Helicobacter pylori (HP) is a common infection of the gastrointestinal system that is usually related to peptic ulcers. However, recent studies have revealed relationships between HP and many other diseases. Although the exact mechanism is unknown, HP can prevent the absorption of certain drugs. A high prevalence of HP has been found in patients with Parkinson’s disease, and this bacterium causes motor fluctuations by affecting the absorption of levodopa, which is the main drug used to treat Parkinson’s disease. Eradicating HP from patients with Parkinson’s disease by applying antibiotic treatment will increase the absorption of levodopa and decrease their motor fluctuations.

Key Words  Parkinson’s disease, Helicobacter pylori, levodopa, motor fluctuations.

INTRODUCTION

Parkinson’s disease (PD) was first described by James Parkinson in 1817 with the name of ‘shaking palsy’. PD is a progressive neurodegenerative disease that occurs due to the loss of dopaminergic neurons in the substantia nigra pars compacta. PD is a complex and multisystem disease of unknown etiology. However, recent studies have found that infection plays a role in the etiology of PD, such as by bacterial overgrowth and involving cytomegalovirus, Epstein Barr virus, herpes simplex virus type-1 and Helicobacter pylori (HP) in the small intestine. The most-common symptoms are related to the motor system (bradykinesia/hypokinesia, rigidity, tremor and postural abnormality), with also non-motor symptoms such as constipation, pain, genitourinary problems, sleep disorders, depression, autonomic dysfunction, cognitive abnormalities, dementia and gastrointestinal dysfunction.

HELICOBACTER PYLORI

HP is a Gram-negative bacterium found on the luminal surface of the gastric epithelium, and it was first isolated by Warren and Marshall in 1983. HP induces chronic inflammation of the underlying mucosa, with the infection usually being contracted in the first years of life and tending to persist indefinitely unless treated. It was initially found to cause gastritis, peptic ulcer and gastric cancer. However, subsequent studies have revealed that it is also related to diseases of other systems such as hematological disorders (iron-deficiency anemia and idiopathic thrombocytopenic purpura), cardiovascular diseases (ischemic heart disease), neurological diseases (stroke, PD, and Alzheimer’s disease), obesity, and dermatological diseases.
PREVALENCE OF HELICOBACTER PYLORI INFECTION IN THE PATIENTS WITH PARKINSON’S DISEASE

A few studies have found the prevalence of HP infection to be high in PD patient. Dobbs et al. found that the urea breath test was positive in 48% of 105 PD patient. While Pierantozzi et al., Lee et al., Dobbs et al., and Tan et al. obtained positive HP results in 36%, 53%, 70%, and 32% of 79, 65, 51, and of 102 PD patients, respectively (Table 1).

Several case-control studies have shown the HP antibody to be five times more common in PD patients older than 80 years. Another study found that positivity in an HP test was three times more common in PD patients than in a healthy control group.

PARKINSON’S DISEASE AND HELICOBACTER PYLORI

The relationship between PD and gastric ulcer was first reported in 1960. An increased prevalence of gastric ulcer in PD patients was first described as an independent component of the disease, resulting in gastrointestinal symptoms being considered one of the symptoms experienced by all PD patients. This means that gastritis as hypokinesia might also be seen in PD patients. Researchers found that there was a relationship between PD and HP, and that HP might actually cause PD.

One proposed hypothesis was that HP shows a neurotoxic effect by increasing cholesterol glucosides, with HP causing PD by degenerating dopaminergic neurons in the brain.

A second proposed hypothesis is that when HP infection is not controlled by the immune system or HP is not eradicated, HP causes the development of PD by damaging dopaminergic cells in the brain. It was stated that HP might lead to the pathogenesis of PD by causing apoptosis of nerve cells after passing the blood-brain barrier after oral ingestion, nasal odor inhalation, or via circulating monocytes.

The primary pharmacological agent used in PD patients to replace dopamine is levodopa. HP not only causes the development of PD but also leads to motor fluctuations in PD patients by affecting the absorption of levodopa. HP infection prevents the absorption of levodopa, thyroxine and delavirdine, with the absorption of levodopa in PD patients being observed to increase by 21–54% following HP-eradication. HP infection is thought to affect drug absorption via its potential effects on intragastric pH.

It was further found that successful eradication of HP in PD patients decreased motor fluctuations by affecting the bioavailability of levodopa. These findings indicate the potential importance of HP eradication in PD patients.

Lee et al. investigated the effects of HP on the clinical response to levodopa and whether motor fluctuations in PD patients could be decreased by HP eradication. Those authors investigated the presence of HP in 65 PD patients using the urea breath test. HP was detected in 35 of these patients, and so the response to levodopa and clinical features were compared between these two groups. The onset of the effect of levodopa, the duration of drug action (on-time), and the motor movements as measured by the Unified Parkinson’s Disease Rating Scale (UPDRS) were evaluated in both groups. There was no difference between the groups in terms of age, duration of disease, scores on the Hoehn-Yahr scale or UPDRS-III, daily dose of levodopa, or frequency of dyskinesia. In PD patients with HP infection, the onset time of levodopa was longer, and the ‘on-time’ was shorter compared to PD patients who did not have HP infection. These data suggest that HP prevents the absorption of levodopa in PD patient. After administering antibiotic treatment to PD patients to eradicate HP, the ‘onset’ time decreased and the ‘on-time’ increased when compared to the pretreatment values. That study concluded that motor fluctuations might be decreased in PD patients by eradicating HP.

Tan et al. found that 32.4% of 102 PD patients were infected with HP. These infected PD patients were older (age, 68.4±7.3 years, mean±SD) and exhibited worse motor function (UPDRS-III score, 34.0±13.0 vs. 27.3±10.0, p=0.04; pegboard test, 6.4±3.3 pins vs. 8.0±2.7 pins, p=0.04; and ‘timed-gait’ test, 25.1±25.4 s vs. 15.5±7.6 s, p=0.08). That study revealed important effects of HP infection on UPDRS-III and ‘timed-gait’ tests of PD patients; it was found that HP status and its relationship with these motor results varied according to age.

Pierantozzi et al. applied HP eradication to 17 patients and administered a common antioxidant treatment to another 17 patients among 34 PD patients with HP infection. They found that the absorption of levodopa was significantly increased in the HP-eradication group relative to the placebo group. That study found that HP affected the absorption of levodopa, which caused motor fluctuations by decreasing the

Table 1. Prevalence of HP infection in patients with PD

| Authors (year) | PD patients (n) | Prevalence of HP infection |
|---------------|----------------|---------------------------|
| Dobbs et al.  | 105            | 48%                       |
| Pierantozzi et al. | 79     | 36%                       |
| Lee et al.    | 65             | 53%                       |
| Dobbs et al.  | 51             | 70%                       |
| Tan et al.    | 102            | 32%                       |

HP: Helicobacter pylori, PD: Parkinson’s disease.
The prevalence of HP infection is high among PD patients. Various studies have revealed that HP causes motor fluctuations in PD patients by affecting the absorption of levodopa. Therefore, PD patients should be evaluated for the presence of HP infection and eradication treatment can be applied in cases where HP positivity is detected. The relationship between HP and PD should be further clarified by more-comprehensive studies in the future.

Conflicts of Interest

The authors have no financial conflicts of interest.

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