Case Report

An Elderly Parkinsonian Patient with Extreme Blood Pressure Fluctuations

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SUMMARY

Blood pressure (BP) fluctuations after long-term levodopa therapy are rarely reported. Patients with Parkinson's disease (PD) often have dysautonomia, and neuropsychiatric and sleep disorders, which influence BP. It is difficult to control BP when hypertension coexists with these complications. We present the case of a 78-year-old man with PD who had hypotensive shock and extreme fluctuations of BP. Fluctuations in BP, with the use of levodopa are more significant in patients with motor symptom fluctuations, autonomic nervous system disorders, primary hypertension, advanced stage of PD, and anxiety or sleep disorders. We controlled BP fluctuations by dividing the total daily levodopa and benserazide (Madopar) dose into smaller doses given more often, adding a sedative, and carrying out some simple nonmedical treatments for postprandial and orthostatic hypotension. At the same time, “dyskinesia” and “wearing-off” were also improved. BP fluctuations have a considerable influence on patients' quality of life and can even be life-threatening. The mechanism is complex, therefore a correct analysis of the underlying causes is needed to carry out comprehensive management. Adjustment of levodopa administration can not only stabilize BP well, but also can control PD motor complications.

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1. Introduction

Parkinson's disease (PD), which occurs mainly in older people, is characterized by movement disorders such as tremor, rigidity, hypokinesia, abnormal gait, and abnormal posture. Levodopa, which is converted to dopamine in the body, can ameliorate all the major clinical features of PD. After long-term levodopa therapy, patients experience nonmotor symptom fluctuations such as fatigue, anxiety, depression, and pain, as well as motor fluctuations, but blood pressure (BP) fluctuations are rarely reported. Most PD patients have dysautonomia, neuropsychiatric disorders, and sleep disorders, which influence the stability of BP, making it difficult to control BP when hypertension also coexists with these complications. It is clinically important to evaluate BP fluctuations and carry out a reasonable management strategy.

We present the case of a 78-year-old man with PD who had hypotensive shock and extreme fluctuations of BP. This case illustrates the value of a correct analysis and comprehensive management (especially the hypertensive effect of levodopa and adjustment of levodopa administration) of BP fluctuations in a PD patient.

2. Case report

A 78-year-old man had been diagnosed with PD 12 years previously and had been taking levodopa and benserazide (Madopar) for 11 years. Dyskinesia symptoms associated with levodopa, that is, head shaking or head and neck twisting to the left, occurred 2 years earlier. Levodopa “wearing-off”, that is, limb stiffness and asthmatic symptoms, occurred 1 year earlier. The patient had been dependent for 6 years and, especially this year, had difficulty moving without support from another person. As a result of dysphagia several months previously, the patient began receiving nasogastric feeding. Before he was hospitalized, his daily oral levodopa dosage was 250 mg four times a day. The patient had pramipexole added to his drug regimen, but had to stop taking pramipexole due to drowsiness and hallucination. Besides having PD, the patient was diagnosed as having primary hypertension 40 years earlier. To treat...
hypertension before being hospitalized, he took oral amlodipine 5 mg/day and candesartan 8 mg/day.

The patient's hospitalization resulted from the sudden loss of consciousness when going to the toilet about 20 days earlier. His BP was 80/44 mmHg. He was given continuous intravenous dopamine for 3 days and prescribed absolute bed rest to maintain sufficient BP while in a community hospital. Although shock did not occur again, his BP fluctuated considerably. In particular, his BP began to decrease significantly after he was administered 250 mg of levodopa. Levodopa had been stopped or postponed for some time, which exacerbated his PD motor symptoms. Therefore, the patient was sent to our hospital for further treatment.

The patient's Hoehn and Yahr stage was 5.0, and 24-hour BP monitoring with the PM-7000 Patient Monitor (Mindray Medical International Limited, shenzhen, China.) showed that the mean systolic blood pressure (SBP) was 144 ± 34 (range 86–198) mmHg. However, daytime BP fluctuated sharply. The SBP decreased by an average of 79 mmHg after he received 250 mg of levodopa, and subsequently began to increase until he received his next dose. At the same time, “dyskinesia” appeared from 30 minutes to 2 hours after he received levodopa and became most significant at the time of lowest SBP. However, “wearing-off” appeared 30 minutes before the next administration of levodopa and became most significant at the time of the highest SBP (Fig. 1). By contrast, nocturnal and early morning BP remained at a high level, and the mean SBP was 165 ± 25 (range 118–198) mmHg. In addition, dizziness or syncope occurred when he sat or stood up.

