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A Case of Hiccups Associated with Dopaminergic Medication

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Abstract

Drug induced hiccups may be associated with a various agents, including corticoste-roid, antibiotics, and benzodiazepines. Rarely, levodopa or dopamine agonist therapy in Parkinson's disease patient, can trigger hiccups. We report a case of persistent hiccup, occurring with dopaminergic medication in a patient with Parkinson's disease.

Key words : Hiccup, Levodopa, Dopamine agonist

Introduction

Hiccups are induced from a contraction of the diaphragm that repeat several times per minute.[1] Hiccups are caused by many central and peripheral nervous system disorders, all from injury or irritation to the phrenic and vagus nerves, as well as toxic or metabolic disorders affecting the aforementioned systems. Hiccups often occur after consuming carbonated beverages, alcohol, dry breads, or spicy foods. In some instance, some medications may induce hiccups. In this report, we present a patient who suffered fromhiccups associated with dopaminergic medication for treatment of Parkinson's disease.

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Case

A 67-year-old man visited neurologic outpatient clinic because of resting tremor on both hands. 4 months ago,he felt down and suffered fracture of left femur, and underwent a surgical operation. During admissionat local orthopedic center, his attending physician noticed resting tremor on both hands and asked the symptoms. On history taking, he noticed gradually progressive slowing of movement and hands shaking since 3 years ago, and developed frequent falling from 6 months ago. On neurological examination, he noticed masked face, monotonous voice, resting tremor on both hands and jaw and bilateral bradykinesia of arms and legs along with cogwheel rigidity. He also showed stooped posture and the pull-test revealed slight postural instability. On gait examination, he noticed shuffering and festinating gait, but did not exist freezing of gait. He was diagnosed with Parkinson's disease, initiated on L-dopa/benserazide. With 300mg L-dopa and 75mg of benserazide, the bradykinesia and gait difficulty improved slightly.

1 month after, L-dopa was further increased to 450mg a day (150mg-150mg-150mg) and pramipexole was introduced to 0.375mg a day, and his bradykinesia more improved. But since after increasing dosage, he experienced severe hiccups. He had never before experienced persistent hiccups, and no prior history of gastroesophageal problems. And he did not take other drugs except non steroidal anti inflammatory drug. On chest X-ray both lung fields were clear. He stopped pramipexole and noticed slight improvement of hiccups. After 3 days, he stopped L-dopa entirely and the hiccups disappeared completely. One week later, L-dopa was reintroduced as 150mg three times a day,and he complaint persistent hiccups again. L-dopa decreased 100mg three times a day and then hiccups were disappeared.

Discussion

Hiccups are the physiologic spasmodic involuntary contraction, manifestation of diaphragmatic myoclonus.[1,2] They are usually benign and have brief duration, but may become persistent. Although the cause of most episodes is never determined, many known associated conditions have been identified, including medications. Cortico-steroids and benzodiazepines have been the drug classes mentioned most frequently in the literatures, but insufficient evidence exists to implicate any one agent in its etiology.[3] But hiccups are rarely associated with antiparkinsonian drugs, such as levodopa and dopamine agonist (DA). Recently, only 6 cases with Parkinson's disease (PD) are reported as hiccups induced by levodopa or dopamine agonist.[2,4-7] In thiscase, hiccups seem to be closely correlated with dopaminergic medications, as hiccup disappeared after stopping levodopa and dopamine agonist, and reappeared after reintroducing same drug. And in this case both dopaminergic medications are responsible to inducing hiccup.

The pathophysiology of hiccups is poorly understood, but probably a dopaminergic pathway could be involved, because many dopamine blocking agents are reported to be useful in its treatment. But the mechanism of hiccups induced by dopaminergic medication remains largely unknown. Daniel et al[7], reported a patient who experienced intractable hiccup after taking levodopa, and he revealed hiccups an dyskinetic side effect of levodopa. We also considered the possibility of levodopa induced dyskinesia, because the reoccurred hiccup were improved after levodopa dosage reduction. But PD dyskinesia related to dopaminergic therapies are typically choreiform or dystonic in nature ; while they can be myoclonic in some patients. And DA are usually not associated with dyskinesia, but our patient experienced some improvement after cessation of pramipexole at first. According to some literatures, the DA implicated in the development of hiccup share a high affinity for D3, and proposed hypothesis that D3 dopamine receptors with stimulation by DA can be involved in generating this symptoms.[5,8] We conclude that dopamine agonist and levodopa may induce hiccups in patients with PD, and this side effect may correlated with dosage of this drugs. Recognition of this association will aid in prompt diagnosis and therapy and avoid unnecessary investigations.

국문초록

약물 유발성 딸꾹질은 코르티코스테로이드, 항생제 그리고 벤조디아제핀 등의 약물에 의하여 발생할 수 있다. 드물게 파킨슨병의 치료 목적으로 사용하는 레보도파나 도파민 효현제가 딸꾹질을 유발시킬 수 있다. 저자들은 파킨슨병의 치료 목적으로 레보도파와 도파민 효현제를 사용한 환자에서 조절되지 않는 딸꾹질을 경험하였기에 문헌 고찰과 함께 보고하는 바이다.

중심단어: 딸꾹질, 레보도파, 도파민 효현제

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