EFFECTIVENESS OF NATURAL SIALAGOGUES IN THE TREATMENT OF PATHOLOGICAL GASTROESOPHAGEAL ACID REFLUX DISEASE (GERD)

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ABSTRACT

Background : GERD is a common gastro-intestinal disorder. It is considered as chronic medical that needs long term medical treatment. Long term acid suppressive therapy, inspite of being considered safe, may result in bacterial overgrowth and secondary hypergastrinemia. The aim of this study is to evaluate the effectiveness of natural sialagogues (sugarless gum) as non-pharmacological treatment to control the pathological acid reflux. Subject and methods: 50 patients were selected from outpatient clinic of tropical medicine department complaining of heart burn and/or epigastric pain. They were confirmed as having pathological GERD by 24 hr pH metry. All patients were subjected

to: full history, thorough physical examination, ECG, and upper G.I.T endoscopy. Ambulatory 24 hrs. esophageal pH monitoring was done in the first day without using natural sialagogues and repeated in second day during using natural sialagogues. Measurement of salivary volume, ph, bicarbonate and Epidermal growth factor (EGF) before and after using natural sialagogues. The result: there was statistically significant symptomatic improvement in patients with GERD. 20% of patients with GERD by ph metry showed normal endoscopy findings. There were statistically significant increase in all measured parameters after chewing gum. 41% of patients who had GERD showed decrease in 24 hrs pH metry score after

chewing sugarless gum. The higher the grade of reflux esophagitis, the lower the response to chewing sugarless gum as regards salivary volume, pH, bicarbonate and EGF. While the highest response in salivary secretion parameters was reported in patients who had GERD with normal endoscopic findings followed by GERD with gastritis and the least response was found in GERD with hiatus hernia (HH).

In conclusion : Chewing sugarless gum as natural sialagogues showed statistically significant increase of salivary volume, pH, bicarbonate and EGF, together with improvement of symptoms of pathological GERD. So, chewing sugarless gum is believed to be good and effective non pharmacological method to control GERD.

INTRODUCTION

Saliva and its component have multiple functions in GI tract. Saliva aids in bolus formation, lubrication, protection and clean pharyngeal and esophageal mucosa. Salivary secretion quantitatively and qualitatively contributes to a protective function of the esophagus (1). When salivary flow decreases, severe symptoms include a feeling of burning or scalding of the

tongue, pharynx and esophagus may occur (2). Patients complaining of symptoms of GERD and those diagnosed as having GERD following 24-h pH monitoring had poorer salivary buffering capacity than normal subjects (3). Gum chewing causes an increase in salivary flow rate and salivary pH (4). Chewing gum might be non pharmacological treatment option for some patients with symptomatic GERD (5).

The aim of the work is evaluating if natural sialagogues can be used as a non-pharmacological method in the control of pathological acid reflux.

SUBJECTS AND METHODS

This study was performed in Tropical Medicine and Medical Biochemistry Departements, Zagazig University.

Selection of patients :

A total number of 50 patients were selected from the outpatient clinic of tropical department complaining of heart burn or epigastric pain confirmed with pH metry study as a pathological GERD.

All selected individuals were :

1- With normal salivary flow by

weighting a 4x4 inch gauze before and after two minutes chewing period (6). Confirmed by volume of saliva collected in first day without salivary stimulation and second day with salivary stimulation.

- 2- Free from systemic disease; hepatic, renal diseases, metabolic, connective tissue diseases and endocrinal diseases especially diabetes mellitus or any malignancy.
- 3- No history of smoking or alcohol consumption.
- 4- No current use of medications including, antidepressants, antipsychotics, antihistamines and antihypertensives (7).
- 5- No history of radiation treatment to the head and neck area.

All patients were subjected to :

- 1- Full history taking and thorough physical examination.
- 2- ECG: To exclude any cardiac cause of chest pain.
- 3- Esophagogastroduodenoscopy :
Using pentax (EG-2940) endoscope to assess the presence of esophagitis. The grading system was done according to Savary-Miller New Endoscopic Grading System (1990).
- 4- Ambulatory 24 hrs esophageal pH Monitoring.

