Current Views on Pharmacological Interventions for Cognitive Impairment in Vascular Parkinsonism and Parkinson's Disease

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ABSTRACT

Parkinson's disease is considered one of the current topics of today's neurology and geriatrics. Today, the etiology, pathogenesis of this disease and the risk of complications caused by the disease are being thoroughly studied[4,6]. One of the risks of such complications is cognitive impairment. Today's neurology shows that cognitive disorders are caused by dopamine metabolism disorders, cerebral blood circulation disorders, changes in substance metabolism and a number of other factors[8.12,13]. One of the proposed causes and theories is the change in the plasma concentration of the hormone cortisol in Parkinson's disease. Although the role of hormone changes in Parkinson's disease in causing cognitive disorders has not been fully confirmed, this theory has been supported by several years of research by a number of scientists [1,5,7].

Keywords: Vascular Parkinsonism, Parkinson's disease, Alzheimer's disease, Chronic cerebral ischemia, mineralocorticoid receptors, Mini Mental State Examination, Temporythmal correction.

Introduction

Vascular Parkinsonism (VP) accounts for 2.5-5% of all parkinsonian conditions. Although there are several cases of VP in the literature today, Jellinger, as a result of his pathomorphological study of more than 2000 patients with parkinsonism, noted various manifestations of cerebrovascular disorders: multi-infarct cases, leukoencephalopathy, lacunar and organic infarcts of the brain base and basal ganglia, these causes 6 Although it is the cause of % of diseases, about 10% of vascular changes can include signs of degenerative damage of the brain[2,6,10]. This article demonstrates modern and effective treatment principles for vascular parkinsonism and Parkinson's disease. The purpose of the study: to study the correlation of cognitive impairment in Parkinson's disease, Vascular Parkinsonism and other neurodegenerative diseases with increased levels of cortisol in the blood serum. Today, cognitive impairment in vascular parkinsonism and Parkinson's disease is detected late in the disease and treatment is started late, indicating that elevated serum cortisol hormone concentrations are an early predictor of cognitive impairment and prevent profound cognitive impairment in the early stages. Temporal correction is a therapeutic and neurorehabilitation method used in Parkinson's

disease, the effectiveness of which is demonstrated in the article. Research methods: Clinical examination was conducted between 2015 and 2022 in the 1st and 2nd neurology departments of Tashkent Medical Academy, 15th and 16th family polyclinics in Olmazor district of Tashkent city. A total of 115 patients participated in the clinical observation. The average age of patients was 56.7 years. Patients were studied in 3 groups.

During the clinical study, Temporithmic Correction (TRC) method based on the neurorehabilitation method was performed in patients. Temporithmic correction is a method aimed at developing small motor skills, and the method is a combination of light physical therapy exercises carried out together with medical treatment. Temporrhythmic correction begins under the supervision of the attending physician, and then the patient continues independently at home. Temporitmal correction was carried out for 10 days with the help of a doctor.

Thus, in the conducted studies, the prevention of cognitive disorders as a re-sult of the increase in the amount of the cortisol hormone and the complex treatment of VP and PD using the TRC method have been proven to be highly effective. Based on the above, we can conclude that the recommended method of treatment is effective, and it is advisable to use it in practice. In this clinical study, we investigated the effects of increased serum cortisol levels on cogni-tive function in parkinsonism, although our clinical study confirms the conclu-sions of clinical studies cited in the literature review above, our study showed only one-time and serum cortisol changes, increased salivary cortisol levels, and An increase in participants in other circadian rhythms can lead to cognitive impairment. In our research, we used only short neuropsychological question-naires to evaluate cognitive function, but the results of complex questionnaires may cause changes in the conclusions of clinical examinations. In addition, in addition to VP, an increase in the amount of cortisol hormone in PD is also ob-served in some cases, but in many cases, cognitive dysfunction may not be observed.