Initially, we found that daytime BP fluctuations were related to levodopa, so we tried to change the manner in which levodopa was administered without changing the total dose (1000 mg/day). We first advised the patient to take 125 mg of levodopa every 2 hours. The SBP decreased by less (average 37 mmHg) after he took levodopa than before adjusting the dose. Dyskinesia was ameliorated and lasted only about 30 minutes, but “wearing-off” was still

**Fig. 1.** Systolic blood pressure (SBP) fluctuations and their relationship to the time of levodopa supplementation and motor complications before and after adjusting levodopa. The X axis is time and the Y axis is SBP level. The triangles indicate points of SBP monitoring and the squares indicate points of SBP monitoring and levodopa supplementation. (A) SBP fluctuations with 250 mg levodopa four times per day; (B) SBP fluctuations with 125 mg levodopa every 2 hours; (C) SBP fluctuations with 62.5 mg levodopa per hour. The SBP usually decreased 30 minutes after levodopa supplementation and reached its highest point just before the next administration. SBP decreases became less and less from (A) to (C) (mean 79 mmHg, 37 mmHg, 17 mmHg for A, B, C, respectively). “Dyskinesia” also appeared 30 minutes after levodopa was taken and became most significant at the time of the lowest SBP. However, “wearing-off” appeared 30 minutes before the next administration and became most significant at the time of the highest SBP. “Dyskinesia” lasted for 1.5 hours in (A) and for 0.5 hours in (B), but disappeared in (C). The “wearing-off” that occurred in (A) and (B) disappeared in (C).
evident 30 minutes before the next dose was administered. We then advised the patient to take 62.5 mg levodopa per hour. The SBP decreased much less (average 17 mmHg) after he took levodopa, and “dyskinesia” and “wearing-off” almost disappeared (Fig. 1). Next, considering that nocturnal and early morning BP was much higher, we ordered the patient to take amiodidine and can-desartan at bedtime, but this change in drug regimen had no effect. When we further increased the dosage of these two drugs, the daytime BP decreased unexpectedly with no change in nocturnal and early morning high BP. Because the patient had insomnia and anxiety, we added a sedative (estazolam 1 mg) at bedtime, and the mean nocturnal and early morning SBP decreased to 135 ± 6 (range 122–142) mmHg. Finally, in view of the frequency of autonomic nervous system disorders in PD, the postprandial and orthostatic hypotension was tested. Postprandial and orthostatic hypotension coexisted in this patient, because SBP decreased by 42 mmHg 1 hour after a meal and by 40–50 mmHg from supine to standing position. We advised the patient to control carbohydrate intake, to eat less but more often, to avoid quick activity immediately after each meal, to sleep in the head-up position, to stop eating a low-sodium diet, and to wear elastic stockings. After the above treatments, SBP decreased by about 20 mmHg with position change, and no dizziness or syncope occurred while sitting or standing up. The patient and his family members were all provided written informed consent for this report, which was approved by the institutional review committee of the General Hospital of the Air Force.

3. Discussion

Several factors can affect BP fluctuations. The first factor is levodopa. On the one hand, levodopa reduces supine BP through a central mechanism, which is more significant in patients who have received long-term levodopa treatment and have motor symptom fluctuations. This effect is heavily dependent on the levodopa concentration. BP is lowest while the symptom is in the “on” phase and peaks while the symptom is in the “off” phase. On the other hand, a large dose of levodopa can induce orthostatic and/or postprandial hypotension through a peripheral mechanism. The second factor is autonomic nervous system disorder—it is common in PD, and is the main reason for postprandial and/or orthostatic hypotension. The third factor is primary hypertension and advanced PD. High baseline level BP and Hoehn and Yahr stage can enhance the effects of levodopa and autonomic nervous system disorder on BP fluctuations. Finally, PD is often associated with anxiety and sleep disorders, which can cause nocturnal and early morning hypertension.

For PD patients with BP fluctuations, we are inclined to suggest a comprehensive treatment strategy. Firstly, the mechanism for levodopa-induced BP fluctuations might be similar to that for motor symptom fluctuations, that is, pulsative dopaminergic stimulation and dopamine receptor hypersensitization. To avoid these effects, we could choose levodopa sustained-release tablets, dopamine receptor agonists, continuous infusions of levodopa or dopamine agonists by intraduodenal administration, or deep brain stimulation. However, we could not carry out the above strategies for several reasons, including dysphagia, agonist side effects, and lack of availability of intraduodenal infusion and deep brain stimulation, so we changed the manner of levodopa administration by dividing the total daily dose into smaller doses and more frequent drug administration. Secondly, sedative and anxiolytic drugs can modify nocturnal and early morning hypertension in mood and sleep disorders. Thirdly, although some drugs (e.g., caffeine, glycosidase inhibitors, octreotide, vasoactive agents, and plasma volume expansion agents) can be used to treat postprandial and orthostatic hypotension, considering these drugs’ uncertain effects, serious side effects, or high costs, as well as baseline primary hypertension, we used some simple nonmedical methods instead.

In conclusion, in older PD patients, BP fluctuations will influence the patient’s quality of life considerably, and can even be life-threatening. The mechanism of the BP fluctuations is complex, so the reasons for the fluctuations (especially the hypotensive effect of levodopa) should be carefully analyzed and comprehensive management to control the BP fluctuations should be carried out. If only the adjustment of antihypertension drugs is considered, this will not only result in the failure of BP control, but also cause hypotensive shock. The adjustment of levodopa administration can not only stabilize BP well, but also control PD motor complications.

References