

TRABAJO DE FIN DE GRADO

Grado en Odontología

GERD (GASTROESOPHAGEAL REFLUX DISEASE) AND ORAL MANIFESTATIONS

Madrid, curso 2020/2021

Número identificativo

Abstract

<u>Introduction</u>: gastroesophageal reflux disease (GERD) is "a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications". The prevalence of GERD has increased in the last years and currently it is one of the most ordinary chronic disorders, with a great variety of symptoms and various degrees of severity.

<u>Objectives</u>: to describe the most common oral lesions associated to GERD in both hard and soft tissues, focusing as well on their management and on a possible relationship between GERD and bruxism.

<u>Methodology</u>: a bibliographic research of biomedical literature published between 2010 and 2021 was performed using PubMed and Medline, resulting in 32 scientific articles. <u>Discussion of results</u>: there is a great amount of evidence proving that dental erosion is a considerable manifestation of GERD in the oral cavity. With regard to mucosal lesions and bruxism, the literature suggests an association to GERD. Despite this, the available information is insufficient to establish a proper connection.

<u>Conclusion</u>: erosive tooth wear is a confirmed oral manifestation of GERD, while the relationships with soft tissue lesions and bruxism require further investigations. It is clear that the dentist plays a key role in the diagnosis of GERD and, as such, will need to cooperate with the patient's family doctor/gastroenterologist so that both a complete and long-lasting treatment will be provided.

<u>Resumen</u>

<u>Introducción</u>: La enfermedad por reflujo gastroesofágico (ERGE) es "una condición que se desarrolla cuando el reflujo del contenido del estómago causa síntomas molestos y/o complicaciones". La prevalencia de la ERGE ha aumentado en los últimos años y actualmente es uno de los trastornos crónicos más comunes, con una gran variedad de síntomas y varios grados de gravedad.

<u>Objetivos</u>: describir las lesiones orales más comunes asociadas a la ERGE tanto en tejidos duros como blandos, centrándose también en sus manejo y en una posible relación entre ERGE y bruxismo.

<u>Metodología</u>: se realizó una investigación bibliográfica de literatura biomédica publicada entre 2010 y 2021 utilizando PubMed y Medline, dando como resultado 32 artículos científicos.

<u>Discusión de los resultados</u>: existe una gran cantidad de evidencia que demuestra que la erosión dental es una manifestación considerable de la ERGE en la cavidad bucal. Con respecto a las lesiones de las mucosas y el bruxismo, la literatura sugiere una asociación con la ERGE. A pesar de esto, la información disponible es insuficiente para establecer una conexión adecuada.

<u>Conclusión</u>: el desgaste dental erosivo es una manifestación oral confirmada de la ERGE, mientras que las relaciones con las lesiones de los tejidos blandos y el bruxismo requieren más investigaciones. Está claro que el dentista juega un papel clave en el diagnóstico de la ERGE y, como tal, deberá cooperar con el médico de familia/gastroenterólogo del paciente para que se le brinde un tratamiento completo y duradero.

Index

1. Introduction	
1.1 Gastroesophageal reflux disease (GERD): definition	1
1.2 Risk factors and pathophysiology of GERD	4
1.3 Clinical manifestations of GERD	14
2. Objectives	
3. Methodologies	23
4. Discussion of results	25
4.1 Dental lesions in chronic GERD (adults and children)	25
4.2 Soft tissue lesions associated to GERD	
4.3 GERD and bruxism	
4.4 Patients with GERD at the dental office	
5. Conclusion	35
6. Social responsibility	
6.1 Responsibility of the dental professional	
6.2 Responsibility of the patient	
6.3 Responsibility of the government	
7. Bibliography	
8. Annexes	41

1. Introduction

1.1 Gastroesophageal reflux disease (GERD): definition

First of all, it is important to differentiate gastroesophageal reflux (GER) from gastroesophageal reflux disease (GERD) (1).

On one hand, GER is a natural physical occurrence taking place when momentary resting of the lower esophageal sphincter favors the retrograde flow of gastric juice into the esophagus and beyond. The rate of occurrence of reflux and the length of episodes differ according to the age, with newborns going through more numerous and frequent episodes than older toddlers and teenagers (1). As far as the adult group is concerned, the prevalence of GER manifestations seems to differ by population. According to the available data, symptoms of GER are more common in Occidental countries (10-20%) than in Oriental ones (~5%) (2).

On the other hand, gastroesophageal reflux disease (GERD) is manifestations or difficulties due to pathological GER (3).

The prevalence of GERD has broadened in the last years and at the moment it is one of the most ordinary chronic illnesses, with a wide range of symptoms and different grades of seriousness (4).

The current notion of reflux esophagitis was created in 1935 when a milestone publication in JAMA first proposed that gastric excretions could produce damage of the mucosae. Afterwards, the cardinal pathophysiological process was described by Allison in 1946 and the term "reflux esophagitis" was introduced (5).

Until recently, GERD was described in many different ways as the absence of a gold criterion for identification made it hard to accept an adequate definition (6).

An International Consensus Group in 2006 established a categorization of GERD and named it "The Montreal Classification". This new arrangement determined a foundation for globally acknowledged terminology, allowing the connection of different countries' cultures and facilitating the handling of GERD (7).

According to the Montreal definition, GERD is "a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications". In agreement with this description, GERD can be divided into two syndromes: an esophageal and an extraesophageal ones (table 1) (6).

Esophageal syndromes
Syndromes with symptoms
Typical reflux symptoms
Reflux chest pain
Syndromes with esophageal injury
Reflux esophagitis
Reflux stricture
Barrett's esophagus
Esophageal adenocarcinoma
Extraesophageal syndromes
Established associations
Reflux cough syndrome
Reflux laryngitis syndrome
Reflux asthma syndrome
Reflux dental erosion syndrome
Proposed associations
Pharyngitis
Sinusitis
Idiopathic pulmonary fibrosis
Recurrent otitis media

Table 1. The Montreal description of GERD and its constituent syndromes. Modified from: Nwokediuko SC (6).

This global consensus admits that a diagnosis of GERD could be carried out in primary care taking solely into account the presence of symptoms, without any further diagnostic examination. This path is suitable for the majority of the patients and does not involve superfluous assets (6).

The verge at which symptoms account for the disease is reached when they are bothersome to patients and alter their daily actions. This patient-centered way to reach the diagnosis involves as well questioning how their daily routine is influenced by their symptoms (7).

Heartburn and regurgitation are the defining symptoms of GERD. The former is described as a stinging feeling in the retrosternal area, while the latter is outlined as the impression of movement of refluxed stomach contents into the oral cavity or hypopharynx. These manifestations are considered characteristic enough to perform а diagnosis of GERD. In addition. esophageal and extraesophageal symptoms/syndromes that constitute part of the structure of GERD involve pain to the chest, alterations of sleep, cough, wheezing, status asthmaticus and dental erosive wear (6).

According to endoscopy detections, patients affected by GERD can be classified as either presenting harm to the esophageal mucosa (erosive esophagitis and Barrett's esophagus) or no injury to it (endoscopy-negative reflux disease or nonerosive reflux disease: NERD) (7).

This recent evidence suggests that the genetic makeup of each single individual exposed to comparable environmental influences may finally decide the particular phenotypic appearance of GERD. Once GERD phenotypes are determined, they remain true to form (6).

Though, it is important to distinguish between GERD in the adult population and the same disease in the pediatric one (1)(3).

It is for this reason that in 2009 another International Consensus Group similar to the Montreal one was held and a proper definition of GERD in the children community was created (1).

GERD in a child occurs when the cause of inconvenient symptoms and/or difficulties is the reflux of gastric contents. Its symptoms change depending on the age (3) and are considered bothersome when they affect adversely the comfort of the child and not just guardian's one. If the reflux symptoms are not troublesome in neither the infant, nor in the older child or nor in the teenager (1-17 years old), the diagnosis should not be GERD (1).

Endoscopy gives the possibility to identify and classify the esophageal mucosal damage and the likely complications of GERD, while the use of histology is limited in finding or ruling out a GERD diagnosis as its principal role is to eliminate other disorders and/or affections of GERD (1).

1.2 Risk factors and pathophysiology of GERD

Despite the economic stress that GERD causes on the health care system of some areas in the world, at the moment it is considered and studied as a multifactorial illness (1).

In order to understand the pathogenesis of GERD, it is important to analyze two main sections of interest. The first one concerns the processes by which reflux happens and the aspects that make them possible, while the second one is constituted by the elements that affect the awareness of GERD symptoms (4).

The first factor to include in the former is sliding hiatal hernia. The esophagogastric junction (EGJ) works as an anti-reflux blockade and is constituted by the smooth muscle of the lower esophageal sphincter (LES), which is enclosed by oblique gastric fibers. These are attached to the striated muscle of the crural diaphragm by the phreno-esophageal ligament. A hiatal hernia is described as the proximal dislocation of the EGJ making the intrinsic sphincter lie proximal to the hiatus constituted by the crural diaphragm, which is probably provoked by the weakening or fracture of the phreno-esophageal ligament (4).

The evidence suggesting that individuals with hiatus hernia present more reflux events and higher exposition to esophageal acid than the ones with no hiatal hernia is indubitable. Moreover, on endoscopy it is possible to appreciate that people with hiatus hernia suffer from a more serious esophagitis. In addition, it is proved that a bigger hiatal hernia is related to a longer exposure to esophageal acid and protracted acid clearance times (4).

Many investigations have been carried out to understand how hiatus hernia gives origin to GERD. Generally, during straining-related augmented abdominal pressure and in the course of inhalation, a contraction of the crural diaphragm occurs giving origin to a raise in LES pressure. This increase makes up for the enlarged pressure gradient between the stomach and the esophagus. Moreover, the LES pressure is also affected by the crural diaphragm. This way, it is possible to find a high-pressure gradient at the level of the LES and one at the height of the crural diaphragm. In addition, in subjects presenting hiatal hernia no overlap is found between the LES and the crural diaphragm. As a consequence, a more inefficient anti-reflux barrier and a greater probability of reflux are originated (4).

Therefore, it is possible to claim that impaired crural diaphragm function is firmly related to GERD (4).

