MEDICINES USED TO TREAT PARKINSONISM AND EPILEPSY

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Annotation

This article provides a review of the literature on modern drug treatments for patients with Parkinson's disease. The main groups of drugs used in practical medicine and the effectiveness of using non-ergoline dopamine receptor agonists in clinical practice in comparison with levodopa drugs are considered. The pharmacoeconomic aspect of drug therapy for Parkinson's disease is touched upon. The main aspects when choosing a drug to initiate therapy in patients with Parkinson's disease are presented. An algorithm for initial therapy for this pathology is presented.

Key words: *Parkinson's disease, drug treatment, dopamine, Levodopa/carbidopa.*

Introduction: Despite the wide range of currently available non-drug methods of rehabilitation of patients with Parkinson's disease (PD): kinesiotherapy, physiotherapeutic techniques, diet therapy, correction of speech and cognitive impairments, drug therapy remains the leading direction in the treatment of patients with this pathology.

Drug treatment for PD includes:

1) treatment of motor manifestations of PD;

2) correction of motor fluctuations and dyskinesias;

3) treatment of non-motor manifestations of PD.

In the treatment of any disease, it is customary to distinguish etiotropic, pathogenetic and symptomatic therapy.

Based on a considerable amount of data on PD, it was not possible to identify an etiotropic factor, drug

exposure to which would lead to a cure

patient from PD; in the development of which genetic, exogenous factors, as well as processes play a role

natural aging [15, 23, 24].

Pathogenetically substantiated in PD is considered therapy aimed at preventing and slowing down the neurodegenerative process. According to a number of authors, dopamine receptor agonists (DRA) and the MAO type B inhibitor rasagiline have a neuroprotective effect. However, in the 21st century, the main focus in terms of effective pathogenetic therapy for PD is on the development of genetic therapy methods, as well as on the widespread introduction of cellular technology methods into practice.

Thus, at present, drug treatment of PD is mainly carried out using symptomatic therapy, which is aimed at correcting the neurotransmitter imbalance that occurs within this pathologies (decreased dopamine levels and increased activity of cholinergic and glutamatergic systems).

This allows us to regard the antiparkinsonian drugs used in treatment as pathogenetic therapy. There are 6 groups of antiparkinsonian drugs:

1. Levodopa preparations.
2. Dopamine receptor agonists.
3. MAO inhibitors type B.
4. COMT inhibitors.
5. Amantadine preparations.
6. Anticholinergics.

Levodopa preparations

Levodopa/carbidopa: nacom 250/25; duellin 250/25, 100/10 (10:1); tidomet 100/25

Levodopa/benserazide: madopar 200/50, 100/25.

Slow-release drugs: madopar GSS 100/25.

Instantly dissolving drugs: Madopar D 100/25 (4:1).

The effective dose of levodopa for each patient is selected individually by titration. Start with a dose of 50 mg/day, after 3–5 days – 50 mg × 2 times a day, after 3–5 days – 50 mg × 3 times a day, further increasing the dose – once every 2 weeks. The daily dose of levodopa should not exceed 1000 mg. The most effective dose is considered to be 300–800 mg/day. in 3–5 doses.

Levodopa is a dopamine precursor that can cross the blood-brain barrier (BBB). Most of the drug taken orally is converted to dopamine in peripheral tissues by decarboxylation. “Peripheral” dopamine, unable to penetrate the BBB, is the cause of the development of side effects when taking levodopa, such as tachycardia, orthostatic hypotension, nausea, vomiting, constipation, urinary retention and

incontinence. Thus, it is advisable to take a drug containing, in addition to levodopa, an inhibitor of peripheral dopa decarboxylase (carbidopa, benserazide).

For initial therapy of PD, standard forms of levodopa preparations with a relatively higher content of a peripheral dopa decarboxylase inhibitor (madopar, tidomet) are used in order to minimize the likelihood of developing undesirable effects after taking levodopa preparations.

Levodopa affects all motor symptoms of PD to varying degrees and with different latency periods at all stages of the disease, which allows us to rightfully consider this drug the most effective in the treatment of PD. But, unfortunately, over time, taking levodopa drugs leads to the development of motor fluctuations and dyskinesias.

