Two cases of Parkinson's disease with the dissection of the motor function and blood levodopa levels

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Abstract

We examined the association between blood levodopa levels and motor symptoms in two patients with Parkinson's disease who were exhibiting the wearing-off phenomenon. Patient 1 was a 69-year-old woman. In the morning and at noon, the blood level increases the motor function was improved after levodopa internal use. In the evening, the blood level did not increase after levodopa internal use, but there was improvement of the motor function. Patient 2 was a 59-year-old man. In the morning, the blood level increased after levodopa internal use, but the motor function was improved since before remedy. At noon, he was in an 'off' state before internal use. The blood level showed a delayed rise after levodopa internal use, but no improvement of the motor function was found. In the evening, he was in an 'off' state before internal use. The blood level increased after internal use, but the motor function improved a little. These findings suggest that endogenous DA secretion or a placebo effect was possible in addition to levodopa malabsorption in both patients. For both patients, these disorders may be linked to poor control by the antiparkinson agent being used.

Keywords: Parkinson's disease, blood levodopa levels, motor symptoms, dissection, wearing-off phenomenon

Introduction

Parkinson's disease is a neurodegenerative disease with symptoms of passive tremors, muscle rigidity and akinesia. The pathologic findings are characterized by the dopaminergic neuronal degeneration / loss of the midbrain substantia nigra. The effect of levodopa is sustained in initial-stage Parkinson patients, and a good motor function can be preserved all day long. However, when levodopa is used for the long term, for five years or more, changes in the motor functions such as dyskinesia, the wearing-off phenomenon, and the on-off phenomenon develop in many patients, and the ADL of the patients is affected.

To suppress the change in the motor function, a little frequent internal use and dopamine agonists, and the combination of selective MAO-B inhibitor and /or the COMT inhibitor have been carried out. It seems that a treatment

plan can generally be devised, including diet cures, if the mechanism of the circadian rhythm in the individual patient can be

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determined. In this study, the levodopa blood level of Parkinsonian patients with the wearing-off phenomenon was measured. We considered the circadian rhythm of the motor function and its association with the levodopa blood level.

Method

Two patients with Parkinson's disease enrolled in this study. The two patients had good response to levodopa, but the wearing-off phenomenon had become particularly apparent recently. On the day the blood was drawn, the patients took an antiparkinson agent, and the state of the motor symptoms was recorded hourly according to the following scales: 1, cannot move (off); 2, can move a little (an intermediate of on-off); 3, can move well (on); 4, dyskinesia. Blood was collected before levodopa internal use and one hour 30 minutes to three hours afterwards. The levodopa blood level was measured by HPLC.

Patient 1

Patient 1 was a 69-year-old woman who had contracted the disease eight years previously. The disease caused slow movement of the left shaking of hands and the right lower extremity. When Parkinson's disease was diagnosed, treatment using an antiparkinson agent for internal use including levodopa was started. The response to medication was good, but off came to develop before supper and lunch for half a year. Madopar (100mg/28.5mg of levodopa/beneserazide) and ropinirole (2 mg) was taken three times a day (at 8:00 a.m. at 11:00 a.m. 4:00 p.m.). The patient also took cabergoline 1 mg to (before supper) once a day. The levodopa blood level rose to 3.17μM after levodopa internal use at 8:00 a.m., and decreased to 1.73μM at 11:00 a.m. (Figure 1a). The levodopa blood level rose to 3.45μM at 1:00 p.m. after lunch, and decreased to 2.72μM at 4:00 p.m. The blood level of 7:00 p.m. was 1.31μM in spite of levodopa internal use at 4:00 p.m. The motor symptom was in the 'on' state from 9:00 a.m. to 2:00 p.m. An 'off' state developed from 3:00 p.m. through 4:00. The 'off' state disappeared with levodopa internal use at 4:00 p.m., but reappeared with a blood level fall after 7:00 p.m.

Patient 2

Patient 2 was a 59-year-old man who had contracted the disease 12 years previously. The disease occurred for slow movement of the right shaking of hands and the right lower extremity. He was diagnosed as having Parkinson's disease five years after the onset, and treatment with an antiparkinson agent for internal use was started. The effect was good at the beginning, but the fluctuation of the motor symptoms became dramatic from the twelfth year after onset. An 'off' state developed before and after lunch. The 'off' state before lunch was improved by levodopa internal use after lunch, but the 'off' state which developed in the evening did not improve after the internal use of the antiparkinson agent. The patient took Madopar (100mg/28.5mg of levodopa/beneserazide) 100/28.5mg,and Entacapone 100 mg four times a day (after every meal and before sleeping), Seregiline 2.5mg once a day (after breakfast), Pramipexole 1 mg three times a day (after every meal). The blood level of levodopa rose to 2.82μM at 9:00 a.m., and decreased to 0.8μM at 0:00 p.m. (Figure 1b). The blood level was still low at 1.54μM after lunch, but rose to 0.43μM at 6:00 p.m. After levodopa internal use at 6:30 p.m., it was 2.7μM at 8:00 p.m. The motor symptoms were 'on' after getting up until 11:00 a.m. However, an 'off' state developed at 0:00 p.m. The off state continued in the afternoon. Though the blood level increased ante prandium, there was no improvement of the motor symptoms.