Another suggested process by which hiatal hernia produces GERD is the one in which the content of the stomach is trapped in the sac of the hiatal hernia (between the LES proximally and the crural diaphragm distally) and refluxes in the following swallowactivated relaxations of the LES. As the esophageal clearance in patients presenting hiatal hernia is impaired, then the acid clearance is damaged too (4).

To conclude, it is sometimes difficult to see a small difference between two pressure peaks. As a consequence, small hernias may not be discovered while implications to the pathogenesis could still happen. So, hiatus hernia can cause GERD by means of different processes (4)(8).



Fig. 1. Image of a hiatal hernia. Source: J.L. Jameson, A.S. Fauci, D.L. Kasper, S.L. Hauser, D.L. Longo, J. Loscalzo: Harrison's Principles of Internal Medicine. 20th Edition.

The second factor to include in the first section is low pressure of the LES. This second factor is less important because a continuous low LES pressure is found in just a small number of patients (4).

A greater role is played by the transient relaxation of the lower esophageal sphincter (TRLES) (8). As opposed to the esophagus, which undergoes a short shrinkage when ingesting, the LES remains in a continuous mode of contraction. By doing so, it acts as a natural blockade and prevents the reflux of stomach contents (4).

The resting tone of the LES is roughly 10-30 mmHg greater than both gastric and esophageal luminal pressures (4).

TRLESs are involuntary and sudden reductions in LES pressure, which are not associated to the action of swallowing (1) and are induced by the vagal nerve (4). As opposed to relaxations produced by the act of ingestion (generally lasting 6-8 seconds), the ones of the TRLEs persist for a longer time (usually more than 10 seconds). Moreover, they are typically described as presenting a lowest-point pressure of 2 mmHg or even less and are mainly provoked by gastric distension. Consequently, they are more likely to occur in the postprandial state (1). TRLESs are also common when standing in an erect posture and new investigations found that patients presenting reflux disease do not necessarily have more recurrent TRLESs, but rather, the latter in patients with GERD are more prone to be correlated with acid reflux (4).

The first section also includes the study of the acid pocket (4).

A paradox that was overlooked at for a long time is that in GERD the majority of acid reflux events happen in the postprandial period, although intragastric pH reaches its greatest value just after a meal because of food's buffering effect (4).

Recent studies assured that following meals, the esophageal refluxate appeared to be generally more acidic than the body of the stomach. This is also known as acid pocket, which is located at the EGJ and gets away from the buffering effect of the meals. Furthermore, it is proved that the proximal margin of the acid pocket could reach and even cross the LES. This extension of the pocket is related to the severity of both GERD and hiatal hernia. In addition, further research also suggests that the supradiaphragmatic location of the acid pocket has a greater importance in the evolution of GERD than its extent (4).

A great emphasis is also put on the presence of a hiatus hernia. A bigger hiatal hernia catches a greater acid pocket in the hiatus sac and, as a consequence, reflux increases. So, the main factor that affects the position of the acid pocket is the existence of a hiatus hernia (4).

It is also relevant to analyze in the first section the increased distensibility of the EGJ. Radiographic investigations indicate that patients affected by GERD present a more compliant LES both in rest and during swallowing relaxation (especially in patients with a hiatal hernia). Furthermore, it is claimed that this factor may demonstrate the decreased capacity to restrict reflux to gas (belching) in individuals presenting GERD. A greater distensibility has a strong importance because it produces greater reflux volumes per event. Additionally, many studies prove that there is a correlation between an increased flap valve grade, a raise in reflux esophagitis and an atypical esophageal acid exposure (4).

So, a connection between flap valve grade and EGJ distensibility is predictable. Despite this, it is not yet clear which measure has a greater relevance. Lately, it was confirmed that the esophagogastric insertion angle was more obtuse in subjects with

GERD and it is for this reason that the reflux protection carried out by the flap valve mechanism could be negatively affected (4).

Sixth factor to investigate in the first section is the impaired esophageal clearance. Currently, it is understood that both LES and esophagus are very relevant in the antireflux mechanisms (8).

The two principal processes that work in the clearance of GER events are gravity and esophageal peristalsis (primary and secondary). Moreover, salivary and esophageal bicarbonate are necessary to neutralize an acidic reflux event. Manometric studies on the esophageal pH in GERD patients prove that the principal clearance event after GER in a standing posture is primary peristalsis. This type of peristalsis following an event of reflux, as the first motor happening, is a more frequent occurrence in GERD individuals. Despite this fact, secondary peristalsis is significant at night because it is the earliest event in 80% of GER experiences. This is probably a consequence of the restriction of the deglutition reflex (8).

Esophageal motility alterations can be found in about 30% of the patients affected by GERD, being ineffective esophageal motility (IEM) the most common disorder (8).

The last mechanism that is included in the first section is delayed gastric emptying. This factor may cause GER because the stomach is full for a larger time arising the likelihood of GER episodes. Furthermore, the intra-gastric pressure over the resting LES pressure is greater and raised gastric distension can generate TRLES. The occurrence of total delayed gastric emptying in patients with GERD is very common. Despite this, there are investigations suggesting that the prevalence of delayed gastric emptying in GERD is very small or equal to zero. Though, other analyses prove an occurrence of more than 40%. This discrepancy could be partly due to different

methods of investigation. Delayed gastric emptying happens as well in NERD, displaying a prevalence that could be compared to the one in patients with erosive esophagitis (8).

After analyzing all the previous aspects, it is possible to assert that the pathophysiology of GERD is affected by the rate of occurrence and severity of reflux. Despite this, severe symptoms can be found in patients with a reasonably low esophageal acid exposure, while patients presenting a high one may have few symptoms (4).

The second section includes aspects other than acid reflux per se affecting the symptoms of GERD and the first one of interest is the pH of the reflux (4).

It is currently accepted that even a pH greater than four can produce reflux symptoms. Despite this, heartburn and regurgitation are more prone to be caused by reflux events in which the drop of the pH is greater. Moreover, it is proved that in GERD patients who are not undergoing a proton pump inhibitor (PPI) therapy 37% of reflux episodes show a weak acidity or a poor alkalinity, while in patients taking these drugs there is an increase to 80%. It is also possible to confirm that symptomatic poorly acidic reflux events are anticipated in the last 15-30 minutes by larger cumulative acid exposure than the asymptomatic refluxes. As a conclusion, it is possible to confirm the relevance of non-acid reflux in the perception of reflux symptoms (4).

The second section also includes the proximal extent. It is demonstrated that events of acid reflux presenting a large proximal extent are more probable to be felt. Furthermore, it is possible to assert that all kinds of reflux episodes with a great proximal extent (acid and non-acid) are more likely to produce symptoms. Other investigations show that patients with serious esophagitis have a tendency to present a higher average proximal extent than the ones with mild esophagitis. In addition, it is

proved that proximal extent is lower in NERD patients when related to subjects affected by esophagitis. This increased perception in reflux events with a high proximal extent may be due to the fact that reflux episodes with bigger volumes reach higher levels, causing a larger mechanical (distension) and chemical (acid) stimulation of the afferent nerves. The importance of the dilatation of the esophagus for symptom perception is proved by analyses in patients taking PPI drugs as proximal extent is connected to reflux perception despite a decreased acidity. In addition, GERD patients present smaller thresholds and, as a consequence, a greater mechano-sensitivity (4).

Another important aspect is gas reflux. In NERD individuals, the presence of gas in the refluxate significantly increases the likelihood of reflux perception. Moreover, pure gas reflux events can produce symptoms as well. This is due to the fact that GERD patients undergoing refractory PPI therapy engulf air more often during meals and present more reflux events which contain gas. Gas reflux can cause symptoms because of the stimulation of mechanoreceptors by esophageal luminal distention (4).

A great relevance in this second section is also constituted by the duodenal-gastricesophageal reflux. In gastroesophageal reflux it is also possible to find harmful components other than acid. These constituents include pepsin, trypsin and bile acids. Analyses inspecting the bilirubin concentration in the esophagus show that in GERD subjects who are not undergoing PPI therapy only 6-9 % of reflux symptoms are related to bile reflux and 12% to mixed (acid-bile) reflux. The mixture of bile acids and pepsin can produce disruption of the epithelial barrier function and cause harm of the mucosa (4).

This section also comprises the longitudinal muscle contraction. It is very common to find uninterrupted contractions of the esophagus preceding events of chest pain. This

shrinkage can also produce a heartburn sensation in patients affected by GERD. A possible phenomenon by which these contractions can generate symptoms of reflux is transient ischemia of the esophageal wall. Furthermore, it is proved that TRLESs are related to a specific arrangement of longitudinal muscle contractions which have a similar duration to the one of a TRLES. In addition, this muscle shrinkage is associated to a reduced blood perfusion of the esophageal wall (4).

An important role is also played by the mucosal integrity (8). An esophagus in good conditions is surrounded by a compact barrier of squamous epithelium which holds harmful substances in the lumen detached from peripheral nociceptors. In people presenting esophagitis there is a clear rupture in this barrier making it possible for components of the refluxate to arrive at the nociceptors in the lamina propria. Nevertheless, this sharp crack is not detectable in many of the GERD subjects who present a normal gastroscopy. Recently, microscopic deterioration of the esophageal mucosa was proposed as a pathophysiological factor in the manifestation of symptoms in individuals affected by NERD. This suggestion is due to the fact that a connection between defective mucosal integrity and empirical sensitivity to acid appears to exist (4).

Mucosal factors show a great pertinence in this second field of interest. It is confirmed that acid perfusion in the lower esophagus causes dilated intercellular spaces (DISs) in the epithelial tissue. It appears that DIS is originated by flow of ions (chloride ions included) through the epithelium because of an initial raised permeability. This is afterwards followed by water which, due to osmosis, penetrates the intercellular spaces producing dilation. Moreover, it is proved that therapy with PPIs overturns DISs. Lately, it was confirmed that in healthy individuals DIS can be produced not only

by acid (pH 2.0) but also by poorly acidic solutions (pH 5.5). In addition, it is possible to claim that distal perfusions also cause DIS in more proximal and unexposed mucosa. It must be noted as well that, together with structural signs of deterioration of the mucosal barrier in GERD, functional signs of its impairment can be present too. Cell-to-cell adhesion proteins (like tight junctions, e-cadherin and desmosomes) preserve the stability of the esophageal epithelium and separate its mucosal side from the serosal one. In GERD patients the epithelial tissue of the esophagus presents a raised permeability and is related to the proteolytic cleavage of e-cadherin, showing the relevance of the cell-to-cell adhesion proteins (4).

