The Use of Psychostimulants in Children With Disruptive Behavior Disorders and Developmental Disabilities in a Community Setting

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This study was done to provide information about the use of stimulants in children with disruptive behavior disorders and developmental disabilities in a community setting. A randomized retrospective chart review was conducted for 115 children, ages 3-13 years, who as outpatients, were referred for a multidisciplinary workup. Twenty-one (18.2%) of the children had a diagnosis of attention-deficit/hyperactivity disorder (ADHD) only, while 94 (81.8%) had comorbid diagnoses, with intellectual disabilities being the most common developmental disability (N=27, 23%). The target symptoms were hyperactivity, inattention, impulsivity or aggression. Four different preparations of two stimulants were used. The children were treated for as long as nine years. Satisfactory responses were noted in 76% of the children with ADHD only, and in 69% of the children with comorbid diagnoses. Side effects were reported in 42 children (36.5%). Stimulants were augmented with other drugs in 25% of the cases. Thus, the use of stimulants for symptoms of ADHD in children with developmental disabilities and disruptive behavior disorders is effective when ADHD occurs alone, and is also effective, with augmentation in some cases, when comorbid conditions are present.
Keywords: ADHD, developmental disabilities, disruptive behavior disorders, hyperactivity, intellectual disability, mental retardation, psychiatric disorder, stimulants

In 1992, the National Institute of Mental Health began a multisite clinical trial to compare three different types of treatment of attention-deficit/hyperactivity disorder (ADHD) with routine community care. This Multimodal Treatment of Attention-Deficit Hyperactivity Disorder (MTA) study compared monthly medication management (usually with a stimulant) following weekly titration (Med Mgt), intensive behavioral treatment (Beh), and the combination (Comb), with each other and with community care (CC). The results indicated that Comb and Med Mgt treatment were superior to Beh and CC for symptoms of ADHD.[41] Beginning before the initial reports of the results of this study, there had been an increase in interest and concern about the use of stimulants in community settings.[22,56]

There have been reports that stimulants are being used inappropriately with children who do not meet diagnostic criteria for ADHD.[7,39,71] There is also concern that they appear to be overprescribed in some geographical areas and underprescribed in others,[19,40] and that stimulant use has increased concomitantly with improved identification of ADHD symptoms in preschoolers, latency age children, adolescents, adults and in inattentive children of all ages.[68] Reports show also that in some areas of the country, Black and Hispanic students are receiving methylphenidate at approximately half the rate of their white counterparts.[53,54]

One of the areas of concern about possibly inappropriate use of stimulants is the evidence of what is called "off label" use of at least one stimulant (methylphenidate or MPH) in preschool age children.[73] In this case, the "off label" use concerns a package insert prohibiting the use of this medication in children under the age of 6 because "safety and efficacy in this age group have not been established."[29]

Some reasons for "off label" use of medications such as stimulants are: a shared body of personal experience attesting to the safety and efficacy of so called "off label" use of stimulants;[14,51] some double-blind placebo controlled trials of MPH in preschoolers with ADHD which provide evidence to show that MPH is superior to placebo;[5,17] and a sense that research data used to obtain official approval of many psychotropic medications is flawed in that the data do not apply to the so called "real world" or "naturalistic" conditions of

routine clinical practice.[70] With regard to children, the flaw may be a study in which children's common comorbid conditions are screened out.[42] Or, the flaw may be a study with such a rich supply of clinical and environmental supports that the results seem suspect with regard to what is realistically available to most children with this disorder.[10,63]

In response to this absence of information about safety and efficacy of stimulants in young children, a six site, double-blind, placebo-controlled study using four doses of MPH given three times a day to children ranging in age from 3 to 8 years has been instituted. The doses are 1.25, 2.5, 5 and 7.5 mg with the possibility of going up to 10 mg/dose. The effects and side effects will be measured by structured diagnostic interview, classroom observations and actometer measurements.[30]