- 5- Measurement of salivary volume, PH, bicarbonate, EGF before and after using natural sialogogues:

I- Saliva collection and measurement of salivary volume (8)

II- Measurement of salivary pH (9)

III- Measurement of salivary bicarbonate (10,11)

IV- Measurement of sEGF: Salivary epidermal growth factor was determined by using Med-Genix EGF-ELISA using a kit manufactured by BIOSOURCE EUROPE S. A, Belgium (12)

STATISTICAL ANALYSIS

The following statistical methods were used for analysis of results of the present study (13). The descriptive statistics: We use the arithmetic mean (X) as an average describing the central tendency of observations and the standard deviation (SD) as a measure of dispersion of the results around the mean.

While comparison of means: The comparison was done using the student "t" test for comparison of means of two independent groups and analysis of variance (ANOVA or F test) for comparison of means of more than two groups.

Calculating the significance of difference between two proportions: We use the standard error of the difference (z).

RESULT

Heart burn was the common presenting symptom. It was found in 66% of patients followed by epigastric pain 41% and the least presenting symptoms were cough and water brash 5%.

After stimulation of salivary flow, there were symptomatic relieve in heart burn, epigastric pain, regurgitation and nausea with no symptomatic relieve in hoarseness of voice, dysphagia, cough with increase incidence of water brash.

There were very high statistically significant in all parameters before and after salivary stimulation in all studied groups.

NB:

Three groups according to pH metry score.

P1 included patients with score less than 22 after salivary stimulation.

P2 included patients with score more than 22 after salivary stimulation but less than the score recorded be-

fore salivary stimulation.

P3 included patients with score more than 22 after salivary stimulation and more than the score recorded before salivary stimulation.

There were very high statistically significant increase in all parameter before and after salivary stimulation in all studied groups.

N.B:

C1 included patients with GERD only by upper endoscope.

C2 included patients with GERD and gastritis by upper endoscope.

C3 included patients with GERD and H H by upper endoscope.

Normal included patients with free upper endoscope.

There were very high statistically significant increase in all parameters before and after salivary stimulation in all studied groups.

N.B:

G1 included patients with GERD grade I.

G2 included patients with GERD grade II.

G3 included patients with GERD grade III.

Normal included patients with free upper GIT endoscope.

Table (1): Frequency of symptoms in patients with pathological GERD before and after salivary stimulation.

Symptom	Before stimulation of salivary flow		After stimulation of salivary flow	
	No	Percentage	No	Percentage
- Heart burn	26	66%	5	12%
- Epigastric pain	16	41%	11	28.2%
- Regurgitation	7	17%	4	10%
- Nausea	11	28%	10	25%
- Hoarseness of voice	3	7%	3	7%
- Cough	2	5%	2	5%
- Water brash	2	5%	4	10%
- Dysphagia	9	23%	9	23%

Table (2): Comparison between mean values of different salivary parameters before and after salivary stimulation in different groups according to pH metry

G	Volume				pH				HCO ₃				EGF			
	Before	After	t	P	Before	After	t	P	Before	After	T	P	Before	After	t	P
P1	0.8	2.29	1.8	0.01	6.8	7.4	8.9	0.01	3.3	9.9	18.2	0.01	1.5	2.8	6.4	0.01
P2	0.72	1.6	7.3	0.01	6.8	7.4	18.3	0.01	3.2	9.7	2.3	0.01	1.4	2.7	6.8	0.01
P3	0.33	0.77	5	0.01	6.69	7.3	6.5	0.01	2	8.5	12.4	0.01	0.7	1.4	4.6	0.01

Table (3): Comparison between mean values of different salivary parameters before and after salivary stimulation in different groups according to endoscopic finding of upper GIT.