Last factor to take into account in this second section is sensitization (peripheral and central). As far as the former is concerned, GERD symptoms can be perceived as a consequence of an enhanced responsiveness of the esophagus to various stimuli. An exaggerated stimulation of the peripheral receptors of the afferent nerve endings can generate their upregulation through the dispensation of intracellular inflammatory mediators and produce a decreased threshold of transduction as a consequence. This primary sensitization leads to a hypersensitivity at the location of injury (4).

It occurs that many receptors are implicated in peripheral sensitization. Among them, it is possible to include the transient receptor vanilloid 1 (TRPV1) receptor, the acid-sensitivity ion channels and the purinergic (P2X) receptors (4).

TRPV1-receptor expression is greater in the sore esophageal mucosa. It is suggested that TRPV1 activation caused by acid-generated inflammation produces synthesis and discharge of P substance and calcitonin gene-related peptide from submucosal neurons and of platelet-activating factor from the cells of the epithelium. The first two are relevant inflammatory mediators, producing in this manner greater inflammation

which could induce a heightened permeability of the mucosa and farther peripheral sensitization (4).

An essential role in esophageal hypersensitivity is played not only by peripheral but also central sensitization. Acid provocation of the esophagus sensitizes as well the insula and cingulate cortex to subliminal and liminal non-painful mechanical stimulations. Intensified nociceptor input causes repeated warning cascades in the spinal dorsal horn neurons which later generates facilitated excitatory synaptic responses and decreased restriction, producing magnified reactions to both harmful and inoffensive inputs. Investigations conducted on the influences of negative and neutral emotional states on the perception of non-painful expansion of the esophagus found that the same stimulation was felt more strongly during an adverse emotional situation and was connected to a raised cortical activity in the anterior insula and the dorsal anterior cingulate gyri than during an indifferent emotional context. Furthermore, it is proved that exposure to acid in patients with GERD generates a faster and bigger cerebral activity than in healthy ones (4).

1.3 Clinical manifestations of GERD

In order to study the possible clinical presentations of GERD, it is important to distinguish between the appearance of this disease in children/adolescents and adults. As far as the first group is concerned, the most ordinary form of manifestation is self-perception. Despite this, it is hard for children younger than 8-12 years to describe their symptoms due to their development and ability to communicate. Moreover, most of the characteristic symptoms of GERD are non-specific and present a great variation depending on the age. On the contrary, the majority of teenagers has the capability to report their symptoms and to establish how burdensome they are. As a consequence,

an accurate history and bodily examination may be enough to confirm a diagnosis of GERD in the group of older children and teenagers without the need of further research (1).

The most frequent presentations of juvenile reflux are regurgitation (flow of gastric refluxed content into the oral pharynx) and vomiting. The ordinary manifestation of a trouble-free GER in an evidently healthy child presenting a typical growth is uncomplicated and innocuous regurgitation (9), which is also known as "happy spitter" (3). In these cases, spit up is frequently painless and non-bilious with no or minimal annoyance. In order to establish a diagnosis in these young children, it is necessary to collect data on the feeding history focusing on the quantity and regularity of formula or breastfeeding, the position of the toddler when the feeding is carried out, the burping and the behavior during this process (9).

Gasping and coughing during the feeding or an important irascibility can be alerting signs of GERD (3). If vigorous regurgitation of gastric contents occurs, laboratory and radiographic examinations of the upper gastrointestinal tract should be performed to differentiate other sources of vomiting (9).

Another possible clinical manifestation of GERD in infants includes unexplained crying and distressed behavior (3). These two are non-specific symptoms and could be related to a large range of aspects, which may be either pathologic or not. Toddlers on average weep or fuss two hours daily. However, personal differences of crying in newborns and awareness of the parents must be taken into account. Irritation associated to arching in babies is believed to be a non-spoken correspondent of pyrosis or chest pain in older kids (9).

Failure to thrive or poor weight gain should also be added to the group of the clinical manifestations of GERD in infants. Even in this case, a thorough feeding history should be realized. Together with the quantity of consumption and its regularity, it is also important to collect information on the description of the toddler's sucking and swallowing reflex. If the child is not gaining weight despite the presence of a proper amount of calories, it is necessary to start an analysis on origins of regurgitation and loss of weight other than GERD (9).

Clinical presentations in toddlers that should also be studied are the extraesophageal ones. It is possible to find evidence suggesting a likely association between GERD and an array of extraesophageal symptoms (3). Among them, it is important to analyze apnea and apparent life-threatening events (ALTEs). These two are commonly studied as extraesophageal presentations of GERD but causality is not often proved. Apnea of prematurity (AOP) is a developmental sleep disease which is not totally known yet. Feeding is a meaningful cause for AOP to occur. Hypoxemia during the feeding process is most likely associated to an inexperienced coordination between suction, ingestion and respiration. Despite this, it may also be caused by an immature laryngeal chemoreflex. Hypoxemia after feeding may be produced by diaphragmatic fatigue and GER infrequently takes part into it. Even though an apparent temporal association based on history is found in some cases and testing in single infants is generally noticed, the current evidence shows that there is no connection between GER and either apnea or ALTEs. It is also possible to claim that anti-reflux drugs do not decrease the frequency of apnea events in premature toddlers (9).

Last clinical presentation to take into account in the group of young children is Sandifer Syndrome. This final manifestation is an uncommon particular presentation of GERD

and is a spasmodic torsional dystonia that is associated to arching of the back and opisthotonic posturing. It is indispensable to make a differential diagnosis with other neurologic conditions such as seizures, infantile spasm and dystonia. The pathogenesis of this condition is not completely understood yet but it is hypothesized that it happens following a vagally-mediated reflex as a reaction to esophageal acid exposure. This condition answers well to an anti-reflux therapy (9).

As far as the group of adults is concerned, the symptomatology of GERD generally includes heartburn or pyrosis, regurgitation and dysphagia. Heartburn shows a specificity of 89% and a positive predictive value of 81% for GERD. Regurgitation presents a specificity of 95% and a positive predictive value of 57% for the disease. The combination of the former and the latter has a veracity larger than 90% for the diagnosis of GERD (5).

Recent investigations provide knowledge on the extraesophageal manifestations of this disease. There are patients that do not present any complaint of associated heartburn and regurgitation. This led to the description of the "atypical" presentations of GERD. It is possible to find at least one extraesophageal symptom in 80% of the patients with GERD. The most ordinary atypical symptoms include asthma, cough and laryngitis (5).

Together with asthma and post-nasal drip, it is possible to claim that GERD is one of the three major origins of chronic cough, computing for 20% of the cases (7). Refluxrelated cough should be presumed in patients presenting chronic non-productive cough without proof of asthma or post-nasal drip, non-smokers who are not on coughproducing drugs and in individuals whose symptoms get worse after big meals or when in a supine position (10).

Chronic laryngitis is a continuous inflammation of the larynx produced by either outer irritation from smoking, alcohol or intrinsic factors such as asthma and GERD (7). It is possible to estimate that 50-60% of chronic laryngitis and sore throat that is difficult to treat may be connected to GERD (10). Reflux of gastroduodenal contents in patients affected by chronic laryngitis is generally cited as laryngopharyngeal reflux (LPR), where presenting symptoms mostly comprise dysphonia, globus pharyngeus (perception of lump in the throat), moderate dysphagia, hoarseness, chronic cough and nonproductive throat clearing (7).

Asthmatic patients who either present symptoms that worsen after eating or who do not respond to anti-asthmatic therapy should be thought of presenting GERD-related asthma. In the same way, patients presenting GERD symptoms before the beginning of asthma's ones should be counted as affected by reflux induced asthma (7).

Occasionally, GERD can also produce esophageal injuries due to caustic inflammation (peptic or reflux esophagitis) such as hemorrhages and perforations. As far as the former is concerned, chronic bleeding and anemia that is iron-deficient may occur in the case of esophageal erosions and ulcers. The latter ones are a very rare complication of GERD and they generally occur as a result of an esophageal ulcer, causing mediastinitis (5).

Other two possible chronic esophageal complications include strictures and Barrett esophagus (BE). Peptic strictures are severe end stages of reflux disease, which happen in 4-20% of patients affected by reflux esophagitis. Among these patients, 25-50% develop concomitant columnar metaplasia of the squamous epithelium (BE). This is the most severe histological repercussion of GERD and it is studied as a precancerous lesion (5).

Risk factors involve chronic reflux symptoms, smoking, white race, male sex, raising age (especially older than 50 years), hiatal hernia and obesity. If warning signs are present, an endoscopy is recommended (7).

GERD is often described as a progressive disease, in which effective intervention is necessary to avoid going from a nonerosive illness to an erosive one and an eventual BE. This "spectrum of disease" analysis is contrasted by the perspective that GERD is an illness characterized by phenotypical categories such as nonerosive disease, erosive esophagitis and Barrett esophagus. This means that change from one presentation to another one is not common and individuals tend to stay in their primary category. This is also supported by the reported rates of change over a period of 20 years, which are relatively small. In individuals in whom it was possible to rule out in the site of a healed mucosa at index endoscopy stricture and BE, the chance of developing them during the following 7 years is respectively 1.9% and 0.0% (7). Finally, GERD can also produce pathological alterations to both hard and soft oral tissues (11). Among them, the most predominant one is dental erosion (12) while oral changes in the mucosa related to GERD are seen less commonly (11). Undiagnosed tooth erosion can produce really severe injuries to the dentition over time and it is quite regular to find patients unaware of the condition. For this reason, dentists acquire a very important role as they may be the first ones to find signs of the disease allowing

them to perform the first diagnosis (12).

2. Objectives

Primary objectives:

- To describe the most common dental lesions produced by chronic gastroesophageal reflux disease (GERD).
- To review the most frequent oral mucosa problems associated to chronic GERD.

