

# Correlation Between the Age, Motor Subtypes and the Necessity of Advanced Therapy in Parkinson Disease

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*Levodopa (L-dopa), a precursor of dopamine, remained the gold standard among antiparkinsonian drugs and virtually, in different stages, all patients will require the more powerful symptomatic effect of L-dopa. In addition, continuous Levodopa/Carbidopa intestinal gel (LCIG) infusion therapy, via a percutaneous endoscopic gastrostomy (PEG) and a portable infusion pump, is well established for the treatment of advanced Parkinson's disease (PD), substantially improving motor symptoms and quality of life in these patients. This study aimed to evaluate the necessity of LCGI depending the PD motor subtypes and age at onset of the disease. Seventy patients diagnosed with PD were included in our study. The Unified Parkinson's Disease Rating Scale (UPDRS) was performed in on state. The patients were classified as tremor-dominant type (TDT), akinetic-rigid type (ART) and mixed type (MT). Depending on form of levodopa, thirty-six patients were on L-dopa orally and thirty-four patients were on LCIG. The results of our study showed that there was a statistically significant correlation between the age at onset of PD and the motor subtype of the disease. Also, we observed that the lower the age at diagnosis, the more our patients have reached the need for LCGI. Regarding the motor subtype, our study showed that the mixed typed request more frequent LCGI. Our data show that age and motor profile at onset can predict the necessity of advanced therapy.*

**Keywords:** levodopa, oral administration, intrajejunal gel, Parkinson disease, age

Parkinson disease is a neurodegenerative disorder caused by substantia nigra neuronal loss and Lewy body inclusions and presented in a variety of ways [1].

The classical triad of motor symptoms includes resting tremor, akinesia and rigidity. However, the expression of these cardinal motor symptoms varies markedly between patients. PD, a heterogeneous condition, can be classified into different subtypes: tremor-dominant type (TDT), akinetic-rigid type (ART) and mixed type (MT) [2].

Many studies support the idea that akinesia-rigidity phenotype and tremor-dominant phenotype reflect different pathophysiological phenomena in the basal ganglia [3-4].

Also, clinical observations suggest that distinct subtypes of PD have a different clinical course. It has been shown that patients with ART develop a faster clinical progression with more severe cognitive deficits [5]. These data were confirmed in pathological studies, which showed that the more favorable course of TDT was related with a less

widespread pallidal and striatal reduced dopamine level in comparison with ART [6].

Levodopa/carbidopa intestinal gel is an advance therapy first established in Scandinavian countries and then extended to other European countries. With this treatment, although invasive and expensive and requiring special experiences, the patients with refractory fluctuations and dyskinesias can achieve marked and sustained improvement [7-8].

In our study we want to evaluate the necessity of advanced therapy depending of motor subtype of Parkinson's disease and, also, if there is a possible correlation between the patient's age at diagnosis and motor subtype of this disease.

## Experimental part Methods and Materials

We studied 70 cases (28 females and 42 males), mean age  $67.79 \pm 7.77$  years, diagnosed with PD according with

United Kingdom Parkinson's Disease Society Brain Bank criteria[9]. For each patient details of demographic data, age at onset, disease duration, symptoms at onset, medications, motor fluctuations, L-dopa induced dyskinesia and family history were recorded. The patients were assessed using United Parkinson's Disease Rating Scale – motor section (UPDRS part III) [10]. The Hoehn and Yahr Scale was used for disease staging. Both scale (UPDRS and Hoehn and Yahr scale) were evaluated while the patients were in *on* state, all patients receiving L-dopa (either orally, or intrajejunal) [11].

The subgroups of PD that include TDT, ART and MT were classified by means of UPDRS part III, using a method similar with Lewis at all [12]. First, we calculated a *tremor score* from the sum of item 20 of UPDRS (tremor at rest) and 21 (action and postural tremor) divided at 7 (the number of single subitems). Then, we calculated a *non-tremor score* from the sum of UPDRS item 18 (speech), 19 (facial expression), 22 (rigidity), 27 (arising from chair), 28 (posture), 29 (gait), 30 (postural instability) and 31 (body bradykinesia and hypokinesia), divided by 12 (the number by single subitems).

For the non-motor symptoms we used Non-motor Symptoms Questionnaire for Parkinson's Disease (NMSQ). It is an questionnaire with 30 items and different non-motor domain like memory, sleep, gastrointestinal and others[13].

