Case Report

Visual disorders with psychostimulants: A paediatric case report

Julie Soyer, PharmD^{1,✉}, Jennifer Jean-Louis BSc¹, Luis H. Ospina MD PhD², Stacey Ageranioti Bélanger MD PhD⁴, Jean-François Bussières BPharm MSc MBA FOPQ^{1,3}, Niina Kleiber MD PhD^{4,5}

¹Pharmacy Practice Research Unit, Pharmacy Department, Sainte-Justine Hospital, Montréal, Québec; ²Department of Pediatric Ophthalmology and Neuro-Ophthalmology, Sainte-Justine Hospital, University of Montréal, Montréal, Québec; ³Faculty of Pharmacy, University of Montréal, Montréal, Québec; ⁴Department of Paediatrics, CHU Sainte-Justine, Université de Montréal, Montréal, Québec; ⁵Clinical Pharmacology Unit, Department of Paediatrics, CHU Sainte-Justine, Université de Montréal, Montréal, Québec

Correspondence: Niina Kleiber, Centre Hospitalier Universitaire Sainte-Justine, Département de pédiatrie générale, 3175, chemin de la Cote-Sainte-Catherine, Montreal, Quebec H3T 1C5. Telephone 514-345-4931, fax 514 345 4822, email niina.kleiber@umontreal.ca

Abstract

Methylphenidate- and amphetamine-based psychostimulants are the most common medications used to treat the symptoms of attention-deficit/hyperactivity disorder in children. Ocular side effects including dry eyes, mydriasis, accommodation disturbance, and blurry vision are listed in the product monograph but interestingly, are rarely reported in the paediatric literature. Our patient, a 9-year-old boy, presented a significant decrease in visual acuity secondary to accommodation disorder after being treated with methylphenidate hydrochloride controlled release (Biphentin) and lisdexamfetamine (Vyvanse). The unusual acute adverse effect, altered accommodation leading to a decline in visual acuity, emphasizes the importance of considering any change in vision following the introduction of psychostimulant medication as a potential adverse effect. This case highlights the importance of pharmacovigilance especially in paediatrics where data are lacking.

Keywords: *Attention-deficit disorder with hyperactivity; Central nervous system stimulants; Coloboma; Visual disorders*

Attention-deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental disorder leading to impaired everyday function and development. Methylphenidate- and amphetamine-based psychostimulants are the most common medications used to treat the symptoms of ADHD in children and youth (1). Psychostimulants bind to the presynaptic transporter protein, inhibiting dopamine and norepinephrine reuptake into the presynaptic neuron, hence enhancing central nervous system dopaminergic and noradrenergic neurotransmission.

Decreased appetite, insomnia, abdominal pain, and headaches are common side effects of psychostimulants. Ocular side effects including dry eyes, mydriasis, accommodation disturbance, and blurry vision are listed in the methylphenidate monograph (2) but rarely reported in the paediatric literature.

We present a case of significant decline in visual acuity in a child following treatment with psychostimulants.

CASE PRESENTATION

A 9-year-old boy previously treated with carbamazepine for generalized epilepsy and followed in ophthalmology for bilateral congenital optic nerve, ciliary body and iris colobomas, myopia and astigmatism was diagnosed with attention-deficit disorder. He was treated with methylphenidate hydrochloride controlled release (Biphentin) at an initial dose of 10 mg (0.4 mg/kg) titrated gradually to 40 mg daily (1.6 mg/kg). One month later, although improvement was seen in the core symptoms of ADHD he was referred to the ophthalmologist complaining of disturbed visual acuity

Table 1. Naranjo's score

Questions	Yes	No	Don't know	Score given
1. Are there previous conclusive reports on this reaction?	1	0	0	1
2. Did the adverse event appear after the suspected drug was administered?	2	–1	0	2
3. Did the adverse event improve when the drug was discontinued or a specific antagonist was administered?	1	0	0	1
4. Did the adverse event reappear when the drug was readministered?*	2	–1	0	2
5. Are there alternative causes (other than the drug) that could on their own have caused the reaction?	–1	2	0	2
6. Did the reaction reappear when a placebo was given?	–1	1	0	0
7. Was the drug detected in blood (or other fluids) in concentrations known to be toxic?	1	0	0	0
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	1	0	0	1
9. Did the patient have similar reaction to the same or similar drugs in previous exposure?	1	0	0	0
10. Was the adverse event confirmed by objective evidence?	1	0	0	1
Total Score: 10				
Total Score	Interpretation of scores			
≥9	Definite. The reaction followed a reasonable temporal sequence after drug exposure had been established in body fluids or tissues, followed a recognized response to the suspected drug, was confirmed by the improvement on withdrawing the drug and reappeared on re-exposure.			
5–8	Probable. The reaction followed a reasonable temporal sequence after a drug exposure, followed a recognized response to the suspected drug, was confirmed by withdrawal but not by exposure to the drug and could not be reasonably explained by the known characteristics of the patient's clinical state.			
1–4	Possible. The reaction followed a temporal sequence after a drug exposure, possibly followed a recognized pattern to the suspected drug, and could be explained by characteristics of the patient's clinical state.			
≤0	Doubtful. The reaction was likely related to factors other than a drug.			

