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Aggravating influence of atomoxetine on the severity of stuttering and successfully treated with methylphenidate: a case report

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Abstract

Stuttering is a communication disorder characterized by a disruption in normal fluency and time patterning of speech. None of the pharmacological agents for stuttering could be recommended for general use. Therefore, specific a drug treatment which is simultaneously effective for both stuttering and attention deficit hyperactivity disorder (ADHD) is currently unknown. In this article, it is presented a case affected by severe developmental stuttering and attention-deficit/hyperactivity disorder who exacerbated with atomoxetine but favorably responded to treatment with methylphenidate.

Keywords: Stuttering; atomoxetine; methylphenidate; attention deficit hyperactivity disorder; child/adolescent

Atomoksetinin kekemeliğin şiddeti üzerine ağırlaştırıcı etkisi ve metilfenidat ile başarılı bir şekilde tedavi edilmesi: olgu sunumu

Öz

Kekemelik, konuşmanın normal akıcılığı ve zamanlama örüntüsünde bir aksaklık ile karakterize bir iletişim bozukluğudur. Kekemelikte hiçbir farmakolojik ajan genel kullanım için önerilmemiştir. Bu nedenle, hem kekemelik hem de dikkat eksikliği hiperaktivite bozukluğu (DEHB) için aynı anda etkili olan spesifik bir ilaç tedavisi şu anda bilinmemektedir. Bu makalede, atomoksetin ile şiddetlenen ancak metilfenidat tedavisine olumlu yanıt veren ciddi gelişimsel kekemelik ve dikkat eksikliği hiperaktivite bozukluğu olan bir olgu sunulmuştur.

Anahtar Kelimeler: Kekemelik; atomoksetin; metilfenidat; dikkat eksikliği hiperaktivite bozukluğu; çocuk/ergen

Introduction

Stuttering is a communication disorder defined as a disruption in which normal fluency and time patterning of speech. Its main characteristics include frequent prolongations and/or repetitions of spoken sounds and/or syllables, audible or silent blocking, interjections and word production with excess physical tension (1,2).

Stuttering has a lifetime prevalence of up to 8.5% and affects especially boys. The most common pattern is developmental stuttering and appears during childhood. Stuttering is often self-limiting and approximately 75% of cases resolve spontaneously. Speech therapy is the main treatment modality of stuttering (2).

It is known that there is a relationship between stuttering and attention skills. Recently, a study has described that 58% of stutterers have symptoms of attention deficit hyperactivity disorder (ADHD) (3).

No pharmacological agent has been recommended for general use without acceptable side effects. Therefore, specific a drug treatment which is simultaneously effective for both stuttering and ADHD is currently unknown. Yet, it has been recommended to avoid psychostimulants which increase dopamine and to prefer the use of atomoxetine or clonidine when the two disorders co-exist (4). On the other hand, several case reports and clinical anecdotes have reported both favorable (5-7) and reverse (8,9) consequences regarding the effects of methylphenidate on stuttering.

As for the non-stimulant atomoxetine, no data which has linked the use of atomoxetine with the onset and/or exacerbation of stuttering was found. It has even been reported that atomoxetine has a beneficial effect on stuttering (10).

Here, an adolescent affected by severe developmental stuttering and ADHD, who exacerbated with atomoxetine but favorably responded to treatment with methylphenidate was explained. Written informed consent for case presentation and publication was obtained from patients and his parents, on condition that the patient's anonymity must be preserved.

Case Report

A 14-year-old male was referred to the clinic with complaints of attention deficit, concentration difficulties and stuttering since he was 7 years old. Primary complaints were attention problems, and poor organizational skills because these problems were an obstacle to high-school entrance exam. In addition, his social functioning was impaired because of stuttering. He had never received speech therapy due to economic and transportation limitations. The relationship of stuttering with anxiety and social situations was not so obvious. It was detected that he had severe stuttering and secondary symptoms within his efforts to get his words out, and hence his communication was severely disrupted. He did not have dysarthria or aphasia.

After clinical examination and taking information from family and case, he was diagnosed with developmental stuttering and ADHD predominantly inattentive presentation according to the DSM-V (1). His neurological and otorhinolaryngologic consultation, all routine laboratory investigations, thyroid function tests, and electrocardiogram showed no abnormality. His ADHD diagnosis was made when he was 7 years old but he had not used the recommended medication. There was no important feature in his background. All developmental steps, including speech-language development phases had been timely. He did not have epileptic seizures, traumas, or other significant physical diseases. In his family history, his uncle had permanent developmental stuttering.

