to preschoolers. Debar et al. studied the psychotropic utilization in children 5 years old and under in an HMO in the Pacific Northwest during the years 1997–1998 (DeBar et al. 2003). They noted that approximately 17% of the preschoolers with behavioral problems were given psychotropics. The majority of the prescribing physicians (74%) in this study were pediatricians. However, they excluded 6.25% of the children with behavioral problems from the analysis, because these children had behavioral disturbances associated with major medical morbidity. They also did not collect data on the prescription of hypnotics, such as benzodiazepines and anticonvulsants, which are frequently used as mood stabilizers. Moreover, adverse events were not tracked by this study.

As noted earlier, the specialty of the prescribing physicians is unknown in the study by Zito et al. and almost three-quarters of the prescribing physicians in the study by Debar et al. were pediatricians (DeBar et al. 2003; Zito et al. 2000). The prescribing practices of physicians who receive the most extensive formal education in the prescription of psychotropics to young children, i.e., child psychiatrists, is unknown. Given the importance of the issue of use of psychotropics for very young children, as recognized by the National Institute of Mental Health (NIMH) (www.nimh.nih.gov/child/blueprin.pdf), further scientific study of this issue is warranted. With these considerations in mind, the objective for this naturalistic, retrospective study was to examine the prevalence and nature of psychotropic prescriptions written by child psychiatrists for hospitalized children under the age of 7 years. In addition, we examined the clinical context (such as diagnoses, functional impairment, characteristics of children and their families) in which these psychotropics were prescribed. The goal of this study was to capture the widest age range of very young children for whom little psychotropic efficacy data is available. Thus, the age cutoff of less than 7 years was chosen (as opposed to 4 or 5 years in the previous studies), as little safety and efficacy data is available for this age range for antidepressants, antipsychotics, and mood stabilizers. No selective serotonin reuptake inhibitors (SSRIs), atypical antipsychotics, alpha-2 agonists, or anticonvulsants are approved by the U.S. Food and Drug Administration (FDA) for psychiatric indications under the age of 7 years (except sertraline, which is approved for Obsessive Compulsive Disorder (OCD) for children 6 years old or more). Moreover, there is little or no safety data for these agents spe-

cific to this age group. Therefore, safety and tolerability data for psychotropics in this sample was also collected.

METHODS

The Institutional Review Board had approved this study, and the study protocol adhered to the privacy requirements of the Health Insurance Portability & Accountability Act of 1996 (HIPAA). The medical charts of 93 children who were admitted consecutively to an inpatient psychiatric unit during the calendar year 2002, and who were less than 7 years old at admission, were retrospectively reviewed. This psychiatric unit is part of a premier pediatric hospital in the Mid-West United States, and during the period under review had 39 child and adolescent psychiatric beds. It had 15 beds exclusively for preteens. For patients who had multiple admissions during the year 2002, the first admission during the year was considered for data analysis. A structured chart review form was utilized to collect data. The data gathering and review included a comprehensive review of all staff notes, including the child psychiatrist's note, discharge summary, nursing notes, vitals, laboratory results, electroencephalogram (EEG), brain-scan results, if any, medication sheets, and physician's orders. In addition, the charts were reviewed for documentation of adverse effects to medication. Adverse events were defined as any unwanted health changes identified after admission, or a medical symptom present at admission, which increased in severity. All treating physicians were board-certified or board-eligible child and adolescent psychiatrists. All diagnoses were made in accordance with *Diagnostic and Statistical Manual of Mental Disorders*—Fourth Edition (DSM-IV) criteria, as recorded by the treating psychiatrists. Demographic and clinical data obtained included sex, age, race, living arrangement, and history of abuse or trauma, as recorded by the treating psychiatrists. The insurance information was collected and classified as Medicaid, private insurance, or no insurance/self-pay.

