Voice Quality and Orofacial Strength as Outcome of Levodopa Effectiveness in Patients with Early Idiopathic Parkinson Disease: A Preliminary Report

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Summary: Introduction. Sixty to 90% of patients with idiopathic Parkinson disease (IPD) developed early dysphonia and subtle speech impairment, which is usually related to orofacial muscular dysfunctions. The aim of this preliminary study is to assess the usefulness of voice quality and orofacial strength (involved in speech) as outcome of levodopa challenge test used for the IPD diagnosis.

Material and Methods. A total of 20 patients with early IPD were recruited and evaluated for clinical findings (Hoehn and Yahr scale), voice handicap index, maximal phonation time, phonation quotient, percent jitter, percent shimmer, noise-to-harmonic ratio, and orofacial muscular strength (Iowa Oral Performance Instrument) at baseline, throughout the levodopa challenge test and after therapeutic stabilization.

Results. The intake of a standardized dose of levodopa (levodopa challenge test) significantly improved phonation quotient and percent shimmer. We did not find similar improvement after medical stabilization of patients (based on levodopa medication) despite an improvement of Hoehn and Yahr mean score. The intake of levodopa significantly improved cheeks and lips strength involved in speech quality both along the challenge test and after the therapeutic stabilization.

Conclusions. These preliminary findings support a differential impact of levodopa on voice and speech functions in early diagnosed IPD and a mismatch between the clinical examination, orofacial strength, and voice quality improvements once the patient is medically stabilized.

Key Words: Parkinson−Voice−Speech−IOPI−Acoustic.

INTRODUCTION

Idiopathic Parkinson Disease (IPD) is a neurodegenerative disorder characterized by the development of subtle voice and speech impairments at the time of diagnosis in 60%−90% of cases.[1,2] The IPD diagnosis is mainly based on the clinical examination and, in many cases, the realization of a levodopa challenge test, which consists of the administration of a standardized dose of levodopa and the objectification of clinical improvements. IPD is first confirmed in patients who respond well to levodopa, whereas nonresponders or doubtful diagnoses can usually benefit from additional examinations. Once the diagnosis has been confirmed, an appropriate treatment (based on low doses of levodopa ± other drugs) is prescribed to stabilize the clinical state of patients. The clinical improvement evaluation throughout the levodopa challenge test is usually made by the neurologist and, depending on the experience of the physician, it still remains subjective. For this reason, since many decades, some studies are interested to the identification of objective tools able to precisely assess the impact of levodopa on the clinical state. Among these objective tools, some authors proposed voice quality[3−6] and speech[7] but they reported mixed results on little cohorts.[8] Indeed, as reported in a recent review,[8] levodopa could subtly improve voice quality along the levodopa challenge test[8] with improvements of maximal phonation time (MPT),[9,10] phonation quotient (PQ),[10] and some acoustic measurements.[3,4,7,11] Concerning the latter, the results are particularly controversial as the most usefulness acoustic parameters are not yet identified.[8] The aims of this preliminary research are to study the evolution of orofacial strength (involved in speech) and voice quality throughout levodopa challenge test; and to assess the midterm evolution of voice and orofacial strength once the patient is considered as clinically stabilized.

MATERIAL AND METHODS

From January 2014 to February 2017, we prospectively recruited 20 patients with early IPD at Neurology Departments of Epicura Hospitals (approved protocol by ethics committee: ref.A2014/001). First, patients were examined by an experienced otolaryngologist to exclude comorbidities impacting voice and speech qualities. Patients with comorbidities exhibited in Table 1 were excluded. All included subjects received a standardized dose of levodopa (375 mg) during the hospitalization to perform clinical, orofacial strength, and voice measurements and, once the diagnosis is confirmed, they were treated by conventional medical treatment of IPD (Figure 1).

