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### **Original Study**

# Pathophysiology of Oropharyngeal Dysphagia Assessed by Videofluoroscopy in Patients with Dementia Taking Antipsychotics



Marta Miarons MS, BPharm <sup>a,\*</sup>, Pere Clavé MD, PhD <sup>b,c</sup>, Robin Wijngaard BPharm <sup>a</sup>, Omar Ortega PhD <sup>b,c</sup>, Viridiana Arreola SLP, PhD <sup>b</sup>, Weslania Nascimento SLP, PhD <sup>b</sup>, Laia Rofes PhD <sup>c</sup>

- <sup>a</sup> Pharmacy Department, Hospital de Mataró, Mataró, Spain
- <sup>b</sup> Gastrointestinal Physiology Laboratory, Hospital de Mataró, Universitat Autónoma de Barcelona, Mataró, Spain
- <sup>c</sup> CIBERehd, Instituto de Salud Carlos III, Madrid, Spain

#### ABSTRACT

Keywords: Antipsychotics dementia oropharyngeal dysphagia aspiration *Objectives:* The objective of this study was to assess the pathophysiology of oropharyngeal dysphagia (OD) in patients with dementia, specifically in those taking antipsychotics (APs).

*Design:* A cross-sectional study was performed from January 2011 to May 2017 in a general hospital. *Setting and Participants:* We included 114 patients with dementia, of which 39 (34.2%) were taking APs (82.5  $\pm$  7.8 years, Barthel Index 52.28  $\pm$  30.42) and 29 patients without dementia (82.4  $\pm$  6.7 years, Barthel Index 77.71  $\pm$  24.7) and OD confirmed by a videofluoroscopy.

Measures: Demographical and clinical factors as well as swallowing function of patients with dementia with OD were compared with older patients without dementia with OD. We also compared patients with dementia taking and not taking APs. Impaired efficacy during videofluoroscopy was defined as the presence of oral and/or pharyngeal residue, and impaired safety (unsafe swallow) was defined as aspiration or penetration. Receiver operating characteristic curves were drawn for laryngeal vestibule closure (LVC) time to predict unsafe swallow.

Results: 87.7% of patients with dementia presented impaired efficacy of swallow and 74.6% impaired safety [penetration-aspiration scale (PAS)  $3.94 \pm 1.94$ ]. 86.2% of patients without dementia presented impaired efficacy and 44.8% impaired safety (PAS  $2.21 \pm 1.92$ ). Time to LVC was significantly delayed in patients with dementia taking APs in comparison with patients without dementia (LVC  $0.377 \pm 0.093$  vs  $0.305 \pm 0.026$ , P = .003). In contrast, there were no differences in the PAS and LVC time in patients with dementia taking and not taking APs (PAS  $3.96 \pm 0.26$  vs  $3.88 \pm 0.22$ , LVC  $0.398 \pm 0.117$  vs  $0.376 \pm 0.115$ , NS). LVC time  $\geq 0.340$  seconds predicted unsafe swallow in patients with dementia with an accuracy of 0.71.

Conclusions/Implications: Patients with dementia presented high prevalence and severity of video-fluoroscopy signs of impaired efficacy and safety of swallow and a more severe impairment in airway protection mechanisms (higher PAS and LVC delay). Clinical practice should implement specific protocols to prevent OD and its complications in these patients. AP treatment did not significantly worsen swallowing impairments.

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Dysphagia, or swallowing disorder, can be a result of behavioral or sensory impairments, and problems with coordination, position, level of consciousness, and motor function (or a combination) and is common in patients with advanced dementia.<sup>1,2</sup> Oropharyngeal

E-mail address: mmiarons@csdm.cat (M. Miarons).

dysphagia (OD) is one of the most frequent causes of aspiration, and aspiration pneumonia has been reported to be one of the most common cause of death in people with dementia at advanced stages.<sup>3,4</sup>

The reported prevalence of dysphagia in persons with dementia ranges from 13% to 84%, depending on several factors such as the selection criteria. Prevalence of dysphagia is higher in more severe phases of the disease, 1.5–8 with 28% to 55% suffering from aspiration. Mechanisms involved in swallowing difficulties vary with different types of dementia. In patients with Alzheimer's disease, deficits in the sensory aspects of swallowing tend to occur, leading to

The authors declare no conflicts of interest.

<sup>\*</sup> Address correspondence to Marta Miarons, MS, BPharm, Pharmacy Department, Hospital de Mataró, Cirera Street s/n 08304 Mataró, Spain.

delayed oral transit time. <sup>11,12</sup> In patients with vascular dementia, the motor aspect of swallowing is affected, resulting in difficulty with bolus formation and mastication. <sup>12</sup> Sensory deficits, autonomic dysfunction, and fluctuation in cognition can lead to swallowing problems in patients with dementia with Lewy bodies and Parkinson disease dementia. <sup>13</sup>

OD has recently been recognized as a major geriatric syndrome <sup>14,15</sup> because of its high prevalence of multiple complications, risk factors, and precipitating diseases in older people. <sup>16</sup> Cognitive impairment or dementia is also recognized as a geriatric syndrome <sup>17</sup> and has been identified as a risk factor for aspiration pneumonia. <sup>18</sup>