Discussion

In this study, the levodopa blood level of Parkinson patients with the wearing-off phenomenon was measured, and it was compared with the circadian fluctuation of the motor function. The levodopa blood level and the motor function showed almost equilateral correlation in Patient 1, but blood level and a motor function let loose in the afternoon. After having taken window par at 4:00 p.m., there were no blood level rises.

There was equilateral correlation in Patient 2 for levodopa blood level and motor function in the morning, but there was no correlation at all in the afternoon.

Though blood level increased after supper, the motor function was not improved. The blood level rise was very slow after window soft-headed internal use after lunch. After levodopa is absorbed in the small intestine, levodopa shifts in blood and brain successively. After it is absorbed by the striatal dopaminergic neuron terminal, the medicine is converted into dopamine. Dopamine released in the synaptic cleft binds to the dopamine receptor of the subsynaptic membrane. As for the change of the motor function, the three following mechanisms are assumed; 1) change of levodopa absorbency in the small intestine, 2) fall of the ability to hold levodopa of the dopaminergic terve terminal in the striatum, 3) change of the sensitivity of the dopamine receptor in a subsynaptic membrane [1]. In both patients, no rise of the levodopa blood level was observed after the levodopa internal use. A fall in gastric-acid secretion and a high fat diet delay excretion of the food from the stomach, and absorption of levodopa is consequently decreased. Also, the protein in food inhibits effective levodopa absorption from the mucosa of the small intestine [2]. The following measures are reported to stabilize levodopa absorption in the small intestine; combination of use of an enterokinesis accelerating agent, low protein diet, and low fat diet [3]. Because levodopa is hard to dissolve in water but easy to dissolve in acidic solvent, it is effective to dissolve tablets in carbonated water and lemon-oil water, and to take medicine this way. Also, an 'on' state was found in both patients before and after the levodopa remedy though blood levodopa levels were low. A placebo effect or an increase of the endogenous dopamine secretion is considered as the mechanism. We have previously studied a Parkinson's disease case in which impairment of the motor symptoms was improved by rehabilitation. Rehabilitation may be equally effective. The measurement of the levodopa blood level is a useful method which is in considering the mechanism of the change of motor function in patients with Parkinson's disease.

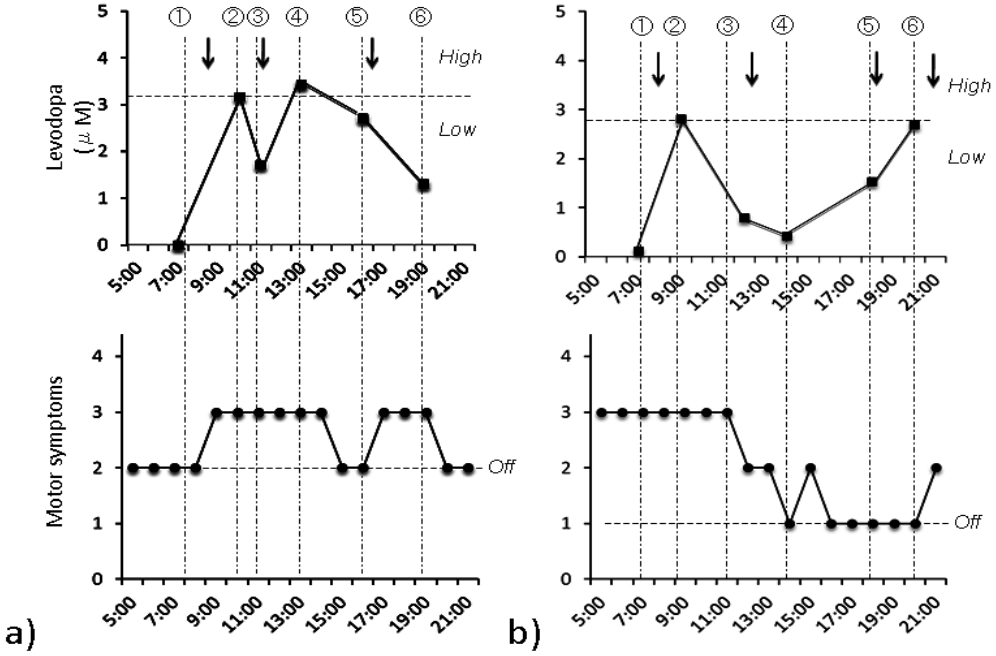

Figure 1.Changes of levodopa blood level (upper panels) and the motor symptom (lower panels). a, Patient 1. b, Patient 2. The arrows of the upper panels show levodopa internal use.

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