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Conflict of interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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TABLE 1.
Exclusion Criteria

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Psychiatric illness
Upper respiratory tract infections (last month)
Significant cervical surgery
Chest or head and neck radiotherapy
Significant laryngeal trauma
Vocal cord paralysis/paresis
Seasonal allergies
Asthma, treated asthma (corticosteroid inhalation)
Benign vocal fold lesions
Pharyngolaryngeal malignancy
Chronic obstructive pulmonary disease (Gold II to IV)
Levodopa hypersensitivity
Chemical exposure causing laryngitis
Untreated thyroid disease
Prior antireflux surgery
Chemical exposure causing laryngitis
Chronic laryngitis due to systemic disease
Other neurological disease
Active smokers & alcoholics

Notes: Exclusion criteria applied in this study.

Clinical, orofacial strength, and voice evaluations

Patients were assessed at baseline (t0), at 45 minutes after the levodopa intake (t1), and once clinically stabilized (3−9 months postdiagnosis [t2]). The clinical stabilization was assessed by the neurologist with Hoehn and Yahr scale, which is a validated grading system for the description of the Parkinson disease symptoms. At these three times, we evaluated:

1. The muscular strength of tongue, lips, and cheeks with Iowa Oral Performance Instrument (IOPI) (IOPI Medical, Redmond, WA). Evaluations were made by the same physician (JRL),
2. The subjective voice quality: Voice Handicap Index (VHI) (only at t0 and t2), and grade, roughness, breathiness, asthenia, strain (GRBAS) (blinded assessment by an experienced speech therapist). To validate the perceptual evaluations, the speech therapist performed the evaluations respecting a test retest procedure that exhibited good intrarater reliability (Spearman correlation coefficient >0.600 for all GRBAS items).
3. The objective voice quality including PQ, MPT, and acoustic measurements (ie, percent jitter, percent shimmer [Shim], and noise-to-harmonic ratio). To calculate PQ, we measured vital capacity with a calibrated spirometer (Spiro-USB100; Medical Electronic Construction, Brussels, Belgium) and MPT was measured with a high-quality microphone (Sony PCM-D50; New York, NY). To measure the acoustic parameters, patients were instructed to produce the vowel /a/ three times (MPT), in a sound-treated room with a high-quality microphone placed at a distance of 30 cm from the patient's mouth. As described in a previous publication,[12] the measurement of the acoustic cues was made on the entire signal of the three vowels (MDVP, KayPentax, Lincoln Park, NJ).

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences for Windows (SPSS version 22.0; IBM Corp., Armonk, NY). According to the distribution of data, the comparison of the mean values of orofacial strength, aerodynamic and acoustic measurements along the clinical course (t0−t2) was made with the Wilcoxon signed-rank test. A level of significance of 0.05 was adopted.

RESULTS

Prospectively, the mean values of Hoehn and Yahr scale at baseline (2.75 ± 0.87) significantly decreased after therapeutic stabilization (0.83 ± 0.72; $Z = -3.36$; $P = 0.001$). Seven, seven, and six patients had axial disease, had left lateralization, and had right lateralization, respectively. IOPI measurements reported a significant improvement of cheeks and lips muscular strength from t0 to t1 and from t0 to t2 (all values increased). The scores of VHI components did not significantly decrease after therapeutic stabilization (Table 2 and Figure 2). We did not find significant perceptual voice quality improvement (GRBAS) between t0 and t1, and t0 and t2. Regarding the objective voice quality assessment, we found significant reductions of PQ and Shim from t0 to t1 (Table 2). Overall, IPD patients did not improve subjective and objective voice qualities from t0 to t2 (Table 2).

DISCUSSION

It has been demonstrated by some controlled studies that IPD patients have more subjective and objective voice disorders from the very beginning of the disease.[8,13,14] Over the years, these subtle voice changes may lead to dysphonia and impaired quality of life,[14,15] and can be associated with speech disorders that usually develop later in the natural history of the disease.[16,17] In this preliminary study, we found that the intake of a standardized dose of levodopa significantly improved PQ and shimmer; both indirectly related with airflow management. Indeed, IPD is known to be associated with impaired chest muscle control leading to alterations of aerodynamic and acoustic measurements.[18,19] From a pathophysiological standpoint, the lack of laryngeal and chest muscle control could induce irregular laryngeal airflow rate that has repercussions on the vibratory process of the vocal folds. Some studies found similar findings regarding PQ,[10] or Shim[5−7] although others did not find significant improvement of shimmer along the levodopa challenge test[6,20] or identified other useful acoustic parameters.[6,7,21] These controversial results can be mainly due to the heterogeneity of the clinical patient profiles included in these studies and the variability of the methods used to measure acoustic parameters.[8]

