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Parkinson's disease: the most common diagnostic mistakes in Lithuania

Research Article

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Abstract: Parkinson's disease (PD) belongs to group of neurodegenerative diseases. PD diagnosis is clinical, based on these signs: tremor, rigidity, bradykinesia, akinesia or hypokinesia. The aim of the work was to determine the frequency of separate clinical forms of Parkinson's disease and difficulties at this disease diagnosis. After examining 267 patients, foreseen clinical criterion of Parkinson's disease correspond 202 (44.0% persons) – 115 women and 87 men and for 65 patients diagnosis of PD was not confirmed, because they did not correspond with accepted criteria of Parkinson's disease. While analyzing clinical peculiarities of disease we ascertained that rigidity–tremor form of disease prevailed for 152 (75.2%, 86 women and 66 men) patients. The rigidity form was more rare – 28 (13.9%, 13 women and 15 men). Not very frequent was a tremor form of disease -- 22 (10.9%, 16 women and 6 men) patients. According to data of our research, for almost one fourth of patients (65, 24.3%) the diagnosis of Parkinson's disease was not confirmed after clinical examination. These patients did not correspond with clinical criteria of PD. The data of our research maintain that for almost one fourth (one fourth of what?) (24.3%) the diagnosis was incorrect. Although these patients did not correspond with accepted criteria of PD, they had been treated with antiparkinsonic medications. The PD diagnosis for them was determined only according to separate symptoms: tremor, gait alterations or memory deterioration and behaviour alternations. It must be noted, that symptoms of Wilson's disease, MSA or brain infarction were estimated as PD. Examining patients at home, we ascertained that not all patients use prescribed L-dopa preparations. A part of patients or their relatives stopped using of this drug independently. We also made note of the fact that urinary incontinence manifested using dopamine agonist ropinirole. This side effect became significant problem for patient himself and for his relatives.

Keywords: *Henoch-Schönlein purpura • Parkinson's disease • tremor • rigidity • bradikynesia • Wilson's disease • ropinirole*

1. Introduction

Parkinson's disease (PD) belongs to the of neurodegenerative diseases group. It is one of the most common progressive neurodegenerative illnesses [1-3]. PD diagnosis is clinical, based on these signs: tremor, rigidity, bradykinesia, akinesia or hypokinesia [4,5]. Accurate assessment of patient's complaints, history and clinical examination data is necessary determining PD diagnosis [6-8]. Unilateral localization of the initial symptoms is also typical for PD [9] however this sign is not reliable for making a diagnosis.

Determining correct diagnosis in the initial stage of the disease is problematical. For one third of patients first symptoms of PD may be rather "misty" (such as general fatigue, depression, gait alterations and limb paresthesias). These symptoms may exist for several months or years until the typical signs of PD manifest. It must be noticed, that even after the manifestation of classical PD symptoms the correct diagnosis is determined not in all cases of the disease.

The most general clinical sign of PD is tremor. It is present in 80-92% of patients [10,11]. Rigidity is common symptom not only for PD. However it can be noticed in 67-99% of patients with this disease [11,12]. Bradykinesia is characterised by gait disturbances and deceleration. 71-99% of patients with PD refer to bradykinesia [12-14].

Study performed by the Norwegian authors in 1995 revealed rigidity-tremor form to be the most common form of PD. By their data it was present in 68.2% of

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cases. Rigidity form was determined in 20.4% and tremor form in 11.4% of patients with PD.

Similar symptoms may also be present in case of other diseases, which may be estimated as PD. Erroneous PD diagnosis is commonly determined in the case of essential (family) tremor, Wilson's disease and various neurodegenerative disorders.

The aim of this study was to determine the frequency of separate clinical forms of Parkinson's disease and difficulties at this disease diagnosis.

2. Study object and methods

Patients who satisfied the following criteria were eligible to participate in this study:

- Parkinson's disease or Parkinson's syndrome was diagnosed from 1978-01-01 to 2004-01-01.
- Patients with PD were alive until 2004-01-01.
- The diagnosis of PD or Parkinson's syndrome and treatment with antiparkinsonic medication was marked in the ambulatoric history of the patients.

