Yonsei Medical Journal
Vol. 27, No. 1, 1986

Parkinson's Disease: Some Clinical Observation Based on the Study of 93 Patients Seen at the Yonsei University Medical Center

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Between 1980 and 1985, 93 patients with Parkinson's disease (paralysis agitans) were seen and examined prior to the initiation of medication. Forty-four of them were men and 49 of them women. Their ages ranged from 32 to 86 years (mean, 56.7 years), with the peak incidence in the seventh decade. The initial symptoms were tremor (67.7%), gait disturbance (16.1%), stiffness (15.1%), back pain, and weakness. Durations of illness until final diagnosis ranged from 2 months to 8 years (mean, 1.5 years). The most frequent signs at first examination were rigidity (95.7%), masked face (94.4%), tremor (89.2%), bradykinesia (87.1%), festinating gait (81.2%), grabella sign, stooped posture, and low voice. No marked dementia was seen in this study, and mild mental change was present in only 7 patients (7.5%). According to the modified Hoehn and Yahr's classification, 13 patients were in stage I, 31 in stage II, 28 in stage III, 13 in stage IV, and 8 in stage V. The more advanced stages were associated with a longer duration of the disease. Fifteen (16.1%) had coexisting disease: 11, hypertension; 3, diabetes mellitus; 2, stroke; and 1, malignant neoplasm. All patients but one responded initially to levodopa (Sinemet).

Key Words: Parkinson's disease, tremor, rigidity, bradykinesia

Parkinson's disease (paralysis agitans) is a chronic disorder of the central nervous system of variable progression and severity, and one of the most common disorders of the nervous system.

Clinically, the disease is usually characterized by rigidity, tremor, akinesia, and gait disturbance. Pathologically, the disease is characterized by a degeneration of the pigmented neurons in the substantia nigra and, to a lesser degree, degeneration of the neurons in the globus pallidus. Biochemically, it is characterized by a decrease in dopamine and serotonin, and their maior metabolities in the corpus striatum (Coasta *et al.* 1966; Pearce 1978; Calne 1978; Yahr 1984). A large body of human and animal experimentation has demonstrated that the decrease of striatal dopamine is specific for Parkinson's disease and is responsible for the clinical symptomatology of it. Repletion of deficient dopamine through the administration of its immediate precursor, Levodopa, has significantly altered the course of the disease.

Since James Parkinson's description of this disorder in 1877, numerous clinical and experimental studies on it have been carried out in America and Europe. However, in Korea few reports about this disorder as it is found in Korea have appeared in print (Lee 1983; Chung *et al.* 1985).

MATERIALS AND METHODS

Between 1980 and 1985, a total of 93 patients were seen at Yonsei University Medical Center and one of its satellite units, Yongdong Severance Hospital, and an initial diagnosis of Parkinson's disease (paralysis agitans) was made.

Secondary parkinsonism due to carbon monoxide poisoning, cerebral arteriosclerosis, drugs, etc., were excluded from this study.

Ninety-three patients were classified according to sex, age, initial symptoms, duration of illness, physical findings, clinical disability, coexisting diseases, and in-

Received January 20, 1986
Accepted February 3, 1986
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itial drug response.

The level of clinical disability was classified into stages I-V, based on the modified Hoehn and Yahr's device (Table 1).

Electroencephalograms (EEG) and computed tomographic (C-T) brain scans were done on all patients for ruling out secondary parkinsonism.

An anticholinergic drug such as trihexyphenidyl (Artane) with either an antihistaminic drug (Benadryl) or Sinemet (levodopa and carbidopa combined), or trihexyphenidyl with both Bendaryl and Sinemet were initially used in attempts to treat Parkinson's disease.

Table 1. Classification of Parkinson's disease

Stage I:	Unilateral involvlement
Stage II:	Bilateral involvement
	(Minimal gait impariment may be present).
Stage III:	Bilateral involvement
	(There is always moderate gait impairement).
Stage IV:	Bilateral involvement
	(There is marked gait impairement).
Stage V:	Bilateral involvement
	(Patient is confined to wheelchair or bed).

(The modified Hoehn and Yahr's device)

RESULTS

There were 44 men and 49 women. Their ages ranged from 32 to 86 years (mean, 56.7 years). Although the age range was wide, in two-thirds of the patients the disease had begun between the ages of 50 and 69. None of the patients was younger than 30 (Table 2).

The initial symptoms of the patients, who were interviewed and examined in detail, are listed in Table 3. Complaints such as back pain, abdominal discomfort, and dizziness are designated as initial symptoms, only if they were specifically and unequivocally related to the onset of the disease.

