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ABSTRACT

of the dissertation submitted for the degree of Doctor of Philosophy in medicine

CLINICAL AND EPIDEMIOLOGICAL FEATURES OF PARKINSON'S DISEASE IN BAKU

Specialty: 3223.01 – Nervous diseases

Field of science: Medicine

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INTRODUCTION

Relevance of the topic and degree of research development. Parkinson's disease (PD) is a chronic neurodegenerative disease mainly affecting older people. According to the World Health Organization data on the global, regional and national burden of PD due to demographic aging of the population, in 1990-2016 this pathology increased by 74%. The disease is 40% less common in smokers. Compared to women, this pathology is 1.4 times more common in men. Taking into account the socio-medical burden of the disease, WHO recommends searching for ways to prevent this pathology on the national level (increasing physical activity, reducing exposure to harmful environmental factors) and organizing high-quality treatment for patients.

Currently, the scientific study of Parkinson's disease throughout the world is based on the study of its epidemiology, prevalence of signs and their mutual connection risk factors for mortality and survival of patients, diagnosis and treatment based on the etiopathogenetic mechanism.[1,2,3] The number of studies conducted is thousands, and a large number of reviews and meta-analyses have been published to systematize them. Early diagnosis of PD, its rehabilitation, treatment and social protection of patients depend on the strategic direction of national health-care.[4,5]

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[3] Bhattacharge, S. Impulse control disorders in Parkinson's disease: review of pathophysiology, epidemiology, clinical features, management, and future challenges // Neurol. India, - 2018. 66, - p. 967-975

[4] Bae, Y.J. Imaging the substantia Nigra in Parkinson disease and other Parkinsonian Syndromes / Y.J.Bae, J.Kim, C.Solm [et al.] // Radiology, - 2011. 300, - p.260 – 278.

[5] Global, regional, and national burden of Parkinson's disease 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016 // Lancet Neurol, - 2018. 17, - p. 939-953

Research was carried out to substantiate national health strategies both in developed and in developing countries.[6] It was revealed that the prevalence of PD, the index of patient mortality, treatment tactics and life expectancy vary depending on the age, lifestyle and ethnic characteristics of the population in individual countries. In the USA and England, countries with simi lar socio-economic status, treatment tactics for patients with PD differ.[7]

It is interesting to note that there is a difference in the early detection of patients.[8] The various clinical symptoms of PD, especially at an early stage, are non- specific. Therefore, in most cases the disease is detected at late stages.The rate at which the disease progresses creates greater challenges for the healthcare system. Despite the presence of a large number of protocols and standards for the treatment of PD, there is no single algorithm for diagnosing, treating and preventing the disease.[9,10,11]

There is no scientifically substantiated provision on the current and future burden of PD on the health care and social protection system in Azerbaijan; i.e. this aspect of PD has been practically unstudied. Therefore, the topic of our planned research is actual.

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[10]Стандарт специализированной медицинской помощи при болезни Паркинсона, требующей стационарного лечения в связи с нестабильной реакцией на противопаркинсонические средства. Приказ МЗ РФ № 1583н, от 28 декабря, 2012 г.

[11]Труфанов, Е.А. Стандарты диагностики и лечения болезни Паркинсона // East European Journal of Parkinson's disease and Movement Disorders, - 2015. Vol. 1, №2, -p. 19-36.

Subject of the study: Patients with a confirmed diagnosis of Parkinson's disease.

Subject of research: Neurological status, vital activity, survival rate in people with PD.

Purpose of the study: To assess the possibilities of reducing the medical and social severity of the disease among the population of the city of Baku based on the prevalence of the disease, risk factors, clinical forms of the disease and the effectiveness of treatment.

Research objectives:

- Determination of clinical and epidemiological characteristics of Parkinson's disease among the population of Baku city aged 50 years and above;
- Assessment of the relationship between clinical characteristics and risk factors of disease;
- Study of the characteristics and effectiveness of drug treament of the disease;
- Identification of predictors of mortality and survival rates of patients with PD.

Research methods:

- Clinical and epidemiological methods;
- Clinical and neurological examination methods;
- Instrumental research methods (transcranial sonography, magnetic resonance imaging);
- Unified Parkinson Rating Scale.

The main provisions put forward for defense:

-The current state and prognosis of the gender and age status of the population of the city of Baku increases the possibility of the spread of Parkinson's disease and turns this pathology into a medical and social problem that attracts special attention;

-The manifestation of the rich clinical symptoms of Parkinson's disease determines the interconnectedness of these symptoms. Morphometric characteristics of the brain are a pattern of clinical manifestations of the disease;

-Treatment of Parkinson's disease in Baku is pathogenetically oriented, carried out by combining drugs such as dopamine precursor,

peripheral decarboxylase inhibitor, dopamine receptor agonists, cholinergic mediator inhibitors, anticholinergics, NMDA receptor blockers, COMT inhibitors. Preference is given to the use of a polytherapeutic model;

- The cumulative risk of mortality from Parkinson's disease is relatively high. The likelihood of survival is relatively low. The probability of survival depends on the gender of the patient, age at the initial manifestation of the disease and the presence of comorbid pathology.