Two child and adolescent psychiatrists (SP and AD), with established inter-rater reliabilities for the Clinical Global Assessment Scale (CGAS; 1 = poor functioning, to 100 = outstanding functioning) (Kappa > 0.9), systematically conducted an independent review of the medical records (Shaffer et al. 1983). They then retrospectively assigned a CGAS score independently. Later consensus ratings, based on the independent ratings and further review of the medical records, were established.

RESULTS

Ninety-three patient charts were reviewed. Consistent with previous reports on the utilization of psychotropics, most children were male (67%) (Table 1). The inpatient staff had obtained informed consent for admission, and later for medications, if prescribed, from all guardians or the Department of Human

TABLE 1. DEMOGRAPHIC CHARACTERISTICS OF THE STUDY SUBJECTS

Variable	n *(%)*
Total number of subjects	93 (100)
Mean age in years ± (SD)	5.4 ± 1.1
Range in years	4.25
Maximum age in years	6.92
Minimum age in years	2.67
Race:	
White	60 (64.5)
African-American	28 (30.1)
Other	5 (5.4)
Gender:	
Male	67 (72)
Female	28 (28)
CGAS: mean ± SD	14.4 ± 6.7*
Primary Caretaker	
Intact family	17 (18.3)
Mother	52 (55.9)
Father	3 (3.2)
Grand parents	5 (5.4)
Foster parents	12 (12.9)
Other family member	1 (1.1)
Other	2 (1.1)
Insurance status	
Medicaid	66 (71)
Private	24 (25.8)
Self-pay	3 (3.2)

*The CGAS is retrospectively assigned and expressed as mean ± SD.

CGAS = Clinical Global Assessment, SD = standard deviation.

Services (DHS), if the state had legal custody. All patients had baseline laboratory work ordered, which included a complete blood count with differential, liver function tests, thyroid-stimulating hormone, lead level, and renal function tests. All except 1 patient had a physical examination by a pediatrician, as well as a psychiatric evaluation by a board-certified or board-eligible child and adolescent psychiatrist. The 1 child who was not seen by a physician was discharged against medical advice, and the period of hospitalization was less than 24 hours. All children received individual, group, and milieu therapy during the hospital stay.

Sixty-six children (71%) in this group were Medicaid recipients, 24 children (25.8%) had private insurance, and 3 children (3.2%) had no insurance. Most children had some kind of instability at home. Both parents were listed as primary caretakers for only 17 children (18.3%) (Table 1). Single mothers were commonly the only caretaker (n = 52, 55.9%). Twelve children (12.9%) were in foster care. Other people, such as aunts, uncles, or family friends, cared for 4 children (4.3%). Physical, sexual, and both physical and sexual abuse was documented in 19 (20.4%), 9 (9.7%), and 14 (15.1%) of the children, respectively. Exposure to other trauma (such as ongoing parental divorce, neglect, or domestic violence) was recorded for 37 patients (39.8%). Only 33 patients (35.5%) had no recorded trauma or abuse. The mean hospitalization duration was 8.6 ± 4.6 days. Of the children who were placed on medications, 61.6% (n = 57) of the patients had received psychotherapy prior to the hospitalization. The majority (52.7% of the total, n = 49) were already on psychotropic agents before admission to the hospital. Twenty-eight percent (n = 26) of the patients had psychiatric hospitalizations one or more times before the present admission.

