

Verification of the effects of Levodopa on the swallowing of patients with Parkinson's disease

Verificação dos efeitos da Levodopa na deglutição de pacientes com doença de Parkinson

Douglas Monteiro¹, Maria das Graças Wanderley de Sales Coriolano², Luciana Rodrigues Belo³, Etenildo Dantas Cabral², Amdore Guescel Asano⁴, Otávio Gomes Lins⁵

ABSTRACT

Purpose: To evaluate the effects of Levodopa on the swallowing of patients with Parkinson's Disease (PD). **Methods:** The study was carried out in the Pro-Parkinson Program of the *Hospital das Clínicas* of the Federal University of Pernambuco. Twenty patients with idiopathic PD and 12 normal subjects (control group) were studied. The surface Electromyography (sEMG) was recorded over the suprahyoid musculature during swallowing of 3 ml and 10 ml of water and yogurt. Each volume was repeated five times. This protocol was carried out on the group with PD before and after the medication, *off* and *on* periods, and on the control group, a single time. **Results:** The amplitude of the sEMG was significantly greater for subjects of the control group than for the patients with PD (*off*), regarding swallowing of each volume of water. The duration of the sEMG was significantly greater for the swallowing of 3 ml of water and yogurt in patients with PD (*off*). During the *on* phase, no significant differences were noted. **Conclusion:** The administration of Levodopa on patients with PD seems to influence the amplitude and duration of the sEMG of suprahyoid muscles, approximating the variables to the values of normalcy.

Keywords: Parkinson disease; Deglutition, Dysphagia; Electromyography; Levodopa

RESUMO

Objetivo: Avaliar os efeitos da Levodopa na deglutição de pacientes com Doença de Parkinson (DP). **Métodos:** O estudo foi realizado no Programa Pró-Parkinson do Hospital das Clínicas da Universidade Federal de Pernambuco. Foram estudados 20 pacientes com DP idiopática e 12 sujeitos normais (grupo controle). A eletromiografia de superfície (EMGs) foi registrada sobre a musculatura supra-hióidea, durante a deglutição de 3 ml e 10 ml de água e iogurte. Cada volume foi repetido cinco vezes. Esse protocolo foi realizado no grupo com DP antes e após a medicação, período *off* e *on*, e no grupo controle, uma única vez. **Resultados:** A amplitude das EMGs foi significativamente maior nos sujeitos do grupo controle do que nos pacientes com DP (*off*), na deglutição de cada volume de água. A duração das EMGs foi significativamente maior na deglutição de 3 ml de água e iogurte em pacientes com DP (*off*). Durante a fase *on*, diferenças significativas não foram notadas. **Conclusão:** A administração de Levodopa em pacientes com DP parece influenciar a amplitude e duração da EMGs dos músculos supra-hióideos, aproximando as variáveis aos valores de normalidade.

Descritores: Doença de Parkinson; Deglutição; Disfagia; Eletromiografia; Levodopa

Research study carried out by the Pro-Parkinson Program, Hospital das Clínicas, Universidade Federal de Pernambuco – UFPE – Recife (PE), Brazil.

(1) Centro Universitário Maurício de Nassau – UNINASSAU – Recife (PE), Brazil.

(2) Universidade Federal de Pernambuco – UFPE, Anatomy Department, Recife (PE), Brazil.

(3) Universidade Federal de Pernambuco – UFPE, Post-Graduate Program (Doctorate) in Neuropsychiatry and Behavioral Science, Recife (PE), Brazil.

(4) Universidade Federal de Pernambuco – UFPE, Hospital das Clínicas, Pro-Parkinson Program, Recife (PE), Brazil.

(5) Universidade Federal de Pernambuco – UFPE, Neuropsychiatry Department, Recife (PE), Brazil.