The scientific novelty of the research:

-The role of the sex and age structure of the population in the formation of clinical and epidemiological characteristics of Parkin

son's disease has been proven;

- It has been substantiated that the distribution and severity of clinical symptoms of Parkinson's disease depend on the demographic characteristics of patients, the age at which the disease manifests itself, family history, comorbid pathology, the status of the substantia nigra, changes in morphometric parameters of the brain;

- The effectiveness and regional features of the structure of drug treatment for Parkinson's disease were revealed;

- Mortality rates, survival probabilities and features of the cause of death of people with Parkinson's disease were identified

Theoretical significance of the study:

In the case of Parkinson's disease, the position is substantiated that the spread of the disease and its symptoms, the medical and social consequences of the disease depend on demographic, social and national-regional health care conditions.

Practical significance of the study:

Results of the study:

- Provide condition for strengthening the role of primary care in the early detection of Parkinson's disease;

-Show ways to optimize treatment tactics for Parkinson's disease;

-Suggest ways to improve the possibility of survival in people with Parkinson's disease.

The approbation and application of the dissertation . The results of the dissertation were presented at conferences and congresses held both in the country and abroad:

- "Modern medicine: new approaches and current research. International scientific and practical conference." Moscow, (2021);
- "XXII international Multidisciplinary Conference Recent Scientific investigation", Shawnee, USA (2021);
- International scientific-practical congress dedicated to the 100th anniversary of Honored Scientist, Professor Tamerlan Aziz Aliyev on "Actual Problems of Medicine-2021"; Baku, (2021);
- Scientific-practical conference dedicated to the birthday of Aziz Mammadkarim Aliyev, Baku, (2022)
- International scientific-practical conference dedicated to the 100th anniversary of National leader Haydar Aliyev, Baku(2023)
- "Actual problems of medicine" international scientific and practical congress of the Azerbaijan Medical University dedicated to the 100th anniversary of birth of national leader Heydar Aliyev, Baku (2023)

Preliminary discussion of the dissertation work was conducted by the Department of Neurology, Department of Epidemiology, Department of Clinical Pharmacology, Department of Internal Diseases of the Azerbaijan Medical University at the inter-departmental meeting Protocol N11, 15.05.2023). It was reported and discussed in 3223.01 scientific seminar at ED2.05 Dissertation council of Azerbaijan Medical University (protocol N1, 14.09.2023).

Publications. The main results of the study are presented in 5 journal articles, including 2 in Russia (journals in the international indexing system), 3 in Azerbaijan and 5 conference proceedings. The journals in which articles are published are journals recommended by the Higher Attestation Commission.

It is applied In Therapeutic Clinic of Azerbaijan Medical University, United city hospital number 18, Baku city policlinics N 1,2,5. The results obtained in the dissertation are used as evidence in the

training of medical specialists and residents in the direction of "Health Organization".

Name of the organization where the dissertation work was carried out: Azerbaijan Medical University

The structure and total volume of dissertation: Introduction - 8004 characters; Chapter I (Literature Review) – 45272 characters; Chapter II (Materials and methods of research) – 9368 signs; Obtained results (Chapter III – 36022 characters; Chapter IV – 38953 characters; Chapter V– 33494 characters; Chapter VI – 19567 points;) Chapter VII (discussion and conclusion of the obtained results) – 10810 points; results – 2502 characters; practical recommendations – 481 characters. The list of references contains 3 literary sources in Azerbaijani, 31 in Russian and 175 in English.

The total volume of the dissertation with notations (excluding tables, figures and bibliography) consists of 204473 characters, 40 tables, 19 diagrams.

MATERIALS AND METHODS OF RESEARCH

The observation object was a patient with a confirmed diagnosis of Parkinson's disease according to the current clinical protocol. In order to assess the incidence of Parkinson's disease among the population, medical records of patients with a firstly confirmed diagnosis (primary disease) and all patients with PD diagnosis (overall incidence) registered in outpatient clinics in Baku in 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2017, 2018,2019 were used. In 2019, both the medical documents of 703 registered patients were studied, and a comprehensive examination of these patients was carried out.

Data collected from observation subjects (observation program) includes: age, gender, signs reflecting the possibility of Parkinson's disease (muscle rigidity, resting tremor, postural instability), signs to exclude Parkinson's disease (history of repeated stroke, severe brain injury, encephalitis , taking antipsychotics, period of remission and remission of unilateral symptoms for more than 3 years, computer tomography and morphometric characteristics of the cerebellum,

early-onset dementia, hydrocephalus, lack of response to levodopa, contact with neurotoxic substances), confirmation of the diagnosis of symptoms of Parkinson's disease (unilateral onset of symptoms, rest tremor, intensity of progression, asymmetry of symptoms, positive reaction to levodopa, manifestation of choreiform dyskinesias when using levodopa, duration of the disease, etc.).

The age of the patients at the time of the first symptoms, duration of the disease, clinical form, comorbidities, family history and treatment options were recorded for persons with a confirmed diagnosis of Parkinson's disease (presence of at least three of the above symptoms in one patient).

Clinical and morphological examination of the observed patients included an objective assessment of their somatic condition and a comprehensive study of their neurological status. All patients underwent a general laboratory examination; in targeted selection, ultrasound examination of the substantia nigra and magnetic resonance imaging of the brain with determination of morphometric indicators of brain structures were performed.