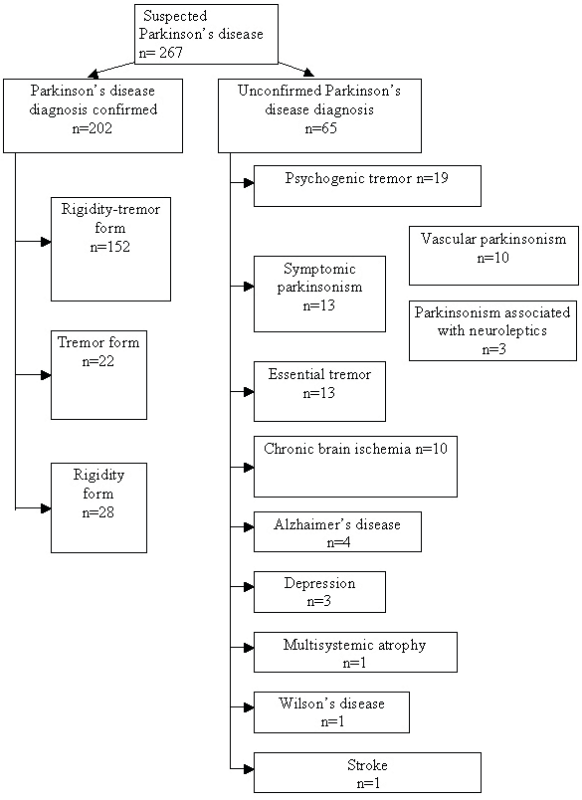
After analyzing of medical documentation (i.e. dispensary histories, registration journals and other kinds of documents) registered by neurologist at primary health care centres of Vilnius city since 1978 patients with the final diagnosis of "Parkinson's disease", "Parkinson's syndrome" and "parkinsonism" were selected. These patients were alive until 2004-01-01 and treatment with antiparkinsonic medication was registered in their ambulatoric histories.

After coordinating all the lists made and adding together all the information obtained about every person the final list of "suspected Parkinson's disease" included 459 patients. Medical interview and neurologic examination were used for these 459 patients. PD diagnosis was confirmed following its clinical criteria: tremor, bradykinesia, hypokinesia or akinesia, rigidity. Bradykinesia, hypokinesia or akinesia were considered to be main criteria of PD. PD diagnosis was confirmed for the patients who satisfied these clinical criteria.

After examining 267 persons, to foreseen clinical criteria of Parkinson's disease correspond 202 (44.0% persons) – 115 women and 87 men and for 65 patients diagnosis of PD was not confirmed, because they did not correspond with accepted criteria of Parkinson's disease.

Analyzing history of the illness main attention was paid to the character of the initial symptoms: if it was tremor or rigidity, unilateral or bilateral. Assessing the data obtained from medical documentation and from the patient and his relatives we tried to ascertain if the correct diagnosis had been determined during the first visit at neurologist after manifesting o the initial symptoms. In case of incorrect initial diagnosis made at the first visit we asked for the initial diagnosis.

Figure 1. Diseases diagnosed for the patients with unconfirmed Parkinson's disease and disease clinical forms.



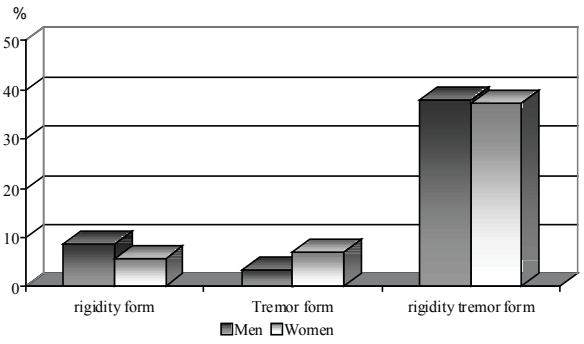
Physical state and neurologic condition was evaluated for every patient. Especial attention was paid to the symptoms, which are typical for PD: i.e. rigidity, bradykinesia and tremor.

Analyzing performed instrumental and laboratory tests attention was paid to the computer tomogram (CT) of the head, electroencephalogram (EEG), neurosonographic researches (i.e. transcranial doplerogram, double-scanning of cervical vessels), coagulogram and lipidogram.