Surprisingly, all subjective (VHI and GRBAS) and objective assessments did not improve from baseline to the therapeutic stabilization time, whereas the clinical state is stabilized. At this time, we observed a mismatch between clinical, orofacial

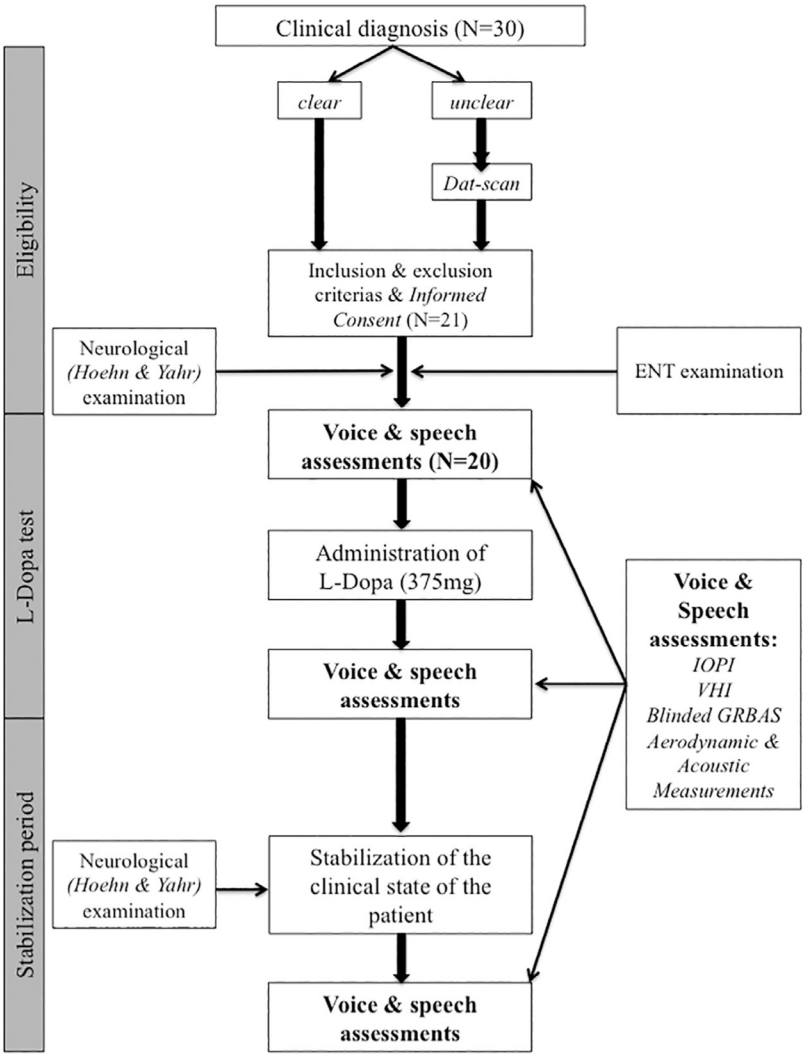

FIGURE 1. Flowchart describing the algorithm for assessment and management of patients. Thirty patients were initially recruited and 21 met the inclusion and exclusion criteria. One patient did not complete the study. After the levodopa test, patients were treated by levodopa ± rasagiline ± artane ± pramipexole ± selegiline ± entacapone.

strength, and voice quality improvements. As already explained, the improvements of PQ and shimmer with a standardized dose of levodopa support the occurrence of an airflow disorder (including laryngeal and chest muscles), and the lack of improvement once the treatment is stabilized (with lower levodopa dose) may support a dose-effect of levodopa on voice quality.