Patients under our care were assessed using the Unified Parkinson's Disease Rating Scale (UPDRS).

In 2009–2010 a cohort of 110 people with primary manifestations of Parkinson's disease was followed to study the risk of mortality and survival of patients with PD. In 2010-2019, medical certificates of annual deaths were reviewed, and the primary (main) and immediate cause of death was established.

The materials collected during the study were processed using adequate methods for this purpose. During statistical processing, descriptive statistics methods were mainly used. Descriptive statistics of quantitative indicators (age of patients, duration of illness, etc.) were calculated.

CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF PARKINSON'S DISEASE AMONG THE POPULATION AGED 50 YEARS AND OLDER IN BAKU

The primary incidence of Parkinson's disease in the population aged 50 years and older was 7.4 (95% confidence interval 5.23–9.55) per 100,000 people in 2010.

In subsequent years, the incidence was high. From year to year, the rate increased in most cases, and only in 2012, 2014, 2016 and 2018 it remained relatively stable compared to the previous year. In these years, when comparing the difference in the primary incidence of PD population according to the χ^2 criterion and the 95% confidence interval, a statistically significant (P>0.05) difference was not proven, but when checking the main trend in the primary incidence using the least squares method, it is noteworthy that it represents a direct line and is expressed by the following regression equation: y=0.4739x, where y is the initial incidence rate, x is the serial number of calendar years (2010 – 1; 2011 – 2; .....2019 – 10). The degree of reliability of the regression equation is 95.46% (approximation index R^2= 0.9546). Projections from this model are as follows: in 2029-2039, the incidence rate could be 16 and 20 $^0/_{0000}$, respectively.

In Baku, the overall morbidity rate (the number of all diseases registered in a calendar year) for the population aged ≥50 years was 101.4 (95% confidence interval 82.13 - 120.80) per 100,000 population in 2010. In subsequent years, the overall incidence was different (102.13–110.6$^0/_{0000}$), but the difference was not statistically significant (P>0.05). It is noteworthy that the change from year to year is characterized by dynamic growth, the correlation between calendar years and the level of general morbidity is high. The change in overall incidence (y) by calendar year (x) is expressed by the following regression equation: y=0.9696x+100.93.

The reliability of the regression equation is 92.4%, its approximation is high (R^2=0.9244). The overall incidence is estimated at 120 and 130$^0/_{0000}$ in 2029 and 2039, respectively.

In 2010-2019, the primary incidence was in the range of 9.6-15.0 $^{0}/_{0000}$ in the male population, 5.5-9.4 $^{0}/_{0000}$ in the female population, the incidence of women in all years was relatively low, statistical significance differences have not been proven. In both populations, the initial incidence trend was characterized by an age-related increase in one direction. During the observation period, the relative risk of primary morbidity in the male population compared to the female population was: 1.75; 1.39; 1.72; 1.46; 1.57; 1.41; 1.75; 1.62; 1.73 and 1.60. The prevalence rate (overall incidence) of PD in the male and female population ranged from 130.6 - 147.7 and 76.3 - 83.8 $^{0}/_{0000}$ in 2010 - 2019. respectively. During the entire observation period, the level of PD in the male population was statistically significant ($p<0.05$). The level of relative risk compared to the female sex is respectively: 1.71; 1.67; 1.74; 1.70; 1.68; 1.65; 1.76; 1.68; 1.66 and 1.69. The occurrence of PD and associated mortality depend primarily on the age of the patients. The age at onset of the disease and the duration of the disease during the observation period are important from an epidemiological point of view. The table shows the primary and general incidence of PD in the population depending on age and gender. The prevalence of PD (overall incidence) per 100,000 population aged 50-59 years was 88.3 (95% confidence interval 72.8-103.7) in the male population, 42.7 (95% confidence interval 32.6-52 ,7) in the female population. and are statistically significantly different from each other ($p<0.05$). This figure is 198.7 and 102.0 $^{0}/_{0000}$ in male and female populations aged 60-69 years, respectively (95% confidence interval 170.6 - 226.8 and 83.0 - 121.0 $^{0}/_{0000}$ statistically significantly exceeded the corresponding indicator in 50-59 years, statistically significantly different from each other in the female and male populations ($p<0.01$).The total incidence of PD among men and women aged 70-79 years is 232.0 and 152.2 per 100,000 people (95% confidence interval 171.1–292.8 and 109.2–195.2) in previous age groups increases between the ages of 50 and 80. This trend reverses after 80 years: the overall incidence in the male population ($136.2^{0}/_{0000}$; 95% confidence interval 109.7 – $195.2^{0}/_{0000}$) decreases, but increases in the

female population (178.6$^{0}/_{0000}$; 95% confidence interval 128.1–229.0 $^{0}/_{0000}$ (table).

Thus, the main feature of the prevalence of PD in male and female populations aged 80 years and older is that the rate is higher in the female population and tends to increase compared to previous ages.