Secondary objectives:

- To analyze the relationship between GERD and the parafunctional habit of bruxism.
- To review management of patients with GERD at dental offices.

3. Methodologies

In order to realize this investigation, a bibliographic research of biomedical literature was performed using PubMed (US National Library of Medicine) and Medline (Medical Literature Analysis and Retrieval System Online). The latter was accessed through the library of the European University of Madrid.

The Mesh-Terms used included "reflux", "GERD", "definition of GERD", "risk factors of GERD", "GERD treatment", "GERD pathophysiology and pathogenesis", "clinical manifestations and presentations of GERD", "oral manifestations of GERD", "GERD and dentistry", "regurgitation", "dental erosion", "GERD in the oral cavity", "GERD and bruxism" and "GERD in the dental office". The titles and the abstracts (when present) of the different analyses were checked to determine if the publications could be useful for the research goal of the investigation.

Inclusion criteria:

- Only articles in English were inspected.
- Only studies with the full text available were selected.
- The time frame chosen to perform this inquiry was between 2010 and 2021.

The investigation resulted in 32 scientific articles and a narrative approach was chosen to carry out this examination.

The literature was used with the following distribution:



4. Discussion of results

4.1 Dental lesions in chronic GERD (adults and children)

Erosive tooth wear is described as the loss of dental structure caused by both physical and chemical processes of cleavage of hard tooth tissue as a result of the presence of acid inside the oral cavity, with no bacterial involvement (13).

The development of dental erosion involves different factors, which could either be extrinsic or intrinsic. The former ones comprise acidic food and drinks, while the latter involve chronic regurgitation, repetitive emesis and GERD (14).

The demineralization of the enamel starts at a pH of 5.5 and hydrochloric acid contained in the digestive secretions of the stomach frequently presents a pH lower than 2 (15).

Moreover, a common problem associated with GERD is xerostomia (16).

As a consequence, the association of the acidic pH of gastric juice and the decrease of salivary discharge causes a reduction of the hardness of the tooth enamel (17).

For this reason, it is possible to claim that dental erosion is a considerable oral manifestation of GERD, as described in the Montreal Definition and Classification (15).



Fig. 2,3. Erosive tooth wear following chronic exposure to GERD in the palatal surfaces of the upper incisors. Sources: Wilder-Smith CH. et al. (19) and Lee RJ. et al. (31).



Fig. 4,5. Early and advanced erosion produced by chronic GERD. Sources: Ranjitkar S. et al. (11) and Lee RJ. et al. (31).

This statement is also supported by different studies in which the relationship between

being affected by GERD and presenting dental lesions was investigated.

A distinction between tooth injuries in adults and children was performed.

As far as the adulthood group is concerned, six relevant analyses were taken into

account and erosive dental wear lesions were found in a range between 24% and 88%

(table 2).

Dental lesions in adults				
Authors	Sample size	Age	Dental tissue lesions	Prevalence
Alauraudanjoki et al. (18)	1962	46-47	Erosive wear	Odds ratio: 3.80
Ramachandran et al. (13)	50	18-40	Dental erosion	GERD: 88% Control: 32%
Wilder-Smith et al. (19)	72	29.1-38.5	Erosive tooth wear	88%
Warsi et al. (20)	187	19-80	Dental erosion	33.5%
Picos et al. (21)	120	20 or older	Dental erosion	35%
Yoshikawa et al. (22)	70	42-79	Dental erosion	24.3%

Table 2. Dental lesions in adults.

Alauraudanjoki et al. studied the connections between self-assessed GERD and the preponderance/severeness of dental erosion. For this purpose, using questionnaires assessing the existence of GERD, a subgroup of the Northern Finland Birth Cohort of 1966 (NFBC 1966) was selected and had their oral cavities analyzed. The results proved that, on an individual base, regular troubles with GERD appear to be evident risk signals for a serious dental erosion. The advantage of this analysis compared to the others is the great number of people involved in it and a possible disadvantage is that silent reflux (GERD with no symptoms) was not taken into account. For this reason, it is suggested that an investigation involving the asymptomatic form of GERD could show a greater association with dental wear (18).

Ramachandran et al. examined as well tooth wear in GERD patients by performing a cross-sectional descriptive analysis in which simple randomness was applied. Individuals included in this investigation had received a previous diagnosis of GERD using upper GI endoscopy and were evaluated for dental erosion clinically. The results of this study show that dental erosion is predominant in patients affected by GERD. Despite this, it is recognized that a bigger sampling is required. The advantage of this examination is the technique used to identify GERD (upper gastrointestinal endoscopy), which is considered the gold standard one at the moment (13).

Wilder-Smith et al. performed a longitudinal investigation of 1 year on GERD and dental erosion. In this analysis, all the individuals presented an important tooth erosion and 88% of them a raised exposure to esophageal acid by 24-hour multichannel intraluminal pH-impedance measurement (MII-pH). After being prescribed esomeprazole 20 mg twice a day, they were re-evaluated after 1 year. The results showed that dental erosion did not progress in 74% of the individuals. This further

proves that GERD can cause erosive tooth wear, even though the size of the sample is not a very large one (19).

Warsi et al. realized a cross-sectional analysis, which included patients who had been confirmed GERD positive with an esophagogastroduodenoscopy and a complete gastrointestinal exploration. These individuals underwent an obligatory exam of the oral cavity to study both soft and hard tissue lesions produced by GERD. The former will be described in the next session. Regarding the latter, this investigation strengthens erosive tooth wear as related to GERD in around 33% of the patients (20). Picos et al. carried out a study on the existence of erosive tooth wear in GERD and found a considerably greater risk of dental erosion in 35% of the individuals affected by GERD, even though this is a small analysis performed in preparation of a larger one (21).

Yoshikawa et al. is the only investigation that did not just search for the presence and cause of dental erosion, but also for the surfaces of the teeth involved in this process. The lesions of tooth wear were present in the palatal surfaces of the upper anterior teeth and in the lingual surfaces of the lower premolars and anterior ones. The palatal areas of the superior teeth may be sensitive to the erosive process because they are the first ones that get in contact with the gastric juice. Moreover, it is important to take into account two factors (22).

The first one is the relative distance between the major salivary glands and these areas, while the second one is the fact that the tongue keeps the juice against them. The involvement of the lower lingual surfaces may be due to the decreased amount of saliva produced. The more GERD is allowed to act, the more surfaces and teeth are affected (22). This agrees with the Montreal accord, which asserts that there is a direct
association between the appearance of GERD and erosive tooth wear, especially when present on the palatal and lingual areas of the teeth (20).

As far as the dental lesions in children are concerned, the available information is still insufficient. Only two significant investigations were selected (table 3).

Dental lesions in children				
Authors	Sample	Age	Dental tissue lesions	Percentage of
	size			appearance
Drummond de	179	2-14	Dental erosion	GERD: 25.6%
Oliveira et al.				No GERD: 5.9%
(23)				
Farahmand et	112	3-12	Dental erosion	GERD: 98.1%
al. (24)				Control: 19%

Table 3. Dental lesions in children.

Drummond de Oliveira et al. realized a case-control study with children who had been diagnosed GERD positive with the 24-hour pH monitoring test. The results of this analysis found an important relation between erosive tooth wear and GERD in about 26% of the involved juveniles. In addition, these lesions appeared on the lingual and incisal/occlusal areas of the teeth and were mainly present in the temporary dentition as just two permanent teeth in one kid were affected by tooth erosion. As an explanation to this fact, the authors claim that the amount of time spent by the permanent teeth in the mouth is not enough to show signs of erosion by the acid. Despite this, it is recognized that the temporary teeth present differences in both structures and histology when compared with the permanent dentition (23).

Farahmand et al. evaluated dental erosion in 54 patients presenting GERD and in 58 as the control healthy group, finding an association between GERD and tooth erosion in about 98% of the sample. In patients with GERD presenting temporary dentition, erosive tooth wear was mainly encountered in superior posterior occlusal areas. In the healthy group, tooth erosion was for the most part present in superior anterior labial

29

surfaces. In the GERD patients with permanent teeth, dental erosive wear chiefly occurred on the inferior posterior occlusal surfaces. The problem of this investigation is that the diagnostic method was not uniform as three different techniques were used (endoscopy, questionnaires and 24 hour pH monitoring). For this reason, it is possible to claim that the number of patients with GERD and of lesions attributed to it is higher. Thus, there are other factors responsible for the appearance of these lesions and this study is not as valid as the previously cited one (24).

To conclude this first section, both the studies in adults and kids prove that the appearance of erosions in teeth can suggest the presence of GERD. For this reason, it is necessary to recognize the importance that dentists have in the diagnosis of GERD as they may be the first ones to notice these dental signs (13).

4.2 Soft tissue lesions associated to GERD

Oral soft tissue injuries may appear because of GERD as a result of either direct acid or acidic vapor contact inside the mouth (11).

Still, there is a large lack of information regarding the effects of GERD on the oral mucosa (11).

For this reason, just two relevant publications were selected. In this case, it was not possible to perform a differentiation between mucosal lesions in adults and children as there were not available investigations (table 4).

Soft tissue lesions				
Authors	Sample size	Age	Soft tissue lesions	Prevalence
Warsi et al.	187	19-80	Xerostomia	Odds ratio: 3.005
(20)			Aphtoid mucosal	Odds ratio: 6.609
			ulceration	
			Gingivitis	Odds ratio: 7.516
			Angular chelitis	Odds ratio: 4.028
Watanabe et	130	28-70	Oral dryness	Complaints: 56.2%
al. (25)			Gingivitis	Inflammation of
				mucosa: 15.2%

Inflammation of tongue, buccal mucosa and palatal regions	
--	--

Table 4. Soft tissue lesions.

The research of Warsi et al., which has been previously mentioned, concluded that patients presenting dental erosion had worse oral manifestations than those in which erosive tooth wear had not been encountered. This investigation detected a confident association between heavy conditions of GERD and oral expressions, which included xerostomia, aphtoid ulcerations of the mucosa, gingivitis and angular cheilitis. Despite this, it is suggested that further studies are necessary to increase the knowledge on these oral symptoms (20).

