Incidence of Parkinson's disease in Estonia

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Key words

Parkinson's disease – Epidemiology – Incidence

Abstract

The incidence of Parkinson's disease (PD) was studied over a nine-year period (1990 through 1998) in Tartu county with a mean population of 156,417. Based on 264 patients, the average crude incidence rate of PD was 18.8 per 100,000 person years. The age-adjusted incidence was 16.8/ 100,000: 18.3 for urban and 14.0 for the rural group, 16,6 for men and 17,1 for women. The age-specific incidence increased from 1.0 /100,000 in the age range of 30-39 years, reached a maximum 117.2 /100,000 population in the age range of 70-79 years, and declined in the elderly. The incidence of PD was comparable with that found in developed countries, except for slightly but not significantly higher incidence rate in urban compared with the rural population in Estonia.

Introduction

Epidemiological studies show that Parkinson's disease (PD) is common among the elderly people. Incidence is the most accurate estimate to evaluate the risk of PD in different populations and races, as it is relatively unaffected by factors influencing disease survival. However, incidence has been studied less often than prevalence [1-4]. In those community-based studies the annual incidence rates vary from 4.5 to 21 per 100,000 population [5-15]. The observed differences in defined populations suggest the possible role of environmental and genetic factors but also methodological variability of the research design and differences in the diagnostic criteria set used for case ascertainment.

The purpose of this study was to evaluate the incidence rate of PD during the period of 1990-1998 in Tartu county, South Estonia, among men and women, residing in the urban and rural areas. The results of the study were compared with those investigations carried out in other populations.

Patients and methods

Estonia is the northernmost Baltic country with a population of 1.5 million inhabitants. Estonia has a long tradition of universally available medical services; there is one physician per 300 inhabitants. The patients are registered at a family doctor and have access to medical care. Traditionally, the patients with chronic neurologic diseases are followed up and treated by neurologists. The Department of Neurology and Neurosurgery of Tartu University is the neurologic center for the whole of South-Estonia.

The epidemiological study was carried out in the Tartu district in South Estonia with an area of 3110 km^2 and a mean population of 156,417 during the period from 1990 to 1998: 46% men and 54% women; 68% living in urban and 32% in rural areas. Population data was obtained from the annual publications of the Statistical Office of Estonia [16].

In order to making case ascertainment, information was obtained yearly from several sources. The hospital and outpatient records of the Department of Neurology and Neurosurgery of Tartu University were reviewed. All 72 general practitioners and family doctors in the Tartu district reported about parkinsonian patients under their care. Eleven nursing homes and regional hospitals in Tartu county were visited. Tartu Parkinson's Disease Society was contacted for case finding. The Tartu Sick Fund providing health insurance supplied regularly data about the prescriptions for anti-parkinsonian drugs. The cases were searched through the year 2000 to ascertain patients who developed parkinsonism in the study period but were brought to medical attention later. The identified patients were interviewed and examined by the authors. The structured questionnaire included details of the medical history, living conditions, occupation, family history and medication.

The diagnostic criteria set of the United Kingdom Parkinson's Disease Society Brain Bank was used for verification of the diagnosis [19]. Idiopathic PD was established by the presence of bradykinesia and at least one of the signs of resting tremor, rigidity, or impaired postural reflexes, if no other cause of parkinsonism was apparent. Unilateral onset and persistent asymmetry, progressive course, and good response to levodopa were considered as supportive criteria; any atypical sign – as exclusion criteria. Secondary parkinsonian syndromes related to stroke, use of neuroleptic drugs, head injury, brain tumor or infection, were diagnosed according to the history. Parkinson plus syndromes were diagnosed if the parkinsonism was in association with additional neurologic signs indicating the degeneration of defined neuroanatomical systems [20, 21].

Incidence rate was defined as the ratio of new PD cases as compared with the population at risk, expressed as cases per 100,000 person-years. Incidence rates were age-adjusted to the Estonian general population (1989) by direct method of standardization. The statistical analysis was performed with the SAS system for Windows, version 6.12 (Cary). The 95% confidence intervals (CI) for incidence rates were calculated. The differences in proportions were analyzed using the t-test and chi-square test. A p value less than 0.05 was considered significant.

The Ethics Committee of Clinical Research Studies of University of Tartu approved the study.
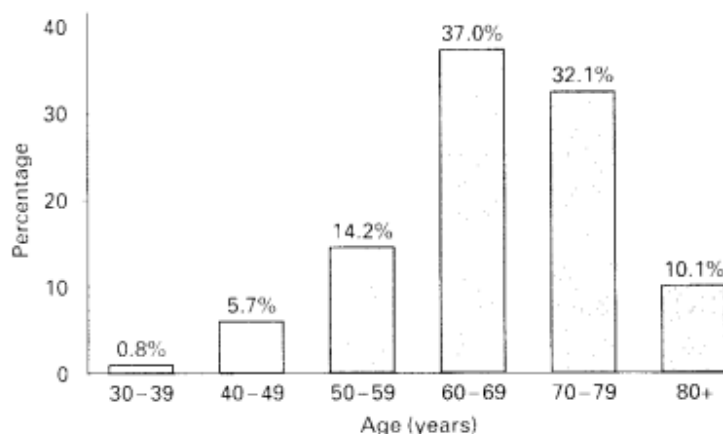
Fig. 1. Distributon of patients with PD by age at onset.