Another area of concern is the use of stimulants in children with development disabilities. Most research on the use of stimulants in children has involved the exclusion of children with intellectual disabilities (ID), pervasive developmental disorders, and other developmental disabilities. There has been some research suggesting that children with ID and ADHD respond in a similar manner to MPH as do children with ADHD in the general population.[32,33,35,37] If there is a difference, it may be that the children with ID and ADHD are more vulnerable to the side effects of MPH.[27,34,35] Reported therapeutic trials of stimulant drugs in children with autism or pervasive developmental disorder NOS (PDDNOS) have consisted of relatively small numbers of children[1] with reported areas of improvement being attention and social responsiveness,[62] irritability[49] and hyperactivity.[12,35] Here again, children with these developmental disorders seem to be particularly susceptible to adverse side effects but there are also reports of high levels of side effects on placebo.[36] Despite the somewhat meager research support, stimulants may be the most commonly prescribed drugs in school age children with pervasive developmental disorders.[3]

Another possible area of concern is the increasingly common phenomenon of the combination of stimulants with other psychotropic medications for children with ADHD with or without comorbid disorders.[11,55]

In response to a stated need for documentation of evolving patterns of psychotropic drug use in young children,[31,61] we present data on 115 children treated with stimulants after being diagnosed as having ADHD. The diagnoses were made using DSM-IV[6] criteria after a multidisciplinary workup at a university based community clinic in an urban area.

SUBJECTS

The data were compiled by means of a randomized chart review of the 460 children treated with pharmacotherapy at this clinic.

There were 91 boys and 24 girls ranging in age from 3-13 years. There was no difference in mean ages between the boys and girls. (Table 1). Twenty of the children had ADHD as a sole diagnosis. The most common comorbid diagnoses were mild to severe intellectual disabilities (26 children) and learning disability and/or language disorder (26 children). There were 10 children with comorbid oppositional defiant disorder (ODD) and 10 children with comorbid borderline intellectual functioning (BIF). There were 8 children diagnosed as having both ADHD and a pervasive developmental disorder, either PDDNOS or an Autistic Disorder (AD). Although DSM-IV advises against the use of the ADHD diagnosis when a PDD is present, we have done so when symptoms of ADHD (i.e., hyperactivity/impulsivity/inattention) were prominent and were the target symptoms of pharmacotherapy, and when symptoms of PDD (i.e., repetitive or perseverative behaviors, social skills deficits, oddities of communication) were not the target symptoms.[28] Other comorbid diagnoses included: an anxiety disorder, other than Posttraumatic Stress Disorder (4 children); Dysthymic Disorder (4 children); Psychotic Disorder NOS (3 children, here too the focus of treatment were symptoms of ADHD); an Adjustment Disorder (3 children); encephalopathy with a seizure disorder (3 children); Posttraumatic Stress Disorder (PTSD; 2 children); 2 children with Multiple Complex/Multiplex Developmental Disorder (MCDD);[16,44,59] and 1 child with Borderline Personality Disorder (Table 2). PTSD was separated from the other anxiety disorders as epidemiological, biological and treatment evidence has shown that PTSD is a unique psychiatric disorder that is different from anxiety or depressive disorders.[57]

In all cases the target symptoms were hyperactivity, impulsivity and inattention. In addition, aggression was a target symptom with 59 children.

TABLE 1. GENDER AND AGE OF 115 CHILDREN DIAGNOSED AS HAVING AN ATTENTION DEFICIT/ HYPERACTIVITY DISORDER

SEX	AGE RANGE (YRS.)
M 91	3 - 13-1/2
F 24	3-1/2 - 12-1/2

TABLE 2. COMORBID DIAGNOSES

COMORBID DIAGNOSIS	N
None	20
Developmental disorders intellectual disabilities (mild to severe) learning disability/language disorder borderline intelligence	 26 26 10
Oppositional Defiant Disorder	10
Pervasive Developmental Disorder NOS	6
Anxiety disorder[a]	4
Dysthymic disorder	4
Adjustment disorder	3
Psychotic disorder NOS	3
Encephalopathy + seizures	3
Autistic disorder	2
Multiple complex developmental disorder	2
Borderline personality disorder	1

[a]excluding posttraumatic stress disorder

METHOD

The children were referred for a multidisciplinary evaluation by schools, pediatricians, hospital-based and community-based general pediatric or pediatric specialty clinics, or parents. After the multidisciplinary evaluation, the children were referred for pharmacotherapy as part of a more comprehensive set of treatment recommendations e.g., integrated nursery school programs, special education, speech and language therapy, educational therapy or psychotherapy.