Watanabe et al. performed a single-site, cross-sectional and retrospective study. This analysis took into account subjects who had been diagnosed GERD positive and both older and younger groups of control. The average ages of these three groups were respectively 66.4, 68.3 and 28.7 years old. The diagnosis of GERD was based on the existence of characteristic reflux manifestations including pyrosis and regurgitation of acid occurring more than twice a week. All the individuals involved were previously interviewed and finally received four oral explorations, which were focused on salivary discharge, swallowing function, hard and soft oral tissues. As far as the mucosal lesions were concerned, the most prevalent oral manifestation was dryness of the mouth. This is due to the fact that salivary discharge was greatly decreased in GERD patients. Moreover, gingival inflammation levels (including both gingivitis and redness of the tongue, palate and buccal mucosa) were fairly larger in GERD positive individuals. Exacerbation of gingivitis may be either due to a decreased amount of saliva or bruxism, which appeared to be increased in GERD patients and will be

discussed in the following section. The redness in the palate was believed to be caused by the direct contact with the gastric acid, while the one in the other two areas by the biting induced by bruxism. Despite this, further bigger and looking forward investigations are needed to confirm these results (25).

As a conclusion, it is possible to assert that the connection between GERD and oral soft tissue lesions is still a disputed one. For this reason, more assessing investigations are required (20) and oral mucosal lesions are not considered as extraesophageal manifestations of GERD yet (15).

4.3 GERD and bruxism

New literature suggests the association between GERD and bruxism (26).

The processes of dental erosion may be more complex in individuals with bruxism if the relation between this and GERD is considered. There are many studies proving the connection between erosion and bruxism or the one between dental wear and GERD. Despite this, very few investigations have been performed to study the association between GERD and bruxism (27) (table 5).

GERD and bruxism				
Authors	Sample size	Age	Parafunction and lesions	Prevalence
Watanabe et al. (25)	130	28-70	Bruxism Tooth wear	17.1%
Sakaguchi et al. (28)	1840	12-15	Association among problem behaviors, bruxism and GERD.	23.8%
Li et al. (27)	726	18-72	Bruxism Tooth wear	Odds ratio: 4.70

Table 5. GERD and bruxism.

The analysis conducted by Watanabe et al., which was earlier described, found that patients affected by GERD presented a higher frequency of bruxism than both their

older and control groups. For this reason, it is suggested that bruxism does not only contribute to increase dental erosion, but also may exacerbate gingivitis (25).

An association between bruxism and GERD was also detected by Sakaguchi et al., who performed a cross-sectional inquiry using some questionnaires in adolescents (28).

Despite this, the only study that has investigated so far the interconnection among GERD, bruxism and dental erosion is the one performed by Li et al. This group designed a case-control analysis to confirm the association between GERD and bruxism and a cross-sectional examination on the same cohort to demonstrate if there is a link between GERD and erosion in patients affected by bruxism. The result of this investigation was a positive one, suggesting the importance that dentists have in identifying the proper cause of tooth wear when they see a patient (27).

As a conclusion, it is possible to understand how difficult it is to differentiate single conditions since they are all connected to one another. Therefore, more studies are required to get a better knowledge of these clinically significant associations (26).

4.4 Patients with GERD at the dental office

Dental professionals are very commonly the first health care providers to detect systemic diseases by inspecting their oral expressions. Among them, GERD has become one of the most widespread (29).

Therefore, a close collaboration between the dentist and the patient's family doctor/gastroenterologist is required for the complete management of this disease. Patients with GERD present a greater frequency of dental sensitivity, facets due to erosion, loss of mineral tissue, dished-out distortions and sharpened edges of the dentition (13).

33

The longer the condition acts, the more teeth get affected and the more serious the damages are (15).

The loss of dental structure can as well produce discrepancies at the occlusal level (14) such as a decrease in the vertical dimension giving origin to complications in the mastication (13).

GERD is not associated to an increased amount of dental cavities (30), but the loss of dental surface close to restorations can originate breaches and as a consequence secondary decays (13).

Once the patient is receiving GERD treatment, it is possible to start dental rehabilitation (31). If enough tooth structure is available, minimal invasive treatments are the recommended ones. Otherwise, ceramic restorations including the use of fiber or metal posts can be successful. Moreover, the dental professional can reinforce the tooth structure with the use of fluoride so that the process of remineralization is activated (32).

To sum up, the dentist has two important duties. The first one is to realize a detailed anamnesis and a careful exploration, while the second one is to make the patient aware of the damages that GERD can produce in the oral cavity (32).

34

5. Conclusion

- This analysis reinforces the Montreal agreement by proving that dental erosion is a relevant manifestation of GERD.
- 2. Tooth erosion is the most common lesion related to GERD and it occurs in around 25 35 % of patients.
- The lesions of tooth wear associated to chronic GERD were present in the palatal surfaces of the upper anterior teeth and in the lingual surfaces of the lower premolars and anterior ones.
- It is suggested that GERD is also responsible of lesions at the soft tissue level.
 Despite this, more investigations are required as there is not enough data available at the moment.
- 5. Associations between GERD and bruxism have been found, but this complex connection requires further analyses.
- 6. Patients affected by GERD are commonly detected in the dental office. For this reason, a partnership between the dentist and the patient's family physician/gastroenterologist is vital in order to fully rehabilitate these individuals.

6. Social responsibility

6.1 Responsibility of the dental professional

This investigation shows the relevance that dentists have in the detection of GERD. As previously explained, the dentist is commonly the first health professional to detect the signs of this disease. The importance of the dental professional is even greater in the cases in which GERD is asymptomatic.

Therefore, this proves that Dentistry is a meaningful specialty of the medical field. In the recent years, it has become quite popular to consider dentists and physicians as two separate entities. For this reason, it is very frequent to encounter dentists who only take care of the dental lesions without delving into the roots of the problem.

This analysis demonstrates the real duty of the dental practitioners. The dentist is a health specialist and as such has the obligation to fully treat the patient.

As a consequence, it is possible to claim that the collaboration between the dentist and any other medical specialist is vital.

Once the cause of the lesions is established and treated, it will also be possible to restore the oral cavity of the patients and to perform long-lasting treatments.

6.2 Responsibility of the patient

This bibliographic review shows that GERD is a very prevalent disease in the modern society, affecting individuals of all ages from toddlers to elderlies. Despite this, GERD often displays either an asymptomatic or a slightly symptomatic presentation.

For this reason, the signs of this disease may often go unnoticed.

As stated in the previous section, the dentist has the capacity to detect and to recognize GERD manifestations on the oral tissues.

37

Therefore, this is a further example for individuals considering the oral health as an accessory care that dentists play a role as necessary as the one of any other physician in the medical field.

As a result, this investigation reinforces the importance of visiting a dental clinic once or twice a year. By doing so, it will be possible for the dental practitioner to identify signs of disorders and to provide a proper treatment in collaboration with the required health specialists.

6.3 Responsibility of the government

As stated in the previous two sections, the dental professional is an essential entity in the modern society.

For this reason, the government has the duty to teach their citizens how relevant the oral health is for the complete well-being of the individual.

This could be performed by introducing simple commercials in the most common channels of communication such as the radio or the tv and by using both direct and easy to understand messages.

A greater effect could also be achieved if the government organized their finances so that a visit to a dental clinic is favored at least once a year.

Health is one of the fundamental rights of the individual and it is an obligation of the authorities to favor it in any of its aspects.

38

7. Bibliography

- 1. Carroll MW, Jacobson K. Gastroesophageal Reflux Disease in Children and Adolescents When and How to Treat. Pediatr Drugs. 2012; 14(2): 79-89.
- 2. Pandeya N, Green AC, Whiteman DC, Webb PM, Hayward NK, Parsons PG, et al. Prevalence and determinants of frequent gastroesophageal reflux symptoms in the Australian community. Diseases of the Esophagus. 2012 Sep 1; 25(7): 573–83.
- 3. Poddar U. Gastroesophageal reflux disease (GERD) in children. Paediatrics and International Child Health. 2019; 39(1): 7–12.
- 4. Herregods TVK, Bredenoord AJ, Smout AJPM. Pathophysiology of gastroesophageal reflux disease: new understanding in a new era. Neurogastroenterology and Motility. 2015; 27(9): 1202–13.
- 5. Mushtaque AR. Gastroesophageal Reflux Disease An Update. Bangladesh Journal of Medical Science. 2010; 9(1): 14-26.
- 6. Nwokediuko SC. Current Trends in the Management of Gastroesophageal Reflux Disease: A Review. ISRN Gastroenterol. 2012; 2012: 1–11.
- 7. Almutairi MBG, Alsulaimi MS, Ali R, Alghamdi RAI, Alrehaili KA, et al. Evaluation of GERD Diagnosis, Management, and Outcomes. The Egyptian Journal of Hospital Medicine. 2018 July; 72(9): 5195-5202.
- 8. Farré R. Pathophysiology of gastro-esophageal reflux disease: A role for mucosa integrity? Neurogastroenterology and Motility. 2013 Oct; 25(10): 783–99.
- 9. Czinn SJ, Blanchard S. Gastroesophageal reflux disease in neonates and infants: When and how to treat. Pediatr Drugs. 2013 Feb; 15(1): 19–27.
- 10. Hom C, Vaezi MF. Extra-esophageal manifestations of gastroesophageal reflux disease: Diagnosis and treatment. Drugs. 2013; 73: 1281–95.
- 11. Ranjitkar S, Smales RJ, Kaidonis JA. Oral manifestations of gastroesophageal reflux disease. Journal of Gastroenterology and Hepatology (Australia). 2012; 27: 21–7.
- Cãlin DL, Mitrea M, Frâncu LL. Dental erosion and other oral anatomical changes caused gastroesophageal reflux. Revista Română de Anatomie funcţională şi clinică, macro-şi microscopică şi de Antropologie. 2012; 11(3): 364–8.
- 13. Ramachandran A, Raja Khan S, Vaitheeswaran N. Incidence and pattern of dental erosion in gastroesophageal reflux disease patients. J Pharm Bioallied Sci. 2017 Nov 1; 9(5): S138–41.
- 14. Picos A, Badea ME, Dumitrascu DL. Dental erosion in gastro-esophageal relux disease. A systematic review. Med Pharm Reports. 2018 Oct 30; 91(4): 387–90.
- Durazzo M, Lupi G, Cicerchia F, Ferro A, Barutta F, Beccuti G, et al. Extra-Esophageal Presentation of Gastroesophageal Reflux Disease: 2020 Update. J Clin Med. 2020 Aug 7; 9(8): 2559.
- 16. Raibrown A, Giblin LJ, Boyd LD, Perry K. Gastroesophageal Reflux Disease Symptom Screening in a Dental Setting. The Journal of Dental Hygiene. 2017 February; 91(1): 44-48.
- 17. Petrovici CS, Petcu LC, Puscasu CB, Petrovici DF, Petcu A, Ion I. Changes induced by the decrease of salivary pH on the hardness of the dental enamel. Section Sociology and Healthcare. 409-416 Available from: https://doi.org/10.5593/SWS.ISCSS.2019.3

