Transient Worsening of Parkinson's Disease after Cigarette Smoking

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**We report a patient with probable Parkinson's disease who experienced a temporary worsening of his symptoms and signs after cigarette smoking. Deterioration of tremor, rigidity, and writing disturbance began soon after the inhalation of cigarette smoke and persisted for 15 minutes. Chewing nicotine gum also induced a brief worsening of the patient's symptoms. Aggravation of parkinsonian symptoms after cigarette smoking appeared to be caused by nicotine alone, although the mechanism for this effect remains unclear.
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Key words: nicotine, neurotransmitter

Introduction

Cigarette smoking aggravates cerebellar ataxia in patients with spinocerebellar degeneration and multiple sclerosis (1). However, smoking has been reported to protect against parkinsonian symptoms (2, 3). In addition, neurochemical studies have demonstrated that nicotine enhances central dopaminergic neurotransmission and increases the firing rate of nigral neurons (4, 5). These observations support the theory that cigarette smoking has a beneficial effect on parkinsonian symptoms (6). The present report describes a patient with probable Parkinson's disease (PD) who experienced a transient worsening of symptoms after cigarette smoking.

Case Report

A 47-year-old Japanese man was referred to the outpatient clinic of our department in August 1992 for the evaluation of parkinsonism. He had exhibited a writing disturbance since 1988, and had been diagnosed elsewhere as having hemiparkinsonism. Treatment consisted of anti-parkinsonian drugs, including levodopa, trihexyphenidyl hydrochloride, bromocriptine mesilate, and amantadine hydrochloride. In 1990, he developed a gait disturbance, tremor at rest, and bradykinesia on the right side that gradually worsened. The patient had smoked 20 cigarettes a day for 27 years, since the age of 20, but had not experienced any involuntary movements, such as finger tremor, after smoking. However, toward the end of 1991, he noticed that all of his symptoms worsened transiently whenever

he smoked a cigarette. In March 1992, he developed starting hesitation and dysarthria. There was no history of hypertension, diabetes mellitus, heart disease, or alcohol abuse. His mother had exhibited finger tremor since her late fifties and had been treated for PD at a neurological clinic.

On admission, the patient had an alert but expressionless face with infrequent blinking. He spoke slowly and in a low voice with dysarthria. Examination of the cranial nerves and muscle power yielded normal results. Cogwheel rigidity was noted in all four limbs, and was marked in the right arm. Bradykinesia and micrographia were present. Deep tendon reflexes were within the normal range. Resting tremor was present in his right fingers. There was no sensory impairment. His walking was stable, although start hesitation and diminished arm swings were noted. Pulsation phenomenon was not apparent. No cerebellar signs were detected. There was no orthostatic hypotension or rectovesical disturbance. Electroencephalography, magnetic resonance imaging, and cerebral angiography were normal. Cerebral blood flow measured by the xenon-133 (¹³³Xe) inhalation method, was also within the normal range. The patient was treated with levodopa (300 mg daily), benserazide (30 mg daily), trihexyphenidyl hydrochloride (6 mg daily), and bromocriptine mesilate (15 mg daily).

Discontinuation of levodopa worsened his symptoms. His condition improved upon reinstitution of levodopa (300 mg daily). The effect of smoking one cigarette that contained 0.8 mg nicotine and 9 mg tar was evaluated 2 hours after taking the antiparkinsonian medications. Motor symptoms began to dete-

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Figure 1. Pentagons drawn by the patient with Parkinson's disease before and after smoking one cigarette. The first set of figures was drawn 2 hours after the ingestion of antiparkinsonism drugs. The second set of figures was drawn 5 minutes, after the patient had smoked a cigarette that contained 0.8 mg of nicotine. The adverse effect of the cigarette on parkinsonism symptoms, including the handwriting disturbance, lasted approximately 15 minutes.

riorate soon after the inhalation of cigarette smoke and lasted for 15 minutes. Tremor and rigidity increased slightly, and his writing disturbance was aggravated (Fig. 1). However, his gait disturbance remained essentially unchanged. One week later, he chewed nicotine gum, which contained 4 mg nicotine, 2 hours after taking the antiparkinsonian medications to evaluate the effects of nicotine alone. A temporary worsening of his symptoms as seen after cigarette smoking was noted and lasted for 15 minutes. These challenges were repeated three times with consistent results. Cerebral blood flow measurements were done before and 10 minutes after smoking. A single photon emission computed tomography using the technetium-99m-ethyl cysteinate dimer infusion method was used. No marked changes in cerebral blood flow were found after smoking.

Discussion

In the present case, parkinsonian symptoms temporarily worsened after the patient smoked a cigarette. A few patients with juvenile parkinsonism have reportedly had a transient worsening of their parkinsonian symptoms following smoking (6, 7). However, other reports (2, 8) suggest a beneficial effect of smoking or nicotine on parkinsonian symptoms. A meta-analysis by Morens et al (9) found no evidence for symptomatic effects of smoking in patients with PD. Furthermore, none of the 3,693 patients interviewed by Golbe et al (10) reported a worsening of hypokinetic-rigid features following cigarette smoking.

In view of the unexpected result in this case, we considered whether the diagnosis of Parkinson's disease was correct in this case. The patient exhibited the three salient clinical features of Parkinson's disease – resting tremor, rigidity, and bradykinesia – which were responsive to levodopa. He was diagnosed as

having “clinically definite PD” using the criteria developed by Calne et al (11). His clinical signs also fulfilled the diagnostic criteria of Hughes et al (12). In addition, his mother had Parkinson's disease. Therefore, the patient most likely did have Parkinson's disease, although other diseases with hypokinetic-rigid features could not completely be ruled out. Post-mortem findings showing Lewy bodies (13) would be needed to rule out all other diseases.

We considered that smoking induced transient ischemia, perhaps by causing vasospasm. However, no change in the cerebral blood flow was observed after smoking. These findings suggest that vasospasm was an unlikely explanation for the effect of smoking on the patient's symptoms.

Among the many substances in cigarette smoking such as nicotine, carbon monoxide and polycyclic aromatic hydrocarbons (14), the effect of cigarette smoking in this case was probably due to an effect of nicotine on the central nervous system since chewing nicotine gum aggravated his parkinsonian symptoms to the same degree as smoking a cigarette. The effects of nicotine on the peripheral nervous system have been established (15), but its effect on the central nervous system has not been established. Acting through nicotinic cholinergic receptors, nicotine stimulates many central neurotransmitter systems, including the adrenergic and cholinergic systems (16). There are many central neurotransmitter system abnormalities in PD (17). A possible explanation for the temporary aggravation of parkinsonian symptoms by nicotine is that nicotine may have induced an imbalance of dopamine-acetylcholine in the basal ganglia. This imbalance may have been influenced by the duration of illness or by long-term levodopa treatment. Although the worsening of parkinsonian symptoms after smoking is unusual in patients with PD, the present case should warrant further study of the effects of nicotine in patients with this

disease.

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