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LETTER TO THE EDITOR

Stuttering worsened with atomoxetine treatment in a child with attention deficit and hyperactivity disorder

Dikkat eksikliği ve hiperaktivite bozukluğu olan bir çocukta atomoksetin tedavisi ile kötüleşen kekemelik

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To the Editor,

Stuttering is defined as an -age and linguistic skill-inappropriate impairment in the fluency of timing of speech that can emerge at any age. Recent studies have reported a lifetime incidence of in the general population of approximately 10%. It is twice as common in males compared to females and this rises with age to three or four times1. Environmental and genetic factors can play a role in the emergence of stuttering. One environmental factor is the use of medication. Several drugs can cause or exacerbate stuttering. Medications known to exacerbate stuttering include tricyclic antidepressants, bupropion, antipsychotics, propranolol, theophylline and memantine2.

Atomoxetine is a selective norepinephrine reuptake inhibitor psychotropic agent. It is a safe and effective agent frequently employed as a first-line treatment in children and adolescents with attention-deficit hyperactivity disorder (ADHD)3. Side effects frequently encountered during atomoxetine use include headache, abdominal pain, decreased appetite, nausea, vomiting and sedation4. Rare side effects such as Raynaud's phenomenon, priapism and flushing may also be seen5,6,7.

There are few cases involving progression of stuttering with atomoxetine use in the literature. We describe a case of stuttering worsening in a dose dependent manner during atomoxetine therapy for ADHD symptoms in a seven year old girl.

A seven year old girl was brought to our clinic by her family due to hyperactivity and irritability. History taken from the family revealed that she had been over active and fidgety since infancy, had frequent accidents, was only capable of playing with her toys for very brief periods, was easily bored, failed to pay attention in class after starting school, had difficulty in doing homework, regularly chattered in class, had difficulty in waiting her turn and found it difficult to remain seated in class. At evaluation in terms of comorbidity we also learned that she had developmental stuttering. In the light of the history given by the family, clinical examination and information obtained from her teacher, she was diagnosed with ADHD.

Treatment in the form of 1 mg/kg/day atomoxetine was planned. The patient was started on 10 mg/day atomoxetine and this was maintained for one week. In the second week the dosage was raised to 18 mg/day. No side effect was observed at 18 mg/day, but the symptoms of ADHD persisted, and the atomoxetine dosage was increased to 25 mg/day. At interview three weeks subsequently, we learned that the patient's stuttering had worsened significantly from the second day of the latest dose increase and that she had become almost incapable of speech. The neurology department was consulted, but no neurological cause was identified. We also learned from the family that no medication, herbal product or substance had been used during atomoxetine therapy. Discontinuation of atomoxetine therapy was recommended at control examination. The patient's

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stuttering complaints resolved within one week after discontinuation of atomoxetine. No stuttering related worsening was determined at three monthly follow up after discontinuation. We planned to monitor the patient's ADHD symptoms at two monthly intervals. Verbal consent to the publication of this case was received from the parents and the patient.

This report described a case of stuttering that worsened with atomoxetine therapy. Our review of the literature revealed very few case reports of stuttering developing in association with atomoxetine. Çicek et al. reported a case of stuttering worsening with atomoxetine in a 14-year-old boy8. The side effect emerging during atomoxetine use in the present case was dose dependent and resolved after discontinuation of the medication. Similarly in the case reported by cicek et al., the side effect was dose dependent and resolved after the medication was stopped. No increase in stuttering related symptoms was observed at follow ups following discontinuation in either case. The side effect emerging in our case was assessed using the Naranjo Adverse Drug Reaction Probability Scale (NADRPS), on which scores≥9 are regarded as definite and scores between 5 and 8 as doubtful. Our case was scored as 8 (probable) on the NADRPS. The fact that our patient received atomoxetine as the first and monotherapy, that the stuttering worsened immediately after the atomoxetine dose increase, and that the side-effect disappeared immediately after discontinuation of atomoxetine all suggest that the stuttering was 'probably' (with a score of 8) associated with atomoxetine therapy.

Although the mechanism of the therapeutic effect of atomoxetine is not yet fully understood, a number of hypotheses have been proposed. Atomoxetine is thought to raise the concentrations of norepinephrine and dopamine in the synaptic cleft by inhibiting the norepinephrine reuptake pump, particularly in the prefrontal cortex.

Atomoxetine exhibits no significant effect on serotonin reuptake pumps. In the prefrontal cortex, however, it specifically increases dopamine concentrations. However, it has no such effect on the motor or reward center of the striatum9. The etiology of stuttering is also not fully understood, although cases benefitting from antidopaminergic therapy have been reported in the literature. This adverse effect may be best explained by atomoxetine raising dopamine levels.

This report describes a case of stuttering exacerbated with atomoxetine therapy. There are very few similar case reports in the literature. It will be useful, in terms of side-effect and treatment management, for clinicians to remember that stuttering may worsen during atomoxetine use in cases of stuttering comorbid with ADHD. Further, more extensive studies with larger case series or samples are now needed to confirm the results of this report.

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