Table 1. The age-adjusted incidence rates of PD with SE (standard error) and CI (confidence interval).

	Cases	Incidence rate	SE	95% CI
Total	264	16.8	1.09	14.7-19.0
Men	90	16.6	1.60	13.5-19.8
Women	174	17.1	1.51	14.2-20.1
Urban	190	18.3	1.38	15.6-21.0
Rural	74	14.0	1.77	10.6-17.5

Results

During the period of 1990-1998, a total of 264 new cases of PD were identified in the resident population of Tartu county: 90 men and 174 women, 190 urban and 74 rural inhabitants. The mean age of the patients at onset of symptoms was 68.8 ± 8.9 years with an age range from 36 to 86 years; 90% of the patients were over 55 years old. The mean age at onset of symptoms did not differ when comparing men and women, or urban and rural people. In distribution of patients by age at onset, the biggest groups of patients were in age 60-69 years and 70-79 years (fig. 1).

Based on 264 patients, the average crude incidence rate was 18.8 per 100,000 person years, 13.8 for men and 23.0 for women, 19.8 for people living in the urban area and 16.5 in the rural area. After age-adjustment to the Estonian general population in 1989, the incidence rate was 16.8 per 100,000 person years, 16.6 for men and 17.1 for women, 18.3 for urban and 14.0 for the rural group (table 1). The crude incidence rates showed a female preponderance due to the specific demographic situation with the female predominance in the older age groups but there was no significant difference between the age-adjusted incidence rates of men versus women (relative risk 0.97). Comparing the incidence rates in urban and rural areas, the urban predominance was not statistically significant as a whole (relative risk 1.3; $p=0.0956$), but only in the elderly groups with age over 65 years ($p=0.0132$).

The age-specific incidence increased from 1.0 per 100,000 population in the age group of 30-39 years, reached a maximum 117.2 per 100,000 population in the age group of 70-79 years, and declined somewhat in the elderly (fig.2). The cumulative risk for developing of Parkinson's disease during lifetime was 1.6% among the population of Tartu county.

The mean time from the the first symptoms to the verification of the diagnosis of PD was 2.2 years; mean time from the first symptoms to the beginning of medication was 2.4 years and to the treatment with levodopa – 3.7 years. There was a statistically significant difference in the mean time from the first symptoms to the diagnosis between the patients living in urban and rural areas: 2.0 and 2.6 years, respectively (p=0.0418). Tremor was the most frequent initial symptom, occurring in 68% of the patients (table 2). There was no statistically significant difference in the mean time from the onset of symptoms to the identified diagnosis of PD between the patients with initial symptom of tremor or hypokinetic-rigid signs (2.1 and 2.3 years, respectively).
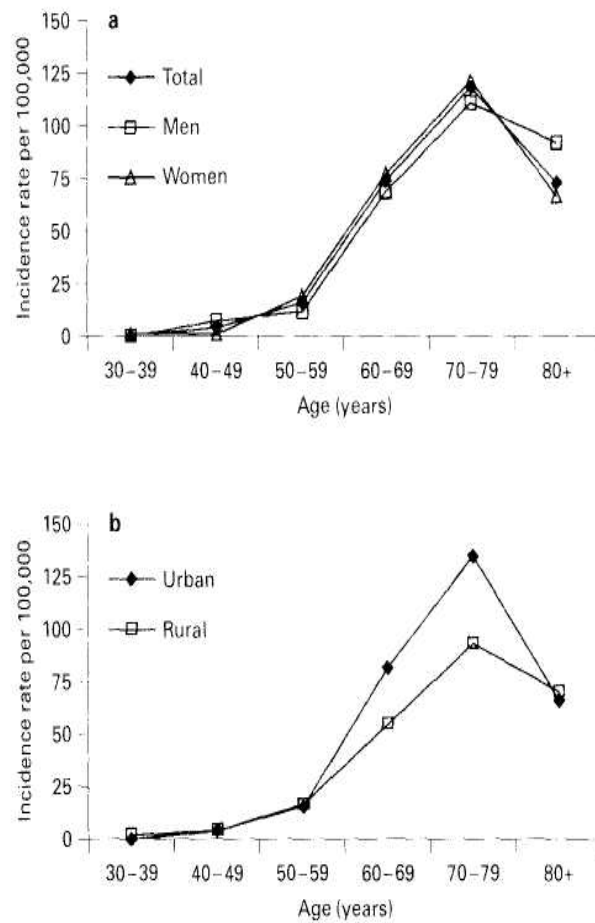

Fig. 2. Age-specific incidence rates of PD. **a** Total incidence rate and rates in men and women, **b** Incidence rates in urban and rural groups.