The patients were classified as TDT if the *tremor score* was at least twice the *non-tremor score*, or ART if the *non-tremor score* was at least twice the *tremor score*. The remaining patients, in whom the *tremor score* and *non-tremor score* differing by less than a factor 2, were classified as MT.

The statistical analysis was performed using IBM SPSS Statistics V20. We made descriptive and exploratory data analysis.

For comparison we used Pearson R correlation - test, the statistical significance was established when  $p < 0.05$ .

## Results and discussions:

We included in this study 70 patients with PD, 28 females and 42 males. When analyzing the provenience there were 32 from rural areas and 38 from urban areas. The disease stage was between 1 and 5 with an average of 3.21 and a standard deviation of 0.99. Age of onset was between 38 and 76 years with an average of 58.2 years. After we analyzed the motor type of the disease using UPDRS part III there were 24 patients in the tremor dominant type, 26 in the akinetic-rigid type and 30 in the mixed type (table 1)

**Table 1**  
DESCRIPTIVE STATISTICS

Variable	No. Patients(N=70)
Sex	
Men	42
Women	28
Average age (years)	67.69
Disease duration (years)	9.49
Hoehn & Yahr Stage (average)	3.21
Score UPDRS motor (UPDRS III)	49.83

**Table 2**  
CORRELATIONS BETWEEN ADMINISTRATION FORM AND MOTOR SUBTYPE

Correlations		Administration form	MOTOR_SUBTYPE
Administration form	Pearson Correlation	1	.493
	Sig. (2-tailed)		.000
	N	70	70
MOTOR_SUBTYPE	Pearson Correlation	.493	1
	Sig. (2-tailed)	.000	
	N	70	70

\*\*. Correlation is significant at the 0.01 level (2-tailed).

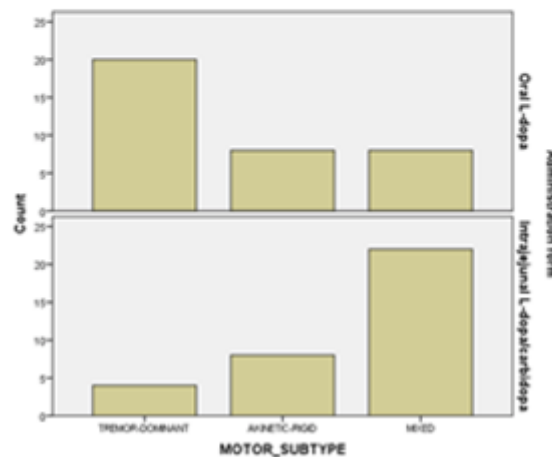


Fig. 1. Correlations between administration form and motor subtype

This study revealed statistically significant correlation with  $p < 0.001$  between the motor subtype of PD and the administration form of L-dopa. Therefore, it seems that the mixed type is treated especially with LCGI infusion therapy (table 2, fig. 1)

Our study analysis showed that the patient age at diagnosis could have an important meaning. In the group we have studied there was a statistically significant correlation with  $p = 0.007$  between the age at onset and the motor subtype of the disease. This shows that the tremor-dominant form of the disease is more likely diagnosed at an older age then the other forms. Also, it seems that our younger PD patients at diagnosis presented predominantly a mixed form (fig. 3, table 2)

**Table 3**  
CORRELATIONS BETWEEN AGE OF ONSET AND MOTOR SUBTYPE

Correlations		AGE_OF_ONSET	MOTOR_SUBTYPE
AGE_OF_ONSET	Pearson Correlation	1	-.322
	Sig. (2-tailed)		.007
	N	70	70
MOTOR_SUBTYPE	Pearson Correlation	-.322	1
	Sig. (2-tailed)	.007	
	N	70	70

\*\*. Correlation is significant at the 0.01 level (2-tailed).

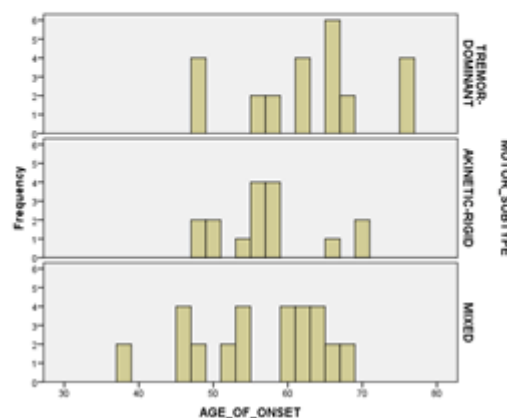


Fig. 2. Correlations between age of onset and motor subtype

There was a statistically significant correlation between the age of onset and the form of L-dopa administration with  $p < 0.001$  (table 4).