TABLE 2. PSYCHOTROPIC UTILIZATION

Agent	n (%)
Heterocyclic antidepressants	
imipramine	1 (1.1)
Selective serotonin reuptake inhibitors	
Total	18 (19.3)
fluoxetine	4 (4.3)
sertraline	2 (2.2)
paroxetine	8 (8.6)
citalopram	3 (3.2)
escitalopram	1 (1.1)
Other antidepressants	
bupropion	15 (16.1)
Mood stabilizers	
Total	16 (17.2)
lithium	2 (2.2)
valproic acid	11 (11.8)
carbamazepine	1 (1.1)
oxcarbazepine	2 (2.2)
2nd mood stablilizer*	
Total	3 (3.2)
lithium	1 (1.1)
valproic acid	1 (1.1)
carbamazepine	1 (1.1)
Stimulants	
Total	39 (41.9)
Adderall®	10 (10.8)
dextroamphetamine	6 (6.5)
Concerta®	21 (22.6)
methylphenidate	2 (2.2)
Typical antipsychotics	
Total	2 (2.2)
haloperidol	1 (1.1)
thiothixene	1 (1.1)
Atypical antipsychotics	
Total	45 (48.4)
risperidone	40 (43.0)
olanzapine	2 (2.2)
quetiapine	3 (3.2)
Antihistamines	
diphenhydramine	22 (23.7)
Alpha-2 agonists	
Total	19 (20.4)
clonidine	16 (17.2)
guanfacine	3 (3.2)
Others	
melatonin	5 (5.4)

*These children were already on another mood stabilizer.

Psychotropic medications prescription patterns

Information was collected on all psychotropic medications given during the hospitalization. These included antipsychotics, antidepressants, mood stabilizers, anticonvulsants used for psychiatric target symptoms, alpha-2 agonists, stimulants, benzodiazepines, etc. Owing to the small sample size, and the nature of the report, most data are descriptively reported (Tables 2, 3, and Fig. 1). Seventy-three patients (78.5%) were started on medications. Use of multiple, different classes of medications during the hospital stay was common. Fifty (68.5% of all who were given psychotropics) children received 2 or more medications during their stay.

TABLE 3. PRIMARY AXIS I DIAGNOSES AND PSYCHOTROPIC PRESCRIPTIONS

Diagnoses	*Total* n (%)	*Anti-psychotic* n (%)	*Anti-depressant* n (%)	*Stimulant* n (%)	*Mood Stabilizers* n (%)	α_2 *Agonist* n (%)
Total (Affective disorder)	57 (61.3)	34 (36.5)	39 (41.9)	25 (26.9)	13 (14.0)	10 (10.7)
Affective Disorder only	23 (24.7)	13 (14.0)	8 (8.6)	4 (4.3)	5 (5.4)	5 (5.4)
Affective Disorder + other disorders						
(Affective Disorder) + DBD	19 (20.4)	12 (12.9)	1 (1.1)	11 (11.8)	4 (4.3)	2 (2.1)
(Affective Disorder) + PTSD	4 (4.30)	1 (1.1)	1 (1.1)	2 (2.1)	1 (1.1)	0 (0)
(Affective Disorder) + DBD + PTSD	11 (11.8)	8 (8.6)	10 (10.7)	8 (8.6)	3 (3.2)	3 (3.2)
(PTSD)*	7 (7.5)	1 (1.1)	0 (0)	1 (1.1)	0 (0)	0 (0)
(PTSD)* + ADHD	8 (8.6)	1 (1.1)	3 (3.2)	3 (3.2)	1 (1.1)	3 (3.2)
(DBD)**	18 (19.3)	10 (10.7)	1 (1.1)	9 (9.7)	2 (2.2)	5 (5.4)
Other†	3 (3.2)	1 (1.1)	0 (0)	1 (1.1)	0 (0)	1 (1.1)

*Children who had diagnoses of affective disorders are not included.

**Children who had diagnoses of affective disorders or PTSD are not included.

( ) Diagnoses in parentheses are the primary diagnoses. All subjects diagnosed with affective disorders had affective disorder as the primary diagnoses.

DBD = disruptive behavioral disorders (includes attention-deficit/hyperactivity disorder (ADHD), oppositional defiant disorder, and disruptive behavioral disorder NOS); PTSD = posttraumatic stress disorder.

Affective disorder includes major depressive disorder, depressive disorder NOS, mood disorder NOS, bipolar disorder, and bipolar disorder NOS.

†One child was diagnosed with pervasive developmental disorder NOS who received all the medicines in this category (1 antipsychotic, 1 stimulant, and 1 α_2 agonist). One child was diagnosed with feeding disorder of early childhood, and another child had a diagnosis of anxiety disorder NOS.