Table. Dynamics of the initial and overall incidence of PD in the population depending on age and gender

Age, years	Gender	Population, thousand people	Number of patients with Parkinson's disease		Primary incidence, per 100 thousand people.		Prevalens, per 100,000 population	
			Primary	General	Level	95%Cİ	Level	95%Cİ
50 -59	Man	14,73	7	130	4,8	1,2 – 8,3	88,3	72,8 – 103,7
	Woman	16,86	4	72	2,4	0 – 4,7	42,7	32,6 – 52,7
60 – 69	Man	10,00	14	200	13,9	6,5 – 21,4	198,7	170,6 – 226,8
	Woman	11,27	10	115	8,9	3,3 - 14,5	102,0	83,0 – 121,0
70 – 79	Man	25,000	15	58	60,0	29,0 – 90,9	232,0	171,1 – 292,8
	Woman	32,85	10	50	30,4	11,2– 47,7	152,2	109,2 – 195,2
80 and much more	Man	2,056	8	28	38,9	11,4 - 66,4	136,2	84,7 – 187,6
	Woman	2,800	8	50	28,6	8,4 – 48,8	178,6	198,1 – 229,0

One of the factors influencing the severity of PD is the rate of its progression. If the transition of the disease from one stage to another occurs in less than 2 years, the rate of progression is considered rapid. Rapid progression was observed in 5.1% of patients (95% confidence interval 3.5–6.8%). This rate of progression was recorded in 5.3% (95% confidence interval 3.1-7.5%) of cases in men and 4.9% (95% confidence interval 2.3-7.4%) of cases in women and did not differ statistically from each other ($p>0.05$).

A moderate rate of progression (the transition of the disease from one stage to another occurs within an interval of 2-5 years) was noted in 87.5% (95% confidence interval 85.0-90.0%) of patients.

This type of progression was observed in 87.3% of men (95% confidence interval 84.0–94.5%) and in 7.8% of women (95% confidence interval 83.9–91.7%), gender differences were not statistically significant ($p>0.05$).

The rate of slow progression (the transition of the disease from one stage to another occurs over more than 5 years) was noted in 7.4% of patients (95% confidence interval 5.1-9.3%).

Stage I of the disease (manifestation of unilateral symptoms) was registered in 18.8% (95% confidence interval 15.9-21.7%) of patients. At this stage, the values for men (21.6±4.0%) and women (14.6±4.1%) were different, but the statistical significance of the difference was not confirmed ($p>0.05$). Stage II of PD (bilateral signs, without postural instability) was detected in 37.6% (95% confidence interval 33.9–41.9%) of patients, in men (39.2±8.2%) and women (35, 2±5.6%) values were close to each other ($p>0.05$). Stage III PD (manifestation of bilateral symptoms against the background of mild postural instability) in 26.6% of patients (95% confidence interval 23.3–29.9%), did not differ in men (23.8 ± 4.2%) and women (30.7±5.4%) ($p>0.05$). Stage IV of PD (severe impairment of motor activity, difficulty in independent movements) and stage V (inability to get out of bed) were noted in 17.0% of patients (95% confidence interval 14.3–19.9%) was observed in 15.4±3.5% of men and 19.5±3.7% of women ($p>0.05$). The distribution of PD by clinical forms shows that in most cases (57.6%; 95% confidence interval 54.0-61.3%) a mixed form of

the disease is observed. The akinetic-rigid form was noted less frequently (16.9%; 95% confidence interval 14.2–9.7%). The tremulous form was detected in 25.5% of patients (95% confidence interval 22.2–28.7%). The proportions of mixed, akinetic-rigid and tremulous forms of the disease in men (60.1±4.8; 19.0±3.8 and 20.9±4.0%, respectively) and women (54.0±.5,9; 13.9±4.1 and 32.1±5.5% of groups) differed ($p<0.05$).

Polymorbidity (comorbidity) is considered one of the factors that complicates the course of PD and increases the likelihood of death in patients.

Diabetes mellitus was found in 23.5% of patients. The prevalence of diabetes in men (21.4±4.0%) and women (26.5±5.2%) was not statistically different. Arterial hypertension was registered in 38.1% of patients with PD (95% confidence interval 34.5–41.7%). The intensity of this pathology was similar in the male (36.1±4.7%) and female (41.1±5.8%) populations. IHD was observed in 8.4% of patients (7.0% in men, 10.4% in women). 29.7% of people with PD did not have severe chronic diseases (95% confidence interval 26.4 - 33.1%), including 26.4% of men and 34.5% of women. The proportion of this category of patients is statistically significantly higher in the female population ($p<0.05$).

The clinical manifestation of PD is characterized by a wide range of symptoms. The most common symptom of autonomic disorders is pathological salivation. This sign was recorded in 69.0% of patients (95% confidence interval 65.5 - 72.5%). Constipation is one of the most common symptoms of PD. Constipation was recorded in 69.8% (95% confidence interval 66.4–73.3%) of patients under our supervision.

Orthostatic hypotension was registered in 61.3% (57.6 - 65.0%) of patients under our supervision. In our study, 50.6% (95% confidence interval 46.8–54.4%) of patients had agitation, 74.3% had irritability (95% confidence interval 71.0–77.3%), 64 .6% - drowsiness (95% confidence interval 61.0–68.2%). , inhibition in 63.6% (95% confidence interval 59.9 - 67.2%), in 67.7% (95% confidence interval 64.2 - 71.2) signs of memory impairment were recorded.