This is largely due to the progressive neurodegenerative process in the central nervous system, as a result of which the ability of cells to deposit dopamine is lost, which is responsible for the long-term effect of levodopa drugs, leading to an irregular (non-physiological) effect on dopamine receptors.

Thus, the most effective period for use in the treatment of levodopa drugs is the period at the end of the 2nd and beginning of the 3rd stage according to Hoehn-Yahr.

Relative contraindications to the use of levodopa drugs: angle-closure glaucoma and malignant melanoma. They should be used with caution during pregnancy, bronchial asthma, gastric ulcer, arrhythmia, heart attack (including history).

Levodopa preparations are prescribed with caution in combination with the following medications: antihypertensive drugs (risk of orthostatic hypotension), non-selective MAO inhibitors (risk of circulatory disorders - stop taking MAO inhibitors 2 weeks before starting levodopa), inhalational anesthetics - halothane (risk of cardiac arrhythmias - from changing levodopa drugs 12–24 hours before anesthesia), tricyclic antidepressants (increased blood pressure, dyskinesias), lithium preparations (risk of dyskinesias, hallucinations), beta-agonists.

Dopamine receptor agonists

There are ergoline (bromocriptine, cabergoline) and non-ergoline (piribedil, pramipexole, ropinirole, rotigotine, apomorphine) ADRs. But taking into account the presence of a number of serious side effects in ergoline ADRs (pleuropulmonary, retroperitoneal fibrosis, cardiac valve fibrosis, vasospasm, erythromelalgia), non-ergoline ADRs are currently used in clinical practice:

Piribedil (pronoran): initial dose of 50 mg per day in 1 dose, followed by dose titration by 50 mg every week with a frequency of 2, 3, 4 doses per day, respectively, the maximum daily dosage is 250 mg in 5 doses.

Pramipexole (Mirapex, Mirapex PD): initial dose of 0.375 mg per day in 3 doses, followed by dose titration by 0.375 mg in the second week of taking the drug and 0.75 mg each subsequent week with a frequency of 3 doses per day, maximum daily dosage – 4.5 mg in 3 divided doses. For pramipexole with gradual release, the daily dosage and titration regimen are the same, the drug is taken once.

Ropinirole (requip mobutab): initial dose 0.75 mg per day in 3 divided doses followed by titration doses of 0.25 mg every week from 2 to 4 and 0.5 mg every week from 5 to 8, with a frequency of 3 doses per day, maximum daily dosage – 9.0 mg in 3 doses. For ropinirole with gradual release - a single dose of the drug: the initial dose is 2.0 mg, then during the first month of taking the drug, titrate the dose every week by 2.0 mg, and during the second month - by 4.0 mg every week; the maximum daily dosage is 24.0 mg.

Rotigotine (Newpro transdermal patch): initial dose 2.0 mg, then during the first month of taking the drug, titrate the dose every week by 2.0 mg, during the second month - by 4.0 mg every week; the maximum daily dosage is 16.0 mg.

Conclusion

Currently, from the pharmacoeconomic side, the problem of choosing between the original drug and the generic is relevant. Based on literature data, the following recommendations regarding the use of generics in clinical practice have been identified:

1. It is not advisable to switch to a generic drug from the original drug in the following category of patients: elderly people; patients with constipation; patients taking maximum dosages of the original drug and/or for a long time.

2. Titration patterns and the spectrum of side effects of the generic and the original drug differ; additional clinical studies are needed.

Based on the studies conducted, it has been proven that Mexidol, hopantenic acid and citicoline have demonstrated their effectiveness in the complex therapy of patients with PD. Mexidol is recommended to be used as a course of infusions (10–15) 2–3 times a year, followed by taking the tablet form of the drug at a dose of 0.25 g 2–3 times a day for a month. Hopantenic acid is effective in the treatment of asthenic syndrome and daytime sleepiness; Citicoline is recommended for use in the correction of affective (anxiety-depressive), cognitive disorders, rigidity and hypokinesia.

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