Case Report

Sertraline-related hiccups in a girl with obsessive-compulsive disorder

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Abstract

Hiccups are the products of simultaneous involuntary spasmodic contractions of the diaphragm and glottic closure, resulting in the failure of air to enter the trachea. Multiple causes have been attributed to the etiology of hiccups, including drugs. Selective serotonin reuptake inhibitor (SSRI)-related hiccups are rarely reported in the available literature. Hereby, we present a 10-year-old girl with obsessive-compulsive disorder who developed persistent hiccups with sertraline treatment.

Keywords: girl, hiccups, sertraline

Introduction

Hiccups are the products of simultaneous involuntary spasmodic contractions of the diaphragm and glottic closure, resulting in the failure of air to enter the trachea [1]. The hiccups reflex arc consists of the phrenic and vagus nerves and the sympathetic chain from thoracic segments T6–T12 in the afferent limb. Phrenic nerve, brain stem and midbrain areas including the respiratory center, phrenic nerve nuclei, medullary reticular formation, and hypothalamus are contained in the efferent limb. The C3–C5 cervical segments and the brain stem probably form the central link between the afferent and the efferent limbs [2]. Multiple causes have been attributed to the etiology of hiccups, including gastric distension or gastroesophageal reflux, drugs, lesions or infections of the central nervous system, and irritation of the phrenic or vagus nerves. Although the exact pathophysiological processes have not yet been established, the neurotransmitters dopamine, serotonin, and gamma amino butyric acid (GABA) have been documented to play a significant role in the generation of hiccups [3]. A 10-year-old girl with obsessive-compulsive disorder who developed persistent hiccups with sertraline treatment is presented below.

Case

A 10-year-old girl was referred to our clinic with complaints of washing her hands more than 20 times in a day, spending long hours in the bath, feeling excessive distress while using school toilets and touching anywhere except in her house. Developmental milestones
were within normal range. Psychiatric history revealed no psychiatric diagnoses. Physical examination was unremarkable. Screening for organicity was negative. Children’s Yale-Brown Obsessive-Compulsive Scale (C-YBOCS) and Clinical Global Impressions Scale (CGI-S) scores were 30 and 5, respectively. With the diagnosis of obsessive-compulsive disorder according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, sertraline 50 mg/day was initiated gradually. Psychoeducation was given to the parents and child in order to alleviate their distress. The patient and her family reported that within 24 hours of taking sertraline 50 mg/day, the patient began having hiccups continuously, for which she consulted a general medical practitioner. After a preliminary examination, she was advised to stop sertraline. The patient and her family reported no history of gastrointestinal disease, polydipsia, or substance abuse. Results of a neurologic examination were grossly normal. The blood, biochemistry, and thyroid function test results were unremarkable. No medication was started to stop hiccups because of the symptoms ceased substantially after the last dose of sertraline. Two weeks after the hiccups stopped, sertraline treatment was restarted and the hiccups started again. Sertraline was immediately stopped and fluoxetine 20 mg/day was started. After one month, the dosage was increased to 40 mg/day. At the 2nd month of the fluoxetine treatment, the scores of C-YBOCS and CGI-S were 20 and 3, respectively. The hiccups did not recur during maintenance treatment of 40 mg/day fluoxetine for 6 months and obsessive complaints were decreased substantially.

Discussion
Persistent hiccups are usually induced by diseases of gastrointestinal (e.g. gastroesophageal reflux), mediastinal (e.g. pneumonia, myocardial infarction) and central nervous system origin (e.g. tumors of posterior fossa) and toxic-metabolic conditions (e.g. uremia) [3]. Drugs are rarely the cause of hiccups but should be screened for especially in persistent cases [4]. Diagnosis of drug-induced hiccups is difficult and often achieved only by a process of elimination. In our case, no evidence of an organic origin for hiccups was found. Additionally, a close temporal relationship between symptom onset and sertraline treatment, relief of the symptom with discontinuation of the drug support the presence of sertraline-related hiccups in our case. The Naranjo adverse drug reaction probability scale score was also 8 out of 13, which indicates a probable adverse reaction [5].

To our knowledge, there are only a few cases which reported SSRI-related hiccups in the available literature [6-8] and our case is the second one which is reported under the age of 18. There are some similarities between these two cases. Both of them consist of patients with obsessive-compulsive disorder and the suggested cause of hiccups was the same SSRI (sertraline) [8].

The action of sertraline as an antidepressant and an anti-ob sessive agent is assumed to be as a result of its inhibitory effect on the re-uptake of serotonin in the central nervous system. In vitro studies in animals suggest that it is a potent and selective inhibitor of neuronal 5HT re-uptake and weakly affects norepinephrine and dopamine neuronal uptake [9]. There are a variety of serotonin receptors and various subtypes of them that have been related to different diseases [10,11]. Although sertraline is a selective inhibitor of serotonin, it has a varied side-effect profile consequence of its effects at various 5HT receptors. For example, the most common gastrointestinal side effects of sertraline are thought to be mediated through peripheral 5HT receptors (e.g., 5HT3 for nausea and 5HT4 for reduced gastric motility) potentially causing gastroparesis. Sertraline acts on 5HT1A receptors to affect the autonomic nervous system, resulting in increased sweating and saliva, mydriasis, ejaculatory failure, cold clammy skin, and dry mouth. Given the above information, it can be hypothesized that sertraline may affect the hiccup reflex arc by one or more ways. Firstly, although little is known of the exact mechanism of respiratory system side effects of sertraline, it causes hypoventilation/hyperventilation, which may affect the hiccup reflex arc. Secondly, although serotonin is not directly implicated in the reflex arc, it may be hypothesized that SSRIs or sertraline may trigger other neurotransmitter systems at an increased dose and affect the reflex arc via this pathway [12]. Thirdly, Silverman et al. suggested that increased phrenic motoneuronal activity at the level of the spinal cord due to enhanced serotonergic activity may cause hiccups [13].

All in all, there are some suggested mechanisms of sertraline which are led to hiccups, but the exact mechanism is not known according to current studies. Therefore, further studies are warranted to understand how SSRIs may affect the hiccup reflex arc. Additionally, clinicians should be aware of this side effect and all patient who are on SSRI treatment should be screened for hiccups and other probable adverse events.

Conflict of interest
All authors declare that they have no conflict of interest.

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References