

Doctoral School of Interdisciplinary Medicine
Preventive Medicine Program

EPIDEMIOLOGY OF PARKINSON'S DISEASE – QUALITY OF
LIFE AS A CHALLENGE FOR REHABILITATION

Summary of PhD Thesis

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INTRODUCTION

According to the current knowledge in medicine, Parkinson's disease or "paralysis agitans" is an incurable but treatable neurodegenerative disease. It is a neurological disease with slowly progressing movement disorders. James Parkinson (1755–1824) was the first to describe the disease; thus, the disease is named after him. Parkinson's disease poses a very complex problem system for researchers and clinicians, as its diagnosis is sometimes less clear, the cure is still pending, and there are many symptoms and accompanying problems in the lives of Parkinson's patients that are very challenging to live with in everyday life. In many cases, the physicians tend to focus only on physical symptoms, but in the enchantment of organ system function, it might be forgotten that patients who are mentally healthy are also challenged by a disease that they must be able to live with for several years knowing that their condition will get worse over time.

Parkinson's disease (PD) is a long-term degenerative disorder of the central nervous system. It has the second highest incidence in neurodegenerative diseases in the world, caused by the selective loss of nigrostriatal dopaminergic neurons. These neurons are responsible for voluntary and involuntary motor functions; thus, in their absence, the classic symptoms of PD, such as tremor, muscular rigidity, bradykinesia, and postural imbalance are manifested.

The etiology of the disease is still not completely understood, but it is suspected that the pathological process of the disease is mainly due to the combination of genetic and environmental factors. Several studies have attempted to investigate the association between Parkinson's disease and environmental risk factors, such as air pollution, certain infectious diseases, or toxic harm.

PD is a common neurodegenerative disease in the world population, the incidence of PD is forecast to be doubled by 2030, primarily as a result of the ageing of the population. According to the European Brain Council Survey, 1.2 million people have been affected by PD in Europe. The economic and social costs of PD are sufficiently high, an estimated 13.9 billion Euros all across Europe, whereas the overall estimates of annual cost for PD, together with the cost of the treatment of the disease is 35 billion Euros.

AIMS

The overall aim of the study is to give a more detailed analysis of the epidemiological aspects of PD patients in Hungary.

Specific research aims:

- to analyze the clinical data and to characterize how certain risk factors/diseases (hypertension, diabetes, dyslipidemia, and obesity) affect PD in patients treated at the Neurology Department, Albert Szent-Györgyi Clinical Centre, University of Szeged;
- to measure the quality of life (QoL) of PD patients and to determine whether self-help groups may influence the quality of life and health behavior of Parkinson's patients. We consider that the concept of quality of life (QoL) is multidimensional and many factors may have an effect, such as those connected to the individual, social networks, the environment and society, but health status is also a key factor in determining how good a person's QoL is. Our study focuses on a special group of PD patients who are attending a "PD Club" in Szeged and Budapest

Our working hypotheses were the following:

1. There is a correlation between cardiovascular diseases and PD.
2. Obesity and diabetes mellitus are significantly related to PD.
3. Alternative rehabilitation methods have a positive effect on the quality of life of PD patients.

MATERIALS AND METHODS

Three main stages of the research can be distinguished. In the first stage, the research was planned and prepared, in the 2nd stage we performed a case-control study based on patient documentation among the patients treated in the university hospital, and in the 3rd stage, we examined the quality of life and health behavior of patients attending the Parkinson's Club.

The case-control study was conducted at the Department of Neurology, Albert Szent-Györgyi Medical Center, University of Szeged, Hungary. We collected our data from the computerized MedSolution integrated hospital information system between January 1, 2000 and January 1, 2013.

The total sample consisted of 1299 subjects who were hospitalized during the study period at the Department of Neurology, Szeged, Hungary, out of which 620 patients were

identified as cases and 679 as controls. Cases included all hospitalizations in the study period if they had a diagnosis of PD (ICD-10 code: G20H0). Controls were matched to cases by age and sex, and they were selected from the patients with the diagnosis of epilepsy (ICD-10 code: G40) or back pain (ICD-10 code: M54) at the same department. The exclusion criteria for the control group were previous diagnoses of PD, Alzheimer's disease, multiple sclerosis, myasthenia gravis, or secondary Parkinsonism.

