

Buspirone Use in the Treatment of Atomoxetine-Induced Bruxism

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To The Editor:

ATENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) is a neurobehavioral disorder characterized by common inattention and hyperactivity-impulsivity symptoms, leading to psychosocial impairments. In society samples, the prevalence of ADHD in school-age children varies between 2% and 18% (Rowland et al. 2002). Pharmacotherapy is the most important component of ADHD treatment. Psychostimulants are the most common treatment for ADHD (Taylor et al. 2004).

Atomoxetine is a selective noradrenergic reuptake inhibitor that was approved by the United States Food and Drug Administration (FDA) in 2002 for the treatment of ADHD in children ≥ 6 years of age (Michelson et al. 2002). The most common side effects of atomoxetine are headache, abdominal pain, loss of appetite, asthenia, nausea, vomiting, and vertigo (Michelson et al. 2002; Wolraich et al. 2007). These effects are generally temporary and do not require the tapering of therapy (Wolraich et al. 2007; Garnock-Jones and Keating 2009).

Bruxism is a common disorder defined as excessive activity that results from grinding or clenching of the teeth and certain strong jaw movements (Clark and Ram 2007). Bruxism affects 8–21% of the population. It is more common at young ages and its incidence decreases with age (Bader and Lavigne 2000).

The etiology of bruxism is a controversial issue, but it is thought to be multifactorial (Jaffe and Bostwick 2000). Bruxism can occur in association with anxiety, benzodiazepines, use of alcohol, or selective serotonin reuptake inhibitors (SSRIs). It is thought that dopamine agonist medications can cause bruxism or worsen pre-existing symptoms (Ellison and Stanziani 1993; Micheli et al. 1993; Bader and Lavigne 2000; Wise 2001; Winocur et al. 2003; Clark and Ram 2007). Bruxism can cause serious damage to tooth enamel, and temporomandibular articular pain in severe cases (Bader and Lavigne 2000; Clark and Ram 2007).

SSRIs have significant effects on bruxism, and their use has increased in recent years. However, bruxism seems to be less frequent, as bruxism is overlooked by psychiatrists or not presented as a complaint by patients especially when it is mild. There are previous reports of bruxism induced by SSRIs or venlafaxine (Ellison and Stanziani 1993; Jaffee and Bostwick 2000; Wise 2001). Various agents such as buspirone, gabapentin, and tandospirone have been used to treat SSRIs-induced bruxism (Ellison and Stanziani 1993; Jaffee and Bostwick 2000; Wise 2001; Winocur et al. 2003).

A patient with aggravating bruxism caused by atomoxetine was reported in the literature (Mendhekar and Lohia 2009). As far as we know, this is the second reported case of bruxism related to atomoxetine.

Case Report

An 8-year-old boy was presented to our outpatient clinic with complaints of lack of attention, lack of concentration, getting bored with activities quickly, failure in school, and behavioral problems. These complaints appeared when he was 3–4 years of age. The presenting symptoms included difficulty in paying attention to lessons at school, getting bored easily, and hyperactivity (swinging leg, fidgeting). Following clinical assessment, the patient was diagnosed with ADHD according to American Psychiatric Association, *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. (DSM-IV) criteria (American Psychiatric Association 1994).

The patient was prescribed atomoxetine 10 mg/day. After 10 days of medication, atomoxetine dosage was increased to 18 mg/day. In the 3rd week, the patient's parents and teachers reported significant improvement of attention deficit symptoms and school-related problems. When interviewed, the family did not mention any side effect except for loss of appetite. In the 4th week, atomoxetine dosage was increased to 40 mg/day. Approximately 1 month after medication onset, the parents noticed that the child was grinding his teeth every night for ~40–50 min. Bruxism was sufficiently loud to be heard from other rooms. The patient's 4-year-old sibling previously had shared the same bedroom, but was unable to remain in the room because of the noise of teeth grinding. In subsequent days, the patient began to complain of jaw pain, which lasted all day but was more severe in the mornings. The parents presumed that the jaw pain might originate from a tooth problem and visited a dentist. The dentist identified temporomandibular pain related to teeth grinding and started paracetamol treatment. However, the patient continuously had severe discomfort because of teeth grinding and jaw pain. Treatment was, therefore, discontinued on the suspicion that the bruxism was related to atomoxetine. Following discontinuation of atomoxetine, bruxism ceased. Atomoxetine was restarted 4 weeks later, and subsequently bruxism reappeared. Then, buspirone 5 mg was added to the treatment; after 10 days, a significant reduction of bruxism was observed. Bruxism was not observed during 4 month follow-up. The possibility of medication side effect was assessed via the Naranjo Probability Scale (Naranjo et al. 1981). It was concluded that there was a possible relationship between atomoxetine and bruxism.

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Discussion

Bruxism is characterized by nonfunctional teeth locking, and grinding leads to temporomandibular articular dysfunction, weakening of teeth, periodontal diseases, hypertrophy of masseter, and headache (Bader and Lavigne 2000; Clark and Ram 2007). It has been reported that benzodiazepines, β -blockers, anticholinergic agents, botulinum toxin, and buspirone can be beneficial in bruxism treatment (Micheli et al. 1993; Bader and Lavigne 2000; Winocur et al. 2003; Clark and Ram 2007). There is no reliable information on the time range of the onset of medication-induced bruxism. It has been reported that bruxism can appear between 6 hours and 11 months after starting drug therapy (Winocur et al. 2003).

In our case, ADHD symptoms were exacerbated when atomoxetine was discontinued. We decided to start methylphenidate, but the family declined this psychostimulant treatment because of concerns about possible side effects. Atomoxetine was significantly beneficial to the patient. As it was reported to be effective in SSRI-related bruxism, we added buspirone to the current treatment (Bostwick and Jaffee 1999; Jaffee and Bostwick 2000; Wise 2001).

Buspirone's mechanism of action is unclear, but is thought that it has a partial agonistic effect on serotonin-1A (5HT_{1A}) receptors. Buspirone has effects on both presynaptic somatodendritic 5HT_{1A} autoreceptors and postsynaptic 5HT_{1A} receptors (Stahl 2002). The effect of buspirone on the dopaminergic system is not clearly understood, and it is thought that these effects have limited clinical importance (Hudziak and Waterman 2005).

A review of PubMed identified a case in which a patient was reported to have existing bruxism that got worse with atomoxetine (Mendhekar and Lohia 2009). There are no reports of newly developed bruxism in response to atomoxetine treatment. This side effect of atomoxetine has not been defined before or after its marketing (Strattera prescribing information 2013).

We conclude that there was a possible relationship between atomoxetine and nocturnal bruxism in this case, based on observation that bruxism reappeared with the resumption of atomoxetine. Substances related to dopaminergic, serotonergic, and adrenergic systems can increase or suppress bruxism activity (Ellison and Stanziani 1993; Micheli et al. 1993; Winocur et al. 2003). It is thought that atomoxetine's mechanism of action, which improves ADHD symptoms and sustains this effect, functions via very specific inhibition of presynaptic norepinephrine reuptake (Garnock-Jones and Keating 2009).

Conclusion

To conclude, while prescribing atomoxetine, it should be remembered that it may cause bruxism, and the presence of bruxism should be questioned during psychiatric visits. Buspirone is used to improve treatment in various psychiatric conditions, and was reported to be very beneficial in bruxism treatment (Bostwick and Jaffee 1999; Jaffee and Bostwick 2000; Stahl 2002; Hudziak and Waterman 2005).

Further systematic studies are required in order to establish the relationship between atomoxetine and bruxism.

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