Of the total 93 children, 16 children (17.2%) were prescribed 2 psychotropics, 17 children (18.3%) were given 3 psychotropics, and 17 children (18.3%) were given 4 psychotropics.

Adverse events were recorded for 12 patients (12.9%). Eight patients (8.6%) had neurological side effects, such as sedation, insomnia, or tremors. Three patients (3.2%) developed gastrointestinal side effects, such as nausea or diarrhea. One patient (1.1%) developed incontinence. Out of those patients who had adverse effects, 1 patient was on risperidone only, and another patient was on Concerta® only. Five children who developed adverse effects were on a combination of an atypical antipsychotic, stimulant, and antidepressant (3 medicines each). Another 5 children with adverse effects were on a combination of 4 drugs each (which included antidepressants, stimulants, typical antipsychotics, atypical antipsychotics, and valproic acid). Two children (2.2%) had increased liver enzymes at the time of admission. One child was on carbamazepine, and the other was on valproic acid as outpatients. No serious adverse effect was noted as a result of drugs given in the hospital. One child was diagnosed with stimulant-induced psychosis, which was prescribed as an outpatient prior to the admission, and it had precipitated the admission. Another child reportedly had a seizure before admission while withdrawing from clonazepam. Eight children (8.6%) had a routine EEG done. All the results were within the normal range.

Diagnostic profile of the children

The majority of the patients were diagnosed with affective disorders (61.3%) (Table 4). Depressive disorder NOS (n = 22, 23.7%) and bipolar disorder NOS (n = 16, 17.2%) were frequently used diagnostic categories. Less than half of the children were diagnosed with attention deficit hyperactivity disorder (ADHD) (48.4%). Anxiety disorders were the third most common category utilized after affective disorders and ADHD (39.8%). Post-traumatic stress disorder was diagnosed in 30 (32.3%) patients. Thirteen children (14%) were diagnosed with reactive attachment disorder. Pervasive development disorders were diagnosed in 3

