Advances in Medical Sciences 59 (2014) 281–287

Contents lists available at ScienceDirect

Advances in Medical Sciences

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

Original Research Article

A distinct salivary secretory response mediated by the esophago-salivary reflex in patients with Barrett's esophagus: Its potential pathogenetic implications

Harathi Yandrapu [a], Marek Marcinkiewicz [b], Cezary Poplawski [c], Zbigniew Namiot [d], Tomasz Zbroch [e], Jerzy Sarosiek [a,*]

[a] Molecular Medicine Research Laboratory, Department of Internal Medicine, Paul L. Foster School of Medicine, Texas Tech University Health Sciences Center, El Paso, TX, USA
[b] Department of Medicine, Columbia County Health System, Dayton, WA, USA
[c] Department of Endoscopy, University Hospital 1, Collegium Medicum Bydgoszcz, Nicolaus Copernicus University Torun, Bydgoszcz, Poland
[d] Department of Physiology, Medical University of Bialystok, Bialystok, Poland
[e] Department of Reproduction and Gynecological Endocrinology, University Clinical Hospital, Bialystok, Poland

ARTICLE INFO

Article history:
Received 31 March 2014
Accepted 13 August 2014
Available online 24 August 2014

Keywords:
Barrett's esophagus
Salivary pH
Bicarbonate
Glycoconjugate
EGF

ABSTRACT

Purpose: A significantly compromised epidermal growth factor (EGF) secretion by basal parotid saliva may contribute to the development of Barrett's esophagus (BE). The rate of secretion of EGF as well as a wide spectrum of protective factors in total basal and stimulated saliva in BE patients remains to be explored. We therefore studied the rate of secretion of salivary buffers, glycoconjugate, protein, EGF, transforming growth factor α (TGFα) and prostaglandin E_2 (PGE_2), evoked by esophago-salivary reflex, in patients with BE and controls (CTRL).
Material/methods: Salivary secretion was collected during basal condition, mastication, and intraesophageal mechanical and chemical stimulations respectively, mimicking the natural gastroesophageal reflux scenario.
Results: Salivary pH in BE was significantly lower than in controls during mechanical ($p < 0.001$) and chemical stimulations ($p < 0.001$). Bicarbonate and protein outputs in BE were significantly lower during mechanical ($p < 0.05$) and chemical stimulations ($p < 0.01$). The non-bicarbonate and glycoconjugate outputs in BE were lower during chemical stimulation ($p < 0.05$) and during mechanical ($p < 0.05$) and chemical stimulations ($p < 0.05$) respectively. The rate of salivary EGF output in BE was significantly lower during mechanical stimulation ($p < 0.05$). We observed a higher TGFα output during mastication ($p < 0.05$) and PGE_2 secretion during basal and masticatory condition ($p < 0.05$) in BE.
Conclusions: Patients with BE demonstrated significantly compromised salivary pH and rate of secretion of bicarbonate, non-bicarbonate, glycoconjugate, protein and EGF. This impairment could potentially predispose to the development of accelerated esophageal mucosal injury. Potential restoration of this impairment by masticatory stimulation of salivary secretion using sugarless chewing gum justifies further clinical exploration.
© 2014 Medical University of Bialystok. Published by Elsevier Urban & Partner Sp. z o.o. All rights reserved.

1. Introduction

There is compelling evidence that Barrett's esophagus (BE) evolves in the setting of prolonged, relentless, gastroesophageal reflux [1,2]. Little is known, however, regarding the sequence of events that lead from gastroesophageal reflux disease (GERD) through the erosive reflux esophagitis (RE) to a gradual intestinalization of the esophageal mucosa [3]. The mechanism by which this specialized columnar epithelium undergoes further dysplastic changes resulting ultimately in malignant transformation remains poorly understood [4]. In some patients BE develops in the absence of any heartburn symptomatology even though 24-h pH monitoring data frequently reveal excessive acid exposure characteristic of GERD [1,5]. In other patients with GERD, BE is preceded by reflux

* Corresponding author at: Molecular Medicine Research Laboratory, Department of Internal Medicine, Paul L. Foster School of Medicine, Texas Tech University Health Sciences Center, 4800 Alberta Avenue, El Paso, TX 79905, USA.
Tel.: +1 915 215 5255; fax: +1 915 545 6636.
E-mail address: jerzy.sarosiek@ttuhsc.edu (J. Sarosiek).

http://dx.doi.org/10.1016/j.advms.2014.08.005
1896-1126/© 2014 Medical University of Bialystok. Published by Elsevier Urban & Partner Sp. z o.o. All rights reserved.

symptoms and erosive reflux esophagitis with or without stricture [2,6]. This clearly indicates that the pathogenesis of BE is multifactorial. Evidence is accumulating that endoscopic RE that sets the stage for the development of BE, results from a disequilibrium between aggressive factors and protective mechanisms [7–11]. In patients with GERD accompanied by erosive RE, salivary contribution to the esophageal pre-epithelial barrier is predominantly driven by esophago-salivary reflex evoked by chemoreceptors stimulated by the presence of acid and pepsin in addition to heartburn-driven nociceptive stimulation [7,11–14].

Interestingly, BE almost never develops in the upper one third of the esophageal mucosa that remains under the strongest impact of salivary secretion, but may develop within the lower two thirds where salivary protection may become compromised especially because of significant impairment of protective factors. Of note, a significant impairment in the rate of secretion of epidermal growth factor (EGF) in basal parotid saliva in patients with Barrett's esophagus (BE) has been demonstrated [15]. Therefore, an insight into the rate of secretion of a wide range of protective components of total saliva, including total salivary EGF, collected both in basal conditions and after stimulation with mastication or through mechanical and chemical receptors in patients with BE can provide new information regarding the efficacy of the salivary component of pre-epithelial barrier and a better understanding of the pathophysiology of this enormously clinically challenging disease.

