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Pharmacological Treatment Pattern and Comorbidities in Parkinson's Disease Outpatients at Dr. Hasan Sadikin General Hospital Bandung in 2013–2018

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Abstract

Background: Parkinson's disease (PD) is one of many neurodegenerative diseases with symptomatic management, and with the correct pattern of pharmacological treatment PD may have an improved quality of life for a minimum of three years. This study aimed to illustrate treatment patterns and comorbidities in PD patients at Dr. Hasan Sadikin General Hospital, Bandung.

Methods: This study was a cross-sectional descriptive study by using total medical records of the period of 2013 to 2018. PD patients receiving pharmacological treatments such as levodopa, anticholinergics, dopamine agonists, or combined therapy were included. Patients with incomplete data and with the previous history of other neurological diseases before PD were excluded from this study.

Results: In total, there were 57 patients with PD, of whom most of them were males (79%). Age-wise, PD was most common in 60 to 69-year-olds (32%). The most commonly used treatment pattern was the administration of levodopa (33%). Patients aged younger than 30 years were administered anticholinergics, whereas the older patients (>60 years old) mostly were given levodopa. Comorbidities after PD diagnosis were mostly stroke, dementia, and epilepsy.

Conclusions: Males are most affected by PD, and the most commonly used treatment pattern is levodopa monotherapy. PD is most commonly found in patients aged 60 to 69 years. Patients aged below 30 years are administered anticholinergics. The most common comorbidities found are a stroke, followed by dementia and epilepsy. By recognizing the patterns and comorbidities of this disease, the study may provide some insights into choosing the most effective pharmacological therapy for PD.

Keywords: Comorbidities, Parkinson's disease, pharmacological treatment

Introduction

Parkinson's Disease (PD) is a neurodegenerative disorder of the central nervous system that affects the motor system and causes motor dysfunction.[1,2] The main cause of PD is the decreasing production of dopamine which is caused by the degeneration process of neurons in the substantia nigra.[3] Prevalence of PD in North America was estimated at around 160 per 100,000 population.[3]

Patients with PD might experience some motoric and non-motoric symptoms. In PD the most common symptoms are tremor, rigidity, and bradykinesia. In this disease there is no curative treatment, most are given to treat the symptoms experienced by patients.[4] One of the primary treatment given is the provision of pharmacological therapy. The first-line of pharmacological therapy given to the patients is levodopa with dopa decarboxylase inhibitors such as benserazide, dopamine agonist, anticholinergics and a combination therapy by using anti-Parkinson drugs. However, each pharmacological therapy must consider many factors such as age, cost needed, dominant symptoms occurrences, the disease that can be caused by the administration of anti-Parkinson drugs, and others.[5]

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Parkinson's diseases patients with the right treatment pattern are believed to be able to improve their quality of life for at least three years.[6] Consequently, this disease needs appropriate treatment. The result of the treatments depends on several factors such as giving the right medication the patient required. The objective of this study was aimed to describe an overview of therapeutic patterns for PD patients in Dr. Hasan Sadikin General Hospital Bandung.

Methods

A descriptive study was conducted using secondary data from medical records of Parkinson's disease outpatients admitted to Dr. Hasan Sadikin General Hospital Bandung from January 2013 to June 2018. The inclusion criteria for this study were medical records of patients diagnosed with Parkinson's disease and receiving pharmacological therapy, such as levodopa with dopa decarboxylase inhibitors, dopamine agonists, anticholinergics, or combination therapy. Medical records with incomplete data and patients who experienced other neurological disorders before the patients diagnosed with Parkinson's disease were excluded from this study. Data were analyzed using Microsoft Office Excel 2010 and presented in percentage.

The variables used in this study were age, sex, the given pharmacological therapy, and the patients' staging. The Research Ethics Committee of Universitas Padjadjaran has approved this study with ethics number 726/UN6.KEP/EC/2018.

Results

During the study period, 78 Parkinson's disease patients were registered in the Outpatient at Dr. Hasan Sadikin General Hospital Bandung. The excluded data were 12 subjects who suffered from other neurological diseases before diagnosed PD and 9 subjects with incomplete medical record data. Out of 57 subjects, 47 subjects did not experience other neurological disorders, four subjects had a stroke, three subjects had epilepsy, and three patients had dementia after given pharmacological therapy.