- 18. Alaraudanjoki V, Laitala ML, Tjäderhane L, Pesonen P, Lussi A, Ronkainen J, et al. Influence of Intrinsic Factors on Erosive Tooth Wear in a Large-Scale Epidemiological Study. Caries Res. 2016 Sep 1; 50(5): 508–16.
- 19. Wilder-Smith CH, Materna A, Martig L, Lussi A. Longitudinal study of gastroesophageal reflux and erosive tooth wear. BMC Gastroenterol. 2017 Oct 25; 17(1): 113.
- 20. Warsi I, Ahmed J, Younus A, Rasheed A, Akhtar TS, Ain QU, et al. Risk factors associated with oral manifestations and oral health impact of gastrooesophageal reflux disease: A multicentre, cross-sectional study in Pakistan. BMJ Open. 2019; 9(3): 1–12.
- 21. Picos AM, Poenar S, Opris A, Chira A, Bud M, Berar A, et al. Prevalence of dental erosion in GERD: a pilot study. Clujul Med. 2013; 86(4): 344–6.
- 22. Yoshikawa H, Furuta K, Ueno M, Egawa M, Yoshino A, Kondo S, et al. Oral symptoms including dental erosion in gastroesophageal reflux disease are associated with decreased salivary flow volume and swallowing function. J Gastroenterol. 2012 Apr; 47(4): 412–20.
- 23. De Oliveira PAD, Paiva SM, De Abreu MHNG, Auad SM. Dental erosion in children with gastroesophageal reflux disease. Pediatr Dent. 2016; 38(3): 246–50.
- 24. Farahmand F, Sabbaghian M, Ghodousi S, Seddighoraee N, Abbasi M. Gastroesophageal reflux disease and tooth erosion: a cross-sectional observational study. Gut Liver. 2013 May; 7(3): 278–81.
- 25. Watanabe M, Nakatani E, Yoshikawa H, Kanno T, Nariai Y, Yoshino A, et al. Oral soft tissue disorders are associated with gastroesophageal reflux disease: Retrospective study. BMC Gastroenterol. 2017 Aug 7; 17(1): 92.
- 26. Wetselaar P, Manfredini D, Ahlberg J, Johansson A, Aarab G, Papagianni CE, et al. Associations between tooth wear and dental sleep disorders: A narrative overview. Journal of Oral Rehabilitation. 2019; 46: 765–75.
- Li Y, Yu F, Niu L, Hu W, Long Y, Tay F, et al. Associations among Bruxism, Gastroesophageal Reflux Disease, and Tooth Wear. J Clin Med. 2018; 7(11): 417.
- 28. Sakaguchi K, Yagi T, Maeda A, Nagayama K, Uehara S, Saito-Sakoguchi Y, et al. Association of problem behavior with sleep problems and gastroesophageal reflux symptoms. Pediatr Int. 2014; 56(1): 24–30.
- 29. Călin DL. Severe dental wear caused by association between nocturnal bruxism and gastroesophageal reflux: overview on the clinical and scientific aspects. Revista Română de Anatomie funcțională și clinică, macro-și microscopică și de Antropologie. 2017; 16(4): 379-86.
- 30. Sîmpălean D, Dana G, Petrişor M, Măruşteri M, Bacârea V, Simona B. The frequency of dental caries in adult patients with gastroesophageal reflux disease. Acta Medica Marisiensis. 2015 Aug 18; 61(2): 124–7.
- 31. Lee Rj, Aminian A, Brunton P. Dental complications of gastro-oesophageal reflux disease:guidance for physicians. Internal Medicine Journal. 2017. 47(6): 619-23.
- 32. Jankovitz MV, Pinto HDG, Caldas RJ, Barbosa CCN, Barbosa OLC. The influence of gastroesophageal reflux in oral cavity. Brazilian Journal of Surgery and Clinical Research. 2019 Jun Aug; 27(1):70-3.

8. Annexes

REVIEW ARTICLE

2012 Adla Data information BV. All rights reserved.

Gastroesophageal Reflux Disease in Children and Adolescents

When and How to Treat

Matthew W. Carroll¹ and Kevan Jacobson^{1,2}

1 Division of Gastroenterology, Hepatology and Nutrition, British Columbia Children's Hospital, Vancouver, BC, Canada

2 Child and Family Research Institute, University of British Columbia, Vancouver, BC, Canada

Contents

At	bstract.	79
1.	Introduction	79
2.	Definitions	80
3.	Pathophysiology.	80
	3.1 Transient Relaxation of the Lower Esophageal Sphincter (LES)	80
	3.2 Hypotensive or Incompetent LES.	81
	3.3 The Esophagogastric Junction.	81
4.	Clinical Presentation	82
5.	Diagnostic Evaluation	83
6.	Treatment of Gastroesophageal Reflux Disease in Children and Adolescents	84
	6.1 Lifestyle and Behavioral Changes.	84
	6.2 Surface Protective Agents	
	6.3 Antacids	85
	6.4 Histamine H ₂ Receptor Antagonists	
	6.5 Proton Pump Inhibitors	
	6.6 Prokinetics.	
	6.7 Surgical Intervention	86
7	Conclusions	86
<i>.</i>		00

Abstract

Gastroesophageal reflux (GER) is a common presenting complaint in children and adults, and is a frequent reason for physician consultation. GER disease (GERD), whilst benign in the majority of cases, is frequently a chronic condition that has been shown to result in significantly reduced quality of life in children and adolescents. Furthermore, there is emerging evidence that the prevalence of GERD is rising and may have links to adult obesity and other morbidities. Consequently, accurate diagnosis, appropriate management strategies, and timely referral to specialist services are important principles in the effective management of GERD. Acid-suppressive drugs are effective therapies but are one of the most costly classes of drugs prescribed. Therefore, not only is an accurate diagnosis important to the patient, but it is also of significant interest from a public health and resource utilization standpoint.

1. Introduction

'Gastroesophageal reflux' (GER) is a frequent reason for consultation at all levels, from family practitioners through to

specialist gastroenterologists.^[1,2] In Western adult populations, the prevalence of gastroesophageal reflux disease (GERD) has been estimated to be as high as 10–20%.^[1,3] In the pediatric population, the epidemiology is not as well defined, but there is emerging

Diseases of the Esophagus (2012) 25, 573-583 DOI: 10.1111/j.1442-2050.2011.01287.x



Original article

Prevalence and determinants of frequent gastroesophageal reflux symptoms in the Australian community

N. Pandeya,12 A. C. Green,2 D. C. Whiteman,2 for the Australian Cancer Study*

¹School of Population Health, The University of Queensland, and ²Queensland Institute of Medical Research, P O Royal Brisbane Hospital, Herston, Queensland, Australia

SUMMARY. Frequent gastroesophageal reflux (GER) causes chronic inflammation and damages esophageal mucosa, which can lead to Barrett's esophagus. It has also been consistently found to be a strong risk factor for esophageal adenocarcinoma. The prevalence of GER appears to vary; however, population-based Australian studies investigating the symptoms are limited. This study aimed to estimate the population prevalence and identify the determinants of frequent GER symptoms in the Australian population. Self-reported information on the frequency of reflux symptoms were collected from 1,580 adults from a population register. We estimated age- and sex-standardized prevalence of occasional (<weekly) and frequent (≥weekly) GER symptoms in the Australian population. We also estimated adjusted prevalence ratios (PR) for GER symptoms associated with demographic and lifestyle characteristics. The standardized prevalences of GER symptoms were 10.4% and 38.3% for frequent and occasional symptoms, respectively. Compared with participants with body mass index <25, those with body mass index ≥35 had almost 90% higher prevalence of frequent GER symptoms (PR 1.89; 95% confidence interval [CI] 1.13-3.16). Similarly, the prevalence of frequent GER symptoms was significantly higher among regular users of aspirin or other non-steroidal anti-inflammatory drugs than never users (PR 1.71; 95%CI 1.08-3.16) and regular consumers of medium to well-done barbecued meat (PR 1.75: 95%CI 1.10-2.80) or fried food (PR 2.69: 95%CI 1.66-4.35). The prevalence of frequent GER symptoms was significantly lowered with regular physical activity (PR 0.46; 95% CI 0.32-0.66) and Helicobacter pylori infection (PR 0.53; 95% CI 0.35-0.80). We found no evidence that frequent GER symptoms were associated with smoking, alcohol, spicy food, or coffee consumption. Our results confirm that GER symptoms are common and that frequent GER symptoms are associated with a range of modifiable lifestyle factors.

KEY WORDS: body mass index, cross-sectional survey, gastroesophageal reflux, non-steroidal anti-inflammatory drugs.

Address correspondence to: Dr Nirmala Pandeya, BSc, MMedSc, PhD, School of Population Health, The University of Queensland, Public Health Building, University of Queensland, Herston, QLD 4006, Australia. Email: n.pandeya1@uq.edu.au *The Australian Cancer Study: Oesophageal Cancer:

Investigators: David C. Whiteman, MBBS, PhD; Penelope M. Webb, MA, D Phil; Adele C. Green, MBBS, PhD; Nicholas K. Hayward, PhD; Peter G. Parsons, PhD; David M. Purdie, PhD.