He was prescribed 25 mg/day of atomoxetine and gradually increased to 40 mg/day. Unfortunately, stuttering was appreciably exacerbated within the third week of treatment, so the dose of atomoxetine was reduced back to 25 mg/day. However, the worsening of stuttering did not regress. The patient and his family reported that there were periods with a variable duration from 10 days to 3 months when the frequency and intensity of stuttering increased or decreased without any obvious triggering factor or event, in the patient's history, but this increase reached its peak with the use of atomoxetine. The expected effect of the atomoxetine for ADHD was not also reached. Thus atomoxetine was terminated within the seventh week of treatment. Stuttering regressed to the old level, after 10 days off the medication.

Thereupon, he was started on 10 mg/day of methylphenidate, which was increased to 18 mg/day from the second week. At follow-up 3 weeks later, his stuttering dramatically reduced and the severity of ADHD symptoms greatly diminished. Treatment was continued with methylphenidate at a fixed dose of 27 mg/day for more than one year and improvement of the stuttering was sustained. Even though no scale was used for the stuttering severity during the follow-up period, it was stated by himself and his family that stuttering was significantly reduced, and this well-being was observed during the interviews as well.

DISCUSSION

This study described an unfavorable reaction to atomoxetine on stuttering in a patient who presented with comorbid stuttering and ADHD. However, he demonstrated a remarkable relief of the stuttering after the intake of methylphenidate.

Two results are important in the treatment of the case presented here. Firstly, this may be the first stuttering case presentation which exacerbated by atomoxetine. Because there was no other similar case report about atomoxetine, as far as it can be found within the literature data at the time this case report was written. Conversely, there is evidence that the use of atomoxetine not only reduces symptoms of ADHD but also stuttering behaviors (10). Atomoxetine is a selective norepinephrine reuptake inhibitor and its action mechanism is to increase the release of norepinephrine and dopamine in the prefrontal cortex. It may be recommended as a priority in patients with ADHD who have comorbid anxiety disorders or

depression (11). Even if the relationship between our patient's stutter moments and anxiety is very weak, it is still interesting to note that stuttering is markedly aggravated with atomoxetine. This dramatic worsening may result from atomoxetine affects the dopaminergic system indirectly by raising the noradrenaline level. Atomoxetine simultaneously also increases extracellular levels of dopamine as well as noradrenaline in the prefrontal cortex, because there are very few DA transporter (DAT) proteins in the prefrontal cortex (11-13). Thus, one could speculate that atomoxetine can mediate stuttering by affecting dopamine levels.

Secondly, this case report is one of the few studies that illustrate a striking improvement of stuttering with methylphenidate. Frankly, there are conflicting results regarding the effects of methylphenidate on stuttering. Several case reports have suggested that methylphenidate clearly improves stuttering (5-7), while others have reported that methylphenidate has adverse effects (8, 9). The first clinical evidence for stuttering associated with the use of methylphenidate was presented by Alparslan et al (9). Nevertheless, methylphenidate has not been extensively studied for stuttering treatment, therefore, it is difficult to reach a definite conclusion about the effect of methylphenidate on speech fluency. A study has shown that methylphenidate provides a significant improvement in stuttering compared to placebo (6).

Our patient's pronounced positive response to methylphenidate can be explained by the effect of methylphenidate on the dopaminergic system, which is also implicated in the stuttering mechanism. Some stutter adults heal with Dopamine D1 or Dopamine 2 D2 blockers, and others worsen (4). Methylphenidate stimulates Dopamine 1 (D1) receptors and reduces Dopamine D2 receptors by indirect stimulation (7). Moreover, striato-cortico-thalamic

pathways, which have an important function in executive functions, are involved in both ADHD and stuttering. Methylphenidate enhances executive functions. Because verbal fluency is also considered to be one of the executive functions, methylphenidate may have been effective on stuttering through improving executive functions (6,7). However, given the contradictory effects of methylphenidate on stuttering, there may be other mechanisms than these mechanisms.

Conclusion

As a result, here, it was presented an interesting treatment finding for stuttering which has deteriorated with atomoxetine and has clearly improved with methylphenidate is presented. Although no similar cases have been reported in the literature, clinicians should be aware that atomoxetine may have an adverse effect on the severity of stuttering. On the other hand, methylphenidate may be an option for treatment of stuttering in cases who presented with comorbid stuttering and ADHD. Further extensive and larger sample studies are needed to reinforce or refute the confusing findings obtained from this case. Replicating future studies with these agents will improve our understanding of stuttering and the neurobiological basis of ADHD.

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