Psychotic Side Effects of Psychostimulants: A 5-Year Review

Esther Cherland, MD, FRCPC[1], Renée Fitzpatrick, MB, MRCPsych, FRCPC[2]

Objective: *To examine the rate of psychotic and mood-congruent psychotic side effects of stimulant medications in children treated for attention-deficit hyperactivity disorder (ADHD).*

Method: *A chart review was completed of all children diagnosed with ADHD in an outpatient clinic from January 1989 to March 1995.*

Results: *Over 5 years, 192 children were diagnosed with ADHD. Ninety-eight children received treatment at the clinic with stimulants. Six children developed psychotic or mood-congruent psychotic symptoms during treatment. Children on medication were followed for an average of 1 year and 9 months.*

Conclusions: *Awareness of the potential for psychotic side effects from stimulant medications is important when prescribing for children. A large prospective study would be useful to predict the frequency and classification of the side effects in children.*

(Can J Psychiatry 1999;44:811–813)

Key Words: *children, stimulants, side effects, attention deficit, psychosis, mood-congruent psychosis*

Psychotic symptoms are well-known side effects of all stimulant medications (1). Caplan and Tanguay reported that medications such as pseudoephedrine, antihistamines (promethazine hydrochloride, tripolidine hydrochloride), and methylphenidate (MPH) have been reported to induce hallucinations (2). Psychotic symptoms in children who are prescribed MPH for attention-deficit hyperactivity disorder (ADHD) are described as rare, brief, and occurring with treatment within the therapeutic dose range (3,4). Tactile and visual hallucinations and delusions have been reported (5–9). There is no case in the literature of the psychotic reaction persisting after medications have been stopped (10).

Barkley and others assessed side effects of MPH in a triple-blind crossover study (11). Eighty-three children were on each regimen for 7–10 days. They examined 17 common side effects at high- and low-dosage MPH and placebo. One child was described as exhibiting "excessive speech and disjointed thinking." Another short-term study of stimulant side effects compared MPH and dextroamphetamine in a double-blind crossover trial (12). Side effects were recorded by parents on the Barkley Side Effects Rating Scale (SERS). One child did not complete the MPH trial because of increased aggression and tearfulness; 2 other children stopped the dextroamphetamine trial because of agitation and aggression or overfocus and anxiety. Each of these children completed the trial on the crossover medication successfully. The trial was 2 weeks long and also used the SERS. Unfortunately, the SERS does not contain questions about agitated and unusual behaviour or hallucinations. It does include questions about euphoria, depression, and anxiety.

Schachar and others examined the therapeutic and nontherapeutic effects of MPH for a longer trial, 4 months, in a sample of 91 children (13). Children with comorbid depression and anxiety were excluded. In addition, the average dose was higher, 0.6 mg/kg daily. Three of the 46 children placed on MPH discontinued the treatment during initial titration because of side effects of sadness, deterioration in behaviour, irritability, withdrawal, lethargy, violent behaviour, or rash. One discontinued in the second month and another in the third month. These 2 children had symptoms of withdrawal, mania, and dysphoria. The 3 studies suggest that, despite careful screening, psychotic side effects may occur and occur at rates higher than previously reported (3,4).

We examined any psychotic symptom occurring after the initiation of MPH, pemoline, or dexedrine. These included hallucinations, psychotic symptoms, and mood-congruent psychotic symptoms. The purpose was to determine the rate of these symptoms to help improve the monitoring of these potential side effects of the stimulant medications.

Method

We performed a chart review of all children who attended an outpatient child mental health clinic diagnosed with ADHD from January 1989 to March 1995. Diagnoses were made by 1 of 3 child psychiatrists using *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III-R, DSM-IV) criteria for attention deficit disorder (ADD) or ADHD. The diagnostic work-up included a psychiatric interview and psychometric testing. Conners' Teacher Rating Scale-Revised was used to assess the response to the stimulant (14). Random checks of the charts were made over the period by the senior child psychiatrist to assess the completeness of information and adherence to diagnostic criteria. The checks were not specific to ADD or ADHD. A standard system of recording response to medication was used in the charts.