An initial medication clinic visit with a pediatrician trainee in developmental pediatrics or a pediatric nurse practitioner, and a child psychiatrist, would involve: a review of the clinical material leading to the diagnosis and recommendation for pharmacotherapy, an evaluation of the child with a focused history relating to the diagnosis and proposed target symptoms; a recommendation for appropriate laboratory or other diagnostic tests; a discussion with the parent or guardian about the benefits and possible side effects of the medication to be used; a discussion with the child (when appropriate) about the meaning of taking medication and the proposed benefits and side effects; and obtaining written and oral "informed consent" from the parent or guardian and "assent" (when appropriate) from the child. When a medication was used in an "off label" manner, this was discussed with the parent and an additional consent from was signed by the parent stating an awareness that relevant studies had not yet been done.

The initial medication visit was then followed by periodic revisits to monitor progress and side effects, and to consider medication changes. The followup visits would initially occur at 1 to 2 week intervals. As the type and dose of medication began to stabilize, the frequency of visits began to stretch from once a month to once every three months. Progress was monitored by parent and child verbal reports, phone consultations with teachers or guidance counselors when indicated, and the use of standardized parent/teacher rating scales, e.g., Child Attention Profile (CAP),[23] and ACTeRS.[60]

There were two stimulants used in this group of children: MPH and dextroamphetamine. There were four different preparations of these drugs: immediate release MHP (e.g., Ritalin); OROS-MPH in a 3 pulse system (Concerta); and two forms of immediate release dextroamphetamine salts, Dexedrine (a single salt) and Adderall (a mixed salt). Whenever possible children under the age of 6 were started on a form of dextroamphetamine.

RESULTS

Hyperactivity and impulsivity were the most common target symptoms, followed by aggression and inattention in that order (Table 3).

TABLE 3. TARGET SYMPTOMS

	HYPERACTIVITY IMPULSIVITY	INATTENTION	AGGRESSION
ADHD alone	18	4	4
Comorbid disorders			
Developmental disorders			
intellectual disabilities	25	5	15
borderline intelligence	7	1	5
learning disability/language disorder	25	3	12
ODD[a]	10	1	3
PDDNOS[b]	6	1	5
Anxiety disorders[c]	4	2	0
Dysthymic disorder	4	1	1
Adjustment disorder	3	1	1
Psychotic disorder NOS	3	0	2
Encephalopathy + seizures	3	0	2
PTSD[d]	2	0	2
Autistic disorder	2	0	2
MCDD[e]	2	1	1
Borderline personality disorder	1	0	0

[a] ODD = oppositional defiant disorder, [b] PDDNOS = pervasive developmental disorder not otherwise specified; [c] excluding posttraumatic stress disorder; [d] PTSD = posttraumatic stress disorder; [e] MCDD = multiple complex development disorder

DOSES

Doses of dextroamphetamines and MPH are presented in Tables 4 and 5. The main trends noted are (1) dextroamphetamine was used in 14 children between the ages of 3 and 6 years; there were 29 children between the ages of 3 and 6 years who received immediate release MPH after a trial of dextroamphetamine; (2) the final mg/kg/day and mg/kg/dose of MPH are higher in the youngest age group than with 2 older age groups; (3) the final mg/kg/day and mg/kg/day dose of Dexedrine mixed salts was higher in the youngest age group than in the 7-9 year old group; (4) there was a rather wide range of the final mg/kg/day doses for each stimulant; and (5) there were rather few children treated with either dextroamphetamine mixed salts (N=14), or OROS methylphenidate (N=12).

The final total daily dose range of MPH for the entire sample was 5-80 mg or 0.08 – 2.0 mg/kg/day. The final mean mg/kg/day dose of immediate release MPH for 17 of the children with ID who wound up being treated with this drug was 0.71.

The length of treatment with stimulants in this sample ranged from 2 months to 9 years, with the median length of treatment being 2 years, 8 months.

