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Review Article

Swallowing Difficulty: Etiology, Diagnosis and New Treatments Review

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ABSTRACT

This review pragmatically explains the importance of the normal physiology and pathological entities such as oropharyngeal dysphagia (OPD) which affect the deglutition process. The later is a complex mechanism that involves the proper coordination of the oropharyngeal and upper esophageal sphincter (UES), motor function and proper control by the central nervous system (CNS) that all together enable a proper swallowing function. There are some innovative diagnostic techniques for evaluating deglutition disorders, as well as new therapeutical approaches for OPD, which are also the aim of this review. In regards with the clinical approach for deglutition disorders, there are still limitations in the diagnosis, treatment and building a trustful relationship with the patients due to the presence of comorbid neurological diseases and other factors that challenge the clinicians and scientist to improve their practice and do more research on this topic.

List of abbreviations and keywords: OPD: Oropharyngeal dysphagia, UES: upper esophageal sphincter, CNS: central nervous system, CN: cranial nerves, PNS: peripheral nervous system, VF: videofluoroscopy, FEES: Fiberoptic Endoscopic Evaluation of Swallowing, FEESST: Fiberoptic Endoscopic Evaluation of Swallowing with Sensory Test, HRM: High resolution esophageal manometry, BTX-A: Botulinum toxin A.

INTRODUCTION

The swallowing process involves the correct coordination of a different set of anatomical structures which include the pharynx, the oropharynx and the Upper Esophageal Sphincter (UES). Anatomically the pharynx is delimited by the base of the skull, the cricoid cartilage, nasal cavity and the base of the tongue. The oropharynx is located between the soft palate and the hyoid bone and all together form a duct which communicates the oral cavity with the pharynx to give passage the bolus to the esophagus [1].

The sensory innervation of these structures is provided by the glossopharyngeal nerve (pharyngeal and tonsillar branches) while the motor innervation emerges from the pharyngeal and superior laryngeal branches of the vagus nerve [2].

The UES is a high-pressure zone which involves the functional activity of three adjacent muscles (inferior pharyngeal constrictor, cricopharyngeus, and cranial cervical esophagus) with cartilage and connective tissue. The cricopharyngeus is the most important muscle component. Basal tone depends on the three muscles with the presence of asymmetry in the axial plane [3].

Swallowing is divided into three phases: oral, pharyngeal and esophageal in which other anatomical structures are involved like the lips, oral cavity, tongue, and palate.

The oral phase is voluntary and involves the lips, teeth, muscles of mastication and tongue. In this phase there are to stages involved: preparatory and propulsive. In the first one take place the retention and positioning of liquids and the mastication of solids and in the propulsive phase the positioning of the bolus on the surface of the tongue and moving the tip it against the roof of the mouth which forces the bolus through the pharynx [4].

After the arrival of the bolus to the pharynx a series of muscles are activated (mylohyoid, anterior digastric, geniohyoid, stylohyoid, styloglossus, tongue, pharyngeal constrictors, palatoglossus, and palatopharyngeus) which all together initiate the involuntary phase. Once the process has begun, the relaxation and opening of the UES occur in two phases: reduction of the sphincter tone (inhibition of signals of the vagus nerve) and contraction of the suprahyoid muscles causes its opening [4]

After the bolus transits along the UES, the high-pressure resting tone is restored.

The swallowing control and the activities of each of the structures involved are located at the spinal bulb. There are three categories of neurons involved in sensitive and motor control [4]:

1) Afferent neurons (cranial nerves V, VII, IX, and X that provide information to the nucleus tractus solitarius (NTS),

2) Interneurons (in the medulla oblongata with the central pattern generator, which works as the primary regulator of swallowing)

3) Efferent neurons (provided by CN V, VII, IX, X, XI, and XII).

There are two variants of the process of normal swallowing: tipper swallowing, wich is the most common, involves the contact of the tip of the tongue with the hard palate (present in 72% of normal individuals) and dipper swallowing where the tip of the tongue deeps below the bolus and lifts it to the tongue´s anterior surface [4].

At the molecular level, the polymodal sensory receptors like the TRP (transient receptor potential channels) or ASIC (acid-sensing ion channels) family receptors have been linked [5].

