Should We Continue Methylphenidate Treatment Despite Orofacial or Extremity Dyskinesias?

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ABSTRACT:
Should we continue methylphenidate treatment despite orofacial or extremity dyskinesias?

Attention-deficit/hyperactivity disorder (ADHD) is the most common neuropsychiatric condition of school-aged children. Its estimated prevalence is around 5.3% for children and adolescents1. Methylphenidate immediate-release (IR), a short-acting stimulant has been used widely more than 60 years to treat ADHD. In this paper 3 cases with orofacial and/or limb dyskinesia after methylphenidate administration are reported. In 2 of our patients, continuation of the methylphenidate treatment did not cause recurrent dyskinesia. We thought that despite dyskinetic side effects, in cases with normal IQ level, continuation of methylphenidate treatment may be safe and do not cause any recurrent dyskinetic movements. Despite dyskinesia, one more chance may be given to methylphenidate treatment.

Keywords: methylphenidate, orofacial dyskinesia, attention-deficit/hyperactivity disorder

INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is the most common neuropsychiatric condition of school-aged children. Its estimated prevalence is around 5.3% for children and adolescents1. Methylphenidate immediate-release (IR), a short-acting stimulant has been used widely more than 60 years to treat ADHD2,3. With the increasing frequency of cases using methylphenidate, in the literature variety of side effects were extensively described3. Headache, irritability, insomnia, appetite suppression, tachycardia, tremor, dizziness, anxiety, hypertension, hallucination, chorea, tics, psychosis, dyskinetic disorders are the most common side effects4,5. Longer acting stimulants such as osmotic-release oral system (OROS) methylphenidate offer greater convenience, confidentiality, and compliance with single daily dosing but may have greater side effects on sleep and appetite6. It is assumed that the effect of methylphenidate is mediated by blocking the reuptake of norepinephrine and dopamine into the presynaptic neurons and increasing the release of these neurotransmitters into the extraneuronal space7. Although the
precise mechanism is not known, it’s thought that the alteration of norepinephrine and dopamine systems may be the reason of dyskinesia after methylphenidate use.

In this paper, 3 cases with orofacial and/or extremity dyskinesia after initial doses of methylphenidate treatments are reported.

**CASE PRESENTATIONS**

All of the three patients had uneventful pregnancy and delivery history. They were born from healthy, nonconsanguineous parents without family history of any psychiatric diseases, movement and muscle disorders. Complete blood count, liver and renal function tests, serum electrolyte levels, and electrocardiography were normal. None of the patients were on any prescriptions other than methylphenidate for ADHD. They did not have any chronic diseases.

**CASE 1**

A 7-year-old boy was admitted to our emergency department after second dose of methylphenidate immediate-release. He was complaining about repetitive facial grim, lip smacking, protrusion of tongue, and involuntary movements of hands and fingers. There were no abnormal movements of upper face and eyes. He had diagnosis of mild mental retardation and had a newly diagnosed ADHD according to the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM 5). Two hours after second dosage of 5 mg methylphenidate IR, his orofacial and limb dyskinesias have started. On physical examination his consciousness level was normal, his body temperature was 36.6°C, pulse 105 per min, blood pressure 105/65 mmHg. His weight was appropriate according to his age (26 kg). There was no abnormality on neurological examination other than dyskinesia. The patient was admitted to the hospital due to dyskinesias and administered 2.5 mg intramuscular biperiden. Two hours after biperiden the involuntary orofacial and limb movements have completely resolved. The parents did not want to use methylphenidate again so the treatment has been ceased.

**CASE 2**

An 8-year-old boy was admitted to our emergency department after administration first dose of methylphenidate IR. He was complaining about repetitive facial contortions and abnormal neck movement. His IQ level was normal and he had a newly diagnosed ADHD according to DSM 5 criteria. On physical examination his consciousness level was normal, his body temperature was in normal range, pulse 110/min, blood pressure 100/70 mmHg. His weight was appropriate according to his age (31 kg). There was no abnormality on neurological examination. His mother told that 3 hours after first dosage of 5 mg methylphenidate IR, his facial contortions and abnormal neck movements have started and in a couple of hours all abnormal movements have decreased by time. There were no abnormal movements when he applied to the hospital. After informing the family about the side effects of the drug we continued the methylphenidate IR treatment. First 2 months, 5 mg methylphenidate IR was used twice a day. There were no side effects depending on the drug. Since the hyperactivity symptoms didn’t resolve completely, the dosage of methylphenidate IR treatment increased as 10 mg twice a day. There was no repetition of dyskinesias in the following 12 months period.