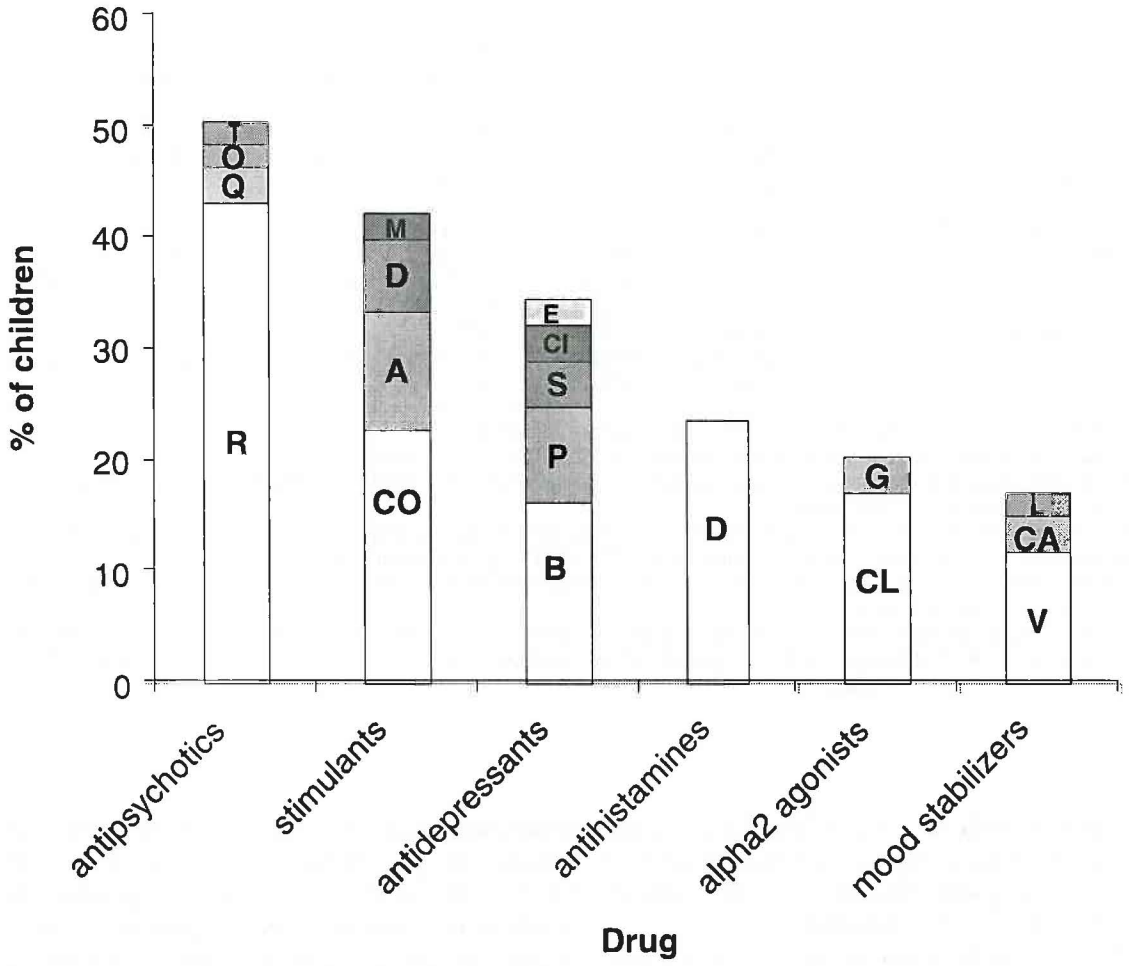

FIG. 1. Commonly used psychotropics.
A = Adderall®; B = Bupropion; CA = Carbamazepine or Oxcarbazepine; CI = Citalopram; CL = Clonidine; CO = Concerta®; DE = Dextroamphetamine; DI = Diphenhydramine; E = Escitalopram; G = Guanfacine; L = Lithium; M = Methylphenidate; O = Olanzapine; P = Paroxetine; Q = Quetiapine; R = Risperidone; S = Sertraline; T = Typical Antipsychotic; V = Valproic Acid.

patients (3.2%). Multiple diagnostic categories were frequently utilized to describe a patient's psychopathology.

DISCUSSION

A major concern with using psychotropics in the very young is that this involves off-label use, as the efficacy and safety of psychotropic drugs has not been established in very young children (Greenhill 1998). Moreover, their impact on the developing human brain is unclear at this time (Huttenlocher 1990; Vitiello 1998). In this study, the children's limited ability to verbalize side effects may have led to an underreporting of adverse effects.

Despite these legitimate concerns, it is important to view the use of psychotropics in light of the nature and severity of psychiatric problems afflicting this age group (Campbell 1995; Hooks et al. 1988; Keenan et al. 1997; Lavigne et al. 1996; Moffitt 1990; Weller et al. 1986; Wilens et al. 2002). In this study, the mean CGAS was 14.4 ± 6.7. Although the numbers are telling, to convey the message more effectively, situations from the histories of a few cases are being reported.