3. Results

After investigating 267 patients PD diagnosis was confirmed only for 202 patients. Other 65 patients didn't satisfy accepted clinical criteria of PD (Figure 1). Analyzing clinical peculiarities of this disease we aimed to determine the most common forms of PD and also their distribution in men and in women. Distribution of clinical PD forms for the both sexes is revealed in Figure 2.

Figure 2. Distribution of PD clinical forms in men ( ) and in women ( ).



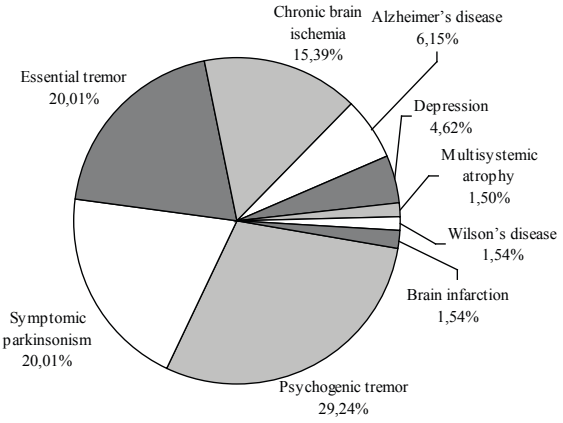
We ascertained that rigidity–tremor form of disease prevailed for 152 (75.2%, 86 women and 66 men) patients; its standardized index was 76.8%, frequency – 1.00±0.16 per 1000. The rigidity form was rarer – 28 (13.9%, 13 women and 15 men); standardized index was 13.7%, frequency – 0.18±0.07 per 1000. Not very frequent was a tremor form of disease -- 22 (10.9%, 16 women and 6 men) patients; standardized index was 9.5%, frequency – 0.15±0.06 per 1000.

By the data of our research for almost one fourth of patients (65 persons of examined 267, i.e. 24.3%) the diagnosis of PD wasn't confirmed after their clinical assessment. These patients didn't satisfy clinical PD criteria. PD diagnosis was confirmed following its clinical criteria: tremor, bradykinesia and rigidity. Diseases, which were estimated as PD for these 65 patients, are presented in Figure 3.

Analyzing out patient histories we ascertained that PD diagnosis had commonly been determined if the patient had presented tremor as prevalent clinical symptom. Specific treatment with antiparkinsonic medications had been administered for these patients by neurologists however after precise examination we diagnosed other diseases.

One group of patients referred that the tremor was boring them since their youth or since middle age however treatment with levodopa preparations or with anticholinergic drugs doesn't relieve the symptoms. Essential tremor was diagnosed for them. This disease is rather frequently misdiagnosed as PD in spite of obvious differences, which these illnesses have. Hypokinesia and rigidity are typical for PD but not for essential tremor. We diagnosed essential tremor for 13 persons (i.e. 20% of 65 patients with unconfirmed PD diagnosis). The majority of these patients were treated with vinpocetine, aspirin and pentoxifylline but for 3 of them (23.08% of all patients with essential tremor) levodopa preparations (levodopa/carbidopa and levodopa/benserazide) were prescribed. It must be noticed that levodopa doses administered for

Figure 3. Diseases diagnosed for the patients with unconfirmed PD diagnosis.



these patents were rather high: 1500-2000 mg daily. Doses of these drugs were constantly being increased because the patients didn't feel better using them. Since all of these patients had tremor anticholinergic drugs (trihexyphenidyl 2-8 mg daily) were also prescribed for them. Medications of other groups were administered for some of these persons: 2 patients used amantadine, one patient used bromocriptine and one patient used amitriptyline.