Durations of illness until final diagnosis ranged from 2 months to 8 years (mean, 1.5 years), but were within 3 years in three-quarters of the patients (Table 4).

The most frequentl physical findings on the first examination were rigidity, masked face, tremor, bradykinesia, festinating gait, and stooped posture in that order. No marked dementia was seen in this study, and only mild mental change was present in 7 patients (7.5%) (Table 5).

Two-thirds were found to be equally divided between stage II and state III; a smaller number was

Table 2. Age at onset

Age (years)	No. of patients	%
30–39	3	3.2
40–49	13	14.0
50–59	22	23.6
60–69	40	43.0
70–79	13	14.0
80–89	2	2.2
Total	93	100.0

Male: Female = 44 : 49

Table 3. Initial symptoms in 93 patients with Parkinson's disease

Symptom	No. of patients	%
Tremor	63	67.7
Gait disturbance	15	16.1
Stiffness	14	15.1
Back pain	7	7.5
Weakness	6	6.4
Abdominal discomfort	2	2.2
dizziness	1	1.1

Table 4. Duration of illness until final diagnosis

Duration (years)	No. of patients	%
0– 1	41	44.1
1– 3	33	33.3
3– 5	14	17.2
5–10	5	5.4

(Range: 2 months to 8 years, mean: 1.5 years)

Table 5. Clinical signs on first examination in 93 patients with Parkinson's disease

Sign	No. of patients	%
Rigidity	89	95.7
Masked face	86	92.4
Tremor	83	89.2
Bradykinesia	81	87.1
Festinating gait	76	81.2
Grabella sign	73	78.5
Stooped posture	65	69.9
Low voice	52	55.9
Mental change	7	7.5

Table 6. Classification on first examination of 93 patients with Parkinson's disease

Stage	No. of patients	%
I	13	14.0
II	31	33.3
III	28	30.1
IV	13	14.0
V	8	8.6
Total	93	100.0

Table 7. Correlation between stage and duration of illness in 93 patients with Parkinson's disease

Stage	Duration (years)			
	0–1	1–3	3–5	5–10
I	8	3	1	1
II	20	11	0	0
III	5	15	7	1
IV	2	4	6	1
V	6	0	0	2
Total	41	33	14	5

found to be in stages I and IV, and only a handful was found to be in stage V (Table 6).

The more advanced stages were associated with a longer duration of the disease. However, there was considerable variation in the duration of illness for some patients in a given stage (Table 7).

Fifteen (16.1%) had a coexisting disease: 11, hypertension; 3, diabetes mellitus; 2, stroke; and only one, malignant neoplasm.

All patients but one responded initially to a combination of levodopa and carbidopa (Sinemet) and/or anticholinergic drugs.

DISCUSSION

Parkinson's disease is one of the major causes of neurological disability, especially in individuals over 60 years of age.

Though its exact incidence is unknown, with the world's population showing an increase in the older age group, this disorder can be expected to be encountered with increasing frequency in the years to come (Yahr 1984).

To date, attempts to discover its cause and pathogenesis have been unsuccessful. Numerous etiologic theories have been brought forth (Barbeau 1962; Lieberman 1974; Barbeau 1976; Pearce 1978; Mann and Yates 1982; Yahr 1984) and one of these has proposed that a premature aging of the CNS is the fundamental cause (Barbeau 1976). In addition, secondary parkinsonism may arise from several causes: encephalitis (Duvoisin and Yahr 1965), drugs (Schmidt and Jarcho 1966), carbon monoxide or manganese poisoning (Pearce 1978; Choi 1983), brain tumor (Sciarra and Sprofkin 1953), and others (Pearce 1978; Mann and Yates 1982; Yahr 1984).

However, advances in our knowledge of the regional biochemisty of the brain, particularly that of the biogenic amines, have made possible a new understanding of this disorder and have established a basis for its rational therapy (Costal *et al.* 1966; Cotzias *et al.* 1967; Marsden 1976).

The age of onset is usually in the sixth to eighth decades of life. The development of symptoms before the age of forty is uncommon (Hoehn and Yahr 1976; Lieberman 1974; Yahr 1984). None of my patients younger than 30.

According to some reported sex ratios (Hoehn and Yahr 1967; Lieberman 1974), it has been found more frequently in men, but, in general, the incidence in the sexes is approximately equal just like that of my study.

As in Mjönes (1949), and Hoehn and Yahr's studies (1967), tremor was the most frequent initial symptom found in this study, occurring as it did, in 67.7% of the patients.

As expected (Hart 1904; Patrick and Levy 1922; Hoehn and Yahr 1967; Lieberman 1974), rigidity, tremor, and bradykinesia were the most frequent physical findings on the first examination. Only 4 patients were free of rigidity, and 10 were free of tremor in this series. Other frequent physical findings were masked face, festinating gait, stooped posture, and low voice.