Studies have shown that the stimulation of some sensory receptors like TRPV1 or TRPA1 with multiple chemical products including capsaisin or piperin can reduce the prevalence of complications such as penetration or aspiration. It is under investigation if the stimulation of other receptors including TRPM8 or ASIC3 with menthol may be other therapeutic targets in the future (5).

DEFINITION

Oropharyngeal dysphagia (OPD) is defined as the difficulty or inability to swallow food caused by the dysfunction in one or more of the swallowing phases [6]. The functional problems affecting the oropharyngeal phase can be divided into oral problems (weakness of the tongue and other muscles of the oral cavity or loss of oral sensation) that can cause spillage of food from mouth or alterations in the formation of the bolus, pharyngeal impairment, transport problems (absence of propulsion forces) and obstruction (problems in the opening of the UES) (4).

EPIDEMIOLOGY

The reported prevalence in the general population varies widely, from 16% to 20.9% from an Australian to a Swedish Epidemiological study respectively. There is a higher prevalence of OPD in patients with a neuro-cognitive disease,. The most robust epidemiological data has been reported in stroke patients with an incidence from 29% to 80% (4). Parkinson´s disease affects the majority of patients and 100% of patients who have Amyotrophic Lateral Sclerosis (ALS) develop it (4).

The rates of morbidity, mortality and the derived costs of OPD are high. For example, it increases the risk of aspiration pneumonia seven times and is considered an independent predictor of mortality [7].

Elderly patients recruited for trials of swallowing physiology have a higher prevalence of complications such as penetration and aspiration also with worse outcomes compared with young subjects (6).

ETIOLOGY

Table 1

Neurogenic dysphagia is the result of alteration in the CNS or Peripheral Nervous System (PNS). The annual incidence worldwide is 400,000 to 800,000 new cases. The reported etiology includes stroke, Parkinson´s disease, dementias, CNS

anomalies, diseases of the basal ganglia and neoplasms among others. Regarding diseases of PNS are included Guillain-Barre, poliomyelitis or drugs.

Neuromuscular dysphagia is the result of various inflammatory muscle diseases such as muscular dystrophies, oculopharyngeal dystrophy or scleroderma and diseases of the neuromuscular union such as myasthenia gravis or metabolic disease (thyrotoxicosis) [8,9].

Table 1: Etiology of OPD
CNS: stroke, Parkinson´s disease, neoplasms, dementias, drugs
PNS: Guillain-Barré, poliomyelitis, drugs
Anatomical causes: Zenker´s diverticulum, cricopharyngeal bar, neoplasms, osteophytes
Neuromyogenic: myasthenia gravis, oculopharyngeal dystrophy, thyrotoxicosis

Anatomical causes

- Cricopharyngeal bar is a common incidental radiological finding which relevance is controversial. This is characterized by a prominent posterior indentation in the UES. There are reports that it is present in up to 5 -19% of patients who undergo to video fluoroscopy for other reasons but the occurrence of dysphagia is rare (13%). A Zenker diverticulum may cause this finding [10].
- Zenker diverticulum is a pouch formed at the posterior wall of the hypopharynx that protrudes through a zone of muscular weakness known as the Killian triangle. The average age of onset is during the eighth decade of life and is characterized by the presence of OPD and regurgitation with bronchoaspiration and pulmonary infections [11-13].
- Cervical osteophytes may be a finding in 6 to 30% of the elderly, but only 0.7% are related to dysphagia, which is caused by mechanical compression of the posterior wall of the pharynx [8].

Functional disorders

Globus is a functional esophageal disorder which is defined by a persistent or intermittent non-painful sensation of a lump or foreign body in the throat. It is a commonly encountered clinical condition and the diagnosis is defined by Rome IV criteria, which must be fulfilled for the last three months with symptom onset at least six months before diagnosis with a frequency of at least once a week with all of the next parameters [14]:

1. There is a persistent or intermittent non-painful sensation of a lump or foreign body in the throat with no structural lesion identified on physical examination, laryngoscopy or endoscopy.
   a) The occurrence of the sensation described between meals.
   b) The absence of dysphagia or odynophagia
   c) An absence of a gastric inlet patch in the proximal esophagus
2. The absence of evidence that gastroesophageal reflux or eosinophilic esophagitis is the cause of the symptom.
3. The absence of major esophageal motor disorders.