For 19 patients (29.23% of 65 patients with unconfirmed PD diagnosis) we diagnosed psychogenic tremor. Psychiatrists consulted them and the diagnosis of somatoformic autonomic dysfunction with psychogenic tremor was determined for these patients. The analyzed persons referred to symmetrical suddenly beginning tremor of arms occurring only in case of stress or nervous strain. This symptom had no progression but ceased by itself. Tremor increased if the patients paid attention to it. 10 patients (52.63% of 19 patients with psychogenic tremor) were nevertheless treated with levodopa medication: 7 of them (36.84% of 19 patients with psychogenic tremor) used levodopa/carbidopa, one patient (5.26%) used levodopa/benserazide and 2 patients (10.5%) used levodopa/carbidopa in combination with levodopa/benserazide. It must be noticed that patients with psychogenic tremor also used rather high levodopa doses: 500-2000 mg daily. In combination with levodopa medication 3 patients (15.79% of 19 patients with psychogenic tremor) used trihexyphenidyl and 4 patients (21.05%) used amitriptyline. In company with these drugs vinpocetine or pentoxifylline were administered for 8 persons (42.10%). Only 2 persons (10.53% of 19 patients with psychogenic tremor) withdrew prescribed levodopa medication on their own account because of nausea and vomiting caused by them. However administration of these drugs was constantly being registered in their

medical documentations because the patients didn't inform health care personnel about those dyspeptic side effects and drugs withdrawal.

Other group of analyzed persons (10 patients, i.e. 15.38% of 65 patients with denied PD diagnosis) presented vertigo in combination with ataxia or with nausea and vomiting. After examining these patients we diagnosed chronic cerebral ischemia with vestibular syndrome. Analyzing medical documentation we tried to ascertain why PD diagnosis had been determined for this group of patients by primary health care center neurologists. We made a conclusion that gait disturbances because of vertigo and ataxia had been evaluated as typical PD sign. It must be noticed that these patients were also treated with levodopa medication. Levodopa/benserazide was prescribed for 4 patients but 3 of them didn't use it because of nausea and vomiting. One patient used administered levodopa/benserazide 500 mg daily. 2 patients used trihexyphenidyl and 3 patients used amantadine. Vinpocetine and aspirin were also prescribed for these patients in combination with the mentioned drugs.

Symptomatic parkinsonism was diagnosed for 13 patients (20% of 65 patients with negated PD diagnosis). These patients besides insignificant signs of parkinsonism had symptoms of pyramidal system and cranial nerves injury. 10 patients of these 13 referred to undergone cerebral infarction. Post-infarctal residual symptoms were observed examining these patients. They complained of vertigo and their neurologic assessment revealed left or right hemiparesis of various degree. Vascular parkinsonism was determined for this group of patients. Only 3 patients in this group were treated with levodopa medication (levodopa/carbidopa up to 1000 mg daily) but they didn't feel significant improvement of their clinical condition using these medicines. Aspirin and vinpocetine were also administered for all of the patients with vascular parkinsonism. They were more effective for this group of patients than levodopa preparations. The patients referred to better health condition and diminution of vertigo using them.

We also ascertained that 3 patients used neuroleptics (haloperidol). Psychiatrists had administered this group of drugs for them. The patients informed us that they had been used haloperidol for a period of 1-2 years and rigidity, bradykinesia, skin desquamation and fatty acids hyperfunction in the face had manifested in a time of 0.5-1 year after its administration. For these 3 persons (4.6% of 65 patients with denied PD diagnosis) we diagnosed drug-induced Parkinsonism. Levodopa medications were also administered for these patients, but only one of them really used levodopa/carbidopa. Other 2 patients withdrew levodopa medication on their own account because felt worse while using them. However administration of these medicines was being registered in their medical documentation and prescriptions were being written constantly. We tried to ascertain why PD diagnosis had been determined and levodopa preparations had been administered for this group of patients. We asked the patients if they had informed their treating neurologist about the usage of other drugs prescribed by psychiatrists. Their answers were negative. Neurologists didn't ask the patients about other drugs used. Information about psychiatrists' consultation and administered treatment also wasn't fixed in ambulatory history because specialized psychiatric ambulatories have separate medical documentation. Thus PD diagnosis was established for these patients without taking detail history of other used medicines.

Willing to evaluate cognitive dysfunction we performed mini-mental test. Significant cognitive dysfunction was determined for 4 persons (6.15% of 65 patients with negated PD diagnosis). For them we diagnosed Alzheimer's disease. Memory deterioration and behaviour alterations were chief symptoms for these patients and they had no other clinical signs typical for PD. Computer tomogram of the head revealed signs of brain atrophy (i.e. considerable dilatation of the third and lateral ventricles and significantly dilated cerebral and cerebellar sulci).