Symptoms determined by the authors as suggesting psychosis were interpreted by 2 independent reviewers. The reviewers rated whether the recorded symptoms were side effects of the medication or part of the child's psychopathology. They used DSM-IV criteria for amphetamine intoxication and definitions for psychotic and mood-congruent psychotic symptoms (15).

Results

Over the entire period, 5 years and 2 months, 192 children were diagnosed with ADHD, 146 males and 46 females. Ninety-eight of the children were treated with MPH at our clinic, 2 of whom were receiving a second medication. The average length of time the children were followed on medication was 1 year and 9 months.

Of the 98 children treated with stimulant medication, 9 children developed psychotic symptoms (Table 1). Three children had amphetamine intoxication, 1 had psychotic symptoms, 3 had mood-congruent psychotic symptoms, and 1 was unclassifiable because information about the event was insufficient. Using the Clinical Global Severity of Illness (CGI-S) scale, the mean rate of impairment caused by the these symptoms was 4.6 (range 4–6). Similar to descriptions in the literature, most of the children and adolescents improved upon withdrawal of the MPH.

Table 1. Children with psychotic effects

Sex	Age	Weight (kg)	Medication	Dose (mg daily)	Time to side effect	Symptom
Male	9 years 5 months		Methylphenidate	5	First dose	Bizarre behaviour
Female	10 years	40	Methylphenidate	35	15 months	Paranoia
Male[a]	12 years	35	Methylphenidate	10	7 years	Visual hallucinations
Male[b]	7 years	25.8	Methylphenidate	10	4 months	Unrealistic fear of being harmed by other children
Male	12 years	42	Pemoline	18.75	2 doses	Auditory hallucinations; aggressive, agitated behaviour
Male	4 years	15.1	Methylphenidate	5	First dose	Bizarre behaviour, giddiness
Female[a]	9 years	32	Pemoline	37.5	1 month	Depression, hallucinations, suicidal behaviour
Male[c]	5 years	21.9	Methylphenidate	15	A few weeks	Euphoria, flight of ideas, decreased sleep, increased energy
Male[c]	17 years	60	Methylphenidate	80	6 months	Concrete thought, severe depression

[a]Received pemoline after a trial of methylphenidate; time between trials was at least 3 months.

[b]Later diagnosed with pervasive developmental disorder, not otherwise specified.

[c]Later diagnosed with bipolar affective disorder.

Three of the 9 children were later diagnosed with another psychiatric disorder, 1 with pervasive developmental disorder not otherwise specified, and 2 with bipolar affective disorder (BPAD). The 2 with BPAD continued to have symptoms following cessation of the stimulant. Three of 9 children were prescribed pemoline 2 to 3 months after stopping MPH. All 3 developed psychotic or mood-concurrent psychotic symptoms within 1 month of beginning pemoline. The symptoms ceased as soon as the medication was

removed. Three children hallucinated, 2 with auditory and 1 with visual hallucinations.

Eleven children developed either mood-only symptoms or mood-congruent psychotic symptoms while being treated with MPH (11.7%). One child with severe depression required hospitalization.

Discussion

Psychotic symptoms in the chart review appear to cluster in 3 groups: MPH-induced hallucinosis, slower-developing paranoia, and mood-congruent psychotic symptoms. All 3 kinds of psychotic side effects have been previously reported in case reports of children (4,5,8,16). The frequency of developing psychotic side effects in large numbers of children treated with stimulants is not known. In our chart review, the frequency was 6%. As there is an inherent bias with such a review for low reporting of side effects, the findings are likely to underestimate the prevalence.

As the study is retrospective, assessments are not fully standardized, nor is the follow-up consistent. However, the size of the review and the rate of side effects suggests that a prospective study would be useful. Considering the importance of stimulant medications in treating children with ADHD, more precise measurement of these side effects, clinically and in the literature, is warranted.

Clinical Implications

- Clinicians need to measure psychotic side effects of stimulants in children with care.
- The frequency of psychotic side effects from stimulants in large numbers of children is unknown.
- A prospective study of psychotic side effects in children is warranted

Limitations

- The study is retrospective.
- The assessments were not standardized.
- The follow-up of the children was routine.