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Correspondence address: Maria das Graças Wanderley de Sales Coriolano. R. Professor Antônio Coelho, 694/102, Várzea, Recife (PE), Brazil, CEP: 50740-020. E-mail: gracawander@hotmail.com

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INTRODUCTION

The surface electromyography (sEMG) should not be used for diagnostic ends, however, it does represent a simple and useful tool to study and monitor swallowing⁽¹⁾. Duration and amplitude are two important electrophysiological parameters that can be analyzed with sEMG during swallowing. The duration of swallowing is calculated by subtracting the first marked time from the second marked time. This parameter characterizes the duration of the oropharyngeal phase of swallowing⁽²⁾.

The amplitude of swallowing, expressed by the value of the root mean square – RMS, can establish the relation between the electric activity and the muscular force⁽²⁾. These two parameters can be important allies in the clinical analysis of swallowing.

Based on a series of studies⁽³⁻⁵⁾, reference values were proposed for these parameters in normal patients. However, the scarce description of technical specifications and the absence of standards for the tests made the method unreplicable⁽⁶⁾.

Some authors^(7,8), who studied swallowing through sEMG in subjects with and without Parkinson's disease (PD), and found differences between them in the electromyographic parameters. However, they did not address the effect of medication on the swallowing of patients with PD.

Considering that the main treatment for PD is dopamine reposition, through the use of Levodopa⁽⁹⁻¹¹⁾, and that the alterations in swallowing along the development of the disease are frequent – the aspiration of food content being the greatest cause of deaths among patients⁽¹²⁻¹⁵⁾ – the objective of this study was to evaluate the effects of Levodopa on the swallowing of patients with PD, through the use of the surface electromyography.

METHODS

This is an analytical cross-sectional study that considers the comparisons of sEMGs between subjects with and without PD, a longitudinal study, by observing the effects of Levodopa on the *on* and *off* swallowing phases of subjects with PD.

This study was approved by the Ethics Committee of Research with Human Beings of the Health Sciences Center of the Universidade Federal de Pernambuco (UFPE), document n° 368/2010. All participants were informed of the objectives of the research study and signed the Term of Free and Conscious Consent.

The study was carried out in the Pro-Parkinson's Program of the *Hospital das Clínicas* at the UFPE, through a partnership with the Pro-Parkinson Extension Project: Phonoaudiology, linked to the Pro-Parkinson's Program. The Program is multidisciplinary and assists patients with PD who come to the hospital for routine medical follow up procedures.

Patients with clinical diagnosis of idiopathic PD were recruited and certified by the neurologist of the Pro-Parkinson's Program, totaling 20 patients. The subjects of the control group, without PD, were recruited from the Nucleus of Attention to

the Elderly (NAI) of the UFPE, through a partnership with the Extension Project Health of the Elderly: An Interdisciplinary Proposal. The patients' companions, friends and family were also invited, totaling 12 subjects.

The research study excluded, from both the PD and control groups, those who presented craniofacial abnormalities, or lesions in phonoarticulatory organs; complaints with swallowing; associated neurological diseases; decompensated systemic diseases; total absence of dental elements, without the use of dental prosthesis; badly adapted prostheses; reduced cognitive level (identified through the Mini Mental State Examination (MMSE))⁽¹⁶⁾; use of alternative feeding and eminent risks of bronco-aspiration, demonstrating weak and ineffective cough.

In the group with PD, exclusively, we excluded those who after being classified with the disease, were found to be in stages 4 and 5 – according to the original version of the Hoehn & Yahr (HY)⁽¹⁷⁾ scale – and who did not use Levodopa.

Both groups were found to have a similar age average and a higher number of male subjects was found in both groups (Table 1).

Table 1. Characterization of the sample

Group	n	Age (years)	Gender (M/F)
PD	20	60.5±10,5	15/5
Control	12	58.2±9,7	8/4
Total	32	59.6±10,1	23/9

Note: PD = Parkinson's Disease; M/F = male/female

For data collection the research study was divided into two phases: in the first, the patients with PD received a confirmation of their clinical diagnosis, of the stage of the disease (HY), and they responded to the questions of a data registration form, where legibility criteria, time of the disease, time of medication use, and the daily dose of Levodopa were recorded (Table 2). Then, a convenient day for the patient's return to the services was scheduled for the second phase: the application of the sEMG.