EFFECTIVENESS

The number of children for whom a given stimulant was initially effective and the number of children for whom a given stimulant was not effective is presented in Table 6. A measure of effectiveness could either be a significant improvement in a score of a rating scale or a verbal report from the parent, teacher or child that the target symptoms had improved and were either no longer a problem or noticeably less of a problem than they had been before the medication was started. Immediate release MPH was effective in 60% of the cases, dextroamphetamine in 68% of the cases, OROS MPH in 67% of the cases and dextroamphetamine mixed salts in 56% of the cases.

The effectiveness rate of any stimulant helping a child with uncomplicated ADHD was 80% (Table 7). Children with comorbid intellectual disabilities had a 73% chance of being benefitted. Seventy-five percent of the children with ID had mild ID while 20% had moderate ID and 5% had severe to profound ID. The children with severe to profound

TABLE 4. DOSES							
Medication		**Initial**			**Final**		
methylphenidate (immediate release)	Age	mg/kg/ dose (mean)	mg/kg/ day (mean)	mean total daily dose (mg)	mg/kg/ dose (mean)	mg/kg/ day (mean)	mean total daily dose (mg)
	3-6 yo's (N=29)	0.24	0.52	10.2	0.4	0.87	26.1
	7-9 yo's (N=54)	0.18	0.35	15	0.27	0.74	27.7
	10-13 yo's (N=17)	0.18	0.38	19.8	0.29	0.57	35.3
Overall range	**0.08 - 1.6 mg/kg/day**				**0.08 - 2.0 mg/kg/day**		
dextroamphetamine	3-6 yo's (N=14)	0.15	0.21	4.5	0.23	0.46	12.2
	7-9 yo's (N=25)	0.21	0.26	8.8	0.26	0.45	17.9
	10-13 yo's (N=0)	-	-	-	-	-	-
Overall range	**0.08 - 0.55 mg/kg/day**				**0.13 - 0.86 mg/kg/day**		

TABLE 5. DOSES							
Medication		**Initial**			**Final**		
dextroamphetamine mixed salts	Age	mg/kg/ dose (mean)	mg/kg/ day (mean)	mean total daily dose (mg)	mg/kg/ dose (mean)	mg/kg/ day (mean)	mean total daily dose (mg)
	3-6 yo's (N=7)	0.12	0.16	3.8	0.3	0.42	9.4
	7-9 yo's (N=7)	0.18	0.24	9.2	0.23	0.3	15
Overall range	**0.05 - 0.76 mg/kg/day**				**0.05 - 0.76 mg/kg/day**		
methylphenidate (OROS)	3-6 yo's (N=6)	1.03	1.03	25.7	1.33	1.33	36
	7-9 yo's (N=3)	0.88	0.88	42.0	1.38	1.38	60
	10-13 yo's (N=3)	0.6	0.6	18.0	0.69	0.69	30
Overall range	**0.36 - 1.38 mg/kg/day**				**0.36 - 2.53 mg/kg/day**		

TABLE 6. RESULTS OF MEDICATION TRIALS FOR EACH STIMULANT

Drug	No. of Positive Cases	No. of Negative Cases	% of Positive Trials
methylphenidate	64	42	60
dextroamphetamine	21	10	68
methylphenidate (OROS)	8	4	67
dextroamphetamine mixed salts	10	8	56

ID were less likely to benefit from stimulants than the children with mild or moderate ID. The children with moderate ID were as likely to benefit from stimulant medication as were the children with mild ID. Children with comorbid learning disabilities/language disorders, and borderline intellectual functioning had a 63% and a 60% chance respectively of benefitting from pharmacotherapy. As for other of the more common comorbid conditions, a stimulant alone benefitted children with comorbid ODD (70% success rate), and a comorbid anxiety disorder (all of the 4 cases). It should be noted that none of the 4 children with a comorbid dysthymic disorder benefitted from a stimulant given alone.

SIDE EFFECTS

Side effects resulting either in a dosage change or a change of medication occurred in 20 children (17%, Table 8), with changes in 15 children (13%) because of side effects. Decreased appetite (N=4) was the most common adverse side effect, and there were 11 different side effects in all.