On the other hand, parkinsonism syndrome accompanied by ischemic strokes in 11% of cases and subcortical form of chronic cerebral ischemia in 14% of cases indicates the prevalence of mild transient forms of VP. In addition, parkinsonian symptoms corresponding to the generally accepted parkinsonian diagnosis are observed in 36% of patients with ischemic stroke. These symptoms are not only signs of disorders of cerebral blood vessels, but also indicate neurodegenerative diseases at an early stage, damage of subcortical structures[7,18,19].

According to the results of clinical studies in recent years, it was found that VP is observed as a result of the impact of small arteries that supply blood to the deep parts of the brain[8,10]. The most common cause of VP is hypertensive microangiopathy (arteriopathy), which is morphologically characterized by lipoglinosis of small arteries and arterioles. General pathology of small arteries causes diffuse bilateral ischemic damage of white matter in the periventricular zone, chiasm and semioval center, as well as numerous lacunar (up to 15 mm) infarcts in the basal ganglia and deep parts of the white matter of the cerebral hemispheres. As a result of repeated transient episodes of chronic ischemia or mild ischemia of the deep layers of the white matter of the cerebral hemispheres, incomplete infarcts develop with demyelination, death of oligodendrocytes, and axonal dysfunction, but the formation of foci of necrosis is not observed[14,16]. An important role in the development of these changes is played by perevascular encephalolysis, which develops as a result of the passage of plasma proteins from the hematoencephalic barrier through the walls of blood vessels during a sharp increase in arterial pressure[3]. In patients without arterial hypertension, the cause of diffuse white matter damage can be considered "senile arteriosclerosis", often associated with pathological changes of arterioles, amyloid microangiopathy, vasculitis, microangiopathy in systemic erythematous, antiphospholipid syndrome, hereditary angiopathy[1,10]. Hemodynamic mechanisms and arterio-arterial embolism in VP can be caused by damage to the

deep structures of the brain as a result of damage to large and medium extra and intracranial vessels. In such cases, in addition to lacunar infarcts, large subcortical infarcts are also observed. One of the less common causes of VP is midbrain hemorrhage, which is often the result of ruptured arteriovenous malformations (See Table 1)[2,8,15].

Table 1. Clinical course of VP.

Features of parkinsonism syndrome	Features of the accompanying syndrome
Bilateral onset of the disease and relative symmetry of symptoms Absence of tremor at rest Less effective than dopaminergic agents Stronger manifestation of symptoms in the axial parts and legs Early development of postural changes and gait disorders	Pyramid syndrome Cerebellar ataxia Early development of severe pseudobulbar syndrome Forehead symptoms (covering reflex, paratonias) Early development of dementia Absence of hallucinations and delusions Focal disorders of higher brain activity (aphasia, apraxia) Early development of neurogenic urinary disorders

VP is observed to develop after one or more ischemic strokes, but also after several transient ischemic attacks, in which extrapyramidal symptoms may appear during the acute period of the disease, or after a period of time, after pyramidal and cerebellar symptoms have regressed. In most cases, VP develops gradually against the background of chronic ischemia of the brain[7,11].

According to new observations, the cortex of the cerebral islets and the hormone cortisol are mutually involved in the development of parkinsonism. Cortical dopaminergic disturbances may be associated with personality changes and the development of hemispheric symptoms in Parkinson's disease[2,13].

In addition, due to the high sensitivity of the dopaminergic system, stress increases the development of neurodegenerative processes[10].

Research Materials And Methodology

Clinical examination was conducted between 2015 and 2022 in the 1st and 2nd neurology departments of Tashkent Medical Academy, 15th and 16th family polyclinics in Olmazor district of Tashkent city. A total of 115 patients participated in the clinical observation.

Analysis

A total of 115 patients participated in the clinical observation. The average age of patients was 56.7 years. Patients were studied in 3 groups (See Table 1).

Table 1. Central Bank key rate and GDP indicators in the Republic of Uzbekistan in 2016-2022.