Table 2. Characteristics of the group with Parkinson's Disease

HY	n	Time of disease (years)	Time of medication (years)	Levodopa (mg/day)
Phase 1	4	3±1.7	3±1.7	500±216
Phase 2	8	5±3.1	4±3.4	525±205
Phase 3	8	6±3.9	5±3.8	640±217
Total	20	5±3.3	4±3.3	566±211

Note: HY = Hoehn&Yahr

On the day of the sEMG examination, the patient arrived at the Service in the *off* period, that is, without having used Levodopa for a minimum of 12 hours, according to previous orientation – however, having with them their medication. After

carrying out test 1, in the *off* period, the patient took his/her medication and waited for an hour to carry out test 2, in the *on* period (Chart 1)

For the sEMG examination, volumes of 3 ml and 10 ml were used for the liquid (water) and pasty (yogurt) consistencies. The patient was asked to swallow each volume, in each consistency, five times. This protocol was carried out in the group with PD before and after medication, *off* and *on* periods, respectively. In the control group, no differences were observed in the values between test 2 and test 1 ($p > 0.05$, paired t-test and test of Wilcoxon). For this reason, only the values of test 1 were used (Chart 1).

All values were measured with syringe. The yogurt was placed with syringe directly into the patient's mouth. The water the patient raised to his/her mouth using a disposable cup. The patient maintained the volume in the mouth and waited until hearing the command to swallow, transmitted after 2 seconds. Each volume offered was recorded during a maximum time of 10 seconds.

To record this, disposable sticker electrodes (Meditrace® 200), placed in the supra-hyoid region were used. Before placement of the electrodes, the skin was cleaned with gauze using 70° alcohol and slightly rubbed with Nuprep (skin prep gel). The ground electrode was placed over the right clavicle.

The two electrodes of Channel 1 of the electromyograph were placed between the chin and the hyoid bone, one in each side. The center of an electrode was separated 2 cm from the center of the other electrode⁽¹⁶⁾. The signal captured by the electrodes was amplified 2000 times, filtered (high pass filter 20 Hz, low pass filter 500 Hz) and digitized (8 KHz, 2 KHz per channel) by a four channel surface electromyograph of the EMG System of Brasil®, model EMG 400c.

The swallowing was considered to begin when the activity of the sEMG increased clearly, above the previous base activity. The end of swallowing was marked when sEMG activity returned to the base activity levels. The difference between the beginning and the end of swallowing determined the duration of sEMG activity, during swallowing.

The recordings were saved as text files (txt) so that they could be read by the sEMG Bioanalyzer^{BR} (version 1.0), that carried out the data analyses obtained through the sEMGs⁽²⁾ (Figure 1).

The variables studied were the duration and the amplitude (average RMS) of swallowing, which are continuous quantitative variables, the root mean square being the most utilized form to express the electromyographic amplitude. The data was tabulated in Microsoft Excel worksheets and the results presented through mean (\pm) standard deviation. The mean obtained represented the mean of the five single swallowings carried out by each subject (Table 3).

Following the prerequisites, the Shapiro-Wilk and the Kolmogorov-Smirnov tests showed that the “amplitude” variable, contrary to the “duration” variable, did not present normal

Chart 1. Testing times for each subject in the PD and control groups

Test 1			Groups	
Consistency	Volume	Repetitions	PD “off”	Control
Water	3 ml	1		
		2		
		3	X	X
		4		
		5		
	10 ml	1		
		2		
		3	X	X
		4		
		5		
Yogurt	3 ml	1		
		2		
		3	X	X
		4		
		5		
	10 ml	1		
		2		
		3	X	X
		4		
		5		
Intervalo de 1 hora				
Teste 2			PD “on”	
Consistency	Volume	Repetitions		
Water	3 ml	1		
		2		
		3		X
		4		
		5		
	10 ml	1		
		2		
		3		X
		4		
		5		
Yogurt	3 ml	1		
		2		
		3		X
		4		
		5		
	10 ml	1		
		2		
		3		X
		4		
		5		

distribution. Thus, the comparison of the amplitude between the group with PD and the control group was carried out through the Mann-Whitney U test, and that between the groups PD (*off*) and PD (*on*) through the Wilcoxon test.