The main description of globus is a non-painful symptom which improves with meals, is episodic and not associated with dysphagia. It is reported in 46% of the healthy population [15-17].

CLINICAL PRESENTATION

The patient with OPD commonly describes an urge to swallow repeatedly to clear the bolus, nasal regurgitation, cough during meals, bronchoaspiration and pneumonia. In the elderly OPD secondary to xerostomia is frequent. A differential diagnosis should be made with globus or disorders of the distal esophagus [8].

Diagnostic evaluation

The objectives of the evaluation are: to assess the functional integrity of deglutition, to identify the presence of structural or mechanical causes, to evaluate the risk of aspiration, to determine if dysphagia is treatable and to prove the effectiveness of treatments [18].

Techniques to study deglutition

1. Clinical evaluation includes the exploration of the pre-oral, oral and pharyngeal phases of swallowing. The Eating Assessment Tool-10 (EAT-10) can detect aspiration in patients with neurological dysphagia. This questionnaire includes 10 questions about the severity of symptoms and each question scored from 0 to 4 (no problem to severe problem). The score is calculated by the addition of each question's score. The higher score is indicative of a higher level of dysphagia severity [19].
2. The dysphagia stress test evaluates swallowing difficulties and pain during a challenge of swallowing five boluses with water, apple sauce, rice, bread, and barium sulfate tablets. After each attempt, the patient rates the difficulty during swallowing (0=very difficult to 10=no difficulty).

Sensitivity to diagnose OPD is between 77 to 91% and specificity 57 to 96% [20,21].

3. Videofluoroscopic assessment (VF) is done by asking the patient to swallow barium in different periods and volumes, with anteroposterior and lateral projections to complete diagnostic evaluation. Sequences at 30 frames per second can assess abnormal movements of the bolus and movements of anatomical structures. The critical elements to assess are [22-24]:
   a) Laryngeal closure
   b) Closure of the nasopharynx
   c) The opening of the UES
   d) Propulsive movement of the tongue
   e) Emptying of the pharynx

VF is an objective, highly sensitive test, considered as the gold standard. Its limitations are mainly due to the exposure to radiation, need to move the patient and the time required to perform it [18] (Figure 1,2).

Figure 1: Patient with OPD: VF showing image compatible with cricopharyngeal bar. (Courtesy of MD Jose Hernandez Suarez, Radiology and Image Department, Hospital Espanol de Mexico).

Figure 2: Zenker´s diverticulum. (Courtesy of MD José Hernández Suárez, Radiology and Image Department, Hospital Español de Mexico).

4. Endoscopic evaluation, also known as FEES (Fiberoptic Endoscopic Evaluation of Swallowing) is an ambulatory and safe procedure done with a rhinolaryngoscope, which has the advantage of being brief. The patient is given different food densities in growing volumes for evaluating the penetration or aspiration of the content and as well if it occurs before, during or after swallowing [18].
5. Endoscopic evaluation with sensory test, known as FEESST (Fiberoptic Endoscopic Evaluation of Swallowing with Sensory Test) is a non-invasive technique to determine the sensitivity of supraglottis and hypopharynx. It consists of insufflating pulses of air through the working channel of the rhinolaryngoscope, therefore, evoking the Adductor Laryngeal Reflex (ALR). This procedure allows setting normal sensitivity limits and its deficits [18].
6. Swallowing laboratory: combines hardware and software that shows physiological signs of swallowing in real time. It includes electromyographic evaluation, measurement of the respiratory cycle and cervical auscultation [18].
7. High-Resolution Esophageal Manometry (HRM): Manometric assessment should be in a sitting position, recording basal pressures for 2-5 minutes. Then ten swallows with 5 ml of water are given and the response is measured. The normal basal pressure and the normal relaxation of the UES are not standardized and vary

according to the software used; due to Chicago's Classification of Esophageal Motor Disorders V3.0 alterations of the UES are not assessed. The normal UES relaxation varies from 200-400 milliseconds for a dry bolus to 300-500 milliseconds for a 5 mL of liquid. High basal pressure indicates high downstream resistance like in the case of a cricopharyngeal bar or a Zenker diverticulum. Near 71% of OPD patients had at least one abnormality in the UES or pharynx manometry. Within the pitfalls on the evaluation of the UES are complex anatomy, asymmetry, and rapid movements. During the intubation some clinicians like to anesthetize the posterior pharynx (but some studies had concluded that the sensory mucosal receptors are important to trigger voluntary swallowing and their dysfunction can contribute to OPD or aspiration). The author recommends not using topical anesthesia if the UES is the objective of the analysis [25,26] (Figure 3,4).