ADDITIONAL MEDICATIONS

There were 31 trials of a switch to another stimulant in an attempt to improve efficiency. Of these, 7 were in children with some degree of ID (27% of the cases), while 24 were in children of average or borderline intelligence (27% of the cases. Four (57%) of the children with ID benefitted from the switch while 15 (62%) of the non-developmentally disabled children benefitted from the switch.

There were 13 different non-stimulant medications added to the pharmacotherapy of 20 of these children at the time of the chart review (Table 9). Nine (45%) were children with some degree of ID. These medications fell into 5 classes: alpha-adrenergic agonists (10 children); antipsychotics (8 children); antidepressants (7 children); antihistamines (3 children); and an anticonvulsant (2 children). Some of the children received more than one additional medication.

Nine of the children with comorbid intellectual disabilities received additional medications: clonidine (7); risperidone (3); gabapentin, trazodone and hydroxyzine (1 each). Four of the children with PDD's received additional medications: quetiapine, olanzapine, gabapentin, clonidine (1 each) and diphenhydramine (1 child). Three of the children with comorbid ODD received additional medications: clonidine (2); trazodone and diphenhydramine (1 each). Two of the children with comorbid borderline intellectual functioning received additional medications: clonidine, trazodone, paroxetine, and gabapentin (2 each). Two of the children with learning disabilities received additional medications: clonidine and hydroxyzine (1 each).

DISCUSSION

This is a report of the use of stimulants in a naturalistic community setting with a population of children with ADHD and a 63% prevalence of a broad range of developmental disabilities (ID, borderline intellectual functioning, learning and language disabilities, PDD's and MCDD). Stimulants have been found to be effective in treating children with ADHD comorbid with ID and other developmental disorders,[2,12,20] with children with IQ's in the mild to moderate range of ID having better responses than those in the severe to profound range.[4] We provide data relevant to the following issues: dosages of several different stimulants in children ranging in age from 3 to 13 years; the relative effectiveness of stimulants in children with ADHD and a wide range of comorbid conditions, with emphasis on how the subsample of children with ID compare to the remainder of the sample; the most common target symptoms when stimulants are used; response rates; efficacy with and without comorbidity; side effects; and the use of adjunctive medications.

There have been some reports of the use of medication to treat children with ADHD who were 3 years of age. In a study of children 3 years old or younger in an office based practice in the Michigan Medicaid fee-for-service health care

TABLE 7. OVERALL EFFICACY OF ANY STIMULANT				
Comorbid Conditions	**Effective**	**Not Effective**	**Equivocal**	**Success Rate (%)**
None	16	2	2	80
Developmental disorder				
intellectual disabilities	19	6	1	73
borderline intelligence	6	2	2	60
learning disability/language disorder	17	7	2	63
Oppositional defiant disorder	7	2	1	70
Pervasive developmental disorder not otherwise specified	4	2	0	67
Anxiety disorders[a]	4	0	0	100
Dysthymic disorder	0	4	0	0
Adjustment disorder	3	0	0	100
Psychotic disorder not otherwise specified	2	1	0	67
Posttraumatic stress disorder	2	0	0	100
Autistic disorder	1	0	1	50
Multiple complex developmental disorder	1	1	0	50
Borderline personality disorder	0	0	1	0
[a]excluding posttraumatic stress disorder				

system, there were 223 children diagnosed as having ADHD over a 15-month period. Of these children, 57% received prescriptions for psychotropic medications. Twenty-two different medications were used. The most common treatment was the "off label" use of MPH (31%) with dextroamphetamine used in 14% of the children.[50]

