Persistent Hiccups with Fluvoxamine: a Case Report

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ÖZET

Fluvoksamin ile İlişkili Dirençli bir Hıçkırık Vak'ası

Majör depresyon tedavisi için fluvoksamin başlanan 59 yaşında bir erkek hastada tedavinin 3. gününde hıçkırık başladı. Hıçkırık hemen bütün gün sürüyordu ve hastayı çok yormaktaydı. Hıçkırık ancak fluvoksamin kesilince durdu. Yaygın olmamakla birlikte, ilâçlar hıçkırığa yol açabilmektedir. Bilgilerimize göre bu hasta literatürde bildirilen ilk fluvoksamin'le ilişkili dirençli hıçkırık vak'asıdır. Fluvoksamin'in aracı olduğu muhtemel vagal bir mekanizma hıçkırık patogenezinde rol oynamış olabilir. İlâcın neden olduğu hıçkırığın kesin teşhisi ancak vücuttan atılması sonrasında tablonun gerilemesinin gözlenmesi yoluyla konulabilir. Fluvoksamin ve muhtemelen diğer SSGİ grubu antidepresanlar dirençli hıçkırık olgularının etiyopatogenezinde akla gelmesi gereken ajanlardandır.
Anahtar Kelimeler: hıçkırık, fluvoksamin, 5-HT reseptörleri, SSGİ

ABSTRACT

Persistent Hiccups with Fluvoxamine: A Case Report.

A 59-year-old man developed persistent hiccups 3 days after initiation of fluvoxamine treatment for major depressive disorder [MDD]. Hiccups were persistent and exhausting. Discontinuation of fluvoxamine finally resolved hiccups. Pharmacotherapeutic agents have been uncommonly associated with hiccups. To our knowledge, this is the first time in literature that persistent hiccups have been described in association with fluvoxamine treatment. A possible vagal mechanism mediated by fluvoxamine is hypothesized for the pathogenesis of hiccups in our patient. Diagnosis of drug-induced hiccups is generally achieved only by a process of elimination. Fluvoxamine and possibly other SSRI drugs should be considered to be ethiopathogenic in development of persistent hiccups.
Keywords: hiccups, fluvoxamine, 5-HT receptors, SSRI

INTRODUCTION

Hiccups are a common phenomenon but little is known about their pathophysiological mechanism. They are often benign and of short duration but they can sometimes be a serious medical problem due to their chronicity and underlying causes. In persistent hiccups, the episodes last for more than 8 hours and may indicate a serious organic disturbance, which may be central or peripheral (Launois et al 1993). Drugs are one of the important intractable causes. Corticosteroids (dexamethasone and methylprednisolone), benzodiazepines (midazolam) and general anesthetics have been the specific agents mentioned most frequently in the literature as being associated with the development of hiccups (Jover et al 2005).

Fluvoxamine is an SSRI [selective serotonin reuptake inhibitor] with proven efficacy as treatment for depression and obsessive-compulsive disorder (Kuloğlu et al 2000). To our knowledge, SSRI associated persistent hiccups has not been reported in the available English literature. In this case report we describe a patient developing persistent hiccups 3 days after initiation of fluvoxamine at 100 mg/day. Hiccups were associated with fluvoxamine, mostly because of the close temporal sequence, and the absence of any alternative explanation for hiccups.

CASE

A 59-year-old man with a history of depressive episodes and anxiety symptoms on and off for 10 years, for which he was treated with several antidepressants was admitted to our psychiatric ward for a recent recurrence of depressive symptoms and active suicidal ideation. Patient's past medical history, physical/neurological examination, ECG, chest X-ray and routine laboratory studies [total blood count, serum electrolytes, blood urea nitrogen, creatinine, liver function tests, thyroid profile and urinalysis] yielded no significant medical pathology. The patient was diagnosed with major depressive episode with vegetative symptoms and treatment with fluvoxamine at 100 mg/day was initiated.

At the 3rd day of fluvoxamine treatment, the patient reported hiccups. Hiccups were continuous throughout the day, exhausting and accompanied by no other physical symptom. As a search for medical causes for the symptom, previously mentioned routine laboratory assessment was repeated. Neurological examination revealed no focal sign. A general physical examination was conducted by a consulting internist, thoracic and abdominal CT's were ordered with an effort to diagnose common causes of hiccups. No organic cause of hiccups was identified despite these investigations. At the 5th day of treatment, the patient was started chlorpromazine 50 mg by mouth every 8 hours with only minimal relief of hiccups. Fluvoxamine was then discontinued at the 8th day of treatment. Two days after discontinuation of the drug, the patient reported that his hiccups were infrequent with brief episodes lasting for 1-2 hours, and the following day the patient finally maintained complete relief from hiccups. Hiccups did not recur during antidepressant treatment with sertraline which was started 5 days after the discontinuation of fluvoxamine.

DISCUSSION

Persistent hiccups are usually evoked by diseases of gastrointestinal [e.g. gastroesophageal reflux disease], thoracic-mediastinal [e.g. pneumonia, myocardial infarction] and central nervous system origin [e.g. tumors of posterior fossa] and toxic-metabolic conditions [e.g. alcoholism, uremia] (Launois et al 1993). Drugs are rarely the cause but should be screened for in cases of persistent hiccups (Miyaoka and Kamijima 1999). Diagnosis of drug-induced hiccups is difficult and often achieved only by a process of elimination. In our case, despite extensive investigations we could not identify an organic origin for hiccups. In addition, close temporal relationship between symptom onset and administration of fluvoxamine, along with gradual relief of the symptom with discontinuation of the drug is good evidence for a causal reasoning.

Fluvoxamine is a potent and selective inhibitor of neuronal 5-HT [serotonin] reuptake in the nervous system. A report on the tolerability and safety of fluvoxamine found that while the drug was generally well tolerated and safe, nausea was the most common adverse event that occurred in >10 % of patients (Figgitt and McClellan 2000). In relation with fluvoxamine's emetic effects, one animal study documented that fluvoxamine induced 5-HT release from enterochromaffin [EC] cells of the intestinal mucosa might stimulate the 5-HT3 receptors on vagal afferent nerve fibers and this depolarization of vagal afferents may result in a 5-HT increase in the brainstem and, thus, lead to emesis. In addition, 5HT3 receptors are implicated in mechanism of vomiting, and the antiemetic effects of certain drugs [e.g., ondansetron] are thought to be mediated via this subtype (Minami et al 2003). An afferent vagal mechanism similar to that observed in the above animal study that focused on fluvoxamine-induced emesis might have been involved in pat-

hogenesis of hiccups in our patient. To support this hypothesis, the hiccup reflex arc consists of an afferent portion that includes the vagus nerve, along with the phrenic nerve and the lower thoracic sympathetic chain and a reflex center in the upper cervical region for hiccups similar to that established for nausea and vomiting response is well documented (Vaidya 2000).

CONCLUSION

Fluvoxamine treatment can result in persistent hiccups that continue for the duration of therapy. Hiccups in this setting can effectively be managed by discontinuation of the drug and switching to a different antidepressant agent. We proposed a possible vagal mechanism mediated by fluvoxamine as an explanation for the emergence of hiccups in our patient. The case warrants further study to understand how SSRIs may affect the hiccup reflex arc.

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