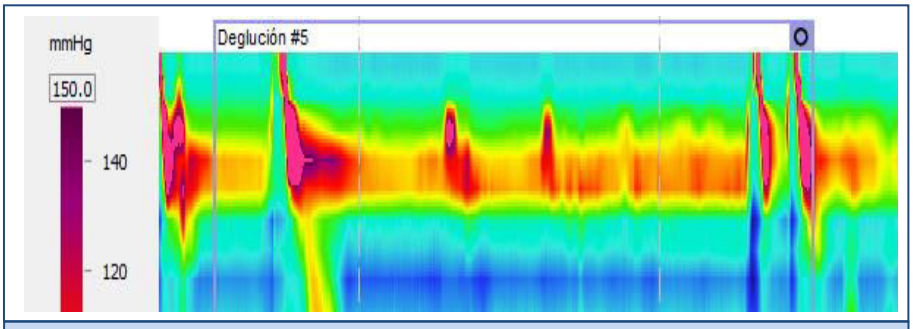

Figure 3: Pharyngeal contraction and UES relaxation in a normal subject. (Courtesy Motility Laboratory, Hospital Juarez de Mexico)

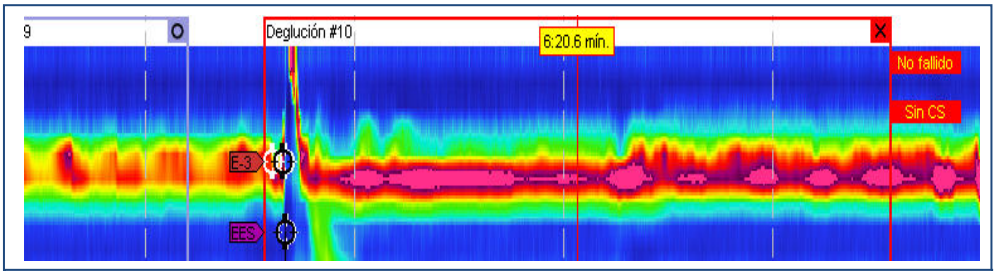

Figure 4: Hypertonic UES in a patient with OPD. (Courtesy Motility Laboratory, Hospital Juarez de Mexico).

8. Additional tests on HRM: The use of different volumes and consistencies of bolus has allowed assessing the power of contraction and pharyngeal accommodation (PSP). For example, the PSP was greater for 20 mL than to 10 mL bolus and was lowest in the thin liquid bolus and highest in the pudding bolus [27]. Other studies demonstrate faster velopharyngeal contraction, longer duration of relaxation and higher closing pressure after swallowing of the UES with higher volumes of liquid [28,29] (Figure 5).

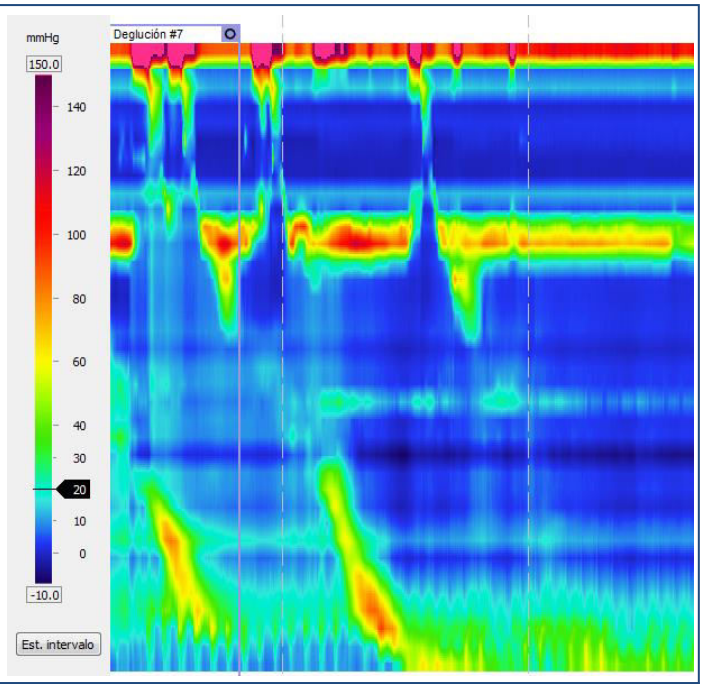

Figure 5: Dysphagia stress test for rapid assessment of swallowing difficulties in HRM.

