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Dysphagia

Esophageal Manometric Abnormalities in Parkinson's Disease

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Abstract. The gastrointestinal tract, and especially the esophagus, is frequently involved in neurological diseases; however, objective studies of gut motor function are few. We carried out an esophageal manometric study in 18 patients with various stages of Parkinson's disease (4 stage I, 4 stage II, 7 stage III, and 3 stage IV) to evaluate the function of the viscus in this disease. Clinical assessment showed that 61% complained of esophageal symptoms such as dysphagia, acid regurgitation, pyrosis, and noncardiac chest pain. Manometric abnormalities were documented also in 61% patients, and were represented by repetitive contractions, simultaneous contractions, reduced LES pressure, and high-amplitude contractions. However, only 33.3% of patients had both symptoms and manometric abnormalities. We conclude that esophageal motor abnormalities are frequent in Parkinson's disease, and may appear at an early stage of the disease.

Key words: Esophagus — Manometry — Motility — Parkinson's disease — Deglutition — Deglutition disorders.

Dysphagia is a well-recognized manifestation of Parkinson's disease (PD) [1,2] and it is associated with increased morbidity from nutritional and pulmonary complications [3,4]. Although in the majority of these patients dysphagia is related to oral-pharyngeal dysfunction [5,6], there is some evidence that the esophageal body may also be involved [7]. Thus, the pathophysiological grounds of dysphagia in PD have still not been characterized [8]. The aim of the present study was to investigate esophageal function in patients with PD of different clinical severity from both a clinical and manometric point of view.

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Patients and Methods

Eighteen PD patients (10 men, 8 women, aged 57–86 yr, average 73 ± 2 [SEM] yr) entered the study. Severity of the disease was determined by the Hoehn and Yahr scale [9]. All subjects were given a previously validated questionnaire focused on the prevalence and severity of symptoms suggestive of esophageal disorders [10]. Patients taking antiparkinson medications withheld them on the day of manometric testing.

Esophageal motility was carried out by a previously described technique [11,12]. Briefly, an 8-lumen standard PVC manometric catheter, with the distal four side holes arranged radially at the same level and the proximal each 5 cm apart (Arndorfer Medical Specialties, Greensdale, WI, type ESM-3R, external diameter 4.5 mm, internal diameter for each lumen 0.8 mm) was used. Each channel was connected to external pressure transducers (Bell & Howell, Pasadena, CA, 4-327-I) and constantly perfused with bubble-free distilled water at 0.5 ml/min by a low-compliance pneumohydraulic system (Arndorfer). At this perfusion rate, the system yields a pressure rise to distal occlusion of more than 300 mmHg/sec. Intraluminal pressures were displayed on a multichanner recorder (SensorMedics R-611 SensorMedics Italia, Milan, Italy) at a paper speed of 1 mm/sec for the lower esophageal sphincter (LES) and 2.5 mm/sec for the esophageal body.

After an overnight fast, the well-lubricated probe was introduced through the nose into the stomach, and then slowly withdrawn in 1-cm increments by station pull-through, to measure resting LES pressure and relaxations with the four radially oriented side holes. Thereafter, the catheter was positioned with its distal recording site 3 cm above the LES, and 10 or more wet swallows (with 5 ml water boluses) were administered every 30 sec to assess peristaltic activity with the three proximal recording ports at 3, 8, and 13 cm above the LES.

Data Analysis

Manometric tracings were analyzed according to previously published criteria [13], taking into account the following variables: (1) LES pres-

sure, recorded in mmHg as an average of four individual pressures, was measured at midexpiration, with mean gastric pressure taken as baseline. Average values less than 10 mmHg were regarded as an abnormally low LES pressure. Relaxations were considered complete if LES pressure fell at least 80% [14]; (2) Wave amplitude, in mmHg, was calculated from the mean intraesophageal baseline pressure to the peak of the wave. A measurable contraction wave was considered at least 10 mmHg in amplitude to differentiate it from potential respiratory artifacts [15].

Contraction abnormalities were defined when a wet swallow was followed by repetitive (three or more peaks with the third peak being at least 10 mmHg in amplitude and at least 1 sec apart from the first) [16,17], nonperistaltic (simultaneous onset of contractions at two or more recording sites) [18,19], and high-amplitude (average >180 mmHg, i.e., >2 SD from the normal upper limit from our laboratory, in the distal recording site) contractions. Spontaneous contractions were also recorded.

Control Group

Thirty six age- (± 5 yr) and sex-matched subjects (2 for each patient) underwent manometric testing as above, and served as control group. None was taking drugs influencing esophageal function, nor had undergone any previously esophageal or abdominal surgery, except appendectomy.

Statistical Analysis

The Student's *t*-test for unpaired data was adopted to compare manometric results. Values of $p < 0.05$ were chosen for rejection of the null hypothesis. Data are expressed as means ± SEM.

Ethical Considerations

After a careful explanation about the aims of the investigation, both patients and controls gave their informed consent, and the study was carried out in accordance with the recommendations of the Declaration of Helsinki.

Results (Table 1)

Clinical Stage

The group included 4 stage I PD (without therapy), 4 stage II, 7 stage III, and 3 stage IV patients. The 14 patients with PD stage II-IV were on dopaminergic drugs (levodopa/carbidopa).

