Extended Abstract Pharmacology & Toxicology
2020
Vol.10 No.2

Parkinson's disease

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Abstract

Parkinson's disease (PD) is a complex neurodegenerative age-related disease associated with loss of dopaminergic cells and both motor and non-motor disorders. PD is the second most common neurodegenerative disease that affects above 85 years of age and affects 2% of the population over 60 years of age. PD is the brain's reward that causes typical motor symptoms such as tremor, bradykinesia, rigidity, contraction, as well as non-motor symptoms such as executive dysfunction, mood and sleep disturbance, with constant loss of dopaminergic neurons in the substantia nigra (black substance) of the midbrain. It is defined as a disease caused by dopamine deficiency, a neurotransmitter that helps control learning and emotional centers [1-4].

This rich and varied symptomatology of PD may cause diagnosis confusion and delay in treatment in the early period of the disease. Symptoms in PD start insidiously and the picture gradually gets more severe over the years. The disease usually begins with a prodrome period with vague and nonspecific symptoms. During this period, fatigue, weakness or personality changes may be observed, and motor symptoms may also be in the form of indistinct complaints (such as weakness, moderate incoordination, and writing difficulty) during this period [5, 6]. Patients may apply to the physician only by complaining of difficulty in writing, slowness or pain. Symptoms in most patients are in one half of the body, and approximately 50% start in tremor. Although the findings gradually pass to the opposite body half, an asymmetric involvement is striking, usually on the first affected side. The onset of PD in one half of the body and usually in one extremity, nonmotor signs and symptoms are features that increase the diagnostic difficulty. In the group that does not start with tremor, early-stage parkinsonian symptoms can often be interpreted as simple arthritis, bursitis, depression, normal aging, Alzheimer's disease, or stroke [5,7]. Sometimes the diagnosis can only be made when the motor findings become bilateral, that is, within months or years.

Dopamine deficiency in PD results in increasing interregional consistency in appearance, excessive oscillations and especially beta band frequencies (13-30 Hz). Such pathological beta oscillations are recorded from the subthalami nucleus, Globus pallidus and the frontal cortex of both PD patients who underwent surgery and in the primate models of PD. Dopamine replacement therapy is still not well understood, although it is still the gold standard treatment to improve motor functions in improving its neural mechanisms in PD. One hypothesis is that the drug reduces pathological vibrations and hyper synchronization, especially in beta frequencies, between and within the cortex and basal ganglia. Thus, it improves communication in corticobasal ganglion circuits [1]. Although etiopathogenesis seems to be poorly understood and in most cases sporadic, genetic variables play an important role in the PD formation of at least 5-10% of PD patients [2].

Parkinson's disease is associated with cardiac sympathetic denervation and severe depletion of myocardial norepinephrine. Catecholamine depletion in PD is estimated to directly reflect the loss of nigrostriatal and sympathetic neurons. However, in the putamen and myocardium, the size of catecholamine depletion in PD is greater than can be calculated by the loss of nigral dopaminergic or post-ganglion noradrenergic neurons. This difference can be explained by the reduced efficacy of vesicular storage of catecholamines in the remaining neurons [8].

Dopa decarboxylase inhibitors are used as part of the treatment for PD. Drugs are used to slow the progression of the disease, as it increases the dopamine levels in the brain of Parkinson's patients and motor symptoms are also due to dopamine deficiency. The main drugs used for PD are levodopa, dopamine agonists and MAO-B inhibitors [9]. In addition, drugs containing levodopa with benserazide, carbidopa, entacapone, and non-ergot agonists such as ropinirole, apomorphine, pramipexole, ergo-derived agonists such as bromocriptine, cabergoline, lisuride, pergolide, anticholinergic drugs such as biperidone, bornaprine, and active ingredients such as amantadine sulphate, domperidone are used in the pharmacological treatment of PD [5]. In treatments using levodopa, it includes converting to dopamine and increasing the level of dopamine in the central nervous system [9]. However, levodopa causes motor complications (motor fluctuations and dyskinesias) that impair the patient's quality of life, its effectiveness gradually decreases over time, and the effect of PD on axial motor symptoms (such as postural instability, dysarthria, palile, dysphagia, flexor posture, freezing) and tremor is limited. Currently, it does not seem possible to talk about the existence of an ideal drug in the treatment of PD [5, 10].

There is a certain balance between acetylcholine, which increases the excitability of nerve cells in the brain, and dopamine, which does the opposite. In Parkinson's patients, this balance is disrupted in favor of acetylcholine and the dopamine deficit should be replaced in treatment. Synthetic dopamine cannot cross the barrier between the blood and the brain. This problem has been solved by the presence of levodopa (L-3,4-dihydroxy-phenylalanine), which turns into dopamine after the blood brain barrier has been overcome [11-18]. Levodopa shows its symptomatic effect by converting it into dopamine in the brain. Therefore, it is used together with decarboxylase inhibitors (benserazide or carbidopa) to prevent it from being converted to dopamine in the periphery. Peripheral decarboxylase inhibitors cannot cross the blood brain barrier. With these additional substances, the amount of levodopa in the blood transforming into dopamine in the periphery is reduced, allowing a higher rate of blood-brain barrier. Thus, the dose of levodopa needed to achieve the same benefit is reduced to one quarter. In addition, since dopamine formation in the periphery decreases, peripheral dopaminergic side effects (such as anorexia, nausea, vomiting, orthostatic hypotension) are partially prevented [5].

The treatment of PD can be thought of as a long marathon that takes years. The general support rule for now is to start treatment as soon as the diagnosis is made. The first drug to be chosen is determined by considering the age of the patient, the type and severity of the symptoms and the degree of functional impairment. Currently, the most effective drugs in the treatment of PD are preparations containing levodopa [5].

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