Dementia is ordinarily not regarded as a manifestation of Parkinson's disease. However, a moderate amount of dementia was present in one-quarter to one-third of the patients (Lieberman 1974; Hakim and Mathieson 1978). No marked dementia was seen in this study, and only mild mental change was present in 7 patients.

As might be anticipated (Hoehn and Yahr 1967; Lieberman 1974), the more advanced stages were found to be associated with a longer duration of the disease. However, there is considerable variation in the duration of illness for some patients in a given

stage.

The leading causes of death in the general population are heart disease, malignant neoplasms, and cerebrovascular accidents. The most striking difference between parkinsonian patients and the general population is the higher incidence of deaths due to bronchopneumonia (Hoehn and Yahr 1967). Certainly this is to be expected in a disease producing chronic immobilization and debilitation.

In general, patientls with Parkinson's disease are resistant to malignancies. In the British Multiple Cause Analysis of 1951, the underlying cause of death was malignant neoplasm in only 2% of those patients with Parkinson's disease as a contributing condition. Doshay, in 1954, stated that cancer was phenomenally rare in paralysis agitans. Barbeau and Joly (1963) also found a much lower incidence of malignancy among their patients than expected. Of the series reported herein, only one patient had coexisiting malignant neoplasm: renal cell carcinoma.

On ther other hand, Westlund and Hougen (1956) found 6 deaths due to cancer in a group of lll patients dying with typical paralysis agitans, against an expected 2 deaths, and in Hoehn and Yahr's study (1967), 62 out of 340 deaths resulting from Parkinson's disease were of patients who were known to have had a malignancy at some time in their lives.

The diagnosis of Parkinson's disease is a clinical one. When the major signs and symptoms are well developed, the average non-neurologist has little difficulty in recognizing it. However, it is frequently confused with a number of other disorders, such as essential tremor (Critchley 1949), normal pressure hydrocephalus (Benson *et al.* 1970), striatonigral degeneration (Andrews *et al.* 1970), pseudobular palsy (Lieberman 1974), the rigid from of Huntington's disease (Bittenbender and Quadfasel 1962), progressive supranuclear palsy (Dix *et al.* 1971), and drug-induced Parkinsonism (Schmidt and Jarcho 1966).

Until the discovery of the levodopa replacement concept in 1961 by Barbeau and Birkmayer (Barbeau 1969), and its development as a therapeutic measure by Cotzias in 1967 (Cotzias *et al.* 1967), the only available treatment for Parkinson's disease was the use of synthetic anticholinergic or antihistaminc drugs which only partially relieved rigidity and tremor (Yahr 1972; Marsden 1976; Bianchine 1976). Stereotactic surgery, with its many variants (leukotome, cryosurgery, and electrically produced lesions), was useful in reducing tremor, particularly if it was of large amplitude and unilateral (Walts *et al.* 1966). Bilateral lesions were too often followed by severe speech disturbances. With the use of neither approach, however, was it possible to modify the akinesia.

The theoretical goal of treatment is the restoration of normal function to the striatum by reducing cholinergic activity or enhancing dopaminergic function, or both (Yahr 1972).

The functional capacity of the dopaminergic system can be enhanced by any of the following: (1) increasing the synthesis of brain dopamine by the administration of its precursor, levodopa (Langrall and Joseph 1972; Mars 1974; Markham and Diamond 1981); (2) delaying the catabolism of dopamine with deprenyl (Eisler *et al.* 1981); (3) stimulating the action of brain dopamine at the reception sites with bromocriptine or pergolide (Fahn *et al.* 1979· Lieberman *et al.* 1979; Lieberman *et al.* 1980; Lieberman *et al.* 1981; Quinn *et al.* 1981; Grimes and Hassan 1983; Lewitt *et al.* 1983); or (4) blocking its reuptake and storage at the synaptic cleft with amantadine (Yahr 1972; Biachine 1976).

At this time, levodopa administered alone or combined with a dopa decarboxylase inhibitor is the most effective treatment for Parkinson's disease (Yahr 1972; Yahr 1984). The numerous other agents must be considered as adjunctive drugs, useful in mild cases or in supplementing the use of levodopa.

Up to 90% patients have been known to respond initially to levodopa (Langrall and Joseph 1972). However, long-term levodopa therapy is associated with a progressively increasing incidence of drug failure as well as drug-induced complications (Langrall and Joseph 1972; Lieberman *et al.* 1979). Of the series reported herein, only one patient initially failed to respond to levodopa therapy.

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