In addition, given that approximately 50% of older people take more than 4 drugs <sup>19</sup> and that patients with dementia are usually older people, they are likely to take drugs that induce swallowing impairment. 19-21 Among them, antipsychotics (APs) (also known as neuroleptics) are frequently associated with the presence of swallowing disorders.<sup>22</sup> There are 2 main types of APs: typical (or first generation) APs, which act on the dopaminergic system, blocking dopamine type 2 receptors; and atypical (or second generation) APs. which have lower affinity and occupancy of the dopaminergic receptors and a high degree of occupancy of the serotoninergic receptors 5-HT2A.<sup>23</sup> Both types of APs are widely used to reduce neuropsychiatric symptoms in patients with dementia, even though they are only recommended when other nonpharmacologic techniques, such as stimulation techniques, group therapy, and sensory interventions including music therapy, have been ineffective.<sup>24</sup> When blocking dopamine receptors, APs can produce both therapeutic and adverse effects, including extrapyramidal symptoms, a consequence of their action on the nigrostriatal pathway, and include acute dyskinesia and dystonic reactions, tardive dyskinesia, parkinsonism, akinesia, akathisia, and dysphagia. APs are usually prescribed for behavioral symptoms of dementia and also for other indications such as schizophrenia or psychosis, delusional disorders, and mood disorders, which can also worsen dysphagia.

A literature review of the relationship between OD and APs<sup>24</sup> concluded that extrapyramidal symptoms-related dysphagia is a dangerous but potentially reversible side-effect in patients receiving APs. Another literature review showed that whereas some studies found a relationship between swallowing impairment and the use of APs, others did not.<sup>25</sup> Therefore, considering the absence of well-designed randomized controlled trials, and that it is difficult to differentiate whether the effect is due to the condition for which the AP is prescribed or from the AP itself, it is clear that more research is needed to evaluate the pathophysiology of OD in patients under antipsychotic treatment.

Hence, the objectives of this study were (1) to characterize the pathophysiology of OD using videofluoroscopy (VFS) in patients with OD and dementia, and (2) to determine if APs can further affect dysphagia, independently of the condition for which they are prescribed.

#### Methods

#### Patients

An observational, retrospective, cross-sectional study analyzed all inpatients with dementia 75 years or older who were discharged from any department of a general hospital, from January 2011 to May 2017, with a positive VFS performed after the discharge and defined as presence of signs of impaired efficacy (oral and/or pharyngeal residue) and/or safety of swallow (aspiration or penetration). Diagnosis of dementia was established according to the *International Classification Diseases*, *Ninth Edition* codes, in which codes for people with dementia are 290.x and 294.x.<sup>26</sup> All VFS parameters of patients with dementia were compared with patients without dementia; older inpatients

with a diagnosis of OD were confirmed with VFS during their hospitalization. Exclusion criteria for both groups were patients with head and neck or esophageal cancer. The study protocol was approved by the ethics committee of the hospital and conducted according to the principles and rules laid down in the Declaration of Helsinki and its subsequent amendments.<sup>27</sup>

#### Data Collection

In accordance with clinical practice, an overall assessment was carried out by a multidisciplinary team on patients with dementia the day of admission and included (1) demographic data, (2) comorbidities carefully collected and later measured with the Charlson comorbidity index, <sup>28</sup> (3) frailty according to the Edmonton Frail Scale<sup>29</sup>; and (4) functional capacity analyzed with the Barthel index. <sup>30</sup> Other variables were measured after the inclusion of the patient in the study and using the clinical history including (5) cognition according to the global deterioration scale<sup>31</sup> and (6) antipsychotic and other drug exposure. <sup>32</sup>

In our hospital, we systematically use the volume-viscosity swallow test (V-VST)<sup>33</sup> for bedside clinical assessment of swallowing function of high-risk populations, such as older patients. The V-VST is an accurate bedside assessment method with good psychometric properties, good reliability, and a detailed and easy-to-perform protocol designed to protect patients' safety. It is capable to evaluate the safety and efficacy of swallowing and has a system to detect silent aspirations. For patients with a positive V-VST, we also perform a VFS study. In this study, we included patients with a positive VFS study who had signs of impaired efficacy (oral and/or pharyngeal residue) and/or safety of swallow (aspiration or penetration) during the VFS study.<sup>16</sup>

#### Videofluorscopic Signs of OD

VFS is the gold standard for studying the oral and pharyngeal mechanisms of dysphagia and for evaluating efficacy and safety of swallow in older patients.<sup>33</sup> All patients were imaged while seated, in a lateral projection that included the oral cavity, pharynx, larynx, and cervical esophagus.<sup>34,35</sup> VFS characteristics are described in Supplementary Material 1.

VFS signs of impaired safety of swallow or unsafe swallow are defined as any swallow showing a significant entrance of part of the bolus into the airway during the VFS and rated according to the penetration-aspiration scale (PAS). Unsafe swallow was predicted by measuring the time between glossopalatal junction opening and LVC. 36,37 Severity of aspiration or penetration was rated according to the PAS and according to whether they were followed by cough (silent aspirations) or not. 35,38 A video demonstration shows impaired swallowing safety (aspiration) associated with a delayed laryngeal vestibule closure time (LVC) (Video 1).

#### Oropharyngeal Physiology

Measurements of oropharyngeal swallow response were obtained during the swallowing of 5 mL-nectar boluses in patients with dementia and patients without dementia. all patients swallowed this bolus and it is highly sensitive to physiological measures of swallowing impairment. LVC time and upper esophageal sphincter opening (UESO) times were measured. LVC time is the time interval in ms from glossopalatal junction (GPJ) opening to LVC and is considered to be the main physiological parameter in assessing impaired airway protection, which leads to aspiration in neurologic patients and older people.<sup>37</sup>

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