Based on the characteristics of the study subjects, PD was often experienced by men with a total of 44 (77%) and women as many as 13 (23%). When classified by age, PD most often occurred in the age range of 60–69 years with a total of 18 data (32%), followed by the age range of 70–79 years as many as 16 (28%) and in the age range of 50–59 years as many as 11 (19%). Based on the staging, 24 subjects (42%) experienced stage II and 16 subjects (28%) experienced stage III (Table 1).

Furthermore, based on the distribution of the most commonly used pharmacological therapy, Levodopa as monotherapy was the most commonly administered drug with 19 (33%) data. Dopamine agonist was rarely given to the subjects with 1 (2%) data (Table 2).

Table 1 Characteristics of Study Subjects

	Staging I	Staging II	Staging III	Staging IV	Staging V	Total
	n=9	n=24	n=16	n=5	n=3	
Sex						
Male	6	17	15	4	2	44(77%)
Female	3	7	1	1	1	13(23%)
Age (Years)						
≤30	2	1	-	-	-	3 (5%)
30-39	1	3	-	-	-	4 (7%)
40-49	-	2	-	-	-	2 (4%)
50-59	1	5	4	1	-	11 (19%)
60-69	3	8	4	1	2	18 (32%)
70-79	2	5	6	3	-	16 (28%)
≥80	-	-	2	-	1	3 (5%)

Table 2 Description of Drugs used in Study Subjects

	n	(%)
Levodopa + BZ*	19	33
Dopamine Agonist	1	2
Anticholinergic	8	14
Levodopa + COMT	8	14
Levodopa+Dopamine Agonist	4	7
Levodopa +anticholinergic	6	11
Levodopa+COMT+anticholinergic	8	14
Levodopa + anticholinergic+ Dopamine Agonist	3	5

Note: *Levodopa + benserazide with a ratio of 1:4

Table 3 Distribution of Drugs Used by Age

Drugs	Age (years)						
	≤30	30–39	40–49	50–59	60–69	70–79	≥80
	n	n	n	n	n	n	n
Levodopa+BZ*	-	2	-	6	6	3	2
Dopamine Agonist	-	1	-	-	-	-	-
Anticholinergic	3	-	-	2	2	1	-
Levodopa+COMT	-	-	-	-	3	4	1
Levodopa+Dopamine Agonist	-	1	-	1	1	1	-
Levodopa+anticholinergic	-	-	2	1	2	1	-
Levodopa+COMT+ anticholinergic	-	-	-	-	4	4	-
Levodopa+anticholinergic+ Dopamine Agonist	-	-	-	1	-	2	-
Total	3	4	2	11	18	16	3

Note: *Levodopa + benserazide with a ratio of 1:4

Table 4 Distribution of Drugs Used Based on Staging

	Staging I	Staging II	Staging III	Staging IV	Staging V
	n	n	n	n	n
Levodopa+BZ*	1	10	6	1	1
Dopamine Agonist	1	-	-	-	-
Anticholinergic	4	3	1	-	-
Levodopa + COMT	1	-	4	1	2
Levodopa+Dopamine Agonist	1	2	1	-	-
Levodopa+anticholinergic	-	6	-	-	-
Levodopa+COMT +anticholinergic	1	2	3	2	-
Levodopa + anticholinergik+ Dopamine Agonist	-	1	1	1	-
Total	9	24	16	5	3

Note *Levodopa + benserazide with a ratio of 1:4

The administration of drugs based on age showed that at the age of under 30 years, all patients were given anticholinergic monotherapy. In the age range of 40–49 years, all patients were given combination therapy with levodopa and anticholinergics. Levodopa was increasingly given along with the patient's increase in age (Table 3).

Moreover, 4 out of57 subjects (7%) of stage I used anticholinergic therapy. In stage II, 10 subjects out of 57(18%) used levodopa. In stage III, as many as 6 subjects out of 57 (11%) used levodopa. In stage IV, as many as 2 subjects (4%) used levodopa+COMT+ anticholinergic. In stage V, there were at most 2 subjects (4%) who used levodopa+COMT.