Considering that PD is a chronic degenerative disease of the brain, patients underwent transcranial ultrasonography brain MRI with analyzing morphometric characteristics. Transcranial ultrasonography examination method was successfully used in 60 of the 703 patients under our supervision.

During transcranial ultrasound examination, changes in the substantia nigra of the brain were symmetrical in 18.3±4.9% of patients, asymmetric in 63.3±6.2%, and normal in 18.3±4.9%. The normal state of the substantia nigra was observed in 10.0±6.7% of patients with the akinetic-rigid form, in 15.0±7.9% with the mixed form of the disease and in 30.0±10.2% with the trembling form of PD, but their difference was not statistically significant (χ^2 <0.38; Ϭ=1.0; p>0.05). Asymmetric changes in the substantia nigra were characteristic of all clinical forms (75.0±9.6% in the akinetic-rigid form, 50.0±11.1% in the mixed form and 65.0±10.6% in the trembling form). According to the proportion of patients with symmetrical changes in the substantia nigra, the clinical forms of PD were statistically different from each other: 35.0±10.6% of PD patients with a mixed form had a symmetrical change in the substantia nigra; this indicator was at a low level in the trembling form of PD (5. 0±4.8%). The proportion of patients with symmetrical changes in the substantia nigra with mixed and trembling forms of PD were statistically significantly different from each other (χ^2=4.5; Ϭ=1.0; p<0.05). Changes in the substantia nigra were more pronounced depending on the stage of PD. According to the stages of disease, changes in the substantia nigra were absent in 60±12.6% of patients at stage I of the disease; the level of this index was slightly lower at stage II of the disease (10.0±6.7%). At stages III - IV of PD, the substantia nigra was changed in all patients. The possibilities of ultrasound are limited by the study of the morphometric characteristics of the brain. Magnetic resonance imaging provides a more reliable study of morphometric parameters. In PD, compared with the control group, the volume of the superior frontal, right precentral, and superior temporal gyrus is statistically larger, while the volume of the lateral insular, orbital H-shaped, and lateral temporo-occipital gyrus is statistically smaller. In PD, there was also a statistical increase in the

total volume of the medial orbitofrontal cortex, hypointense foci in the white matter, and the volume of the insular cortex was statistically less compared to the control group.

Thus, PD is characterized by a change in the substantia nigral of the brain, an increase in some morphometric parameters of the brain, and a decrease in other parameters of the brain.

ASSOCIATION OF CLINICAL CHARACTERISTICS AND RISK FACTORS IN PARKINSON'S DISEASE

At stage I of PD, predominantly its tremulous and mixed forms are observed (29.5±3.9 and 59.1±4.8%), at stage II the proportion of mixed form increases (73.4±2.6%), the proportion decreases tremulous form (15.3±2.3%). At stage III, on the contrary, the proportion of the mixed form decreases (47.6±3.6%), and the proportion of the trembling form increases (38.5±3.5%).

At stages IV - V of the disease, the akinetic-rigid form of the disease is more common (45.0±4.5%). Depending on the duration of the disease, the proportion of its akinetic-rigid form practically does not change (17.1±1.9; 17.7±2.5 and 14.8±3.9% with a duration of 0-4, 5-9, 20 and many years, respectively, $p > 0.05$), PD lasting 10 years or more often manifests itself in the form of a mixed form (64.5±4.3%). The proportion of clinical forms of PD in the male and female groups differs statistically significantly ($p<0.05$): in the male group the proportion of the mixed form (61.5±2.3%), akinetic-rigid form (21.4±2.0) is relatively high, and in the group of women the mixed form of PD makes up the majority (37.6±2.8%).

The most important sign for the prognosis of PD is the rate of its progression. In the population we observed, the proportion of PD developing at a fast and slow pace was 5.1±0.8 and 7.4±1.0%, respectively. In the first and second five-year plans, the distribution of PD according to the rate of progression was stable (3.4±1.4% and 4.4±1.1% rapid rate, 8.4±1.3% and 6.6±1.8% slow speed). The rapid rate of PD lasting 10 years or more was observed up to 3 times or more (11.6±1.8%; $p<0.05$). Depending on the gender of the patients, the

structure did not change significantly due to the rate of disease progression ($p>0.05$).

CHARACTERISTICS AND EFFICIENCY OF DRUG TREATMENT OF PARKINSON'S DISEASE

A wide range of medications are used to treat Parkinson's disease. The choice of drugs depends on the stage of development of the disease.

It is noteworthy that monotherapy was prescribed to a relatively small number of patients: pronoran- 17.1±1.4%; cyclodol– 10.7±1.2% (total 27.8%). Two variants of polytherapy are noticeable: a combined version of two or three drugs (Nakom -Levadopa+Karbidopa, Madopar-Levadopa+Benserazid, Dopalevo-Levadopa+Karbidopa+Entokapon) (respectively 28.2±1.7; 2.4±0.6 and 2.1±0.5%; total 32.7%); polytherapy with a combination of two or three drugs (Nakom +Cyclodol; Nacom+Akineton; Nacom+Midantan; Madopar+Akineton; Madopar+Praxol; Madopar+Stalevo+Amantadine; Stalevo+ Pronoran; Stalevo+Akineton; Levocarb + Madopar; Praxol+Alcheba +Madopar. In other groups, dopamine precursors and peripheral decarboxylase inhibitors are prescribed relatively less frequently (63.2±1.8 and 59.2±1.9 per 100 patients, respectively; 35.5 and 33.2% of drugs used, respectively).