**CASE 3**

A 6-year-old boy was admitted to our child psychiatry department after first dose of 18 mg OROS-methylphenidate. He was complaining about repetitive facial grimaces, lip smacking, and protrusion of tongue. There were no abnormal movements of upper face, eyes and extremities. His IQ level was normal and had a newly diagnosed ADHD according to DSM 5 criteria. On physical examination; his consciousness level was normal, his body temperature was 36.9°C, pulse 115 per min, blood pressure 100/65 mm Hg. His weight
was appropriate according to his age (23 kg). There were no abnormalities on neurological examination other than dyskinesias. Approximately 2 hours after his use of first dose of OROS-methylphenidate, his orofacial dyskinesias had started. The patient was followed for a couple of hours and in 2 hours later all symptoms have resolved. No treatment has been required. After informing the parents, 18 mg OROS-methylphenidate was planned to continue. There was no repetition of dyskinesias in the following 3 months period. After 3 months, despite the persistence of attention deficit and hyperactivity symptoms 27 mg OROS-methylphenidate has been prescribed. Dyskinesia did not repeat in the following 8 months follow up period.

**DISCUSSION**

Abnormal movements such as facial grimaces, lip smacking, protrusion of tongue, and involuntary movements of hands and fingers may occur as a component of tic disorders in the children. Once we observe these abnormal movements in children, first of all we should rule out tic disorders. In DSM-5, tic disorders are classified as Tourette syndrome, persistent tic disorder and provisional tic disorder. In Tourette syndrome and persistent tic disorder, the patients should have symptoms for at least one year and these should not occur due to taking medicine or other drugs. In our cases all of them had presented the symptoms after taking methylphenidate and symptoms resolved in no longer than 1 day and they did not reoccur following discontinuation. Provisional tic disorder is diagnosed when tic disorder occurs in no longer than 1 year and the symptoms are not due to taking medicine or other drugs. Although the dyskinesias may be similar in both of the diseases, our cases differ from tic disorders, due to the fact that for being both persistent or provisional and being secondary to methylphenidate treatment.

Since methylphenidate is both well tolerated and efficacious for ADHD, its prescription is increasing worldwide. Side effects are more recognized with a few serious adverse reactions. Pharmacokinetic half-life of methylphenidate IR is short, and the maximum drug concentration is observed in 2 hours. So side effects are seen mostly during these first hours of administration.

Although drug-induced dyskinesias have been widely described in the literature in association with antipsychotic agents depending on their dopaminergic system blocking effect there are also few case reports in the literature secondary to methylphenidate use. Also there are a few reports about dystonic reactions after discontinuation of methylphenidate treatment. Dyskinesias after both administration of methylphenidate or discontinuation of methylphenidate are not exactly known yet.

Once dyskinesia occurs as a side effect, it may be left untreated or some medications may be used depending on the severity of the dyskinesia. In our first case we used biperiden for dyskinesia and the symptoms resolved. Diphenhydramine, has antihistaminic and anticholinergic effects, is widely used for dyskinesias. However, in some cases biperiden, centrally active anticholinergic drug, is seen effective for the treatment of dyskinesia.

Waugh reported a 23-month-old boy with repetitive tongue thrusting to the left, and less frequent left laterocollis and grimace of the face after accidentally ingestion of methylphenidate. Complete resolution of the movements observed after 2 doses of diphenhydramine (1.1 mg/kg) in 15 hours.

Yilmaz et. al reported a 7-year-old boy presented with orofacial and limb dyskinesia after methylphenidate. He was diagnosed with epilepsy and treated with sodium-valproate. The symptoms resolved completely 15 hours after ingestion of methylphenidate without any treatment. It is assumed that antiepileptic therapy may increase the sensitivity to the side effects of methylphenidate. Balazs et al. and Senecky et al. have reported orofacial and/ or extremity dyskinesias immediately after methylphenidate treatment in patients with lower IQ or borderline intellectual functioning. Our first case similar with these 2 cases calls into questions about
Should we continue methylphenidate treatment despite orofacial or extremity dyskinesias?

different mechanisms involving drug-receptor interaction or individual drug sensitivity dependent on lower IQ level. In all of the cases the presenting symptoms, which developed after first or second dose of methylphenidate, have occurred as the first time in their life. There were no history of convulsions. Due to the character of the dyskinetic movements we did not consider epilepsy or seizure disorder. In the second case the physical examination was normal on presentation. In the first case symptoms were resolved after biperiden so we excluded the epileptic syndromes. In the third case in 2 hours symptoms resolved without any treatment by time. There were no other associated symptoms of epilepsy.

In conclusion, especially children with lower IQ scores and epilepsy should be monitored closely for adverse reactions during the first doses of treatment. These side effects in patients with lower IQ scores and epilepsy will be more resistant to the treatment and will be long lasting. Depending on the symptom severity, dyskinesias can be left untreated and observed for hours until resolving the symptoms or can be treated with biperiden or diphenhydramine. These side effects are assumed to occur due to individual drug sensitivities. In the cases with normal IQ level, continuation of the methylphenidate treatment, despite dyskinetic side effects, may not cause any recurrent dyskinetic movements. If it is necessary to use the medication because of the severity of symptoms depending on ADHD, despite dyskinesia risk, one more chance can be given to methylphenidate in ADHD patients with normal IQ level. There should be more studies about mechanism of the association of drug interaction and IQ level with side effects of methylphenidate treatment to understand the underlying causality.

References:


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