

## ATOMOXETINE AND TICS IN ADHD

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### Letters to the Editor

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#### ATOMOXETINE AND TICS IN ADHD

##### *To the Editor:*

Atomoxetine is a nonstimulant medication shown to be efficacious in the treatment of attention-deficit/hyperactivity disorder (ADHD). There have been no reports to date of tics being precipitated or exacerbated by atomoxetine. We report four patients with ADHD who had developed tics on stimulants and in whom tics reappeared or were exacerbated on atomoxetine. Moreover, the tics resolved or abated significantly when atomoxetine was discontinued. The possibility of tics as an adverse effect of atomoxetine may also shed light on the neurochemical systems involved in patients with comorbid ADHD and tic disorders.

The first patient is a 9-year-old adopted boy with unknown family history and no history of tics. He was first diagnosed with ADHD, combined type, in March 2002 and treated with methylphenidate and then with Adderall (amphetamine/dextroamphetamine) and dextroamphetamine. Upon starting medications, he developed motor tics that ceased upon discontinuation of treatment. He remained medication free for 6 months. Because of the persistence of ADHD symptoms, he was started on atomoxetine at 10 mg every morning in June 2002, and the dose was increased to 20 mg every morning after 1 week. Within a few days of the dose increase, he developed motor tics consisting of rapid, severe eye blinking, similar to those he developed previously on stimulants. There were no vocal tics. The medication was stopped, and the tics ceased within 1 to 2 days. He was then started on guanfacine, on which his ADHD is well controlled, and there has not been a recurrence of tics for more than a year.

The second patient is a 14-year-old white boy diagnosed with ADHD, predominantly inattentive type. He developed an eye-blinking motor tic on Concerta (methylphenidate), which was discontinued. He was then started on atomoxetine 20 mg q.d.; however, the eye blinking worsened, and he started developing a vocal tic of severe bouts of throat clearing. After a few days, atomoxetine was discontinued, the vocal tics resolved, and eye blinking diminished. He is currently on guanfacine with only mild eye blinking persisting.

The third and fourth patients are both boys, 9 and 15 years old, with histories of chronic tic disorder and ADHD. They had also experienced tic exacerbations on stimulants. For the 9-year-old, within a month of starting atomoxetine up to 18 mg q.d., he developed dramatic vocal tics and increased motor tics accompanied by irritability, anxiety, dysphoria, compulsive finger picking, and obsessional ruminations, whereas he only had facial tics when not on medication. For the 15-year-old with Tourette's syndrome, within 5 days of beginning atomoxetine at 10 mg q.d., he developed a very marked increase in tics, impulsivity, and fatigue. The tics and associated symptoms diminished when atomoxetine was stopped in both patients.

Stimulant medications have been the mainstay of treatment of ADHD. However, they are associated with appetite loss, headaches, gastrointestinal symptoms, irritability, dysphoria, and insomnia. Although controversy exists about its prevalence, precipitation and exacerbation of tics are potential adverse effects in a small number of children ( King et al., 2002 ). There has been a continued search for nonstimulant medications. Atomoxetine, a nonstimulant, noncontrolled drug has been reported to be efficacious in the treatment of ADHD ( Michelson et al., 2002 ). It acts as a potent inhibitor of the presynaptic norepinephrine transporter ( $K_i$  4.5 nmol/L) with minimal affinity for other noradrenergic receptors or other neurotransmitter systems. Side effects include decreased appetite; upset stomach, nausea, or vomiting; and tiredness; tics were not listed as a potential side effect ( Wernicke and Kratochvil, 2002 ). McCracken et al. (2003) found that atomoxetine up to 1.5 mg/kg per day did not increase tic severity in 76 children with comorbid ADHD and tic disorder.

The apparent ability of atomoxetine to precipitate or exacerbate tics provides insights into possible neurochemical pathways involved in tic disorders. Dopaminergic, serotonergic, and noradrenergic systems have all been implicated in Tourette's syndrome ( Leckman and Cohen, 1999 ). Noradrenergic involvement is further suggested by the stress sensitivity of tics ( Leckman and Cohen, 1999 ) and the therapeutic effects of the presynaptic  $\alpha_2$ -adrenergic agonists. It might be speculated that atomoxetine, acting as a potent inhibitor of the presynaptic norepinephrine transporter, may increase the synaptic norepinephrine in such a way that tics are precipitated or exacerbated in a predisposed patient.

One confounding factor is that ADHD and tic disorders are often comorbid. Although two of these patients did not have a history of tic disorder, they first developed tics on stimulant medications. However, in all four patients, the discontinuation of atomoxetine was followed by diminution of tics. For patients with ADHD, especially those with preexisting tics, it is important to consider the possibility that atomoxetine can unmask or increase tics in vulnerable patients and alternative medications should be considered.

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