TABLE 4. DSM-IV AXIS I AND II DIAGNOSTIC RUBRICS USED TO DESCRIBE PSYCHOPATHOLOGY*

Disorder	*Subtypes*	n (%)
ADHD	Total	45 (48.4)
Disruptive behavior disorders	Total	33 (35.5)
	DBD-NOS	2 (2.2)
	ODD	31 (33.3)
Mood disorders	Total	57 (61.3)
	Bipolar disorder	1 (1.1)
	MDD	8 (8.6)
	Mood disorder NOS	10 (10.8)
	Bipolar disorder NOS	16 (17.2)
	DD-NOS	22 (23.7)
Anxiety disorders	Total	37 (39.8)
	SAD	3 (3.2)
	Anxiety disorder NOS	4 (4.3)
	PTSD	30 (32.3)
Psychotic disorders	Total	1 (1.1)
	Psychosis-NOS	1 (1.1)
Learning disorders	Total	2 (2.2)
Communication disorders	Total	12 (12.9)
	Expressive language disorder	4 (4.3)
	Mixed receptive-expressive language disorder	8 (8.6)
PDD	Total	3 (3.2)
	PDD NOS	3 (3.2)
Tic disorders	Total	2 (2.2)
	Tourette's Disorder	2 (2.2)
Feeding and eating disorders	Total	1 (1.1)
	Feeding disorder of early childhood	1 (1.1)
Reactive attachment disorders	Total	13 (14.0)
Mental retardation	Total	8 (8.6)
Elimination disorders	Total	
	Encopresis	3 (3.2)
	Eneuresis	1 (1.1)
Impulse control disorders	Total	5 (5.4)
	Intermittent explosive disorder	5 (5.4)
Adjustment disorder	Total	1 (1.1)

*Many children were given more than one diagnoses.
DBD-NOS = Disruptive behavior disorder NOS; ODD = oppositional defiant disorder; MDD = major depressive disorder; DD-NOS = depressive disorder NOS; SAD = social anxiety disorder; PTSD = posttraumatic stress disorder; PDD-NOS = pervasive disorder NOS; NOS = not otherwise specified.

Case 1. A 5-year-old boy was brought to the hospital, as he wanted to kill himself and his mother. He had a history of lifting the dresses of unsuspecting women and touching their breasts. He had been in outpatient treatment for over 2 years, and had received family therapy and a combination of risperidone and valproic acid.

Case 2. A 6-year-old boy became belligerent at school. He spit at the school principal and bit him. The teachers tried to restrain him. These incidents led to his getting more agitated; and as the teachers were unsuccessful in calming him, they called the police.

Case 3. A 6-year-old girl cut herself on the wrist with a kitchen knife with the intention to kill herself.

Consistent with the extant literature, our study suggests that preschoolers have high rates of psychiatric morbidity, comorbidity, and impairment (DuPaul et al. 2001; Hooks et al. 1988; Thomas and Guskin 2001). Furthermore, the emerging literature suggests that serious and chronic disorders, such as anxiety, depression, bipolar disorder, and attention deficit hyperactivity disorder, sometimes have an onset in very young children (Kashani and Carlson 1987; Luby et al. 2002; Wilens et al. 2002). In addition, there is some longitudinal evidence linking be-

havioral and emotional difficulties at age 3 with adult psychopathology (Caspi et al. 1996). Thus, the possible adverse effects of psychotropics at this age needs to be weighed against the long-term sequela (including possible neurotoxicity) of untreated psychopathology. Successful treatment at this stage may change the trajectory of development and lead to a better quality of life and possible containment of psychopathology. It is also very likely that psychiatric disorders afflicting children at this age are very severe and have a pernicious course, necessitating both psychosocial and pharmacological intervention (Jensen 1998). Therefore, it is not surprising that clinicians are compelled to prescribe psychotropics to approximately 1% of preschoolers, despite the scarcity of evidence in this age group (Zito et al. 2000).

The growth in use of psychotropics in children can be attributed to several reasons, as discussed by Jellinek (Jellinek 2003). In this study, use of multiple medications was common. Moreover, many classes of medicines were used for many disorders, and many disorders were treated with many different drugs. For instance, antipsychotics were used for affective disorders, posttraumatic stress disorder, disruptive behavioral disorder, and pervasive developmental spectrum disorder; disruptive behavioral disorders were treated with stimulants, antipsychotics, antidepressants, alpha-2 agonists, and mood stabilizers. One of the main reasons for this pattern of utilization of psychotropics is that no treatment guidelines are available for most behavioral disorders at this age. When faced with a challenging clinical situation, clinicians extrapolate from adult data that may not be applicable at this age. Concomitant medications are usually a result of an inadequate response to the first trial of medications. In an effort to contain the symptoms, the clinician takes recourse to adding more medicines in the hope of helping the child.