In the figure above we can observe that there was a link between the age of onset and the form of L-dopa administration. It seems that while the age at diagnosis decrease it is more likely that those patients need for intrajejunal L-dopa/carbidopa administration (fig. 3)

**Table 4**  
CORRELATIONS BETWEEN AGE OF ONSET AND ADMINISTRATION FORM

Correlations		AGE_OF_ONSET	Administration form
AGE_OF_ONSET	Pearson Correlation	1	-.428
	Sig. (2-tailed)		.000
	N	70	70
Administration form	Pearson Correlation	-.428	1
	Sig. (2-tailed)	.000	
	N	70	70

\*\*. Correlation is significant at the 0.01 level (2-tailed).

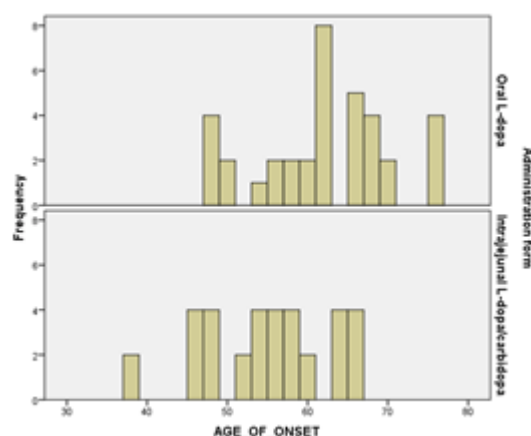


Fig. 3. Correlations between age of onset and administration form

In the table and figure above, we can observe that even if the age of onset showed statistically significant correlation with both motor subtypes and administration form, there is no correlation between the non-motor symptoms and the age at onset ( $p=0.951$ ) (table 5, fig. 4)

**Table 5**  
CORRELATIONS BETWEEN AGE OF ONSET AND NMSQ

Correlations		AGE_OF_ONSET	NMSQ
AGE_OF_ONSET	Pearson Correlation	1	-.007
	Sig. (2-tailed)		.951
	N	70	70
NMSQ	Pearson Correlation	-.007	1
	Sig. (2-tailed)	.951	
	N	70	1048574

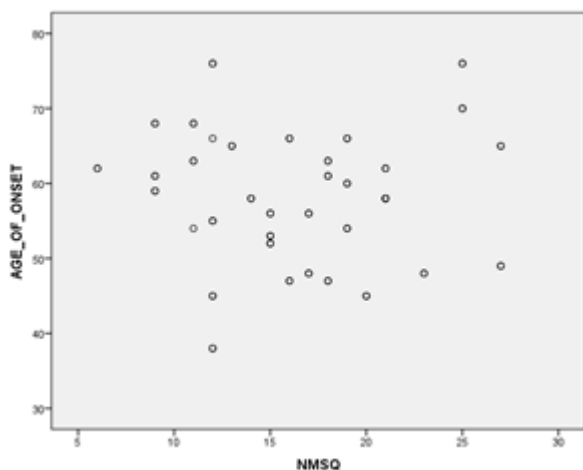


Fig. 4. Correlations between age of onset and NMSQ

Parkinson's disease is a disorder with a variate symptomatology divided in motor and non-motor type. Akinetic-rigid and tremorigen type has different performance once the disease progressed [6].

Currently, there is no cure for Parkinson's disease. The therapy include oral medication (L-dopa, dopamine agonists, monoamine oxidase-B inhibitors, catechol O-methyltransferase inhibitors, anticholinergics), continuous Levodopa/Carbidopa intestinal gel (LCIG) infusion therapy and deep brain stimulation[14]. It is very important that patients receive the right therapy for their type and stage of the disease[15-19]. In our study the mixed type correlated with a frequent need advanced therapy.

Even if the presentation is the same regardless of the age group, there is a difference when we study the age at onset. In our study the mixed type presented a younger age at onset but in other studies the akinetic-rigid form has a higher prevalence on those patients[20].

Our study headlights the importance of the age of onset in PD and its importance on diagnosis and clinical management.

## Conclusions

This study indicates that the age and motor subtype can be a predictor for the necessity of advanced therapy in Parkinson's disease. The younger patients with a mixed form of the disease are the type that request more LCIG.

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Manuscript received: 30.10.2018