Discussion

This study describes an overview of therapeutic patterns for PD patients in Dr. Hasan Sadikin General Hospital Bandung. The majority of PD patients are male (77%), consistent with another study in China.[7] The role of estrogen might support this study result. Estrogen has a protective effect against dopaminergic damage and also prevents the deposition of Lewy body through specific anti-aggregation activities of alpha-synuclein and destabilization of fibrils.[8]

The PD mostly occurs predominantly in late age after 50 years old, supported by the previous study in China[7]and Serbia[8]. Our study has shown that as age increases, the risk of getting higher staging is increased. Increasing age is one of the risk factors for the development of PD, which increases the risk of a derivative neuron function or often called neurodegenerative. The accumulation of damaged cells might trigger poor regeneration cells and compensation system, it might promote the acceleration of PD progressiveness.[9] Increasing age also plays a role in decreasing dopamine production, loss and damage of neurons, especially in dopaminergic neurons in substantianigra.[10]

Patients under 30 years in our study are given anticholinergic therapy. Dopamine agonist can be an alternative therapy for young aged PD patients.[11] There are several consideration for pharmacological therapy for PD patients, such as the predominant symptoms, age, economic burden, and others.[12] For young PD patients who have economic problems, anticholinergic therapy might be given.[12]

However, elderly patients over 60 years in our study are given anticholinergic therapy. Based on WHO, anticholinergic therapy may cause decreased cognitive function, therefore, this therapy is not recommended to be given to patients over 75 years. Anticholinergics are not the first-line treatment for PD because of its limited efficacy and side effects on the patient's neuropsychiatric system.[13] Nevertheless, anticholinergics could be given to PD patients with dominant tremor and should not experience cognitive impairments.[13]

Besides, levodopa is often given to PD patients aged over 60 years in this study as this is in accordance with the PD management algorithm issued by the Indonesian Neurological Association (*Perhimpunan Dokter Spesialis Syaraf*, PERDOSSI) in 2015. The side effects of levodopa such as dyskinesia potentially occur in young PD patients.[14] Long-term levodopa therapy can cause unwanted side effects. Levodopa therapy might increase the potential to experience side effects such as dyskinesia when it is consumed over 10 years. Until now, long-term pharmacological therapy in PD patients has been given, because PD has no curative treatment so that levodopa therapy will be given for a long time to reduce the symptoms.[15] The administration of levodopa is given with consideration of functional disorders, dominant symptoms, and age so that the administration of levodopa is mainly given to patients who experienced non-tremor dominant symptoms and aged over 60 years. Combination therapy can be given to optimizing the therapy. For example, combination therapy with levodopa and COMT inhibitors is to extend the half-life of levodopa levels in the body to stabilize the blood dopamine levels.[16]

Comorbidities for PD in this study are a stroke, epilepsy, and dementia, in which stroke is the most comorbid.[9] The degeneration process of dopamine-producing cells in PD can be caused by an oxidative stress process in which it might damage the endothelial cell function and cause atherosclerosis. Atherosclerosis may cause chronic hypertension which leads to stroke.[12] Stroke can also be caused by homocysteine, PD patients treated with levodopa have elevated plasma homocysteine, which can trigger neuroinflammation. The activated microglia and astrocytes release some factors that initiate an inflammatory response and trigger neuronal death. Furthermore, homocysteine has prothrombotic and proatherogenic effects so that it may promote the progression of stroke in PD patients.[17]

This study has several limitations. Some of the potential subjects are excluded due to incomplete medical records, especially concerning the patient's stage. This study

can be developed by increasing the sample and analyzing the correlation of the pharmacological treatment pattern with the patient's quality of life conducted prospectively.

In conclusion, males are most affected by PD, and the most commonly used treatment pattern is levodopa monotherapy. Parkonson's diseases is most commonly found in patients aged 60 to 69 years. Patients aged below 30 years are administered anticholinergics. The most common comorbidities found are a stroke, followed by dementia and epilepsy. By recognizing the patterns and comorbidities of this disease, the study may provide some insights into choosing the most effective pharmacological therapy for PD.

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