Limitations of the study

Hospitalized children with very severe psychopathology from one clinical setting were included in this study. These results are not easily generalizable to children with psychiatric problems of less severity or those seen in other settings, such as outpatient clinics and other hospitals. This study has also not tracked in detail the treatment received prior to the hospitalization. Although, during the period under study (i.e., inpatient hospitalization), use of single and multiple psychotropic medication is common, it is possible that some of these children received psychosocial treatments alone and for prolonged periods prior to admission. However, as noted earlier, the majority of the children were on psychotropics even prior to admission.

The retrospective design of our study limits results to the documentation practices of individual clinicians. The diagnoses listed in the inpatient records might be different from the diagnoses determined by a full research assessment using a semistructured, validated diagnostic interview. Adverse effects to medications obtained are not a comprehensive list of all adverse health symptoms resulting from taking the medicine, but are limited to the symptoms that the clinician deemed important to document.

CONCLUSION

Clinical research lags behind clinical care in this age group. Society and ethicists have struggled with the issue of pharmacological research in children. However, lack of research compromises the care children receive. Randomized, controlled trials with psychotherapeutic and psychopharmacological interventions for psychiatric problems in this age group are needed. The recognition by the National Institute of Mental Health of the need for research in this area will go a long way in remedying the situation (Vitiello 2001). Legislation, such as the Best Pharmaceuticals for Children Act of 2002 is needed to increase pharmaceutical research in this hitherto ignored area of child psychiatry (www.fda.gov/opacom/laws/pharmkids/contents.html). This act has encouraged pharmaceutical companies to conduct pediatric studies of on-patent drugs that are used in pediatric populations, but are not labeled for such use, by extending their market exclusivity. Extending this approach to

pharmaceutical research in very young children will produce desirable results. In the interim, it would be helpful to examine the management practices of child psychiatrists in other regions for children with severe psychiatric problems as part of future research.

REFERENCES

Anderson LT, Campbell M, Grega DM, Perry R, Small AM, Green WH: Haloperidol in the treatment of infantile autism: Effects on learning and behavioral symptoms. Am J Psychiatry 141: 1195–1202, 1984.

Best Pharmaceuticals for Children Act of 2002. www.fda.gov/opacom/laws/pharmkids/contents.html. Retrieved on February 5, 2002.

Campbell SB: Behavior problems in preschool children: A review of recent research. J Child Psychol Psychiatry 36:113–149, 1995.

Caspi A, Moffitt TE, Newman DL, Silva PA: Behavioral observations at age 3 years predict adult psychiatric disorders. Longitudinal evidence from a birth cohort. Arch Gen Psychiatry 53:1033–1039, 1995.

Charatan F: Mrs. Clinton aims to reduce psychoactive drugs in young children. Bmj 320:893, 2000.

Coyle JT: Psychotropic drug use in very young children. Jama 283:1059–1060, 2000.

DeBar LL, Lynch F, Powell J, Gale J: Use of psychotropic agents in preschool children: Associated symptoms, diagnoses, and health-care services in a health maintenance organization. Arch Pediatr Adolesc Med 157:150–157, 2003.

Del Bello MP, Schwiers ML, Rosenberg HL, Strakowski SM: A double-blind, randomized, placebo-controlled study of quetiapine as adjunctive treatment for adolescent mania. J Am Acad Child Adolesc Psychiatry 41:1216–1223, 2002.

DuPaul GJ, McGoey KE, Eckert TL, VanBrakle J: Preschool children with attention deficit hyperactivity disorder: Impairments in behavioral, social, and school functioning. J Am Acad Child Adolesc Psychiatry 40:508–515, 2001.

Findling R, McNamara N, Branicky L, Schluchter M, Lemon E, Blumer J: A double-blind pilot study of risperidone in the treatment of conduct disorder. J Am Acad Child Adolesc Psychiatry 39: 509–516, 2000.

Ghuman JK, Ginsburg GS, Subramaniam G, Ghuman HS, Kau AS, Riddle MA: Psychostimulants in preschool children with attention deficit hyperactivity disorder: Clinical evidence from a developmental disorders institution. J Am Acad Child Adolesc Psychiatry 40:516–524, 2001.