Table 2. Frequency of initial symptoms of PD.

Symptom	Percentage
Tremor	68.6
Bradykinesia	11.5
Gait disorder	8.1
Rigidity	4.4
Poor balance	2.8
Writing disorder	1.6
Other	3.0
Total	100.0

Discussion

The variations in the results of descriptive epidemiological studies in Caucasian populations [5-10] probably reflect the differences in methodology, particularly in case-finding and diagnostic criteria for case ascertainment, as also in the length of study period, rather than a heterogeneous distribution of PD. In this study, to ensure complete ascertainment, every available source was used to obtain information for the case-collection, including the records of the hospitals, general practitioners and family doctors, nursing homes, Parkinson's Disease Society and Sick Fund.

The correct diagnosis is a prerequisite for valid estimates of the incidence of PD. Since PD has an insidious onset with the various clinical syndromes appearing, the incidence figures cannot be based only on medical history. Therefore, all patients were examined neurologically to identify the cases of PD. The first step in diagnosis is to confirm that the patient indeed has true parkinsonism. For a diagnosis of established parkinsonism, upper body akinesia must be present: the symptom complex containing bradykinesia, hypokinesia, and difficulty initiating movement [21]. For verification of PD in our study, we applied the strict criteria set of the United Kingdom Parkinson's Disease Brain Bank that requires bradykinesia and at least one of the following: resting tremor, rigidity, or postural instability. However, the clinicopathological studies have shown a false-positive rate of PD of around 20%, and a false-negative rate from 5 to 10%, depending on patients' selection [19, 22]. The analysis of features which improve the accuracy of the clinical diagnosis of PD shows that the use of strict exclusion criteria (atypical signs for PD; suggestion of a cause for another parkinsonian syndrome), in addition to inclusion criteria, reduces misdiagnosis [22]. Thus, special attention was paid to distinguishing secondary parkinsonism and Parkinson plus syndromes in our study.

The epidemiological investigations have suggested often male predominance when comparing the incidence rates in men versus women [5, 6, 10, 11, 13], in other studies the sexes are affected almost equally [9, 12]. In this study, no significant difference was noted in the age-adjusted annual incidence of PD between the sexes. However, there was female preponderance when comparing the crude incidence rates in men versus women (ratio 0.6), evidently because the representativeness of the sexes in the population was not equal due to a significantly longer lifespan in women, and casualties of men in the Second World War.

The rural residence has been suspected to be a risk factor for PD [23, 24]. Some studies compare the prevalence rates of PD among urban and rural people but only a very limited amount of data is available about the incidence ratio in urban versus rural people. In the study carried out in Finland [5], the total risk ratio in rural versus urban populations was 1.4, but the rural predominance was not significant. In Italy [9], the study revealed a significantly higher incidence rate among agricultural workers, but for the total rural population the incidence rate was nearly similar to that in the urban centers. On the contrary in this study, the urban predominance was not found statistically significant in all age groups, but only in the older age groups of over 65 years. The urban predominance in Estonia could be explained by the opinion that not rural residence but a specific feature of rural life such as pesticide or herbicide exposure could be distinguished as a risk factor of PD [23,24]. In Finland, the study concerning environmental risk factors revealed that domestic animals, or something that is connected

with the animals, could have a protective effect against PD [25]. On the other hand, the findings suggested that the chronic exposure to occupational toxins and specific metals in the industrial areas was associated with PD [26]. In Ferrara, Italy, the distribution of PD among housewives living in urban and rural areas was homogenous; that seems to reduce the role of environmental factors linked to the residence, and to indicate a greater influence of some specific professional exposures [9].

In our study, the lower incidence rate in rural people may also reflect different referral habits among urban and rural people: the estimated differences would perhaps express different attitudes toward the disease that bias the case collection. This is confirmed by the finding that the time from the onset of symptoms to the identified diagnosis of PD was significantly longer among rural people as compared to the urban people.

The results of the incidence studies reflect an age-related disease and underline the fact that advancing age remains the only certain risk factor for PD. The results of this study agree with the findings from other studies [5, 6, 9, 11-13, 15] indicating an increase in the risk with advancing age. This upward trend was observed, mostly with decreasing incidence in the very old [5, 9, 11-12], or increasing also in the oldest age group [6, 13]. In our study, the incidence rates, very low before the age of 50 years, reached the highest peak in the age of 70 to 79 years and then declined with very old age. The latter phenomenon could be partly caused by the poor ascertainment of the cases due to under-diagnosis of PD in the oldest age group. However, the declining incidence rates in elderly and the differences between various segments of the population show that there could be any exogenous causative factors in addition to the aging. The environmental causative factors, possibly of a toxic nature, may be of importance for the slow neuronal loss in advancing age and for the development of PD, although influence from genetic factors cannot be excluded.

Acknowledgement

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