

Review Article

The Pharyngo-Esophageal Transition Zone in Chagas' Disease

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Abstract

Chagas' disease is caused by the infection of the protozoan *Trypanosoma cruzi* with important impairment of esophageal function. Manifestations of the disease include changes in esophageal motility and megaesophagus, with symptoms of dysphagia and regurgitation, caused by nerve cells loss in the esophageal myenteric plexus. Although the motility of pharynx, upper esophageal sphincter and a short segment of the proximal esophagus are controlled by the central nervous system rather than by the myenteric plexus impairment in bolus transport through the thoracic esophagus may affect the pharyngeal and upper esophageal sphincter transit. We conducted a review of the literature concerning changes in contractions and transit in the pharynx, upper esophageal sphincter and proximal esophagus in patients with Chagas' disease. No data about the amplitude of pharyngeal contraction in Chagas' disease were found in the literature. Pharyngeal transit time is longer and the electromyographic activity of the suprahyoid muscles with swallows decrease in Chagas' disease patients compared with healthy individuals. The upper esophageal sphincter pressure is increased, and the amplitude of contractions in proximal esophagus seems to be comparable to healthy controls. These results strongly suggest that Chagas' disease is associated with functional changes in the pharynx and upper esophageal sphincter.

Keywords: Chagas' disease; Megaesophagus; Pharynx; Upper esophageal sphincter; Esophageal contraction; Dysphagia

Abbreviations

UES: Upper Esophageal Sphincter; HRM: High-Resolution Manometry

Introduction

Chagas' disease (American trypanosomiasis), caused by the infection of the protozoan *T. cruzi*, affects about 6-8 million people worldwide [1-3]. The disease causes important changes in the heart and digestive tract. Chronic cardiomyopathy is the most serious manifestation of the disease and an important health concern in endemic areas [1,2]. The most severe manifestations involving the digestive tract are megaesophagus and megacolon [1,2]. The esophageal involvement in Chagas' disease may be of low intensity [4] or cause megaesophagus, dysphagia, regurgitation and esophageal motility changes typical of achalasia [5], consequence of significant damage of the esophageal myenteric plexus (Auerbach's plexus), with degeneration and reduction in the number of intrinsic neurons [5,6].

Neurons of the myenteric plexus control the motility of the middle and distal esophagus and are present in higher numbers from the proximal to the distal esophagus [6]. In the pharynx, Upper Esophageal Sphincter (UES) and in a short segment of the proximal esophagus, the motility is controlled by the central nervous system [7,8]. Esophageal peristalsis in the cervical esophagus is mediated by vagal fibers that have direct contact with the striated muscle [8].

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Considering the involvement of the central nervous system in chronic Chagas' disease, there is a discrete and unspecific functional cortical disorder that does not cause significant functional damage [9,10], excepted in case of reactivation of chronic disease, which is more commonly reported in immunosuppressed patients [10]. As the central nervous system is spared, functional changes of the pharynx, UES and proximal esophagus during swallowing are not expected. However, with impaired esophageal motility caused by lower esophageal sphincter achalasia and changes in esophageal contractions upon deglutition [5], the pharyngeal-esophageal coordination and transit may alter, and perhaps explain the proximal dysphagia referred by some patients.

The aim of this review is to describe results about the pharyngo-esophageal transit and contractions evaluation in patients with Chagas' disease. Publications from 1990 to 2019 about pharyngeal, upper esophageal sphincter (UES) and proximal esophageal transit and contractions in patients with Chagas' disease were selected.

Pharynx, upper esophageal sphincter and proximal esophagus in chagas' disease

So far, the pharyngeal contraction in Chagas' disease has not been enough studied. One study reported one patient with weak pharyngeal contraction among 22 patients with Chagas' disease, measured by High-Resolution Manometry (HRM) [11]. There are other investigations of esophageal motility in Chagas' disease using high-resolution manometry, however they did not mention cervical esophagus, UES or pharynx [12-16]. This methodology is essential to evaluate the pharynx and the UES, since the method of water perfusion is not sensitive enough to register pharyngeal contractions.

The duration of pharyngeal transit, measured by video fluoroscopy, is longer in Chagas' disease patients compared with controls after swallowing of 10 mL bolus ($0.44 \pm 0.10s$ vs. $0.37 \pm 0.11s$ for liquid bolus; $0.46 \pm 0.12s$, vs. $0.37 \pm 0.07s$ for paste bolus, $p=0.04$) [17]. There is a positive correlation between bolus flow through the pharynx and changes in bolus volume or consistency in Chagas' disease, what is not

seen in healthy subjects [18]. The sequence of events of pharyngeal swallowing of patients with Chagas' disease did not differ from that of normal subjects [19].

The UES pressure in Chagas' disease patients without abnormalities upon radiologic esophageal examination, measured at the point of highest pressure, is higher than in normal volunteers (Chagas: 142.8 ± 47.4 mmHg; volunteers: 113.0 ± 46.0 mmHg, $p < 0.05$) [20]. Similar results, in terms of comparison with normal volunteers, were seen in patients with esophageal radiologic involvement (Chagas: 74.9 ± 24.4 mmHg; volunteers: 52.4 ± 18.0 mmHg) [21]. These results may be explained by the use of the rapid pull-through (instead of the station pull-through) technique. In this method, the water-perfused catheter is withdrawn rapidly, which would increase the response of the sphincter with the catheter movement. Considering this explanation, the UES would have hyper sensitivity to the catheter movement; however, other study showed the same results with the station pull-through technique [22], and another study reported that the UES pressure increased with the catheter movement in normal volunteers but not in Chagas' disease patients [23]. In studies conducted in Europe, 10% to 36% of Chagas' disease patients had hypertensive UES [24,25]. These results suggested that the UES pressure is increased in some patients with Chagas' disease, but not in all of them. The factors which determine the increase in UES pressure are not known, but megaesophagus with food retention may be one of them, situation to avoid pharyngeal reflux from esophagus.