Clinical collaborators: B. Mark Smithers, FRACS; David Gotley, FRACS, PhD; Andrew Clouston, FRACP, PhD; Ian Brown,

FRACP. Project Manager: Suzanne Moore, RN, MPH. Database: Karen Harrap, BIT, Troy Sadkowski, BIT. Research nurses: Suzanne O'Brien, RN, MPH; Ellen Minehan, RN; Deborah Roffe, RN; Sue O'Keefe, RN; Suzanne Lipshut, RN; Gabby Connor, RN; Hayley Berry, RN; Frances Walker, RN; Teresa Barnes, RN; Janine Thomas, RN; Linda Terry, RN, MPH; Michael Connard, B Sc; Leanne Bowes, B Sc; Mary Rose Malt, RN; Jo White, RN, Clinical Contributors

Cunical Contributors: Australian Capital Territory: Charles Mosse, FRACS, Noel Tait, FRACS. New South Wales: Chris Bambach, FRACS, Andrew Biankan, FRACS, Roy Brancatisano, FRACS, Max Coleman, FRACS, Michael Cox, FRACS, Stephen Deane, FRACS, Gregory L. Falk, FRACS, James Gallagher, FRACS, Mike Hollands, FRACS, Tom Hugh, FRACS, David Hunt, FRACS, John Jorgensen, FRACS, Christopher Martin, FRACS, Mark Richardson, FRACS, Garrett Smith, FRACS, David Stephen Seriel Stephen State St FRACS, Ross Smith, FRACS, David Storey, FRACS. Queensland: John Avramovic, FRACS, John Croese, FRACP, Justin D'Arcy, FRACS, Stephen Fairley, FRACP, John Hansen

FRACS, John Masson, FRACP, Les Nathanson, FRACS, Barry O'Loughlin, FRACS, Leigh Rutherford, FRACS, Richard Turner, FRACS, Morgan Windsor, FRACS.

South Australia: Justin Bessell, FRACS, Peter Devitt, FRACS, Glyn Jamieson, FRACS, David Watson, FRACS, Victoria: Stephen Blamey, FRACS, Alex Boussioutas, FRACP, Richard Cade, FRACS, Gary Crosthwaite, FRACS, Ian Faragher, FRACS, John Gribbin, FRACS, Geoff Hebbard, FRACP, George Kiroff, FRACS, Bruce Mann, FRACS, Bob Millar, FRACS,

Paul O'Brien, FRACS, Robert Thomas, FRACS, Simon Wood, FRACS Western Australia: Steve Archer, FRACS, Kingsley Faulkner, FRACS, Jeff Hamdorf, FRACS.

© 2011 Copyright the Authors

Journal compilation © 2011, Wiley Periodicals, Inc. and the International Society for Diseases of the Esophagus

PAEDIATRICS AND INTERNATIONAL CHILD HEALTH 2019, VOL. 39, NO. 1, 7–12 https://doi.org/10.1080/20469047.2018.1489649



Check for updates

Gastroesophageal reflux disease (GERD) in children

Ujjal Poddar

Department of Paediatric Gastroenterology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

ABSTRACT

Background: Gastro-oesophageal reflux (GER) and gastro-oesophageal reflux disease (GERD) are common in infants and children.

Aims: To review the recent literature on GERD in children and to outline the approach to diagnosis and management.

Methods: A literature search in PubMed was conducted with regard to the prevalence, clinical features, diagnosis and management of GER and GERD in children with special attention to low- and middle-income countries. Articles in English published during the last 25 years, the full text of which was available, were considered and the relevant information extracted.

Results: Almost 50% of all healthy infants regurgitate at least once a day which peaks at 4 months of age and subsides by 12 months in 90% of cases. Conversely, the prevalence of GERD increases with age and, by adolescence, is similar to that in adults (20%). While GER in infancy does not require investigation or therapy, an empirical proton pump inhibitor (PPI) for 4-8 weeks is justified in older children with classical symptoms of GERD. There is no gold-standard investigation for GERD. In extra-oesophageal manifestations, a pH/impedance is useful and endoscopy in cases with oesophagitis. PPIs play a pivotal role in the management of GERD but have not been found useful in infants with GER. Anti-reflux surgery plays a minor role in GERD owing to the associated morbidity and high failure rate, especially in high-risk groups who most need it.

Conclusions: Unless there are warning features such as failure to thrive, haematemesis, abnormal posturing, choking/gagging or coughing while feeding, regurgitation in infancy need not be investigated. In older children and adolescents with typical reflux symptoms, empirical PPI therapy is justified. For extra-oesophageal manifestations, a pH/impedance study and endoscopy to detect oesophagitis are the investigations of choice. PPI is the mainstay of therapy in GERD, but not in GER.

Introduction

Gastro-oesophageal reflux (GER) is a physiological process that occurs many times a day in healthy children as well as in adults. It is defined as the involuntary passage of gastric contents back into the oesophagus. Gastrooesophageal reflux disease (GERD) is symptoms or complications associated with pathological GER [1]. GER is one of the most common causes of upper gastro-intestinal symptoms in children.

Prevalence

GER or regurgitation is a common phenomenon in infancy in both high-income countries (HIC) and lowand middle-income countries (LMIC). A study of 948 infants in the USA reported a 50% prevalence of at least one bout of regurgitation a day in infants aged 0–3 months which increased to 67% at 4–6 months of age and then declined sharply to 21% at 7–9 months of age, and, by 10–12 months, only 5% of infants still had regurgitation [2]. A significant proportion of these infants regurgitated more than four times a day and they too

CONTACT Ujjal Poddar 😂 ujjalpoddar@hotmail.com © 2018 Informa UK Limited, trading as Taylor & Francis Group

ARTICLE HISTORY Received 4 March 2018

Accepted 11 June 2018

KEYWORDS

Regurgitation; pH study; impedance; endoscopy; proton-pump inhibitors

followed a similar pattern: 20% at 0-3 months, 23% at 4-6 months and only 3% at 7-9 months and, by 12 months, only 2% of infants still had regular regurgitation. This natural history of GER in infancy has been substantiated by other studies in Australia and Italy [3,4]. The prevalence of GER in infants in LMIC is similar to that in HIC. Studies of 602 patients in India [5] and 103 in Indonesia [6] reported a prevalence of GER in the first 6 months of life as high as 55-73% which had decreased to 4-12% by 12 months of age. On the other hand, a small proportion (5-9%) of all infants with regurgitation have GERD [2,6]. These studies [2-6] suggest that GER is common in early infancy and has almost disappeared by one year of age. The continuation or development of regurgitation after 18 months of age suggests a pathological condition.

The prevalence of GERD is lower in younger children. In a study in the USA [7] of 566 children aged 3–9 years (parental interview) and 615 children aged 10–17 years (directly interviewed), pyrosis or heartburn was reported in 1.8% of the 3–9-year-olds and in 3.5% of the 10–17-year-olds. This figure was much Neurogastroenterology & Motility

Neurogastroenterol Motil (2015) 27, 1202-1213



doi: 10.1111/nmo.12611

REVIEW ARTICLE

Pathophysiology of gastroesophageal reflux disease: new understanding in a new era

T. V. K. HERREGODS, A. J. BREDENOORD & A. J. P. M. SMOUT

Department of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands

Key Messages

- The aim of this review is to provide an overview of the current understanding of the pathophysiological mechanisms causing GERD and the factors which influence perception.
- Pathophysiological factors involved in reflux include: sliding hiatus hernia, low LES pressure, TLESRs, the acid pocket, obesity, increased distensibility of the EGJ, prolonged esophageal clearance, and delayed gastric emptying.
- Mechanisms influencing perception of GERD symptoms include: acidity of reflux, proximal extent, presence of gas in the refluxate, duodenogastroesophageal reflux, longitudinal muscle contraction, mucosal integrity, and peripheral and central sensitization.
- Further research of the pathophysiology of GERD remains necessary despite the recent advances in our understanding.

Abstract

Background The prevalence of gastroesophageal reflux disease (GERD) has increased in the last decades and it is now one of the most common chronic diseases. Throughout time our insight in the pathophysiology of GERD has been characterized by remarkable back and forth swings, often prompted by new investigational techniques. Even today, the pathophysiology of GERD is not fully understood but it is now recognized to be a multifactorial disease. Among the factors that have been shown to be involved in the provocation or increase of reflux, are sliding hiatus hernia, low lower esophageal sphincter pressure, transient lower esoph-

Address for Correspondence Prof. Dr. A. J. P. M. Smout, Department of Gastroenterology and Hepatology, Academic Medical Center Amsterdam, Meibergdreef 9, room C2-326, 1105 AZ Amsterdam-Zuidoost, The Netherlands. Tel: +31 20 5667375; fax: +31(0)205669478; e-mail: a.j.smout@amc.uva.nl Received: 10 February 2015 Accepted for publication: 5 May 2015 ageal sphincter relaxation, the acid pocket, obesity, increased distensibility of the esophagogastric junction, prolonged esophageal clearance, and delayed gastric emptying. Moreover, multiple mechanisms influence the perception of GERD symptoms, such as the acidity of the refluxate, its proximal extent, the presence of gas in the refluxate, duodenogastroesophageal reflux, longitudinal muscle contraction, mucosal integrity, and peripheral and central sensitization. Understanding the pathophysiology of GERD is important for future targets for therapy as proton pump inhibitor-refractory GERD symptoms remain a common problem. Purpose In this review we provide an overview of the mechanisms leading to reflux and the factors influencing perception, in the light of historical developments. It is clear that further research remains necessary despite the recent advances in the understanding of the pathophysiology of GERD.

Keywords GERD, hiatus hernia, lower esophageal sphincter, pathophysiology, reflux perception.