This cross-sectional study was carried out between 2013 and 2014 with the help of the Parkinson's Association "I will hold your hand" (Budapest and Szeged). The Parkinson's Clubs operating within the Delta Hungarian Parkinson's Association organize joint programs, lectures, discussions, and events for patients to discuss their problems, get answers to questions they do not dare to ask, participate in programs and rehabilitation exercises organized for them. The association expressed its support for our research, so we conducted our survey with Parkinson's patients in the auspices of the association. Data were collected by a paper-and-pencil questionnaire about socio-demographic (age, gender, and education level), lifestyle, and QoL characteristics. Participants filled in the questionnaire independently, except when having technical problems (e.g., could not hold the pen).

Altogether 150 questionnaires were allocated to the clubs, and 101 were completed. Three questionnaires were incomplete (high number of missing data), and finally, 98 persons' data were analyzed.

QoL was assessed by the Hungarian version of the PDQ-39 questionnaire. The PDQ-39 contains 39 questions in eight dimensions. Participants were asked to think about their health and general well-being, and to consider how often in the last month they have experienced certain events (e.g., difficulty walking). The answers were scored from 0 (never) to 4 (always), and the scores of dimensions were calculated as a scale from 0 to 100 (0=no problem at all; 100=maximum level of problem), higher scores representing worse QoL.

Simple descriptive statistics were used to characterize the participants in the case-control study. Chi-square tests were applied to compare the basic characteristics of case and control groups. Univariate and multivariate logistic regression analyses were conducted to assess the odds of vascular risk factors (diabetes, dyslipidemia, and hypertension) in PD. All logistic models were developed for the total population, and for males and females, separately. In the regression models, we calculated the odds ratio (OR) and the 95% confidence interval (95%CI) for each predictor.

Descriptive statistics, chi-square, and one-way ANOVA were applied in the questionnaire-based study. Normality was tested by one sample Kolmogorov-Smirnov test: the

data of scores were not normally distributed, so one sample Wilcoxon tests were used to compare the observed and the hypothetical medians.

Statistical significance was set up at p values lower than 0.05. Statistical analyses were performed by using IBM SPSS version 24.0 (IBM Corporation, Armonk, New York, USA).

The study protocol was approved by the Human Institutional and Regional Biomedical Research Ethics Committee, University of Szeged (Registration number: 164/2012). Participants were informed about the purpose, benefits, and risks of the study, and each participant provided written informed consent.

RESULTS

In the univariate logistic regression analyses, diabetes mellitus was positively associated with PD, i.e., the odds of diabetes mellitus was significantly higher in the PD group than in the control group ($OR_{total}=2.65$, 95%CI: 2.05–3.43; $OR_{male}=2.45$, 95%CI: 1.74–3.45; $OR_{female}=2.97$, 95%CI: 2.01–4.40). Dyslipidemia showed a negative association: the odds were 0.62 (95%CI: 0.49–0.79) in the total population; 0.54 (95%CI: 0.38–0.75) in males and 0.71 (95%CI: 0.51–0.99) in females. In the univariate analyses, no significant associations were identified between hypertension and PD in the total population, and among males and females, respectively.

Age (in years) and vascular predictors were involved in the multivariate logistic regression models of the total, the male and the female populations (Table 5). The common analysis of the factors demonstrated that the odds of diabetes mellitus was higher ($OR_{total}=2.86$, 95%CI: 2.19–3.73; $OR_{male}=2.72$, 95%CI: 1.90–3.89; $OR_{female}=3.24$, 95%CI: 2.16–4.84), while the odds of dyslipidemia was lower ($OR_{total}=0.58$, 95%CI: 0.46–0.75; $OR_{male}=0.48$, 95%CI: 0.33–0.69; $OR_{female}=0.70$, 95%CI: 0.50–1.00) in PD patients than in the control group. Hypertension showed a different pattern by gender: the odds of registered hypertension was significantly lower in female PD patients ($OR_{female}=0.68$, 95%CI: 0.48–0.98), whereas in males, the result was not significant ($OR_{male}=0.95$, 95%CI: 0.69–1.32).

Altogether 98 patients with clinically diagnosed PD were included into our quality of life study.