Our doses of immediate release MPH (mg/kg/dose) are in keeping with reports in the literature of 0.3 to 0.5 mg/kg/dose being effective when given b.i.d to preschoolers with ADHD.[18] Our mg/kg/dose and mg/kg/day doses were highest in this 3-6 year old group (MPH only) and lowest in the 10-13 year old group. Our results are in keeping with those of Findling *et al.*[25] who found the "best dose" of a stimulant was inversely associated with weight, so that children in the 4-7 year age group responded to significantly higher weight-adjusted doses than older children. This may have to do with a greater density of dopamine receptors in the brains of younger children. The number of synapses in the human brain is 50% greater at the age of 2 years than in the normal adult brain. The number of synapses then decline until the age of 16 through a process known as synaptic pruning. At that point the adult number of synapses are attained.[52] There may, therefore, be a greater density of dopamine receptors in the brains of younger children. MPH is said to work by binding to the dopamine transporter protein, thus blocking the reuptake of dopamine in the presynpatic neurone, and by increasing the release of dopamine into the extraneuronal space.[68] The greater number of dopamine receptors in our youngest group may explain the requirement for a greater dose of MPH in order to get the desired clinical effect. The highest total daily effective dose of immediate release MPH was 80 mg (20 mg q.i.d), while the highest effective mg/kg/day dose was 2.0. Doses of immediate release MPH in the sample of children with ID was well within the dosage range for the entire population. The average age of this group was 7 years and the 0.71 mg/kg/day dose was well within the range of doses for the entire sample of children in the 7-9 year old group. Doses of OROS MPH tended to be somewhat higher with doses as high as 2.53 mg/kg/day used in some cases.

Most studies of 6-12 year old children with ADHD treated with stimulants report a positive response rate between 70-76%.[39] Our rates varied from 56-68% depending on the stimulant used. Our population differed from most populations reported in the literature in that we had: a younger population (about one quarter of our sample was less than 6 years of age); about a 60% rate of one or another developmental disability; and, a wide range of comorbid conditions in addition to developmental disabilities. Our results indicate that children with ADHD and comorbid ID have similar success rates with any stimulant, when more than one stimulant is tried (73%), as do children with ADHD alone (80%). Our 60% positive response rate for children with BIF is somewhat surprising in the light of a 73% positive

response rate for children with ID. This may be due to the rate and type of comorbidity of the children with BIF who did not respond positively to a stimulant. The four children who did not respond positively each had a comorbid diagnosis (dysthymia, language disorder, PDD, and ODD) which, in our sample, tended to reduce the rate of positive responses.

Most studies of rates of comorbidity in children with ADHD report rates of between 40 and 66%.[5] Studies of rates of comorbidity in

TABLE 8. SIDE EFFECTS RESULTING IN CHANGE OF DOSAGE OR DRUG

Symptoms	Number
Decreased appetite	4
Upset stomach	3
Crying	3
Weight loss	2
Tics	2
Hair pulling	1
Enuresis	1
Blood pressure elevation	1
Day dreaming	1
Moodiness/sadness	1
Drowsiness	1

TABLE 9. ADDITIONAL MEDICATION

Type of Medication	Number
alpha-agonists	
clonidine	9
guanfacine	1
antipsychotics	
risperidone	4
quetiapine	4
olanzapine	1
antidepressants	
trazodone	3
bupropion	1
citalopram	1
fluoxetine	1
paroxetine	1
antihistamines	
diphenhydramine	2
hydroxyzine	1
anticonvulsants	
gabapentin	2

preschoolers with ADHD report a 75% rates with 68% of preschoolers with ADHD having at least two disorders.[64,65] The most common reported behavioral or emotional secondary diagnoses were: conduct/oppositional disorders (40%); depression/dysthymia (18%), and anxiety disorders (6%); and about 15% of children are found to have comorbid learning disabilities.[8] Some reports of comorbid bipolar disorder in children and adolescents range from 11% (outpatients)[24] to 22% (inpatients).[15] Our sample had a 83% rate of comorbidity as we included children with one or more developmental disability.

There are reports that about 23-30% of school age children do not respond to the first stimulant prescribed,[67] but some respond to another stimulant. Sixty-one percent of the children in this sample who failed to improve on one stimulant went on to improve on another. There was little difference in rates of improvement in our ID and non-ID samples when a switch was attempted. Most often the switch was from dextroamphetamine in a preschooler to the "off label" use of MPH.

In keeping with recent reports[17,18,38] that aggression is a treatable target symptom in children with ADHD treated with stimulants, we find that aggression is an appropriate target symptom for children with ADHD and comorbid developmental disabilities. As was found in the MTA and other studies,[21,46] the presence of a comorbid anxiety disorder in our sample was not a contraindication to the use of stimulants. However, stimulants did not appear to be effective in the four cases in which dysthymia was a comorbid condition. It is possible that these children had an as yet undiagnosed bipolar mood disorder which had presented as a depressive disorder.