The comparison of the “swallowing duration” variable

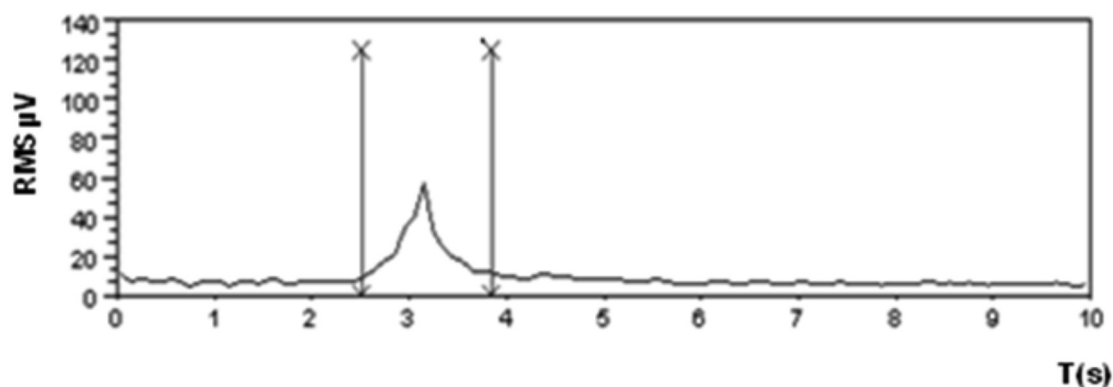


Figure 1. Illustrative electromyogram showing how the markings of the swallowings were carried out

Table 3. Number of single swallowings during electromyographic recording

Consistency	Volume (ml)	Control Mean (\pm)	PD (<i>off</i>) Mean (\pm)	PD (<i>on</i>) Mean (\pm)
Water	3	4.8 (0.5)	3.6 (1.7)	4.2 (1.8)
	10	4.9 (0.3)	2.7 (2.5)	3.3 (2.4)
Yogurt	3	4.8 (0.6)	2.2 (2.5)	3.7 (2.2)
	10	4.8 (0.6)	2,7 (2.5)	3.0 (2.4)

Note: PD = Parkinson's Disease

between the group with PD and the control group was carried out through the independent T-test, and that between the groups PD (*off*) and PD (*on*) through the paired T-test. The study considered $p < 0.05$ as the statistical significant level, the data being analyzed through the statistical program Statistical Package for the Social Sciences TM, version 19.0 (SPSS).

RESULTS

In the group with PD, the time of the disease, time of medication use and the daily dosage of Levodopa, presented increasing values at greater phases of development of the disease, this being verified through the HY scale (Table 2).

To analyze the results obtained with the sEMG, the study merely considered the amplitudes and durations of single swallowings, for all volumes and consistencies. Greater means were observed in the control group than in the group with PD, which had less single swallowings, mainly in the *off* condition. In the control group, no significant differences were observed ($p > 0.05$) in the amplitude and duration of the sEMGs, between tests 2 and 1 (Table 3).

Amplitudes of the sEMGs

The amplitudes of the sEMGs presented greater means in the control group, when compared to the group with PD (*off*), this difference being significant merely for the liquid consistency (water), in both volumes (3 ml: $p = 0.029$ and 10 ml: 0.036). However, the significance of this difference disappears

after administering Levodopa (group PD, *on*), when an increase in the amplitudes happened with near normalcy values, although still lower than normalcy (Table 4).