The sex distribution showed a female dominance, and the most prevalent age-group was between 65 and 74 years. A high proportion (around 70%) of the participants were married, and half of them completed secondary level of education, followed by college or university degree, and only a few persons had primary education level.

The average total score of PDQ-39 was 34.29 ± 17.82 (mean \pm standard deviation). From the eight dimensions, the highest score was found in “bodily discomfort” (42.78 ± 22.20), whereas the lowest score was in “social support” (16.36 ± 18.92). Analyzing all dimensions separately, gender analysis showed a significant difference only in the perception of “mobility” (males: 31.78 ± 26.92 ; females: 44.28 ± 29.70 ; $p=0.046$), age had a significant effect on “mobility” ($p=0.023$), “activities on daily living” ($p=0.035$), and “cognitive impairment” ($p=0.009$). No significant differences were revealed in marital status; “bodily discomfort” was significantly lower in the highly educated ($p=0.021$).

During the further analysis of our quality of life related data (observed group), the results of another Hungarian survey was used as a control (see hypothetical group) in this study. In both studies, the highest score (median) was found in “bodily discomfort” (41.67 and 58.30), whereas the lowest score was found in “social support” (8.33 and 25.00). All dimensions were significantly better in patients attending the PD club ($P < 0.05$ or <0.001), especially in case of “social support”.

The body mass index (BMI) data show that most patients were in the normal weight range, and much more fell in the overweight and obese categories than in the malnourished one. The results exhibited no significant difference between males and females ($p=0.835$).

In the analyzed group, 46% of the subjects consumed fruit at least once a day, and 33.7% consumed more than one time per day; the number of patients who consumed less frequently was very low, indicating that they had never consumed fruit in the sample. There was no significant difference between the genders in fruit consumption ($p=0.435$).

Only 4% of our sample was a daily smoker. Examination of previous smoking patterns found that 31.6% of patients had smoked in previous years (at least one year). There was no significant difference in smoking history between men and women ($p=0.841$).

Examining drinking patterns, we found that 44% of the sample never consumed alcohol as reported. The frequency patterns of alcohol users differed significantly by gender. Occasional alcohol drinkers have a female dominance, while regular alcohol drinkers have a male dominance. The difference between men and women was not significant ($p=0.503$) at the higher alcohol consumption (6 units or more) in the last year, the majority of the sample consumes large amounts of alcohol less frequently than once a month. The alcohol consumption monitoring patterns are especially important because of the increased risk of depressive disorders in PD patients.

DISCUSSION

Our case-control study showed considerable relationship between vascular risk factors and PD. Diabetes mellitus was positively, while dyslipidemia was negatively associated with PD in males and females, whereas hypertension was negatively associated with PD only in females; the association between dyslipidemia and hypertension seemed to be gender-dependent.

If our starting point is that in several health policy analyses we can read that the health condition of the Hungarian population, besides the possible weaknesses of the health care system, is negatively driven by the lack of self-care, then this tendency is perfectly detectable in PD patients as well. All we have to do is to examine the nutritional status and the eating habits.

Maintaining optimal blood sugar, blood fat, and blood pressure levels is also of paramount importance in PD patients. Because it is a chronic disease that accompanies patients for many years, comorbidities accumulated via improper lifestyle can further aggravate the condition and impair the quality of life on a daily basis.

The study of eating habits and nutritional status was induced by the correlation found in the case-control study, according to which blood sugar levels and lipid levels show different ratios in PD patients. Our results showed that some risk factors of PD patients did not fit the national average, as obesity, cholesterol level, diabetes, and ischemic heart disease.

Several international studies report deteriorations in eating habits and nutritional status in PD patients. Decreased taste perception and impaired swallowing reflex function help patients become malnourished.

Due to the peculiarities of PD, we identified some differences. In our study, the sample did not show a decrease in BMI; moreover, the balance tipped towards overweight, as it did in the Hungarian population in general. According to our data, the dietary patterns of PD patients were not significantly different from the unfavorable habits of the entire Hungarian population based on the national health surveys, whereas a fruit and vegetable-rich diet would be important for the whole population, especially for patients with neurodegenerative diseases. Proper nutrition is of paramount importance. Achieving and maintaining the optimal body weight is also very important, as the instability in movement and stagnant gait is further complicated by the extra weight and the cumbersome movement that accompanies it.

