

# Chin Trembling Induced by Combined Use of OROS Methylphenidate and Procaterol Hydrochloride in a Boy with ADHD

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## ABSTRACT:

Chin trembling induced by combined use of OROS methylphenidate and procaterol hydrochloride in a boy with ADHD

Recently, asthma has been reported to be a potential comorbidity of attention deficit hyperactivity disorder (ADHD). It is, therefore, possible to have combined use of medications for both ADHD and asthma although, potential adverse reactions are unknown. The case presented here is that of a 61/2-year-old boy diagnosed as having both ADHD and asthma. He presented with chin trembling after the first administration of OROS methylphenidate and procaterol hydrochloride. This is the first report of an adverse event in patients using a combination of these two types of drugs. It raises an awareness of chin trembling as an adverse effect in patients using a combination of methylphenidate and procaterol hydrochloride, especially among those who are younger and underweight.

**Keywords:** attention-deficit/hyperactivity disorder (ADHD), asthma; adverse effect, OROS methylphenidate, procaterol hydrochloride

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## INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is a common disorder of childhood that affects 5% to 10% of school-age children<sup>1,2</sup>. Psychostimulants such as methylphenidate and amphetamine are the first-line treatment for ADHD<sup>3</sup>. OROS methylphenidate (Concerta, ALZA Corporation, Vacaville, USA), a slow-release hydrochloride formulation, has good efficacy and safety profiles.

However, comorbidity is very common in patients with ADHD. Recently, asthma was reported as a newly-described comorbidity of ADHD<sup>4,5</sup>. The prevalence of asthma was significantly higher in the ADHD patient group than the general population,

and patients with asthma had higher scores on ADHD symptom rating scales<sup>5</sup>. In a prospective population-based study, Mogensen et al. found that children with asthma at age 8-9 years had an almost two-fold increased risk of having one or more symptoms of hyperactivity-impulsivity (HI), and a more than twofold increased risk to have three symptoms or more of HI at age 13-14 years, independent of asthma medications<sup>4</sup>. The multiplicity of ADHD comorbidities renders treatment particularly challenging.

Herein, we report a boy with both ADHD and asthma, who with presented chin trembling after combined use of OROS methylphenidate and procaterol hydrochloride.

## CASE PRESENTATION

A 6<sup>1</sup>/<sub>2</sub>-year-old boy was brought to the psychiatric clinic for his inattentive and hyperactive behaviors. He was in the first grade in primary school. His father described him as a “busy” boy, always “driven by a motor”. He had difficulty engaging in activities quietly and waiting his turn. He could not pay close attention to details in his schoolwork, and often lost his pencils or eraser. He had a short attention span, and was easily distracted by extraneous stimuli. His academic performance was lower than average. His behaviors were assessed by the Vanderbilt ADHD Parent and Teacher Rating Scales, the Conner’s Rating Scale and SNAP-IV. In addition, the WISC-R and WCST were performed. Based on DSM-IV criteria, he was diagnosed with ADHD, combined subtype. He had no history of tics or other severe medical conditions except asthma. He had been diagnosed with acute asthma 4 days before this visit and the pneumologist had prescribed a  $\beta$ 2-receptor agonist, procaterol hydrochloride tablets (Meptin, Zhejiang Otsuka Pharmaceutical Co., Ltd, Lin’an, China), for him. He took 12.5 micrograms every morning and evening. His symptoms of asthma were improved after the medication.

We prescribed OROS methylphenidate at a dosage of 18 mg/day. The boy began to take this medication at 7:00 AM the next day and on the same day, his teacher observed that he had much better concentration, and gave positive comments about him. He became proactive in doing his homework at 16:30 after school. However, his mother found that his chin was trembling and the movement could not be stopped by diverting his attention. His parents took him back to the hospital at 17:30 because they were worried about the side effects of the drugs.

At our clinic, the patient’s vital signs were stable, with a pulse of 89 beats/minute, respiration rate of 18 times/minute, blood pressure 102/60 mmHg, and O<sub>2</sub> saturation 99%. His body temperature was 36.9°C, and the blood glucose was normal at 4.7 mmol/L. His height was 124.5 cm with a body weight of 19.5 kg.