*We accounted both drugs as one class since they share the same pharmacological mechanism. Hence, the positive answers to the questions 1, 2, 3, and 4.

difficulty seeing objects close and at a distance. On examination, there was a significant decrease in visual acuity secondary to an accommodation disorder (Far visual acuity: right eye [RE] 20/40 and left eye [LE] 20/125, near visual acuity: RE and LE 20/100). No etiology for the sudden deterioration in vision was identified. Retinal detachment due to colobomas was excluded. Biphentin administration was stopped immediately resulting in a complete resolution of the visual disturbance within a week. Two months later, lisdexamfetamine (Vyvanse), an amphetamine-based psychostimulant, was initiated and titrated to 20 mg (0.8 mg/kg) daily. Within 2 weeks following initiation of treatment, ADHD symptoms improved but there was a recurrence of

the visual disturbances (Far visual acuity: RE 20/40 and LE 20/80). Lisdexamfetamine was ceased and atomoxetine (Strattera), a nonstimulant second-line medication for the treatment of ADHD was prescribed and titrated to 20 mg (0.8 mg/kg) daily. Four days later, the dose of atomoxetine was increased following visual acuity recovery. One month later, on a dose of 25 mg (1 mg/kg) per day, his vision remained stable and atomoxetine was effective for the patient's symptoms of ADHD.

The adverse effect described was reported to the Health Canada's postmarket surveillance program, a governmental organization that collects and assesses suspected adverse reactions to drugs marketed in Canada.

DISCUSSION

The case reported describes two occurrences of reversible visual acuity deterioration in a child with colobomas while treated with two different psychostimulants namely methylphenidate and lisdexamfetamine but not on atomoxetine, a nonstimulant. With both psychostimulants, vision was restored following drug cessation. The disappearance of an adverse effect when the drug is stopped (positive de-challenge) is highly suggestive of causality. Both drugs are psychostimulants acting on dopamine reuptake. This common pharmacologic pathway suggests a shared causality mechanism. Moreover, the reappearance of the adverse effect after lisdexamfetamine initiation (positive re-challenge) further suggests causality. We used the Naranjo Score (Table 1) to assess the imputability of methylphenidate and lisdexamfetamine on the deterioration of vision. The Naranjo score is a questionnaire designed by Naranjo et al. (3) used to assess the causal relationship between an adverse drug reaction and the suspected drug by taking into account several factors.

Although dysfunction in accommodation is reported in the product monography (2), no reported cases could be identified following a systematic search, conducted with a trained librarian, on the ophthalmologic effects of psychostimulants. A possible explanation is that the loss of visual acuity following the introduction of psychostimulants may be overlooked.

In a prospective pilot study including 14 patients (mean age 11 years), Larrañaga-Fragoso et al. (4) studied the effects of methylphenidate on refraction and anterior segment parameters in children with ADHD. In contrast to the adverse effects reported in our patient, no significant differences in refraction or accommodation, including indirect accommodation were found after 9 months of follow-up. However, there was a significant reduction in the anterior chamber depth raising concerns about a potential risk for glaucoma. Methylphenidate, a sympathomimetic amine classified as an adrenergic agonist, is contraindicated in patients with glaucoma. A case of bilateral complicated cataract and glaucoma in a 10-year old treated with methylphenidate for 2 years has been reported by Lu et al. (5). The postulated mechanism was cytoskeletal change in the chamber angle trabecular meshwork or obstruction of the trabecular meshwork.

A recent prospective study (6) compared the detailed ophthalmological examination of 57 children (mean age 11.2 years) treated with methylphenidate for at least 1 year and 60 healthy controls. Early signs of cataract formation were detected in five patients treated with methylphenidate. The authors concluded that long-term use of methylphenidate may be responsible for lens opacities in a dose-related manner. Neither loss in visual acuity or change in accommodation was reported.

Prospective studies report visual adverse effects in a limited number of patients associated to the intake of psychostimulants. However, acute visual acuity loss and accommodation disturbances experienced by our patient have not been described previously. The presence of colobomas in our patient may explain a higher susceptibility to the adverse effect of psychostimulants. In rare cases, coloboma involving the ciliary body may affect accommodation. We hypothesize that the effect on accommodation was triggered by the activation of the dopaminergic system. For a given accommodation effort, amphetamines, sharing similar pathways with psychostimulants, increase accommodative convergence. Acute intoxication with amphetamines results in severe dilatation of the pupils and paresis of accommodation (7).

CONCLUSION

We presented an unusual acute adverse effect, disturbed accommodation leading to decline in visual acuity, associated with the administration of psychostimulants for the treatment of ADHD. This case highlights the importance of considering any change in vision following the introduction of psychostimulant medication as a potential adverse effect. Unawareness of this adverse effect may explain the lack of reported cases in the literature despite its report in the product monograph. This case highlights the importance of pharmacovigilance especially in paediatrics where data are lacking.

Informed consent has been obtained to publish this case.

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