According to the evaluation of strength of orofacial muscles involved in speech quality, the utilization of IOPI in clinical practice provides objective and helpfulness measurements to evaluate the levodopa effect in the diagnosis procedure. We found better results with the smooth musculature (cheeks and lips) than the tongue musculature that did not significantly improved. Only a small number of studies previously used IOPI as speech quality tool in the management of dysarthria[17,22] but, to our knowledge, no previous trial has used it in the management and the diagnosis of IPD. In practice, we realized that this preliminary experience substantially helped our neurologist to make the IPD diagnosis, especially in cases with unusual IPD presentation. Indeed, beyond the neurological examination and the walking test, IOPI provides objective evaluations of muscular strength along the levodopa challenge test.

In summary, these preliminary findings support a differential impact of levodopa on voice and speech functions in early diagnosed IPD and a mismatch between the clinical, speech, and voice quality improvements once the patient is medically stabilized. In the future, it could be interesting to conduct both videolaryngostroboscopic and electrophysiological examinations to study both the vibratory process of the vocal folds and muscular impairments along the levodopa challenge test. The continuation of this study, the inclusion of a controlled group (with healthy subjects receiving levodopa), and the exhaustive analyses of our voice and speech recordings (ie, singing voice, balanced phonetic text, glides, samples with prosody variations, speech rate, and the assessment of subglottal pressure) is under way and could respond to many unresolved questions about the occurrence of voice and speech disorders in the development of IPD and its utilization in the diagnosis procedure based on levodopa challenge test.

