Parkinsonism and Related Disorders 20 (2014) 1382–1387

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Swallowing disturbances in Parkinson's disease: A multivariate analysis of contributing factors

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ARTICLE INFO

Article history:
Received 19 June 2014
Received in revised form
18 September 2014
Accepted 29 September 2014

Keywords:
Parkinson's disease
Dysphagia
Swallowing disturbances
Dementia
Disease duration

ABSTRACT

Background: Swallowing disturbances are an important issue in Parkinson's disease (PD) as several studies have shown that they are associated with increased risk of aspiration pneumonia and mortality. Information about factors related to swallowing disturbances, such as disease duration, age at assessment and concomitant dementia, is limited and would be useful for their management.
Methods: All consecutive PD out-patients evaluated at a movement disorders clinic over a 7-year period (2007–2014), were included in the present retrospective study. Presence of symptomatic swallowing disturbances was assessed using the specific item of the Non Motor Symptom Questionnaire.
Results: In the whole PD population ($N = 6462$), prevalence of symptomatic swallowing disturbances was 11.7% (95%CI, 10.9–12.5). Multivariable logistic regression analysis (adjusted for education) disclosed a significant interaction between disease duration and gender ($P = 0.009$). In both gender strata, swallowing disturbances were significantly associated with longer disease duration and dementia ($P < 0.001$ for all). A significant effect for age at assessment was also found in male patients. In non-demented patients, swallowing disturbances were associated with male gender, age and disease duration ($P < 0.02$ for all). In demented patients an association was found only with male gender ($P = 0.018$) and disease duration ($P < 0.001$).
Conclusions: Gender, age, disease duration and dementia all seem to contribute to the occurrence of swallowing disturbances independently. However, the role played by these factors in sub-groups of patients stratified by gender and concomitant dementia suggests that swallowing disturbances are likely related to different neuro-degenerative patterns within the brain. The underlying mechanisms deserve further investigation.

1. Introduction

Dysphagia and, more broadly, swallowing disturbances refer to a clinical condition in which the unsafe and/or impaired swallowing of fluids and/or solid foods may be responsible for negative health outcomes, including impaired quality of life, dehydration, malnutrition, aspiration pneumonia, asphyxiation and death [1,2].

Swallowing disturbances are more likely to have a neurologic basis [2,3] and are currently considered as an important issue in Parkinson's disease (PD) [4,5], as aspiration pneumonia often is the cause of death in this patient population [6]. Accordingly, it is important to have reliable prevalence data and identify risk factors. Previous prevalence studies have reported heterogeneous estimates, which could be primarily explained by the method of assessment [7]. Particularly, these studies have not distinguished between dysphagia and swallowing disturbances in broad sense and the presence of these had been generally evaluated by different and not comparable subjective- or patient-rated measures. Besides, there is a consistent discrepancy in prevalence between the use of

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http://dx.doi.org/10.1016/j.parkreldis.2014.09.031
1353-8020/

subjective and objective methods of assessment (35% vs. 82%) [7]. However, other sources of heterogeneity should be investigated, as several factors could play a role. Most studies have included a limited number of patients and little-to-no attention has been paid to the role of disease duration, age at assessment and concomitant dementia. Interestingly, when focusing on the three largest studies (>400 patients), using subjective methods of assessment, it was observed that the prevalence appeared associated with the stage of PD [7]. Some investigators have described dysphagia as a feature of advanced-stage PD, while others suggest that it may be present even in the early stages [4,8]. Likewise, in the general population swallowing disturbances may simply be associated with aging [1–3], and increasing age is the main risk factor for PD [9]. A thorough knowledge of disease-related factors would enable timely assessment and treatment designed to prevent complications and prolong survival.

With this background of considerations, the aim of the present study was to evaluate the presence of symptomatic swallowing disturbances in a large PD out-patient population, in order to investigate the relative contribution of age at assessment, disease duration and severity, and dementia.

2. Methods

2.1. Data source

We conducted a cross-sectional, retrospective study. We used the Parkinson Institute–Milan (Italy) research database [10], which contains computerized demographic, lifestyle and general medical information, as well as disease-specific records collected on all patients assessed for disease.