As already mentioned, in the treatment of PD in clinics of Baku, Nakom (Levadopa+Karbidopa) (28.2±1.7%), Pronoran (piribedil) (17.1±1.4%), Cyclodol (triheksiphenidil) (10.7±1.2%), Nakom (Levadopa+Karbidopa) and Cyclodol (triheksiphenidil) (10.4±1.2%). Nakom (Levadopa+Karbidopa) and Akineton (biperiden hidrochlorid) (10.1±1.1%) were used.

A number of symptoms of mental disorders, including excitability (from 50.5±3.5% to 40.4±3.4%, $p<0.05$), irritability (from 73.1±3.1% to 63. 6±3.4%, $p<0.05$), anxiety (from 24.2±3.0% to 15.6±2.5% to, $p<0.05$), drowsiness (from 64.6± 3.3% to 48.9±3.5%, $p<0.05$), slow thinking (63.6±3, from 4% to 56.0±3.5%, $p<0.05$)

disorders memory (from 67.7±3.3% to 50.0±3.5%, $p<0.05$) statistically significantly decreased in persons with such symptoms. For other symptoms (fatigue, dysphoria, euphoria, mutism, aggression and insomnia), the decrease was statistically insignificant ($p>0.05$).

Similar results are observed regarding signs of sensory disorders, statistically reduced pain (43.9±3.5 and 33.8±3.3%), restless legs syndrome (36.4±3.4 and 27.2±3.1 %) and anosmia (25.3±3.0 and 16.2±2.6%), changed significantly ($p<0.05$), the percentage of signs of paresthesia and akathisia did not change significantly ($p>0.05$).

Thus, the use of Nakom (Levadopa+Karbidopa) in the treatment of PD created a real opportunity to reduce the prevalence of a number of symptoms, but it was not possible to eliminate individual symptoms in all patients.

Pronoran(piribedil) monotherapy was used in 17.1±1.4% of cases in the treatment of PD in Baku. Piribedil contained in Pronoran(piribedil) binds to dopaminergic receptors in the brain and acts as an α-2 receptor antagonist and dopaminergic receptor agonist (biological response enhancer). Statistically significant ($p<0.05$) observed positive changes include: a decrease in the proportion of registered individuals with orthostatic hypotension (from 59.2±4.4% to 45.8±4.5%), agitation (48, s 3±4.5% to 32.5±4.2%), irritability (from 72.5±4.0% to 53.3±4.5%), dysphoria (**37,5 from** 5±4.4% up to 25.8±3.9%), drowsiness (from 62.5±4.4% to 49.1±4.5%), slowed thinking (from 61.7±4.4% to 49.1%)±4.5%), memory impairment (from 65.8±4.3% to 50.8±4.5%), insomnia (from 31.7±4.2% to 22.5± 3.8%), with restless legs syndrome (from 34.1±4.3% to 24.1±3.9%).

According to the Unified Rating Scale as a result of treatment for Parkinson's disease, a statistically significant improvement (decrease in scores) was observed in the following symptoms: tremor (1.68±0.09 and 1.32±0.10 points), rigidity (1.70±0.10 and 1.35±0.11 and 1.33 points±0.10 points), rising from a chair (1.45±0.09 and 1.20±0.10 points), walking (1.68±0. 10 and 1.31±0.11 points), thinking (1.28±0.11 and 1.01±0.10 points), depression (1.42±0.11 and 1.11±0.09 points), salivation (1.84±0.11 and 1.50±0.12 points), swallowing (1.64±0.09 and 1.28±0.10 points), cutting food (1.71±0 .11

and 1.39±0.12 points), dressing (1.70±0.12 and 1.41±0.11 points), hygiene (1.38±0.08 and 1.11±0.09 points). Statistically significant decreases were also recorded for other symptoms. Thus, the use of Pronoran (piribedil) in the treatment of PD can reduce most clinical symptoms and stabilize a number of symptoms.

Cyclodol containing trihexyphenidyl, as a peripheral and central cholinergic blocker is used in the treatment of movement disorders. This drug was prescribed to 10.7±1.2% of patients with PD in Baku. During the treatment, the dynamics of the prevalence of PD symptoms in patients shows that the severity of motor disorders decreased significantly: speech from 1.52±0.08 points to 1.20±0.10 points ($p<0.05$), facial expressions from 1.48±0.09 points to 1.12±0.10 points, tremor from 1.56±0.11 points to 1.20±0.12 points ($p<0.05$), finger tapping from 1.56±0.11 points to 1.16±0, 12 points ($p<0.05$), arm movement from 1.46±0.09 points to 1.12±0.11 points ($p<0.05$) and leg movement from 1.51±0.11 points up to 1.19±0.13 points ($p<0.05$), rising from a chair from 1.54±0.13 points to 1.22±0.11 points ($p<0.05$), walking from 48± 0.09 points to 1.21±0.10 points ($p<0.05$). The reduction in stiffness in these patients (from 1.61±0.13 points to 1.43±0.12 points) was not statistically significant.