Table 4. Values of swallowing amplitude measured through surface electromyography

Consistency	Volume (ml)	Control Mean (\pm)	PD (<i>off</i>) Mean (\pm)	PD (<i>on</i>) Mean (\pm)
Water	3	23 (7)	18 (11)*	21 (11)
	10	23 (7)	17 (5)*	21 (13)
Yogurt	3	26 (9)	21 (9)*	23 (13)
	10	23 (7)	21 (7)*	26 (17)

*Significant values ($p < 0.05$) – Mann-Whitney test

Note: PD = Parkinson's Disease

Duration of the sEMGs

The duration analyses of the sEMGs showed that subjects with PD (*off*) took longer to swallow than subjects of the control group, and that this difference was greater for the smaller volumes. The duration of swallowing 3 ml of yogurt ($p = 0.038$) was significant, and the duration of swallowing 3 ml of water ($p = 0.055$) presented a strong tendency to be significant.

After administering Levodopa, the PD (*on*) group presented a reduction in the time of duration of swallowing of all volumes and consistencies. In spite of the fact that these values continued being greater than the values of the control group, this difference was not significant, indicating approximation of the "duration" variable to the normalcy values after medication (Table 5).

DISCUSSION

The amplitude from the sEMGs of the subjects of the control group was greater than that of the patients with PD (*off*), indicating negative influence of the disease over the amplitude of the suprahyoid musculature. However, the amplitude is one of the only components that have direct relation with the clinical symptoms (muscular weakness) in neurogenic lesions⁽¹⁸⁾.

Table 5. Values of swallowing duration measured through surface electromyography

Consistency	Volume (ml)	Control Mean (\pm)	PD (<i>off</i>) Mean (\pm)	PD (<i>on</i>) Mean (\pm)
Water	3	1.6 (0.2)	1.9 (0.5)**	1.8 (0.3)
	10	1.7 (0.2)	1.9 (0.6)	1.8 (0.4)
Yogurt	3	1.8 (0.3)	2.2 (0.6)*	2.0 (0.4)
	10	1.9 (0.3)	2.0 (0.6)*	2.0 (0.5)

* $p < 0.05$ (Independent t-test); ** $p < 0.055$ (Independent t-test)

Note: PD = Parkinson's Disease

The difference between the amplitude from subjects of the control group and subjects with PD (*off*) was only significant for the water consistency, which probably happened due to a lower sensorial input generated by a thinner and tasteless bolus, because the reduction of the sensorial stimuli as a consequence of the PD is one of the factors that is strongly related to oral dysphasia⁽⁸⁾.

Thinner boluses do not generate resistance to the flux, which can reduce the necessity of oral manipulation, causing spilling in the posterior portion of the mouth and, possibly, in the pharynx – and this could be caused by the difficulty in coordinating movements, slowness and weakness of oral musculature⁽¹⁹⁾.

In the majority of individuals with dysphasia, the aspiration of fine liquids are more probable. Thus, the thicker consistencies produce safer swallowing for patients with PD^(19,20).

The high density of mechanical or chemical receptors implicates the tongue as the main sensorial region to determine the size of the bolus. This type of sensation in the tongue and on other tissues around the entrance of the pharynx, can originate an important fast peripheral feedback mechanism that affects the central motor program of swallowing in the brainstem⁽²¹⁾.

After using Levodopa, the group of patients with PD, in the *on* phase, presented an increase in the amplitudes of sEMGs, in relation to the *off* phase. This increase in amplitude made it so that the difference between the control group and the group with PD was no longer significant – which can indicate influence of mediation on the approximation of the amplitude to the normal values of patients with PD. This finding is consistent with other studies^(1,7) that did not find a significant difference between amplitude of subjects with and without PD – evaluated merely on the *on* phase – in none of the consistencies and volumes studied.