Only patients with a confirmed diagnosis of idiopathic PD, based on the UK PD Society Brain Bank criteria, and having at least a one-year follow-up were included in the present study [11]. We excluded all patients with past history of cerebrovascular disease or major vascular abnormalities (confluent white matter hyperintensities or lacunar lesions in the brainstem) revealed by brain MRI. Patients with incomplete data on main study variables were excluded.

Among all the visits recorded in the database, we considered a single record for each patient, taking the latest as the most relevant. Finally, based on the methods used for the assessment of the study outcome [12], we included only patients examined after 2007.

2.2. Ascertainment of study variables

Study outcome. The ascertainment of any-type of swallowing disturbance was performed by direct interviewing [13] using the specific question included in the "Non Motor Symptom Questionnaire (NMSQuest)" [12]. PD patients were initially asked to answer the following question (with the aid of caregivers whenever necessary): "Have you experienced any difficulty in swallowing food or drink or problem with choking?". Although no cross-validation with objective measures has been performed for this tool, its validity and discriminant proprieties as screening tool has been recently reviewed and supported by an *ad-hoc* task force of the Movement Disorders Society [5]. Therefore, symptomatic swallowing abnormalities were confirmed by the use of the specific item of the Unified Parkinson's disease rating scale (score ≥2 on item 7) [14]. Nevertheless, clinical chart of patients reporting swallowing difficulties were reviewed for the presence of instrumental confirmation of any-type swallowing impairment having occurred within 6 months since assessment.

Covariates. Information on the following variables was considered: gender, education, age at onset, disease severity, age and disease duration at assessment and diagnosis of dementia. Disease severity was rated by means of the Hoehn and Yahr (HY) staging system as assessed in "worst-OFF" condition [15]. Finally, dementia diagnosis was based on the criteria reported in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) [16].

2.3. Ethics

The study was performed in agreement with the principles of the Declaration of Helsinki and the local Ethics Committee was notified in compliance with Italian legislation on retrospective studies. For every patient included we retrieved the written informed consent previously signed to allow the use of clinical data for research purposes.

2.4. Statistical analyses

Based on previous data from the Parkinson Institute [17] and estimates in literature [9], reporting a minimum prevalence of subjective swallowing disturbances around 12%–15%, for a two-sided 95% confidence interval with a precision of 1%, we planned to include in the analysis at least 5000 patients.

Estimates for swallowing disturbance prevalence were computed in 6-year age groups (<60, 60–64, 65–69, 70–74, 75–79, ≥80 years) and 5-year disease duration strata (1–4, 5–9, 10–14, 15–19, ≥20 years). Therefore, multivariable logistic regression analysis was used to evaluate the association of swallowing disturbances with age at assessment, gender, disease duration, dementia and disease severity. Particularly, due to skewed distribution of values, age at assessment, disease duration and education were analyzed as categorical variables taking the first one as reference standard (OR = 1). Before inclusion in the models, collinearity among all covariates was assessed by Pearson's statistic. Accordingly, disease severity (HY stage) and duration were not included in the same model due to high collinearity ($r = 0.48$; $P < 0.001$); they were analyzed separately. The same applied to age at assessment and age at onset of PD ($r = 0.82$; $P < 0.001$). Based on consensus between the authors, only the former has been included in the model, being this variable more relevant to the occurrence of swallowing abnormalities. The interaction among independent variables was also investigated.

Finally, to assess the discriminatory accuracy of age at assessment and disease duration in predicting swallowing disturbances, receiver operating characteristics (ROC) curves were constructed and the corresponding areas under the curve were calculated. Therefore, the optimal cut-off points of these two variables were calculated using the ones associated with the highest Youden index (calculated as: sensitivity + specificity − 1), which is a single statistic that captures the performance of a diagnostic test by combining its the true positive rate (sensitivity = ability to identify a condition correctly) and the false positive rate (specificity = ability to exclude a condition correctly).

All statistical analyses were performed using STATA 13 statistical software (StataCorp, College Station, TX, USA). The level of significance was set at a two-tailed *P*-value <0.05.

3. Results

A total of 6503 out-patients with a confirmed clinical diagnosis of PD were assessed at our Institute between 2007 and January 2014; 6462 had complete data and were included.

The general features of the study population are presented in Table 1.

Prevalence of swallowing disturbances was 11.7% (95%CI, 10.9–12.5; $N = 754$) and 13.2% (95%CI, 12.2–14.1; $N = 692$) in the