Rates of side effects with active medication reported in the literature vary from 3.6% to 70.4%.[9,27,43] This last was in a study of preschool children with developmental disabilities.[27] Some studies of MPH resulted in reports of side effects with placebo in more than 50% of the children who participated.[9] Our rate of side effects (17%) with active drug compares favorably with other studies but this figure represents the number of dosage or medication changes as a result of reported side effects. Many reports of side effects in our study did not result in changes of dosage or medication because of the perceived benefits. In keeping with reports from other community settings,[13,72] we find that some children with ADHD and comorbid disorders require the addition of other psychoactive drugs to maximize the effectiveness of pharmacotherapy.

The use of multiple psychoactive agents for the treatment of psychiatric disorders in children and adolescents is not new. This phenomenon is due to the high rates of psychiatric comorbidity, and the often less than satisfactory response to a single medication.[69] In our sample, children with comorbid ID were no more likely to require additional psychoactive drugs than were children with other comorbid conditions. Whereas other studies have pointed to antidepressants as the most common drug to be co-prescribed with a stimulant,[47,48] in our sample alpha-adrenergic agonists were the most common class of drugs to be added. When antidepressants are used in individuals with developmental disabilities, they are usually used in adolescent and young adult populations and for perseverative or obsessive compulsive symptoms.[45] In our sample, alpha-adrenergic agonists were most often used to treat a sleep disturbance which is often associated with ADHD and was a common complaint. Antihistamines were also used as sleep inducers. Antipsychotics were most often added to treat aggression or self injury in children with ID and/or a PDD. Antidepressants were added to treat anxiety or depression and gabapentin was used to treat a possible mood disorder and/or to help with sleep.

Conclusions

These data from a community sample of children with a diagnosis of ADHD who were treated in a naturalistic setting with stimulants leads to the following conclusions. Stimulants appear to be both safe and moderately effective when treating target symptoms of hyperactivity, impulsivity or aggression, across a range of ages spanning the preschool years to early adolescence. Stimulants, as a class, do not appear to lose their effectiveness over time. The "off label" use of MPH in children less than 6 years does not appear to present problems which are in any way different from the use of MPH in older children. The one difference we found was that children 6 years of age received higher mg/kg/dose and mg/kg/day doses of MPH than the older children, although there was no difference in total daily dosage between the 3-6 year olds and the 7-9 year olds.

Stimulants were effective in the presence of a wide range of comorbid conditions including ID,

PDD's, anxiety disorders, and other disruptive behavior disorders. Stimulants were surprisingly ineffective in the presence of comorbid depression and borderline intellectual functioning.[26] ID as a comorbid condition did not seem to affect the rate of effectiveness of stimulants nor did it appear to affect the dosage range in our ID subsample. The subsample of ID children were no more likely to receive an additional psychoactive medication than children in the remainder of our sample, and were as likely to benefit from the addition as the remainder of the sample.

The overall effectiveness of stimulants in this sample tended to be below that which is reported in the literature but most studies do not include the broad range of comorbid conditions present in our sample and do not include large numbers of children under 6 years of age. It is our impression that when a group of children below 6 years of age present for an evaluation and treatment recommendations due to disruptive behavior, they tend to be a group that is more treatment resistant than older groups. We await the results of the current placebo-controlled study of the use of immediate release MPH in children under 8 and as young as 3 years to see if this impression is substantiated.

As is done in other naturalistic settings, we have augmented stimulants with a number of different classes of psychotropic drugs in an attempt to maximize the effectiveness of pharmacotherapy. In such cases we have found stimulants to be "user friendly" in that they rarely produced serious adverse interactions when combined with other drugs. We have not found that combining stimulants and alpha-adrenergic agonists has resulted in significant side effects despite some concerns about this combination.[58,67]

Finally, as is hinted at in this report, the use of longer acting (sustained release) forms of stimulants may be replacing the use of shorter acting (immediate release) forms in naturalistic clinical settings.[66]

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