The unintentional and persistent chin trembling

was confirmed, but could be partially suppressed by talking to him. He spoke with his parents and physicians reasonably. He had good environmental interpretation and no agitation. He told the physician that he felt well when his chin was trembling, but he could not control the movement. He was not able to figure out when the movement occurred. The mother told us that the boy took 12.5 mg of procaterol hydrochloride in addition to OROS methylphenidate within 30 minutes in the morning before he went to school.

On physical examination, the boy coordinated very well with the physician’s action. His heart rate was regular, and his pulse was strong. The neurological examination found no positive results and no agitation. Electrocardiogram (ECG) and brain CT scan showed normal results. The complete blood count, myocardial enzyme levels, and electrolytes were all within normal range.

The management for this boy was primarily supportive. The patient was given 500 ml intravenous bolus of normal saline and glucose. He was closely observed. Gradually, he improved and showed no more unintentional chin movement about one hour later (6:30 PM). The boy was discharged after three hours of observation.

Two weeks later, his asthma symptoms improved, and he stopped the administration of procaterol hydrochloride. Then, we recommended that he take only OROS methylphenidate again under close monitoring. No chin trembling or other tic-like movements occurred between then and his most recent visit. His ADHD symptoms had improved substantially at his 5-month follow-up.

## DISCUSSION

OROS methylphenidate works for ADHD by blocking the reuptake of both noradrenaline and dopamine at their respective transporters. It has been reported to be well tolerated by ADHD patients in several clinical trials<sup>6</sup>.

In our ADHD patient, chin trembling appeared after the first administration of OROS methylphenidate. We primarily thought it was due to OROS methylphenidate’s adverse effect.

However, when he took the same tablet once again 2 weeks later, the symptom of chin trembling did not appear. We found that the first dose of OROS methylphenidate was administered together with procaterol hydrochloride for his asthma. Although procaterol hydrochloride has the side effect of tremor with an incidence of 2.43% according to FDA data<sup>7</sup>, it showed efficacy without any side effects in the first 4 days of treatment in our patient. It appears that the single use of procaterol hydrochloride or OROS methylphenidate do not induce the symptom of chin trembling; however, combined use of these two medications may have induced chin trembling. Therefore, we speculate that OROS methylphenidate and procaterol hydrochloride had synergistic effects resulting in the adverse reaction. The following hypothesis might partly explain the possible mechanism. As we know, methylphenidate is a central nervous system stimulant, and shares part of its basic structure with catecholamines, which may affect the peripheral nervous system. This effect could be enhanced when used in combination with a  $\beta$ -2-receptor agonist and inducing chin trembling. Nevertheless, a single clinical case cannot allow us to uncover the underlying mechanism. Further studies on animals may help us elucidate the mechanism.

Earlier studies have demonstrated the onset of action of OROS methylphenidate to be 1 hour post dose, with length of activity of no more than 12 hours<sup>8-11</sup>. The time to peak plasma concentration has been found to be  $6.8 \pm 1.8$  hours. Procaterol hydrochloride's time course of action has been reported to be 6-8 hours. Therefore we might expect that the chin trembling would begin between 12:00-16:00. In addition, chin trembling abated 11.5 hours after administration (7:00 AM-18:30). There was no specific treatment except supportive management because of the pharmacokinetics of these two drugs.

The boy had both conditions of ADHD and asthma. Combined use of OROS methylphenidate and procaterol hydrochloride led to chin trembling in our case, which indicated the likelihood of drug interactions between these two drugs. However, this patient had several characteristics that we should take into consideration: 1) he was stimulant-naïve, which meant that he was more sensitive to the medication, 2) he was underweight and one tablet of 18 mg was a relatively high dose for him and 3) he had another medical condition, asthma, and had been using procaterol hydrochloride for its treatment. All of those factors may have contributed to the occurrence of the adverse effect. Thus, psychostimulants are not recommended when the patients were being given a  $\beta$ -2-adrenergic receptor agonist, especially for patients who are younger and underweight.

To our knowledge, this is the first report about this adverse effect in patients after combined use of OROS methylphenidate and procaterol hydrochloride. Since the comorbid condition of asthma is common in the ADHD group, treatment for the patients with both of them is challenging. Our case report has practical implications for psychiatrists and physicians, who prescribe methylphenidate for children with ADHD comorbid asthma. It raises an awareness of chin trembling as a potential adverse effect in patients with combined usage of methylphenidate and procaterol hydrochloride. As emphasized, those in younger ages and who are underweight are more likely to experience this side effect.

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