

## Polypharmacy in a nine year old boy with Attention Deficit Hyperactivity Disorder and Tourette Syndrome: what worsened the tics?

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### ABSTRACT

**Introduction:** Attention Deficit Hyperactivity Disorder (ADHD) and Tourette Syndrome (TS) commonly co-occur, imposing a special challenge in the management. **Case report:** This is a case of a nine year old boy with ADHD and TS, who had been on methylphenidate, risperidone, fluvoxamine and atomoxetine, alone and in combination. Tics worsened with methylphenidate but improved after its withdrawal, and the addition of risperidone and fluvoxamine. Later, atomoxetine was added which worsened the tics, even when it was removed. Significant improvement in the tics were only obvious when fluvoxamine was taken off. **Discussion:** The possible roles of dopamine and serotonin neurotransmission, and metabolism of cytochrome P450 D26 in the pathophysiology were discussed. **Conclusion:** The use of multiple medications need cautious consideration and monitoring in a child patient to avoid unwanted complications and risks.

**Keywords:** Fluvoxamine, Atomoxetine, Worsening tics

### INTRODUCTION

ADHD and TS frequently occur together. Although effective medications are available, the challenge lies in harmonizing the benefit and side-effects of the medications in treating the disorder and its associated conditions. Due to the common comorbid conditions, combination of medications are usual occurrence. Worsening of tics caused by atomoxetine<sup>1</sup> and fluvoxamine alone<sup>2</sup> have been reported previously. We report a case of a young Malaysian boy with ADHD and TS, whereby combinations of atomoxetine and fluvoxamine worsened the tics. The complexity in the management and risk of polypharmacy in children is discussed.

### Case report

MP is a nine year old boy with mild motor tics, and predominantly inattentive symptoms which were first noticed three years ago. His attention span was short and he had difficulty focusing on the given task. He was easily distracted, disorganized, and frequently lost his belongings. Teachers complained that he always made careless mistakes and failed to complete his schoolwork. Similar difficulties were observed at home. He was brought to see a Child and Adolescent Psychiatrist at nine years old, due to worsening of symptoms and impairment in his daily functioning. A diagnosis of ADHD with predominantly inattentive symptoms was made.

He was started on Concerta (Methylphenidate Extended Release) 20 mg daily with improvement in the symptoms but tics worsened four months later. He presented with motor tics involving body parts such as the upper limbs, neck and abdomen. He also had vocal tics such as involuntary shouting. The symptoms impaired his functioning at home and school. A diagnosis of TS was made and Concerta was immediately withdrawn. Risperidone 0.5 mg daily and Fluvoxamine 12.5 mg daily were added. He was then referred to the Child and Adolescent Psychiatric Clinic, Universiti Kebangsaan Malaysia Medical Centre.

When he was seen at our clinic, the tics were mild but symptoms of ADHD started to interfere with his functioning at school and at home. For that reason, decision was made to start atomoxetine 18 mg daily (body weight was 32kg), the only available pharmacological option to treat his ADHD symptoms. Risperidone and fluvoxamine were continued at the same dose.

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Upon starting atomoxetine, motor and vocal tics worsened in frequency and intensity. There were vigorous involuntary movements of the neck, upper limbs and abdomen including 'jumping movement'. On few occasions, he had fallen down the stairs due to the uncontrollable movements. Unfortunately, the medications were continued for two weeks before his mother sought treatment. Atomoxetine was withdrawn, while the dose of risperidone was increased to 0.75 mg daily and fluvoxamine continued at the same dose. There was only slight improvement after atomoxetine was withdrawn. Marked improvement was seen only after fluvoxamine was removed from the treatment regime.

## DISCUSSION

It is of high possibility that combination of atomoxetine and fluvoxamine caused the worsening of tics in this boy. There were no worsening of tics when he was treated with fluvoxamine and risperidone alone. Although worsening of tics occurred after atomoxetine was introduced, marked reduction in symptoms were only seen after fluvoxamine was removed.

Theoretically, atomoxetine does not increase dopamine in the striatum resulting in the absence of motor tics,<sup>3</sup> but it may have broader effects on the neuromodulators than was previously postulated.<sup>1</sup> These may explain the few reported cases of atomoxetine worsening tics in children.<sup>4</sup> Furthermore, atomoxetine is poorly metabolized by cytochrome P450 2D6,<sup>4</sup> resulting in the delay of the symptoms even after withdrawal of the medication. Combination of atomoxetine and fluvoxamine further worsened the tics which disappeared significantly only after removal of both medications. Fluvoxamine use has been reported to worsen tics in a 14 year old boy.<sup>2</sup>

The Malaysian Clinical Practice Guidelines (CPG) for ADHD, recommended pharmacological treatment alone or combination treatment (i.e. pharmacological and non-pharmacological) for the management of ADHD.<sup>5</sup> To date, only methylphenidate and atomoxetine are available pharmacological treatment for ADHD in Malaysia. The limited treatment alternative is a challenge particularly when the child does not tolerate both medications as highlighted in this case. Non-pharmacological treatment alone has not been useful, particularly for moderate and severe symptoms of ADHD.

It is very important that treatment is individualized to the best interest of the child. Medications should always be used with cautious and polypharmacy should be avoided if possible. Given that the child had mild tics at the initial presentation, medication known to trigger or worsen tics such as methylphenidate should not be used. Psychoeducation is probably the most important aspect in the whole management plan. At the meantime, the non-pharmacological treatment of ADHD such as parent training, behavioural intervention, school intervention, and occupational therapy should be strengthened to help the child coping with his symptoms.

Parent training involves teaching parents behavioural intervention to manage the children's behavior. It assists parents to provide structured environment with consistent limits and consequences. Teacher's participation with classroom behavioural intervention improves attention and reduces hyperactivity in classrooms. Occupational therapy facilitates in daily organizing skills and attention training.<sup>5</sup>

In conclusion, although pharmacotherapy is the recommended treatment for ADHD, polypharmacy should be avoided if possible or used with caution in children.

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