G	Volume				pH				HCO ₃				EGF			
	Before	After	t	P	Before	After	t	P	Before	After	t	P	Before	After	t	P
C1	0.8	2.01	6	0.01	6.9	7.4	12	0.01	3.4	10.32	10.9	0.01	1.7	3.5	8.9	0.01
C2	0.55	1.69	5.42	0.01	6.8	7.3	12.7	0.01	2.5	8.9	20.1	0.01	1.01	1.81	4.2	0.01
C3	0.5	1.5	4.2	0.01	6.7	7.3	10.6	0.01	2.8	8.8	16.4	0.01	1	1.8	3.6	0.01
N	1.03	2.1	9.7	0.01	6.9	7.5	5.2	0.01	4.08	11.3	20.1	0.01	2.1	3.9	8.9	0.01

Table (4): Comparison between mean values of different salivary parameters before and after salivary stimulation in different groups according to endoscopic grading of GERD.

G	Volume				pH				HCO ₃				EGF			
	Before	After	t	P	Before	After	t	P	Before	After	t	P	Before	After	t	P
G1	0.9	2.4	1.9	0.01	6.9	7.4	10.8	0.01	3.7	11	22.7	0.01	1.7	3.4	5.7	0.01
G2	0.54	1.4	5.07	0.01	6.8	7.3	15.5	0.01	2.8	8.6	13.1	0.01	1.14	2.02	4.2	0.01
G3	0.37	1.3	3.17	0.01	6.7	7.3	10.4	0.01	2	8.4	2.74	0.01	0.64	1.44	7.8	0.01
N	1.03	2.13	9.7	0.01	6.9	7.5	5.2	0.01	4.08	11.3	20.1	0.01	2.1	3.9	8.9	0.01

Fig. 1 : Esophageal pH metry study in the 1st hour after dinner before salivary stimulation.

Fig. 2 : Esophageal pH metry study in the 1st hour after dinner after salivary stimulation.

DISCUSSION

Gastroesophageal reflux disease is a common GI disorder, particularly frequent in the primary care setting (14). Several powerful drugs were developed for treatment of GERD. Although, they considered to be safe, long-term acid suppressive therapy may result in bacterial overgrowth and secondary hypergastrinemia (15). Some believe that several old therapy, that appeared again, may be effective in treatment of GERD (16). Diagnosis of GERD confirmed by ambulatory 24 hours pH metry, with upper GIT endoscopy was done for all patients.

20.5% of patients with symptoms of GERD showed normal endoscopic findings with high pH metry score. While, 7% of patients whom had been excluded from this study were with severe symptoms suggesting GERD but with normal or very low pH metry score. These symptoms may be related to oesophageal dysmotility or bile reflux rather than pathological acid reflux (17). In this study, as shown in table (1), it was found that after chewing sugarless gum and increasing salivary flow, there was early significant symptomatic relieve especially in heartburn and epigastric pain this was

due to buffering action of alkaline salivation on refluxed acid. The same findings was reported by (Roopovar et al., 1995) (18).

There was no early affect on hoarseness of voice and dysphasia. These symptoms are due to prolonged and chronic acid exposure and need longer duration of follow up of chewing sugarless gum. However, there was increase of water brush which may be due to excess salivation. It was found that 41% of patients showed improvement in their ambulatory 24 hours pH metry score. This can be explained by the fact that chewing gum stimulates salivary secretion and bicarbonate production, which result in dilution of the fluid, acid neutralization, back diffusion of hydrogen ions across the esophageal mucosa, and clearing of acid from the esophagus. Moreover, chewing gum increases esophageal peristalsis by inducing deglutition.

On the other hand 59% of patients showed no improvement in their ambulatory 24 hours pH metry score. This may indicate greater disturbances in their physiological acid clearance mechanisms that could not be overcome by salivary stimulation.

There was very highly significant increase salivary volume, PH, bicarbonate and epidermal growth factor after chewing gum. The same was reported by (Polland et al., 2003) (19) and (Smoak and Koufman 2001) (20).

Table (2) showed all patients, regardless of their ambulatory 24 hours pH metry score, had shown great improvement in their postprandial esophageal pH measured in the first hour after meal during chewing gum. This was in agreement with Moazzez et al., (2003) (4) who found that chewing gum is effective in reducing postprandial esophageal reflux.