The issue of quality of life is very complex in PD patients. After all, there is a disease that is accompanied by a number of symptoms that in itself repels patients from normal social status, isolation creates a feeling of loneliness, and the majority of patients have a mental illness,

such as depression, mood disorder, or panic disorder, due to decreased dopamine function. Social support, the help of the family, and support groups are inevitably important in this case.

In the case of all diseases, it may put a mental burden on the patients that they are limited in anything. In PD patients, it is an even more complex issue, as in addition to the worsening symptoms, they practically experience a situation where the intact mind is locked in a dysfunctional body with the hands and feet do not functioning as before.

These are all factors that affect quality of life. This is also particularly important in patients with PD. As the number of years of life spent in health decreases, which is not very favorable in Hungary anyway, the improvement of the quality of life in the years spent in illness is of paramount importance. Patient organizations, the social sector and mental health professionals are also called upon to advance this process. In PD patients, complete isolation can very easily develop. Loss of hope and the development of depression may further aggravate their condition.

Comparing our results to Hungarian and international results, we can conclude that the QoL of our patients attending the PD club was significantly better than the results in the other Hungarian study. The members of the Szeged Parkinson Club meet once a week regularly, and a qualified physiotherapist helps them stay in shape and improve their coordination skills, and besides this, once a month, they can listen to lectures about nutrition, alternative forms of treatment, and sometimes they have the opportunity to participate in the dance therapy.

According to scientific evidence for the treatment of Parkinson's disease, PD treatment can only slow down the disease progression. A number of studies deal with the medication under which therapy can improve the physical and mental state of the participants. A significant proportion of Parkinson's patients are depressed. Therefore, a priority of physical symptoms in addition to the daily well-being and providing social support to the participants are important priorities. Several studies have addressed treatment options, such as dance therapy, which, in addition to the joy of movement for PD patients, can provide safety to be a member of a community.

Patient clubs provide opportunities for PD patients to learn about new procedures, to learn about new options in rehabilitation or therapy. It is also indispensable in giving patients the feeling of "I'm not alone". In many cases, the feeling of social belonging has a positive effect on quality of life and acceptance, which is essential for such an illness.

The primary element of rehabilitation is physiotherapy in Parkinson's disease, which increases the physical strength of the motor learning ability and reduces spasticity. Based on practical examples, we assume that stretching and strengthening exercises, treadmill exercises,

and the development of balance should be the most useful methods of physiotherapy for PD patients. Our results indicate that participation in club-life may provide added value to rehabilitation services of PD patients by improving mental conditions, preventing isolation, and altogether, strengthening social support.

Our study may be considered unique, since it was conducted among a group of persons with PD, who live an active life in a self-help club. In the light of the results, it would be worthy of support groups to include facilitating the establishment of rehabilitation options, as relevant to the subjective quality of life improves this option. Our results confirmed that the strengthening of social support of chronically ill participants can greatly contribute to the healing of them.

On the base of our results, we can conclude that operating patient organizations, such as the patient clubs seems to be an excellent tool of rehabilitation of PD patients. Mental assistance should be made widely available as part of the therapy. There are a number of excellent efforts to bring diversity to rehabilitation procedures, and central support for this would be a huge step forward for patients. Given the dynamic growth in the number of PD patients, based on age, and that their number could even be doubled by 2040, PD patients are a very important group of the society, not only in terms of patient care, but also in terms of health economics.

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Publications related to the Thesis

- I. Kucsera, M. (2012). A Parkinson-kór epidemiológiájának hatása a háziorvosi ellátásra. *Medicus Universalis*, 45(4), 149-151.
- II. Kucsera, M., & Paulik, E. (2013). Risk of Parkinson's disease in southern great plain, Hungary. In G. Belojevic (Ed.) *Proceedings of the First International Congress on Hygiene and Preventive Medicine*, Belgrade, 22-24 May 2013, Serbian Medical Society, pp. 590-593.
- III. Markó-Kucsera, M., Vécsei, L., & Paulik, E. (2018). Association of cardiovascular risk factors and Parkinson's disease – case-control study in South East Hungary. *Ideggyógyászati Szemle/Clinical Neuroscience*, 71(1-2), 57-62.
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