Contractions of the proximal esophagus following the pharyngeal contractions after a wet swallow are delayed in patients with Chagas' disease [26-28]. Proximal esophageal contraction had normal amplitude in some investigations [26,29-32] and decreased amplitude in another [27], which may depend on the grade of esophageal involvement by the disease, esophageal dilatation or not.

Scintigraphic studies of pharyngeal-esophageal transit revealed longer pharyngeal clearance time for paste and liquid bolus and slower esophageal filling rate for liquid bolus in patients with esophageal manifestations of Chagas' disease [33,34]. The pharyngeal transit time is affected with the changes in bolus volume and consistency in Chagas' disease, but not in normal volunteers [18].

The impairment of pharyngeal transit in Chagas' disease patients may influence water ingestion. These patients required more time to drink a volume of water, and higher number of swallows, showed lower swallowing rate, and took smaller volume in each swallow compared with controls [27,35], however this difficult is more likely to be consequent of the esophageal involvement by the disease.

Individuals with megaesophagus caused by Chagas' disease had reduced electromyographic activity of the suprahyoid muscles during swallows and a greater recruitment of the suprahyoid musculature [36], which may be the cause of longer pharyngeal transit. Results about changes in pharyngo-esophageal transition in Chagas' disease are summarized in Table 1.

Discussion

Carlos Chagas described in 1909 the disease which has his name. He described the etiologic agent, the parasite and its life cycle. The disease is endemic in Latin America but affect people in Europe, North America, Japan and Australia [12,24,25,37,38].

The infection by *T. cruzi* causes in the digestive tract the impairment of the myenteric plexus which is between the longitudinal

Table 1: Summary of the results of the evaluation of Pharyngo-esophageal transition zone transit and pressure in Chagas' disease.

Longer pharyngeal transit [17,33,34]
Longer time for water ingestion [27,37]
Decrease in electromyographic activity of the suprahyoid muscles [36]
Increase in upper esophageal sphincter pressure [20-25]
Normal amplitude of the proximal esophageal contractions [26,29-32]
Delayed propagation of peristaltic contractions from pharynx to proximal esophagus [26-28]

and circular smooth muscles, and affects saliva production, esophagus, stomach, gallbladder, small bowel and large bowel [5,39]. Functional manifestations of Chagas' disease in the esophagus include achalasia of the lower esophageal sphincter, aperistalsis and dilatation. There is no evidence of clinically relevant impairment in the pharynx and upper esophageal sphincter area, since it is composed of striated muscle and are under the control of central nervous system [8,40]. This is true even in the chronic phase of the disease [5,9,10,39]. The esophagus is more intensely affected from proximal to the distal direction, since the striated muscle is gradually replaced by smooth muscle and the myenteric plexus increases in importance. Sensory input has influence in the modulation and initiation of the swallowing sequence [41,42]. There are no results about the evaluation of oral and pharyngeal sensitivity in Chagas' disease; however the results of pharyngeal adaptation to bolus volume and consistency [18] and the timing of pharyngeal swallow events [19] suggest that the sensory input is not affected by the disease.

Esophageal dysmotility represents an obstacle for the bolus transit through the esophagus. An increase in bolus transit time is observed from oral cavity to proximal esophagus, through the pharynx and UES [17,33]. The increase in bolus transit duration is associated with a delay in proximal esophageal contraction after the onset of pharyngeal contraction [26-28]. Since contractions occur at the bolus tail, delayed contractions represent delay in bolus transport. In addition, decrease in suprahyoid muscles activity is observed [36], which lead us to assume that this may be an adaptation to prevent more severe dysphagia, and consequently difficulty swallowing, caused by altered bolus transport through the esophagus and esophageal stasis.

Changes in consistency may facilitate food ingestion [43]. Although changes in bolus volume do not cause changes in pharyngeal transit or pharyngeal pressure amplitude, pharyngeal transit time increases with increase in bolus consistency, without changes in pharyngeal pressure wave [44]. A slow pharyngeal transit may cause difficult in drink water [27,35], although megaesophagus is more likely to cause the symptom. In patients with Chagas' disease swallowing rate adapts to change in bolus volume and consistency, which is not observed in health volunteers [18]. The pharyngeal epithelium is richly innervated by sensory fibers [41], with permitted that oropharyngeal swallowing process to be modulated, both volitionally and in response to different sensory stimuli.

Studies of the pharyngo-esophageal transition are important to understand the pharyngeal and UES behavior in situations of esophageal motility problems such as achalasia of the lower esophageal sphincter. For example, the increase in intra bolus pressure [45]. Observed in patients with cricopharyngeus bar [46] and Zenker diverticulum [47], may be caused by an impairment of the UES opening. However, it is not clear yet whether chagasic megaesophagus is associated with Zenker' diverticulum [48] or increase in intra bolus pressure. In idiopathic achalasia one investigation observed Zenker's

diverticulum in more than 10% of cases [49]. The modern HRM could be very useful in the evaluation of pharynx of patients with Chagas' disease. In idiopathic achalasia hypertonic contraction in pharynx and increased residual pressure in UES was observed [50]. Also, the possible participation of the reflux of the material from the esophagus to the pharynx and its aspiration to the airways, seen in at least 78% of patients with megaesophagus, needs further investigation [51].

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