Analyzing medical documentation we ascertained that memory deterioration had been estimated as typical PD sign. Thus levodopa medication was also administered for this group of patients. Relatives of 2 persons withdrew these drugs independently because by their opinion this treatment didn't relieve the symptoms. However information about treatment with levodopa/carbidopa was constantly being registered in medical documentation of these patients. Other 2 patients (3.1% of 65 persons with denied PD diagnosis) used levodopa preparations. One of them used levodopa/carbidopa and another -- levodopa/carbidopa in combination with levodopa/benserazide.

3 patients (4.62% of 65 patients with denied PD diagnosis) were observed and treated by psychiatrists ambulatorically and in hospital because of depression. But mood and behaviour alterations by neurologists were estimated as typical PD signs. So the diagnosis of PD was made and treatment with antiparkinsonic drugs was also prescribed for this group of patients. At the time of our study these patients used levodopa medication in combination with neuroleptics.

For one woman (1.5% of 65 patients with negated PD diagnosis) we suspected Wilson's disease because of asterixis. However we didn't notice generalized bradykinesis and rigidity. As asterixis by itself isn't

patognomic symptom of Wilson's disease the patient was admitted to neurological and then to gastroenterological departments to determine precise diagnosis. Laboratory findings revealed low blood ceruloplasmin level (101 mg/l, the normal value is more than 200 mg/l). Also cuprum excretion with urine was increased (263 μg per 24 hours, the normal value is less than 100 μg Cu per 24 hours). Marginal pigmentation of cornea was determined after eyes examination with fissure lamp. Computer tomography of the head revealed insignificant dilatation of lateral ventricles and expanded cerebral and cerebellar sulci. Thus diagnosis of Wilson's disease was confirmed for this patient.

For one patient (1.5% of 65 patients with denied PD diagnosis) during neurologic assessment we found symptoms of pyramidal system and cranial nerves injury. This man didn't satisfy other clinical PD criteria. Computer tomography of the brain revealed hypodensal focus. We determined the diagnosis of cerebral infarction for this patient.

For one patient (1.5% of 65 patients with denied PD diagnosis) pathologic symptoms (bilateral insignificant tremor, rigidity and bradykinesia) manifested symmetrically approximately in the age of 50 years. 2 years later dysfunction of vegetative nervous system (urinary incontinence and orthostatic hypotension) shoved up. Computer tomography and magnetic resonance of the head revealed signs of advanced brain atrophy (i.e. dilated both of the lateral third and fourth ventricles and expanded cerebral and cerebellar sulci). Multisystemic atrophy was diagnosed for this man.

4. Discussion

We ascertained rigidity-tremor form to be the most common form of PD. Rigidity and tremor forms were determined more rarely in our study. The data of our research maintain that for almost one fourth (24.3%) the diagnosis was incorrect. Although these patients did not correspond with accepted criteria of PD, they had been treated with antiparkinsonic medications. The PD diagnosis for them was determined only according to separate symptoms: tremor, gait alterations or memory deterioration and behaviour alternations. It must be noticed that PD was most commonly considered as the cause of tremor even in the absence of other typical symptoms for this disease. Thus levodopa medication were prescribed in case of psychogenic and essential tremor. Levodopa doses were constantly being increased because the patients didn't feel better using them.

Memory and behaviour alterations were also identified with PD symptoms. Thus PD was diagnosed for the patients with Alzheimer's disease.

Symptoms of Wilson's disease, MSA or brain infarction were estimated as PD. Antiparkinsonic treatment was prescribed for these patients but it wasn't effective.

We also noticed urinary incontinence manifested using dopamine agonist ropinirole. This side effect became significant problem for patient himself and for his relatives.

Examining patients at home, we ascertained that not all patients use prescribed L-dopa preparations. A part of patients or their relatives stopped using of this drug independently because of appeared dyspeptic symptoms (nausea, vomiting and pain in the epigastrium). Other group of patients withdrew levodopa medication because these drugs by their opinion didn't relieve the symptoms. However information about administration of these unused medicines was constantly being registered in medical documentation of these patients.