References

1. Polchert SE, Morse RM. Pemoline abuse. JAMA 1985;254:946–7.

2. Caplan R, Tanguay PE. Development of psychotic thinking in children. In: Lewis M, editor. Child and adolescent psychiatry: a comprehensive textbook. New York: Williams and Wilkins; 1991. p 310–7.

3. Golinko B. Side effects of dextroamphetamine and methylphenidate in hyperactive children–a brief review. Prog Neuropsychopharmacol Biol Psychiatry 1984;8:1–8.

4. Weiss G. Attention deficit hyperactivity disorder. In: Lewis M, editor. Child and adolescent psychiatry: a comprehensive textbook. New York: Williams and Wilkins; 1991. p 554–61.

5. Young J. Methylphenidate-induced hallucinosis: case histories and possible mechanisms of action. J Dev Behav Pediatr 1981;2:35–8.

6. Lucas AR, Weiss M. Methylphenidate hallucinosis. JAMA 1971;217:1079–81.

7. Spensley J, Rockwell DA. Psychosis during methylphenidate abuse. N Engl J Med 1972;286:880–1.

8. Bloom AS, Russell LJ, Weisskopf B, Blackerby JL. Methylphenidate-induced delusional disorder in a child with attention deficit disorder with hyperactivity. J Am Acad Child Adolesc Psychiatry 1988;27:88–9.

9. Rosenfeld AA. Depression and psychotic regression following prolonged methylphenidate use and withdrawal: case report. Am J Psychiatry 1079;136:226–8.

10. Barkley RA. Attention deficit hyperactivity disorder: a handbook for diagnosis and treatment. New York: Guilford Press; 1990.

11. Barkley RA, McMurray MB, Edelbrock CS, Robbins K. Side effects of methylphenidate in children with attention deficit hyperactivity disorder: a systemic, placebo-controlled evaluation. Pediatrics 1990;86:184–92.

12. Efron D, Jarman F, Barker M. Side effects of methylphenidate and dexamphetamine in children with attention deficit hyperactivity disorder: a double-blind, crossover trial. Pediatrics 1997;100:662–6.

13. Schachar RJ, and others. Behavioral, situational, and temporal effects of treatment of ADHD with methylphenidate. J Am Acad Child Adolesc Psychiatry 1997;36:754–63.

14. Goyette CH, Conners CK, Ulrich RF. Normative data on revised Conners parent and teacher rating scales. J Abnorm Child Psychol 1978;6:221–36.

15. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Appendix C. Washington (DC): American Psychiatric Association; 1994. p 763–71.

16. Koehler-Troy C, Strober M, Malenbaum R. Methylphenidate-induced mania in a prepubertal child. J Clin Psychiatry 1986;47:566–7.

Résumé

Objectif : *Examiner le taux d'effets secondaires psychotiques et psychotiques congruents à l'humeur des stimulants chez les enfants traités pour le trouble d'hyperactivité avec déficit de l'attention (THADA).*

Méthode : *On a mené une étude des dossiers d'une clinique externe pour tous les enfants ayant reçu un diagnostic de THADA, de janvier 1989 à mars 1995.*

Résultats : *Sur 5 ans, 192 enfants ont reçu un diagnostic de THADA. Quatre-vingt dix-huit enfants ont reçu un traitement de stimulants à la clinique. Six enfants ont développé des symptômes psychotiques ou psychotiques congruents à l'humeur durant le traitement. Les enfants prenant des médicaments ont été suivis en moyenne durant 1 an et 9 mois.*

Conclusions : *La connaissance des effets secondaires psychotiques éventuels des stimulants importe lorsqu'on prescrit aux enfants. Une vaste étude prospective serait utile pour prédire la fréquence et la classification des effets secondaires chez les enfants.*

Manuscript received September 1998, revised, and accepted April 1999.

This paper was previously presented at the Canadian Child and Adolescent Psychiatry Convention, Victoria, BC, 1995.

[1]Associate Professor, Department of Psychiatry, Royal University Hospital, Saskatoon, Saskatchewan.

[2]Psychiatrist, Student Health, Queen's University, Kingston, Ontario.

Address for correspondence: Dr E Cherland, Division of Child Psychiatry, Royal University Hospital, 103 Hospital Drive, Saskatoon, SK S7N OW3

email: cherland@duke.usask.ca