	Characteristics of groups	Female	Male	Average 56.7±1.2
1	Patients with Parkinson's disease	n=12	n=24	62.3±1.1
2	Patients with parkinsonism	n=12	n=20	66.7±1.1
3	47 healthy people	n=22	n=25	34.9±1.3

In these 3 groups, clinical neurological and anamnestic examination was conducted according to the standards of neurological examination. Parkinson's disease severity was evaluated according to the Hen and Yar scale[7,8]. Patients with a diagnosis of juvenile Parkinsonism did not participate in the investigation. Vascular parkinsonism criteria were assessed according to Levin's criteria[8].

In all patients, the concentration of cortisol hormone in the morning blood serum was determined by the immunofluorescent method. Nonparametric methods were used for statistical processing of laboratory analysis results and objective clinical data. The significance level of p was equal to 0.05. Clinical

study results were analyzed using STATISTICA for Windows 6.0.

Results

During the clinical follow-up, the results of the concentration of the cortisol hormone in blood serum on the 2nd day of hospitalization in all patients are presented in Table 3.

Table 3. Periods of incidence of main group PD

	1-5 years	5-10 years	More than 10 years
Male	13(19.1%)	18(26.4%)	8(11.8%)
Female	14(20.5%)	8(11.8%)	7(10.3%)

20 patients with vascular parkinsonism (29%) had a normal level of cortisol hormone, 37 patients (54.4%) had a moderate increase in cortisol, and 11 patients (16.1%) had a high level of cortisol (See Table 4).

Table 4. Periods of incidence of main group PD

Groups	50 – 250 mg / ml	250 – 500 mg / ml	500 - 900 mg / ml
Basic group n=68	20 (29.4%)	37(54.4%)	11(16.1%)
Control group n=47	32(68%)	9(19.1%)	3(6%)

During the clinical study, Temporithmic Correction (TRC) method based on the neurorehabilitation method was performed in patients. (See Table 5).

Table 5. Memory impairment in patients was assessed using the MMSE scale. Mini Mental State Examination MMSE scale score results

	Below 10 points	In the range of 11-19 points	In the range of 20-23 points	24-27 points	In the range of 28-30 points
Basic group	n=6	n=19 17.64 ±4.3	n=16 22.34 ±2.1	n=18 26.±2.4	n=9 28.67 ±4.3
	8.2 ±2.1				
%	8.9 %	27.94 %	23.5%	26.47 %	13.23 %
Control group	-	n=12 18±2.1	n=22 22.71 ±5.1	n=6 26.4± 1.1	n=18 29±1.1
%	0%	25.53	46.8%	12.7 %	38.3%

During the clinical study, Temporithmic Correction (TRC) method based on the neurorehabilitation method was performed in patients. Temporithmic correction is a method aimed at developing small motor skills, and the method is a combination of light physical therapy exercises carried out together with medical treatment. Temporrhythmic correction begins under the supervision of the attending physician, and then the patient continues independently at home. Temporitmal correction was carried out for 10 days with the help of a doctor. In the early days of TRC, the doctor only recommended exercises for the distal ends of the arms and legs. From the third day of the TRC, the duration of the exercise was extended. TRC is conducted for 10 days under the supervision of a doctor. Step length, height are measured 5 times during TRC, and patients fill out a special questionnaire. The questionnaire consists of three parts, the first part determines the patient's self-care abilities, the second part determines the patient's daily activity, the third part determines the patient's social activity, it is filled again before the start of TRC and after 10 days, the obtained results and step length changes are compared.

Conclusions: Based on the results of the above-mentioned research and the data of the studied literature, we can say that an increase in the amount of cortisol hormone is associated with the development of cognitive dysfunction in vascular parkinsonism and parkinson's disease. The Temporitmal correction method used in the treatment of vascular parkinsonism and

parkinsonism is highly effective in the therapy of vascular parkinsonism and Parkinson's disease, the gait disorder of patients has been normalized, and the quality of life has been confirmed

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