Thus, in PD treated with cyclodol (triheksiphenidil), it was possible to change both motor functions and other symptoms in a positive direction.

When nakom (levadopa+karbidopa) is combined with cyclodol(triheksiphenidil), two pharmacological effects are achieved (an increase in the amount of dopamine in the brain and cholinergic blockade). This combination was used for PD in 10.4±1.2% of cases.

Notably, the prevalence and severity of all PD symptoms decreased, but the statistical significance of the decrease was not always confirmed. Thus, the number of patients with autonomic disorders with dry mouth (37.0±4.4 and 26.0±2.9%; $p<0.05$), hyperhidrosis (28.8±5.2 and 23.3±4.9%; $p>0.05$) decreased statistically significantly, salivation (68.5±5.4 and 57.5±5.7%; $p>0.05$), orthostatic hypotension (58.9±5. 7 and 47.9±5.8%; $p>0.05$) the decrease in the prevalence of symptoms was not statistically significant. A statistically

significant decrease is also observed in symptoms of mental disorders: with fatigue from 50.6±5.8% to 39.7±5.7% ($p<0.05$), with anxiety from 23.2±4.9% to 9.3±3.8% ($p<0.05$), with memory impairment from 65.8±5.5% to 51.7±5.8%, with euphoria from 16.4±4.3% to 5.4±2.6% ($p<0.05$), with mutism from 24.6±5.0% to 10.6±4.0% ($p<0.05$), with aggression from 16, 4±4.3% to 5.4±2.6% ($p<0.05$), with insomnia 34.8±4.8% from 5.4% to 21.9±4.8% ($p <0.05$). Amoung the symptoms of mental disorders, there was no statistically significant change in the following symptoms ($p>0.05$): agitation (from 49.3±5.8% to 38.3±5.6%), irritability (from 72.6±5.2% to 61.6%±5.6%), dysphoria (from 38.3±45.6% to 27.3±5.2%), drowsiness (from 63.0±5.6% to 52.0±5.8%).

With the combined use of nakom (Levadopa+Karbidopa) and cyclodol (triheksiphenidil) in patients, optimization of all motor functions was recorded.

Thus, the combined use of nakom (Levadopa+Karbidopa) and cyclodol (triheksiphenidil) leads to improvements in movement, thinking and daily activity.

Akineton (biperiden hidrochlorid) is an anticholinergic drug, and its combination with nakom (levadopa+karbidopa) is used to treat all symptoms of autonomic disorders (dry mouth, drooling, hyperhidrosis, orthostatic hypotension), mental changes (excitability, irritability, fatigue, dysphoria, anxiety, drowsiness, slow thinking, weakness, euphoria, mutism, aggression, insomnia), for sensory disorders (paresthesia, pain, akathisia, restless legs syndrome, anosmia) and a positive result was obtained ($p<0.05$).

The effectiveness of complex evaluated treatment options: monotherapy with pronoran and cyclodol, combination of two drugs with nakom, cyclodol (combination of 3 drugs), akineton with nakom (combination of 3 drugs), combination of more than three drugs with stalevo, madopar and midantan allows to get a positive result. Taking into account the age of the patients, the duration and stage of the disease, there was no statistically significant difference in terms of the level of the Unified Rating Scale I, II, III parts and the mean scores as a whole.

MORTALITY LEVEL, CAUSES AND SURVIVAL PROGNOSIS OF PD

After the first detection of PD, the mortality rate of patients dynamically increases within 6.4±2.3% and 42.8±9.3% over 10 years, the cumulative mortality rate over 10 years is 85.5±5.8% (average annual 8. 55%), in men (93.8±2.7% cumulative, 9.38% annual average) compared to women (63.3±8.7% cumulative, 6.33% annual average) is statistically significant ($p<0.05$). The probability of death in patients with PD depends on age and gender, as in the population. In the population, the mortality rate of men and women 60 years of age and older (7 and 6.2%, respectively) is less than the mortality risk in the corresponding groups of people with PD (9.38 and 6.33%), the mortality risk of people with PD is 1.34 times higher in men, 1.02 times higher in women. PD significantly increases the risk of mortality primarily in men. Factors that statistically influence the risk of mortality include: age (both age at first onset of the disease and age at follow-up), comorbidities (diabetes mellitus, cerebrovascular disease, coronary heart disease), stage of the disease and its relationship with dementia. Among the causes of death (primary causes) of patients with PD, the share of Parkinson's disease is 23.4%; in most cases, patients die due to arterial hypertension (51.1%). Among the primary causes of death, the share of diabetes mellitus, malignant tumors, chronic obstructive pulmonary diseases, pyelonephritis and cirrhosis of the liver is 7.4, respectively; 5.3; 4.2; 5.3 and 3.2%. The immediate causes of death were acute myocardial infarction in 24.5% of cases, acute cerebrovascular accident in 36.2% of cases, pulmonary artery thrombosis in 11.7% of cases, pneumonia in 10.6% of cases, uremia in 4.2% of cases, cerebral edema in 7.4% of cases, cardiogenic shock in 5.3% of cases. The probability of 1-10-year survival of patients with PD ranges from 0.94±0.21 to 0.41±0.9 depending on the age at the time of onset of the disease (≤70 and >70 years 0.96±0.20 – 0.50±0.11; 0.91±0.41 – "0"), from the patient's age (≤70 and >70 years 0.96±0.20 – 0.50±0.16 and 0, 91±0.41 – 0.38±0.16), gender (for men 0.93±0.33 – 0.29±0.11 and for women 0.97±0.23 – 0.65±0 .15), from