Greenhill LL: The use of psychotropic medication in preschoolers: Indications, safety, and efficacy. Can J Psychiatry 43:576–581, 1998.

Harmon RJ, Riggs PD: Clonidine for post-traumatic stress disorder in preschool children. J Am Acad Child Adolesc Psychiatry 35:1247–1249, 1996.

Hooks MY, Mayes LC, Volkmar FR: Psychiatric disorders among preschool children. J Am Acad Child Adolesc Psychiatry 27:623–627, 1988.

Huttenlocher PR: Morphometric study of human cerebral cortex development. Neuropsychologia 28:517–527, 1990.

Jellinek MS: Psychiatric drugs and children. Science 300:901, 2003.

Jensen PS: Ethical and pragmatic issues in the use of psychotropic agents in young children. Can J Psychiatry 43:585–588, 1998.

Kalb C: Drugged-out toddlers. A new study documents an alarming increase in behavior-altering medication for preschoolers. Newsweek 135:53, 2000.

Kashani JH, Carlson GA: Seriously depressed preschoolers. Am J Psychiatry 144:348–350, 1987.

Keenan K, Shaw DS, Walsh B, Delliquadri E, Giovannelli J: DSM-III-R disorders in preschool children from low-income families. J Am Acad Child Adolesc Psychiatry 36:620–627, 1997.

Lavigne JV, Gibbons RD, Christoffel KK, Arend R, Rosenbaum D, Binns H, Dawson N, Sobel H, Isaacs C: Prevalence rates and correlates of psychiatric disorders among preschool children. J Am Acad Child Adolesc Psychiatry 35:204–214, 1996.

Luby JL, Heffelfinger AK, Mrakotsky C, Hessler MJ, Brown KM, Hildebrand T: Preschool major depressive disorder: Preliminary validation for developmentally modified DSM-IV criteria. J Am Acad Child Adolesc Psychiatry 41:928–937, 2002.

Moffitt TE: Juvenile delinquency and attention deficit disorder: Boys' developmental trajectories from age 3 to age 15. Child Dev 61:893–910, 1990.

Rappley MD, Mullan PB, Alvarez FJ, Eneli IU, Wang J, Gardiner JC: Diagnosis of attention deficit hyperactivity disorder and use of psychotropic medication in very young children. Arch Pediatr Adolesc Med 153:1039–1045, 1999.

Shaffer D, Gould MS, Brasic J, Ambrosini P, Fisher P, Bird H, Aluwahlia S: A children's global assessment scale (CGAS). Arch Gen Psychiatry 40: 1228–1231, 1983.

Shute N, Locy T, Pasternak D, Brink S, Lord M, MacNeil JS, Madden ME, Schultz S, Sobel R: The perils of pills. The psychiatric medication of children is dangerously haphazard. U.S. News World Rep 128:44–50, 2000.

Thomas JM, Guskin KA: Disruptive behavior in young children: What does it mean? J Am Acad Child Adolesc Psychiatry 40:44–51, 2001.

Vitiello B: Pediatric psychopharmacology and the interaction between drugs and the developing brain. Can J Psychiatry 43:582–584, 1998.

Vitiello B: Psychopharmacology for young children: Clinical needs and research opportunities. Pediatrics 108:983–989, 2001.
Weller RA, Weller EB, Tucker SG, Fristad MA: Mania in prepubertal children: Has it been underdiagnosed? J Affect Disord 11:151–154, 1986.
Wilens TE, Biederman J, Brown S, Monuteaux M, Prince J, Spencer TJ: Patterns of psychopathology and dysfunction in clinically referred preschoolers. J Dev Behav Pediatr 23:S31–S36, 2002.
Zito JM, Safer DJ, dosReis S, Gardner JF, Boles M, Lynch F: Trends in the prescribing of psychotropic medications to preschoolers. Jama 283: 1025–1030, 2000.

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