In spite of representing very important information, the amplitude of sEMGs is a variable that is very influenced by factors such as biological variations, skin-electrode impedance, location of recording electrode in relation to anatomical structure, distance of the muscle from the skin surface, variation of muscle size between the subjects and temperature⁽⁴⁾. Due to this, the parameter “amplitude” is little discussed in the literature, which hampers comparing results.

When we consider the duration of the EMGs, we verify that the time activation of the supra-hyoid musculature during

swallowing is also affected by PD. However, it seems to be more prolonged in lower volumes, because the duration of swallowing of patients with PD (*off*) was significantly greater than that of the group of subjects without PD in the swallowing of 3 ml of yogurt, and tended to be significant for 3 ml of water. This can indicate greater sensibility to the lower volumes – in detecting alterations in the duration of swallowing – since the great majority of subjects, both of the control and the PD groups, reported that the volume of 10 ml was easier to swallow than that of 3 ml.

The prolongation in the swallowing of patients with PD could be explained by the inadequate planning of the voluntary activity of swallowing, in relation to malfunctions of the cortical-subcortical circuits which connect the nodes of the base to the supplementary motor areas and to the pre-motor area of the frontal cortex⁽²²⁾.

After using Levodopa, the differences between the duration of the sEMGs of patients with PD (*on*) and the group of subjects without PD, stopped existing, because the group with PD presented reduction in the duration of the sEMGs, therefore becoming more proximate to the normal values.

This finding contradicts other studies^(1,7,8,23), where the duration of the swallowing of patients with PD, in the *on* phase, was significantly superior to that of the subjects without PD, for all tested volumes and consistencies. However, one of the studies⁽¹⁾ used larger volumes (10 and 20 ml of water and 5 and 10 ml of yogurt), while other researchers^(7,8) evaluated only the swallowing of 3 ml of water, and another merely 2 ml of water⁽²³⁾.

The differences of results among the studies that used the sEMGs could have happened due to the different methodologies applied. Contrary to the other authors, and with the objective of reducing variability, the present study did not consider the amplitude and duration of one single swallowing, but rather the mean of five swallowings for each patient.

As differences were not observed in the control group, in the amplitude and duration of the EMGs, between tests 1 and 2, we believe that the difference found in the group with PD was due to the intervention and not to the variability of the portion.

The dopaminergic mechanism can also play a role in the oropharyngeal control of swallowing, corroborating in this sense with the present study, which showed changes in the amplitudes and durations of the sEMGs of patients with PD, after the use of Levodopa, that is, in the *on* phase – possibly indicating the positive influence of the drug over the variables studied, becoming more proximate to the values of the group of subjects without PD⁽²⁴⁾.

Studies that have investigated the swallowing of patients with PD through sEMGs are scarce, and those which have dealt with the effects of Levodopa on the swallowing of these patients are even more rare. Among the few that have been carried out, there are controversies regarding the real effect of medication and most of them used videofluoroscopy as the evaluating

instrument⁽²⁴⁻²⁸⁾, with the exception of one study⁽²⁸⁾ which used nasoendoscopy to evaluate swallowing and the EMGs merely to verify breathing coordination.

It is important to consider the electrophysiological methods as complementary tests to the videofluoroscopy for the monitoring and study of swallowing⁽²³⁾, the EMGs being a sensitive method to monitor swallowing and its disorders.

This study presented as limitations the non-adequate pairing of the sample, due to difficulties in recruiting subjects for the control group. However, both groups presented a greater number of male subjects. The presence of swallowing in parts (*piecemeal deglutition*), in the subjects with PD, mainly in the *off* phase, caused the exclusion of data of many swallowings, since we could only compare single swallowings.

CONCLUSION

In spite of the limitations presented, we can assert that the electromyograms of the group of muscles of the supra-hyoid region, in the subjects with Parkinson's Disease, suffered alterations after administering Levodopa, which seemed to have influenced the amplitude of the swallowing of finer liquids and the swallowing duration of smaller volumes, approximating the variables to normalcy values.

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