Treatment

The most important point of the treatment is to assess the risk of aspiration to decide the use of an appropriate feeding route for each patient.

To assess the risk of aspiration we have different techniques: clinical or invasive.

In the clinical evaluation we can use:

1. Volume-viscosity swallow test: It is performed at the bedside or in the office. Consists of administering food with three different consistencies in different volumes (water, nectar and porridge) to evaluate data such as nasal regurgitation, cough during swallowing or choking. It is useful to determine if the patient can be fed orally and which density of food will be required [21].
2. EAT-10: (previously described). It has a sensitivity of 61 - 95% and specificity of 17-34% to determine the presence of aspiration [21].

Using HRM we can estimate pressure events in the pharynx and UES. In one study the authors taking a threshold of 105.0 mmHg of pharynx pressure got a sensitivity of 95% and specificity of 70% and taking the threshold 0.45 s for UES relaxation sensitivity of 76.3% and specificity of 57.5% to recommend non-oral feeding [30].

In another study the authors compared VF with HRM to identify risk factors for aspiration. They found that the presence in VF of pyriform sinus residue and vallecular residue and with shorter relaxation UES time interval were at more risk for aspiration [31].

In a Spanish study no correlation was found between clinical evaluation (presence of cough during swallowing, impaired gag reflex) and presence or aspiration. Silent aspirations were more frequent in patients with previous orotracheal intubation or abnormalities in velopharyngeal reflexes in patients in acute phase of stroke [32].

The treatment depends on the underlying cause

- Cricopharyngeal bar: endoscopic dilatations with a dilator of 18 to 20 mm. In one study in infants and children it has a total response in 68% of patients considering it a safe method [33].
- Zenker diverticulum: surgical treatment (diverticulectomy) or endoscopic diverticulotomy [11].
- Neurogenic dysphagia: treatment of the neurological disease if possible or try rehabilitation with a phoniatrist or at specialized clinics on the disease. In some cases botulinum toxin can be useful. Swallow strength training exercise for the elderly is a new technique consisting of the

use of a Swallow Resistance Exercise Device (sRED) what includes an inflatable bag housed in a rigid shell. The concave surface of the insufflated bag rests on the thyroid cartilage and conforms to the surface of the larynx, restricting the anterosuperior excursion of the hyolaryngeal complex to strengthen suprahyoid muscles, improves UES opening and preserves pharyngeal sarcopenia [33].

- Botulinum toxin A (BTX-A): It has shown utility in case series but the infiltration of other muscles can make dysphagia worse. BTX-A should be used in cases of hypertonia of the UES and its effectiveness is observed from the seventh day to the fourth month [34]. The technique is simple and the complication rate low (7/100). Within the factors of effectiveness: injection in the horizontal part of the cricopharyngeal muscle and high initial dose.

In patients with stroke a single injection of BTX-A is efficacious for 12 months in patients with aspiration diagnosed by VF. The number of patients with aspiration decreased to 52% [35].

Key points

- OPD is not a rare entity but is more frequent in the elderly and patients with neurological diseases.
- The diagnosis is based on the clinical features and support with VF and HRM or other new diagnostic techniques
- There is no standardized treatment but the use of training devices, rehabilitation or BTX-A is promising.
- Treatment must be multidisciplinary.

CONCLUSIONS

Oropharyngeal dysphagia is not a rare entity, but it is more prevalent amongst the elderly that have concomitant neurological conditions. The diagnostic is still clinical with confirmation in radiological and functional studies that are both specific and sensible in evaluating the upper esophageal sphincter. There is no standardized treatment for OPD due to the underlying conditions that cause it. This is the main reason why the treatment must be individualized upon the pathogenic and clinical findings. There are emerging therapies but there is still a need for more investigation.

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