2. Material and methods

2.1. Subjects

The study was approved by the Human Subject Committee and conducted on 33 Caucasian asymptomatic volunteers (15 females and 18 males, mean age of 39, range 26–56) and 16 Caucasian patients with BE (3 females and 13 males; mean age of 47; range 30–69) with a history of GERD (heartburn as a predominant symptom). Endoscopically BE patients had a long-segment (extending above the 3.0 cm distance from the gastroesophageal junction) of columnar epithelium without ulcer or stricture, presented histologically as a specialized intestinal metaplasia without dysplasia. Informed consent was obtained from all subjects. All subjects were not afflicted with any acute illness, did not receive any antisecretory medication at least 7 days before the salivary sample collection and never had any dysfunction of mastication.

2.2. Salivary sample collection

Subjects expectorated all saliva collected in their mouth every 10 s and were instructed not to swallow during the procedure. The salivary samples were sequentially collected on ice during the same time of the day for each subject as follows: (1) basal saliva during the first 10 min, (2) saliva produced during stimulation by parafilm chewing (mastication) during the following 5 min, (3) saliva produced by tubing following the placement of the intraesophageal catheter during two consecutive 1.5-min intervals, (4) saliva produced following inflation of both intraesophageal balloons during two consecutive 1.5-min intervals and (5) saliva produced during the esophageal perfusion with initial saline (initial NaCl), hydrochloric acid (HCl), HCl/pepsin and final saline (final NaCl) consecutively, four samples of each totaling 16 consecutive 1.5-min intervals.

2.3. Esophageal perfusion catheter

Esophageal perfusion was performed with a specially designed six-channel catheter manufactured by Wilson-Cook Company, Chapel Hill, NC, USA [16]. The four larger diameter channels were used for infusion and aspiration of the perfusate, gastric juice and incidentally swallowed saliva, which is retained above the upper balloon. The two smaller diameter channels were used for inflation of the upper and lower balloons to compartmentalize the segment of the lower esophagus [11,13,15–20].

2.4. Perfusing solutions

Esophageal perfusion in all subjects was performed using fresh 10 ml solutions for each 1.5-min interval: (1) NaCl (0.15 M) that corresponds to 0.9% saline. (2) HCl (0.01 M; pH 2.1). This concentration and pH of HCl was chosen to closely resemble the content of gastroesophageal refluxate [21]. (3) HCl (0.01 M; pH 2.1) with pepsin. Pepsin (0.5 mg/ml; Sigma Chemical Co., St. Louis, MO, USA) was dissolved in the concentration, which corresponds to the average proteolytic activity of human gastric juice [22,23].

2.5. Esophageal perfusion procedure

Subjects were placed in the semi-recumbent position. The nasopharynx was anaesthetized with xylocaine gel, the esophageal catheter was inserted into the esophagus through the nares and the balloons of the catheter were gently insufflated to seal the esophageal lumen. This procedure allows the compartmentalization of 3.75 cm segment of the esophagus between the balloons [9,10,16,24,25]. Since our BE patients had long segments of intestinal metaplasia replacing the squamous epithelium, compartmentalization with 2 inflatable balloons was taking place within columnar epithelium in BE subjects and squamous epithelium in controls. During each perfusion period of 1.5-min interval, the entire 10 ml solution of perfusate was circulated within the isolated segment of esophagus for a total duration of 24 min for each subject (16 consecutive 1.5-min intervals).

2.6. Analysis of salivary secretion components

Salivary volume was assessed using a sialometer (Proflow Incorporated, Amityville, NY, USA) [11,18,19]. Salivary pH was monitored using the Expandable Ion Analyzer EA 940 (Orion Res., Boston, MA, USA).

The salivary bicarbonate and non-bicarbonate buffers were analyzed by titration and back-titration methodology using TitraLab 90 (Radiometer America Inc., Chicago, IL, USA) [26]. Secretions form a thin film on the mucosa and allow the evolution of carbon dioxide (CO_2) formed from acid–base interactions. Therefore, the esophageal bicarbonate buffer value would be equilibrated with CO_2 tension of the lumen [26,27]. This was the rationale for choosing titration to pH of 4.0 for assessment of esophageal bicarbonate in an open system (without covering with a layer of liquid paraffin oil) with continuous CO_2-free bubbling. The bicarbonate concentration was calculated using the difference in the amount of acid initially required to titrate the sample from its starting pH to pH 4.0 and the amount of base required to back-titrate the sample to its original pH after development of the CO_2. The difference between the back-titration from pH 4.0 to its original starting value and the similar run of the buffer-free blank solution was used to calculate non-bicarbonate buffers [26,27]. In addition, this methodology was always validated by the titration of known concentrations of bicarbonate and non-bicarbonate in the standard solutions.

Salivary glycoconjugate (predominantly mucin) was measured using the periodic acid Schiff (PAS) methodology [9,24]. Salivary EGF was assessed by RIA using a commercially available kit (Amersham, Arlington Heights, IL, USA) [10,11,16,19]. Salivary TGFα was recorded using a commercially available RIA kit based on

Download English Version:

https://daneshyari.com/en/article/2032125

Download Persian Version:

https://daneshyari.com/article/2032125

Daneshyari.com