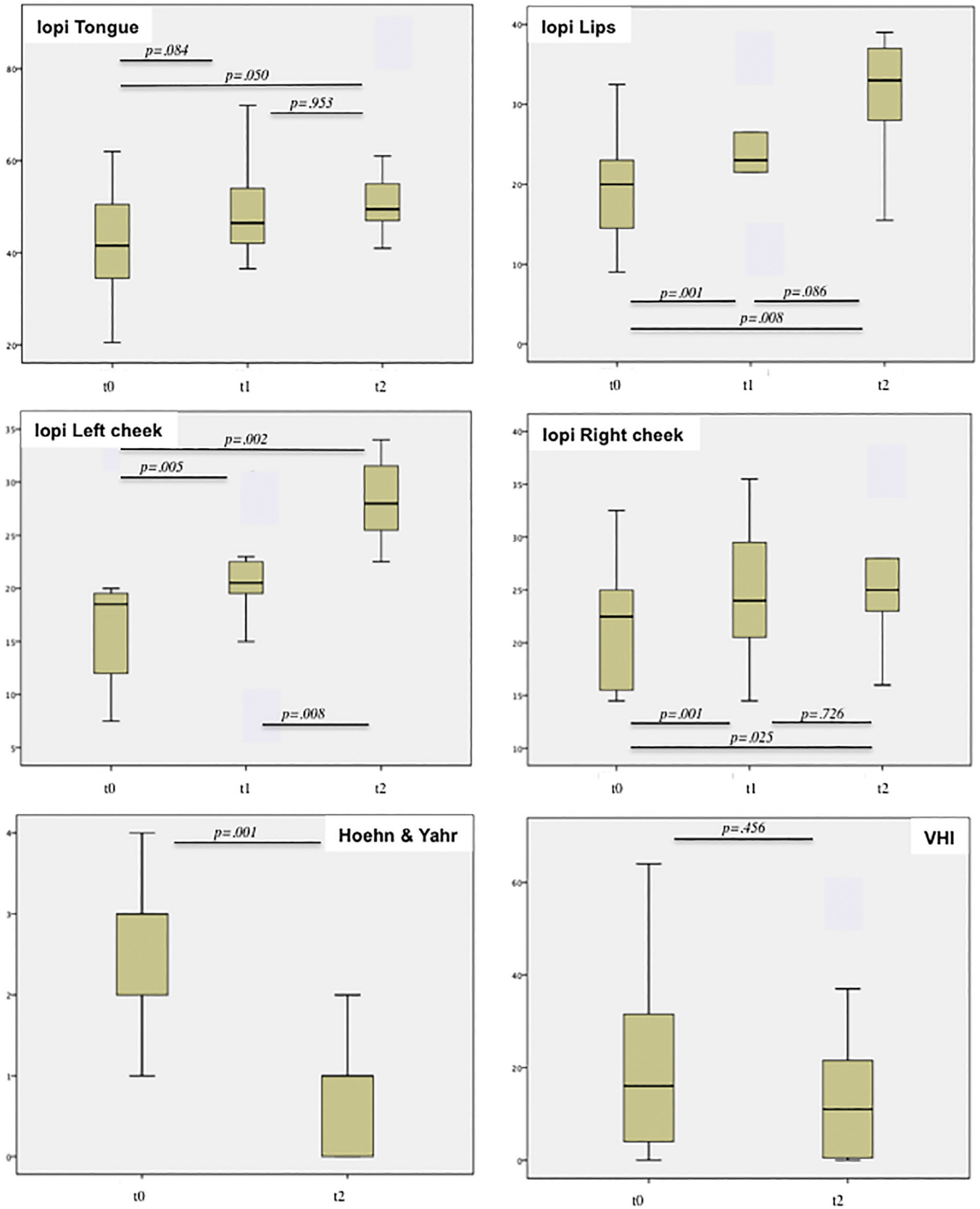

FIGURE 2. Improvement of Hoehn and Yahr, VHI scores, and orofacial muscular strength measurements along the levodopa test (t0, t1) and after the stabilization of treatment (t2). Statistical analyses were performed using Wilcoxon rank tests.

TABLE 2.
Evolution of Voice Quality Along the Levodopa Challenge Test (t0, t1) and After the Stabilization of Treatment (t2)

		Parkinson Patients (N = 20)				
	Units	Mean ± SD	Mean ± SD	Mean ± SD	*P* value	*P* value
Voice Handicap Index		t0	t1	t2	t0 vs. t1	t0 vs. t2
VHI tot	—	19.33 ± 19.60	—	17.42 ± 18.20	—	NS
VHIf	—	5.67 ± 6.14	—	4.42 ± 5.60	—	NS
VHIe	—	7.71 ± 7.56	—	6.83 ± 7.88	—	NS
VHIp	—	6.95 ± 7.41	—	6.17 ± 5.75	—	NS
Perceptual evaluation						
Grade	—	0.85 ± 0.67	0.70 ± 0.66	0.22 ± 0.44	NS	NS
Roughness	—	0.80 ± 0.62	0.65 ± 0.59	0.22 ± 0.44	NS	NS
Breathiness	—	1,15 ± 0.59	1.05 ± 0.69	1.11 ± 0.60	NS	NS
Asthenia	—	0.85 ± 0.50	0.90 ± 0.45	1.00 ± 0.50	NS	NS
Strain	—	0.05 ± 0.22	0.00 ± 0.00	0.00 ± 0.00	NS	NS
Acoustic parameters						
MF0	*Hz*	134.5 ± 35.9	140.4 ± 26.2	1.20 ± 0.77	NS	NS
Jitt	*%*	1.37 ± 1.30	0.94 ± 0.83	1.20 ± 0.77	NS	NS
Shim	*%*	5.77 ± 2.92	4.51 ± 1.83	5.52 ± 2.10	0.033	NS
NHR	—	0.15 ± 0.04	0.13 ± 0.03	0.15 ± 0.01	NS	NS
Aerodynamic						
Maximum phonation time	*s*	13.74 ± 5.23	14.83 ± 6.14	14.36 ± 5.94	NS	NS
Phonatory quotient	*ml/s*	225.7 ± 100.5	194.8 ± 72.1	207.6 ± 129.2	0.030	NS

Abbreviations: Jitt, Jitter percent; NS, non significant; SD, standard deviation; VHIf/e/p, Voice handicap index functional, emotional, physical.

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