polymorbidity (0.87±0.50 – 0 against the background of dementia, 0.88±0.61 – 0 against the background of cardiovascular diseases, 0.97±0.21 – 0.48±0, 11 in persons without chronic diseases). Monotherapy and polytherapy (0.94±0.45 – 0.46±0.28) do not have a statistically significant effect on the probability of survival. Against the background of the existing treatment tactics for patients with PD in Baku, the average annual probability of death (8.55%) is close to the corresponding indicator for people of Asian origin living in the United States of America (8.5%), and is 2 times higher compared to the corresponding indicator for the population of Sweden (4.0%).

RESULTS

1. In Baku in 2010-2019, the primary incidence of Parkinson's disease among the population aged 50 years and older varies in the range of 7.4-12.0$^0/_{0000}$, and the overall incidence is 101.4-110.6$^0/_{0000}$, characterized by an increasing trend , both in the male and female populations changes in a similar trend at different levels (9.6 - 15.0 and 5.5 - 9.4$^0/_{0000}$ primary incidence; 130.6 - 147.7 and 76.8 - 83 ,8$^0/_{0000}$ total incidence), increases mainly depending on age (primary incidence at the ages of 50-59, 60-69, 70–79 years, 80 years and older - 4.8; 13.9; 60.0 and 38.9$^0/_{0000}$ in men, 2.4, 8.9, 30.4 and 28.6 0/0000 in women, overall incidence 88.3, 198.7, 232.0 and 136.2$^0/_{0000}$ in men. 42.7; 102.0; 152.2 and 178.6$^0/_{0000}$ in women) the rate of progression was fast in 5.1% of patients, moderate in 87.5% and slow in 7.4% of patients, 18. 8% of patients were at stage I, 37.6% of cases were recorded at stage II, 26.6% at stage III and 17.0% at stage IV-V, 50.6% of the disease lasted 0-4 years, 32.1 % 5-9 years and 17.2% lasted 10 years or more, 57.6% of patients had a mixed form of the disease, 16.9% had an akinetic-rigid form of the disease, and 25.5% had a tremulous form of the disease.

2. Manifestations of PD and the results of assessment on the Unified Parkinson's Rating Scale show dependence on the patient's age, gender, the presence of this pathology in the family history, as well as the presence of diabetes mellitus and arterial hypertension as

a concomitant disease, the stage and duration of the disease. and morphometric changes in brain structures. The correlation between MRI indicators of brain structures (superior frontal, right precentral, superior occipital fold, lateral, H-shaped orbital, annular insula, volume of the lateral occipital sulcus) and between the intensity of the disease symptoms is statistically significant .

3. Modern drugs aimed at its pathogenesis and symptoms were used in the treatment of PD: 63.2±1.8% dopamine precursors, 59.2± 1.9% peripheral decarboxylase inhibitors, 17.1±1.4% dopaminergic receptor agonists, 10.7±1.2% inhibitors of cholinergic mediators, 14.9±1.9% 1.3% anticholinergic drugs, 8.4±1.0% COMT inhibitors, 2.6±0.6% NMDA blockers receptors, 2.1±0.5% drugs in the treatment of dementia. Treatment is carried out with one drug (monotherapy) in 28.1% of cases, two drugs in 30.6% of cases, three in 31.0% of cases, four or more drugs in 10.3% of cases. The effectiveness of treatment options in reducing disease symptoms and Unified Parkinson's Rating Scale scores did not differ.

4.10-year cumulative and average annual mortality of persons with PD in Baku are 85.5% and 8.55%, respectively, the risk of mortality depends on gender (10-year cumulative 93.8±2.7% and 63.3±8.7 % respectively in men and women), on the age of patients (<70 years old was 85.7±5.9%; 70-79 years old 96.5±3.3% and 100% at the age of 80 years and older), comorbid pathology (according the background of ischemic heart disease, mortality was 92.8±3.9%; 100% according to the background of diabetes mellitus and cerebrovascular diseases), from dementia (96.8±3.0%) and stage of the disease (100% at stages III-V) . The probability of 1, 5 and 10-year survival of patients was 0.94±0.21; 0.76±0.18 and 0.41±0.09, respectively.

PRACTICAL RECOMMENDATIONS

1. Develop a priority for pathogenetically targeted monotherapy in the treatment of PD.

2. Widespread use of the primary health care system (local doctors and family doctors) for early detection of PD.

3. Ensuring the use of transcranial ultrasonography and MRI in the diagnosis of PD and dynamic monitoring of patients with monitoring of the status of the substantia nigra and morphometric parameters of the brain.

4. Training of family and local doctors in the methods of diagnosing PD.

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