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Opinion

DRUG THERAPY FOR PARKINSON'S DISEASE

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INTRODUCTION

Parkinson's Disease (PD) is a neurological disease that worsens over time. The etiology and pathogenesis of the disease are still unknown. There are presently no disease-modifying treatments for Parkinson's disease, and medical care is mostly focused on using medicines to reduce motor symptoms. Because of the long-term nature of the disease, patients may be required to follow complex pharmaceutical regimens targeted at regulating motor symptoms, with the risk of negative side effects. The movement dysfunction of Parkinson's disease is caused primarily by the selective death of neurons in the substantia nigra pars compacta, resulting in dopamine depletion in the striatum. Dopaminergic medications that replace dopamine's function in the depleted striatum are currently the mainstay of PD treatment. This can be accomplished using medications that are converted to dopamine, activate the dopamine receptor, or block endogenous dopamine breakdown. There is no one-size-fits-all treatment method, with pharmaceutical regimens adapted to the particular patient's severity and temporal nature of symptoms, as well as the adverse effects they face. Because dopamine cannot cross the Blood–brain Barrier (BBB), it must be created in the Central Nervous System (CNS) before it can act in the striatum. Dopamine is largely created in dopamine-producing neurons (dopaminergic neurons) in the brain, with minor amounts also produced in the adrenal glands' medulla.

The direct metabolic precursor of dopamine in the traditional biosynthetic pathway is L-

dihydroxyphenylalanine (levodopa or L-DOPA), which can be made directly from tyrosine (a non-essential amino acid) or indirectly from phenylalanine (an essential amino acid). In the liver, the enzyme Phenylalanine Hydroxylase (PH) converts L-phenylalanine to L-tyrosine in the presence of oxygen, iron, and tetrahydrobiopterin as cofactors. Tyrosine is generated in the liver and then transferred into the brain's dopaminergic neurons via an active transport mechanism. Following that, the enzyme tyrosine hydroxylase converts L-tyrosine into L-DOPA via hydroxylation at the phenol ring (TH). L-DOPA is then decarboxylated into 3,4-dihydroxyphenethylamine (dopamine) in the presynaptic terminal by the enzyme L-3,4-dihydroxyphenylalanine decarboxylase (DOPA decarboxylase). After reuptake into dopaminergic neurons or glial cells, dopamine is processed. It undergoes oxidative deamination in the presence of Flavin Adenine Dinucleotide (FAD), catalyzed by the enzyme monoamine oxidase (MAO), to create the reactive aldehyde 3,4-dihydroxyphenylacetaldehyde (DOPAL).

DESCRIPTION

Alcohol dehydrogenase (ADH) converts DOPAL to 3,4-dihydroxyphenylethanol (DOPET). The enzyme catechol-O-methyl transferase then degrades DOPAC to the physiologically inactive metabolite homovanillic acid (HVA) (COMT). COMT, on the other hand, converts dopamine to 3-methoxytyramine, which is then transformed to 3-methoxy-4-hydroxyacetaldehyde by MAO. The ALDH enzyme converts this to HVA, which is then expelled in the urine.

Although there are no disease-modifying medications available for PD, the treatments available can provide significant symptomatic alleviation. They provide modest clinical effect in terms of non-motor PD symptoms. To lessen the impact of unwanted effects, it is common practice to delay therapy until the patient's symptoms become unbearable. Levodopa-based preparations, which are designed to restore dopamine in the depleted striatum, are the cornerstone of contemporary PD treatment. The dopamine precursor levodopa, on the other hand, can cross the BBB and be used as a treatment. DOPA decarboxylase converts it into the neurotransmitter dopamine after absorption and transit across the BBB. Patients are often started on a low dose of levodopa, with the dose titrated increased based on the patient's response to treatment, as well as any side effects.

CONCLUSION

The majority of people require a daily dose of 150–1000 mg, split into many doses. As doses are increased, the likelihood of developing significant side effects increases. In general, levodopa's clinical effect is immediate and might linger for several hours, especially in the early stages of illness. However, as the condition progresses, the drug's impact usually wears off after a shorter period of time, necessitating increasing dose frequency.

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