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CASE REPORT

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Dopamine Agonist-Associated Hiccup in Parkinson's Disease: A Case Report

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ABSTRACT

Hiccup is described as the sudden involuntary contraction of the diaphragm, and the intercostal muscles followed by the immediate closure of the glottis. Corticosteroids, benzodiazepines, and antibiotics may cause drug-induced hiccups. Dopamine agonist-induced hiccups were reported in patients diagnosed with Parkinson's Disease (PD) in small number of cases. Here we report a patient diagnosed with PD who had severe hiccups with the use of two dopamine agonists in treatment, however hiccup was not reported with the use of Levodopa. This information may help to manage the treatment of PD, and avoid the unnecessary diagnostic procedures.

Keywords: Hiccup, dopamine agonist, levodopa, Parkinson's disease

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INTRODUCTION

Hiccup is described as the sudden involuntary contractions of the diaphragm, and the intercostal muscles followed by the immediate closure of the glottis which causes the characteristic "hiccup" sound. Hiccups are considered as physiologic myoclonus of the diaphragm (1). Pathologies of the central, and peripheral nervous system (phrenic, vagal and sympathetic nerves), and ear, nose, throat, toxic-metabolic, neoplastic, pharmacological and psychosomatic pathologies may cause hiccups. Corticosteroids, benzodiazepines, and antibiotics may cause drug-induced hiccups. Dopamine agonists induced hiccups were reported in patients diagnosed with Parkinson's Disease (PD) in small number of cases (2–4). Here we report a patient diagnosed with PD, who had severe hiccups with the use of two dopamine agonists in treatment, however hiccup was not reported in treatment with Levodopa.

CASE

A man aged 45 years developed gradual progressive slowness in the movements, and tremor on the left side of the body last two years who had no previous history of gastroesophageal problems, and persistent hiccups. The neurologic examination revealed normal eye movements, and moderate bradymimia. Resting tremor, rigidity, and bradykinesia were detected on the left side of the body. The magnetic resonance imaging (MRI) of the brain was normal. He was diagnosed as having PD in accordance with the UK Brain Bank criteria. Pramipexole was prescribed before he was admitted to our clinic. The patient had persistent hiccups within the first day use of pramipexole (0.75 mg/day) while he experienced no persistent hiccups before. Pramipexole was continued for two weeks however the hiccups did not resolve. Then, the treatment was switched to daily 2 mg ropinirole. Hiccup was not detected with the use of 2 mg ropinirole, however persistent hiccups again started after the dose was increased to daily 4 mg ropinirole. Ropinirole was discontinued, and rasagiline (1 mg/day) and Levodopa-benserazide (375 mg/day) were initiated. Hiccups resolved one day after the treatment switch. Amantadine (200 mg/day) was included to treatment in the follow-up period. The increased doses caused no hiccups. Tremor, and bradykinesia responded well to the dopaminergic treatment, and the patient experienced no hiccups with this treatment regime in the one-year follow-up.

DISCUSSION AND CONCLUSIONS

Hiccups are accepted to be generated by a reflex arc which has afferent, central, and efferent components (5). Phrenic nerve, vagus, and sympathetic afferent fibers constitute the efferent unit. The central component is midbrain, and the efferent component is composed of phrenic, and accessory nerves to the diaphragm, and intercostal muscles. Although the complete mechanism is still unclear, the use of dopamine antagonists in treatment of intractable hiccups shows that dopamine has a role in the central processing unit.

Persistent hiccups associated with dopamine agonists were previously reported in case reports (2–4). It was suggested that the prolonged dopamine D3 receptor stimulation, and the mild agonistic activity of ropinirole, and pramipexole on serotonergic pathway through 5-HT1A or 5-HT1D were suggested to have a role in the emergence of hiccups (2, 4). Interestingly, levodopa caused no hiccups in those cases similarly as in our case. However, levodopa-induced hiccups were reported in another two case reports, and in a pharmacovigilance study (6–8). The pathophysiology is unclear why the dopaminergic agonists caused hiccups, however levodopa caused no hiccups.

Researchers investigated the frequency of hiccups in PD patients compared with healthy controls, and demonstrated that 20% of PD

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patients had hiccups, however hiccup was detected in 3% in the healthy controls (9). Synucleinopathy was suggested to affect brainstem and might cause hiccups.

In conclusion, persistent hiccups in PD might be drug-related particularly with the use of dopamine agonists. This information may help to manage the treatment, and to avoid the unnecessary diagnostic procedures.

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