Analyzing results of this study we ascertained that patients with unconfirmed PD diagnosis were also treated with levodopa preparations. It must be noticed that the doses prescribed were rather high (500-1500 mg daily). As all we know these medicine are quite expensive. They are compensated for patients with PD. Administration of antiparkinsonic drugs for the patients without PD wastes large amount of money. The patients often withdraw prescribed drugs on their own account without informing their doctors. The doctors continue writing prescriptions of the compensated drugs every month but the patients either don't by the medicines or don't use them and even throw out.

These conclusions may be done by the results of the study: Rigidity-tremor form is the most common form of PD. It occurs in 76.8% of patients. Rigidity and tremor forms are more rare (in 13.7% and 9.5% of patients respectively). PD most generally has to be differentiated from the essential tremor, symptomic Parkinsonism psychogenic tremor and multisystemic atrophy. For 24.3% of analyzed patients PD diagnosis wasn't confirmed after their clinical assessment because they didn't satisfy clinical criteria of the disease. Clinical examination of the patients, neurologic, instrumental ways of diagnostics and mini-mental test enabled to diagnose other diseases for these patients.

References

[1] Lang AE, Lozano AM. Medical progress: Parkinson's disease. Part 1. N Engl J Med. 1998; 339: 1044-53

[2] Nakashima K, Maeda M, Tabata M, Achachi Y, Kusumi M, Ohshiro H. Prognosis of Parkinson's disease in Japan. Versicherungsmedizin. 1997; 49(4): 126-31

[3] Werner M, Fornadi F. Effect of early diagnosis and therapy on prognosis of Parkinson syndrome. Versicherungsmedizin. 1997; 49(4): 126-31

[4] Gibb WRG, Less AJ. A comparison of clinical and pathological features of young and old-onset Parkinson's disease. Neurology. 1988; 38: 1402-6

[5] Valeikiene V, Ceremnych J, Alekna V, Juozulynas A. Differences in WHOQOL -100 domain scores in Parkinson's disease and osteoarthritis. Med Sci Monit 2008; 14(4):CR221 - 227

[6] Calne DB, Snow BJ, Lee C. Criteria for diagnosing Parkinson's disease. Ann Neurol. 1992; 32 (Suppl 1): S125-7

[7] Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinicopathological study of 100 cases. J Neurol Neurosurg Psychiatry. 1992; 55: 181-4

[8] Mieliauskaite D, Valeikiene V, Juozulynas A. Variations of oropharyngeal signs in patients with Parkinson's disease. Gerontologija. 2007; 8(3): 171 – 174

[9] Gimenez Roldan S, Mateo D, Martinez Gines M, Iniesta I. The problem of accurate diagnosis of Parkinson disease. Neurologia. 1999; 14(Suppl 1): 3-16

[10] Mieliauskaite D, Valeikiene V, Juozulynas A. Rijimo sutrikimai sergant Parkinson's disease. Gerontologija. 2006; 7(1): 32-34

[11] Linazasoro G, Gorospe A, Rodriques MC, Guridi J, Ramos E, Mozo A, Obeso JA. Pallidatomy in the treatment of complicated Parkinson's disease: clinical results at two years and analysis of prognostic factors. Neurologia. 1999; 14(2): 53-61

[12] Wenning GK, Litvan I, Jankovic J, Granata R, Mangore CA, Mckee A, Poewe W, Jellinger K, Ray Chaudhuri K, D'Olhaberriagne L, et al. Natural history and survival of 14 patients with corticobasal degeneration confirmed at postmortem examination. J Neurol Neurosurg Psychiatry. 1998; 64(2): 184-9

[13] Valeikiene V, Ceremnych J, D. Mieliauskaite, Alekna V. The prevalence of Parkinson's disease among Vilnius inhabitants. Centr Eur J Med. 2008; 3(2): 195-198

[14] Valeikiene V, Juozulynas A. The incidence of Parkinson's disease among Vilnius inhabitants. Gerontologija. 2006; 7(3): 131-136