Symptom Assessment

Overall, 11/18 (61%) patients complained of esophageal symptoms. Dysphagia for both solid and liquid foods was present in 7/18 (39%) patients. In 3 of these patients (nos. 13, 15, and 17, see Table 1) the dysphagia was probably related to oral-pharyngeal dysfunction, since they reported two or more of the following [20]: a sense of bolus holdup localized to the cervical region, multiple swallows to clear the bolus from the pharynx, difficulty with swallow initiation, postnasal regurgitation, or coughing or choking during swallowing to suggest aspiration. Acid regurgitation was complained of by 7/18 (39%) patients, pyrosis by 4/18 (22.2%) patients, and noncardiac chest pain by 1/18 (5.5%) patients. Association of two or more of the above symptoms was found in 5 (28%) patients. Controls did not complain of any esophageal symptoms.

Table 1. Clinical variables and manometric abnormalities in 18 patients with Parkinson's disease

No.	Stage	Symptoms	Abnormalities
1	I	D	—
2	I	—	—
3	I	CP,P	HAC
4	I	AR	R
5	II	AR,D,P	R,RL,S
6	II	AR,D	RL
7	II	—	S
8	II	—	R
9	III	—	—
10	III	AR	—
11	III	AR	—
12	III	—	—
13	III	D	—
14	III	—	RL
15	III	AR,D,P	RL
16	IV	AR,D,P	RL
17	IV	D	R,S
18	IV	—	R

Abbreviations: AR = acid regurgitations; CP = chest pain; D = dysphagia; HAC = high-amplitude contractions; P = pyrosis; R = repetitive contractions; RL = reduced LES pressure; S = simultaneous contractions.

Manometry

As shown in Table 2 with respect to LES pressure and contractions amplitude, PD patients and controls displayed no significantly different overall manometric values. However, manometric abnormalities of the esophageal body were documented in 11/18 (61%) patients (Table 1), and were represented by repetitive contractions (28%), simultaneous contractions (17%), reduced LES pressure (28%), and high-amplitude contractions (5.5%). No contraction abnormalities were found in controls.

Discussion

Gastrointestinal disorders are frequently encountered in PD; of these, motility abnormalities evoke the most frequent clinical complaints [21]. The esophagus is commonly involved, and dysphagia was first clinically de-

Table 2. Manometric variables[a] in patients with Parkinson's disease[b]

	PD	Controls
LESP	19 ± 2.3	19.5 ± 3.7
body D	98 ± 10	110 ± 11
body M	87 ± 9	90 ± 10
body P	53.5 ± 8	52.5 ± 7

Abbreviations: LESP = LES pressure; D = distal; M = median; P = proximal.
[a]means ± SEM.
[b]n = 18 and controls n = 36.

scribed in PD by James Parkinson himself [22]. However, the pathophysiology of dysphagia in PD is still controversial; in fact, early radiological investigations described segmental esophageal spasm [23], defective tongue movements [24], or cricopharyngeal achalasia [25]. Other studies reported a frequency of swallowing abnormalities in 50% of PD patients [1], although this has been not confirmed in a recent videoesophagographic study [26]. Direct measurements of esophageal motility through manometric techniques suggest that motor abnormalities may be frequent in PD [27,28], as in the present study. In the study of Weber et al. [27] esophageal alterations were more frequent in patients with stage III-IV in the Hoehn and Yahr scale. However, the present study suggests that the esophagus may be involved early in PD.

Many factors, including altered neuromuscular junction function [29], degeneration of the dorsal motor nucleus of the vagus [30], and peripheral dopamine depletion [31] have been implicated in the pathogenesis of gastrointestinal motor abnormalities in PD [32]. It is worth noting that Lewy bodies, the pathological hallmark of PD in the substantia nigra and locus ceruleus [33], have been identified in the enteric nervous system (especially in the distal one-third of the esophagus) [34,35]. A similarity to achalasia, due to the manometric findings of nonperistaltic contractions and absence of LES relaxations [23], has also been suggested because of the presence of Lewy bodies in the degenerated ganglion cells of the esophageal myenteric plexus in 2 patients with achalasia [36].

Although our PD patients were studied during an off period by withholding their medications on the morning of manometric testing, it is possible that their use in the preceding days may have somewhat influenced the results. Of course, a prolonged period off all dopaminergic agents would have been ideal: however, ethical, safety, and patient compliance considerations made it impractical. Previous studies have demonstrated that the presence of gastrointestinal symptoms in PD correlates with the severity and duration of the disease, not with anti-Parkinson therapy [37]. Experimental animal models suggest that levodopa treatment influences esophageal motility facilitating swallowing [38]; it is therefore possible that esophageal motor abnormalities could have been more severe if patients were off all treatment. If peripheral dopamine depletion is indeed a pathogenetic factor of gastrointestinal abnormalities in PD, dopaminergic agents could have improved esophageal dysfunction [39,40].

In conclusion, we have shown that esophageal symptoms and motor abnormalities may be present in a high percentage of patients with PD. We suggest that esophageal manometry may detect gastrointestinal involvement at a relatively early stage. However, no specific motor pattern for PD was identified, and only in about one-third of cases patients had both symptoms and manometric abnormalities. Unfortunately, the lack of correlation between manometric finding and symptoms is a *leitmotiv* in studies of esophageal motor function. In fact, the manometric study identifies a limited spectrum of esophageal functional abnormalities, but it is not perfectly sensitive or specific for a single disease process [41]. Owing to the fact that dysphagia is also frequent in PD, but its pathogenesis is multifactorial involving cognitive and psychological changes in addition to abnormalities of the extrapyramidal and autonomic nervous system [42], further studies are needed, including on-off drug periods, to better understand the pathophysiology of esophageal symptoms in these patients.

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