Also, salivary volume and bicarbonate output were found to be significantly higher in patients showing improvement, than in patients showing no improvement in their pH metry scores after chewing gum. This clearly indicates that simple chemical titration of refluxed acid by bicarbonate with salivary stimulation is a key mechanism in the improvement of GERD patients.

There were also statistically significant differences in measured salivary

volume, pH, bicarbonate and EGF with weaker responses in patients with GERD with HH, than GERD with gastritis than patients with GERD only. The strongest responses were seen in normal endoscopic volunteers as showed in table (3). This observation suggests that the stronger the underlying dysfunctions, the weaker will be the responses to salivary stimulation or pathogenesis of GERD might be due to underlying dysfunction rather than salivary impairment.

Table (4) showed, the maximum responses to chewing gum, concerning salivary volume, pH, bicarbonate and EGF were observed in normal endoscopic volunteers. This response was inversely related to GERD grading by endoscopy being highest in grade I and lowest in grade III. This poor response in more severe diseases means that defective salivary function may have a role in pathological GERD and its complication. This was reported by Kao et al. (1999) (21) who found that patients with reflux esophagitis have poor salivary functions by quantitative salivary scintigraphy.

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فعالية محفزات اللعاب الطبيعية لعلاج ارتجاع المريء المرضى الحمضي

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يعتبر ارتجاع المريء واحداً من أكثر أمراض الجهاز الهضمي شيوعاً. ويعتبر من الأمراض الطبية المزمنة حيث يحتاج للعلاج الباطنى فترة طويلة. ويعتبر العلاج الباطنى بمشبطات الحموضة من العلاجات الآمنة ولكن مع طول فترة استخدامها قد يتسبب فى زيادة نمو البكتريا بالجهاز الهضمي وزيادة نسبة الجاسترين بالدم.

الهدف من الدراسة :

يهدف هذا البحث الى دراسة تأثير محفزات اللعاب الطبيعية فى علاج ارتجاع المريء المرضى الحمضي

المرضى وطرق البحث :

أجريت هذه الدراسة بقسمي المتوطنة والكيمياء الحيوية بكلية الطب جامعة الزقازيق. خضع ٥٠ شخصاً يشكون من حموضة أو ألم بالمعدة أو الاثنين معا الى قصة المرض والفحص الإكلينيكي الدقيق واستبعاد الأمراض والأدوية التى تؤثر على إفراز اللعاب، تم تأكيد المرض بدراسة حموضة المريء على مدار ٢٤ ساعة مع منظار ضوئى علوى للمريء والمعدة والأثنى عشر. كما تم عمل رسم قلب لكل المرضى. تم قياس كمية اللعاب وحموضة المريء والبكتريونات وعامل نمو طبقة الجلد باللعاب قبل وبعد محفزات اللعاب الطبيعية مثل البان بدون سكريات لمدة ساعتين بعد الوجبات الثلاثة.

النتائج :

وجد تحسن ملحوظ فى شكوى مرضى الارتجاع الحمضى بالمرئ كما وجد أن ٢٠٪ من مرضى ارتجاع المرئ لا يوجد مايدل على الارتجاع بالمنظار الضوئى. تحسنت قياس حموضة المرئ لمدة ٢٤ ساعة فى ٤١٪ من المرضى. تحسن واضح ذو دلالة إحصائية فى كل قياسات اللعاب بعد المحفزات الطبيعية. تحسن كامل للارتجاع فى الساعة الأولى بعد الأكل تم قياسه بجهاز قياس حموضة المرئ لمدة ٢٤ ساعة. كانت الاستجابة لمحفزات اللعاب فى إرتجاع المرئ مع وجود مرئ طبيعى بالمنظار أكثر منها فى إرتجاع المرئ مع التهابات المعدة وأقلهم إستجابة هو إرتجاع المرئ مع فتق بالحجاب الحاجز أيضاً. وجدت علاقة عكسية بين قياسات اللعاب بعد المحفزات ودرجة ارتجاع المرئ الحمضى.

الخلاصة :

تعتبر محفزات اللعاب الطبيعية طريقة جيدة وفعالة فى علاج حالات كثيرة من إرتجاع المرئ الحمضى.