1202

© 2015 John Wiley & Sons Ltd

Bangladesh Journal of Medical Science Vol.09 No.1 Jan'10

Review article

Gastroesophageal Reflux Disease – An Update

AR Mushtaque*

Summary

Gastroesophageal reflux disease (GERD) is a common disease and a considerable burden on healthcare resources. Definitions and terminology have been a source of confusion for GERD. The 'Montreal definition' is the first ever global consensus definition of GERD. The esophageal and extraesophageal syndromes are now considered the two constituent syndromes of GERD. The pathogenesis of gastroesophageal reflux is multi-factorial and a failure of the anti-reflux barrier allowing the stomach content to enter the esophagus is the target of interest. Heartburn and acid regurgitation are the typical symptoms of the disease, although some patients may have atypical manifestations of GERD. The long term complication of GERD includes esophageal stricture, Barrett's esophagus with consequent increase in the risk of esophageal adenocarcinoma. Diagnosis of GERD can usually be established on the basis of a careful history and physical examination. Detailed diagnostic studies are not necessary in a patient presenting with typical symptoms with no alarming features. Patients with alarming feature in addition to their GERD symptoms require prompt investigation and usually endoscopy is preferred. Treatment of GERD is directed at acid suppression through the use of lifestyle modifications and pharmacologic agents from over-the-counter (OTC) agents ranging from antacids to proton pump inhibitors (PPIs). New algorithm of treatment of GERD has also been proposed. Antireflux surgery, including open and laparoscopic, and newer endoscopic procedures are alternative modalities of treatment in case of failure of medical therapy.

<u>Key words</u>: Gastroesophageal reflux disease, Montreal definition, Esophageal syndrome, Extraesophageal syndrome, Heartburn, Regurgitation.

Gastroesophageal reflux disease (GERD)

Gastroesophageal reflux disease (GERD) is a common medical problem with a broad spectrum of symptoms and varying degrees of severity¹. The modern concept of reflux esophagitis dates back to 1935 when a landmark article in JAMA first suggested gastric secretions may cause the mucosal damage². Later in 1946 Allison identified the fundamental pathophysiological process and introduced the term 'reflux esophagitis'³.

Definition and Classification of GERD

The first ever global consensus definition of gastroesophageal reflux disease (GERD) is known as Montreal definition which defines the condition as "a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications"⁴.

The patients having GERD is broadly classified into two groups on the basis of endoscopy findings- having esophageal mucosal damage (erosive esophagitis and Barrett's esophagus) and no mucosal damage (endoscopy-negative reflux disease, symptomatic GERD, or non erosive reflux disease) (Box 1)⁵.

Heartburn and acid regurgitation are the archetypal symptoms of GERD and most

Box 1: GERD presentations⁵

Phenotypic presentations of GERD

- 1. Erosive esophagitis (20-30%)
- Non erosive reflux disease (60-70%)
- 3. Barrett's esophagus (6-12%)

^{*}Corresponds to: Dr. Mushtaque Ahmad Rana, Asst. Professor, Department of Medicine, Ibn Sina Medical College, Dhaka-1216. E-mail: ranamushtaque@yahoo.com.

International Scholarly Research Network ISRN Gastroenterology Volume 2012, Article ID 391631, 11 pages doi:10.5402/2012/391631

Review Article

Current Trends in the Management of Gastroesophageal Reflux Disease: A Review

Sylvester Chuks Nwokediuko

Gastroenterology Unit, Department of Medicine, University of Nigeria Teaching Hospital Ituku/Ozalla, PMB, Enugu 01129, Nigeria

Correspondence should be addressed to Sylvester Chuks Nwokediuko, scnwokediuko@yahoo.com

Received 28 April 2012; Accepted 28 May 2012

Academic Editors: P. Correa and C.-T. Shun

Copyright © 2012 Sylvester Chuks Nwokediuko. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Gastroesophageal reflux disease (GERD) is a chronic disorder of the upper gastrointestinal tract with global distribution. The incidence is on the increase in different parts of the world. In the last 30 to 40 years, research findings have given rise to a more robust understanding of its pathophysiology, clinical presentation, and management. The current definition of GERD (The Montreal definition, 2006) is not only symptom-based and patient-driven, but also encompasses esophageal and extraesophageal manifestations of the disease. The implication is that the disease can be confidently diagnosed based on symptoms alone. Nonerosive reflux disease (NERD) remains the predominant form of GERD. Current thinking is that NERD and erosive reflux disease (ERD) are distinct phenotypes of GERD rather than the old concept which regarded them as components of a disease spectrum. Non erosive reflux disease is a very heterogeneous group with significant overlap with other functional gastrointestinal disorders. There is no gold standard for the diagnosis of GERD. A substantial proportion of GERD patients continue to have symptoms despite optimal PPI therapy, and this has necessitated research into the development of new drugs. Several safety concerns have been raised about chronic use of proton pump inhibitors but these are yet to be substantiated in controlled studies. The debate about efficacy of long-term medical treatment compared to surgery continues, however, recent data indicate that modern surgical techniques and long-term PPI therapy have comparable efficacy. These and other issues are subjects of further research.

1. Introduction

Gastroesophageal reflux disease (GERD) is a common chronic disorder prevalent in many countries [1]. Apart from the economic burden of the disease and its associated impact on quality of life [2–5], it is the most common predisposing factor for adenocarcinoma of the esophagus. As a conse-quence of the irritation caused by the reflux of acid and bile, adenocarcinoma may develop in these patients, representing the last of a sequence that starts with the development of GERD and progresses to metaplasia (Barrett's esophagus), lowgrade dysplasia, high-grade dysplasia, and adenocarcinoma. Although there has been a decrease in the incidence of squamous cell cancers, the rate of esophageal adenocarcinoma has increased rapidly, and this has been traced to the advent of obesity epidemic, GERD and Barrett's esophagus [6, 7]. Over the years, several issues have emerged regarding the definition, classification, natural history and treatment of GERD, and complications associated with its treatment. This paper focuses on some of these evolving issues. Recent studies, limited to English language, were identified via PubMed searches (1990–2011) with the search terms GERD, NERD, prevalence, incidence, epidemiology, and management. Recent reviews on epidemiology and management were also examined for appropriate references.

2. Definition

Until recently, there were many definitions of GERD. The lack of a gold standard for diagnosis made it difficult to adopt a satisfactory definition. The first ever global consensus The Egyptian Journal of Hospital Medicine (July 2018) Vol. 72 (9), Page 5195-5202

Evaluation of GERD Diagnosis, Management, and Outcomes Mada Bejad G. Almutairi¹, Salem Muaedh Alsulaimi², Rayan Ali I Alghamdi², Khalid Abdullah Alrehaili², Sohaib Aziz Habhab², Abdulrahman Mohsen Althagafi², Faisal Ali Alghamdi³, Naif Abdulaziz Meighrbl³, Waleed Mohammed Alsuhaymi³, Mohammed Saeed Al_Yahya⁴

Almaarefa College, ²Umm Al-Qura University, ³University of Jeddah, ⁴King Khalid University

ABSTRACT

Background: Gastroesophageal Reflux Disease (GERD) is a condition which develops when the reflux of gastric content causes troublesome symptoms or complications. GERD is arguably the most common disease encountered by the gastroenterologist. It is equally likely that the primary care providers will find that complaints related to reflux disease constitute a large proportion of their practice.(1) GERD condition can present with different presentations and the response to the intervention significantly differs from patient to patient. As a result reviewing the new literatures done in this field will help in providing a better outcomes for the patients.

Objective: Treating patients with GERD is difficult and needs different approaches. In this paper, we reviewed the major and the latest studies regarding GERD symptomatology, risk factors, diagnosis and management.

Method: A comprehensive search was done using biomedical databases; Medline, and PubMed, for studies concerned with assessment of GERD. Keywords used in our search through the databases were as; "GERD Pathophysiology", "GERD Classification", and "GERD Management".

Conclusion: GERD is a condition which develops when the reflux of gastric content causes troublesome symptoms such as heartburn, regurgitation, and sleep disturbance. GERD can be diagnosed by various measures such as GERD Questionnaire, PH Monitoring, and Upper Endoscopy. Initially GERD can be managed by simple life modification measures, then physicians can add Protons Pump Inhibitors (PPIs), and Histamine 2 Receptor Blocker (H2RBs). In case of PPIs and H2RBs failure in reliving GERD symptoms physicians may go for anti-reflux surgical interventions.

Keywords: GERD, Diagnosis, Management, Outcomes.

INTRODUCTION

GERD is defined as heartburn, acid regurgitation, or both, at least once a week. These troublesome symptoms are caused by the movement of gastric contents into the esophagus.

GERD represents a common disorder, particularly in the Western world (about 10%-20% in Western countries and under 5% in Asia) and its prevalence appears to be increasing. The incidence rate, reported by two longitudinal studies was 4.5 and 5.4/1000 people per year, respectively. In Saudi Arabia, *Alsuwat et al.*² found that the prevalence of GERD is suspected to be around 25% of the population, which means it is slightly higher than Western countries and much higher than countries of East Asia.

OBJECTIVE

In this review our aims are: 1) Discussing the pathogenesis that stands behind GERD development. 2) Discussing the various methods of GERD diagnosis, and management 3) Providing a paper that analyzed the recent literatures done in this field.

METHODOLOGY

Sample

We performed comprehensive search using biomedical databases; Medline, and PubMed, for studies concerned with evaluation of GERD published in English language. Keywords used in our search through the databases were as; "GERD Pathophysiology", 5195

Received:23/5/2018 Accepted:2/6/2018 "GERD Classification", and "GERD Management". More relevant articles were recruited from references lists scanning of each included study.

Analysis

No software was used, the data were extracted based on specific form that contain title of the study, name of the author, objective, summary, results, and outcomes. Double revision of each member's outcomes was applied to ensure the validity and minimize the errors.

PATHOPHYSIOLOGY

Normal gastric acid has a pH of 1.5 to 3.5 (similar to lemon juice) secreted by the stomach's parietal cells in response to histamine, acetylcholine, and gastrin. All three of these substances coordinate hydrogen ion generation; however, histamine represents the dominant route and plays an important role in current GERD management strategies.

Lower esophageal sphincter (LES) is located at the juncture of the stomach and the esophagus. When LES pressure is lower than intragastric pressure, LES become lax. Subsequently, acid contents can easily reflux into the esophagus. This will be leading to the mentioned troublesome symptoms (esophageal and extra esophageal) depending on the severity. Transient LES relaxation (TLESR) occurs largely in the postprandial period, Neurogastroenterology & Motility

Neurogastroenterol Motil (2013) 25, 783-799

doi: 10.1111/nmo.12201

REVIEW ARTICLE

Pathophysiology of gastro-esophageal reflux disease: a role for mucosa integrity?

R. FARRÉ*,†

*Translational Research Center for Gastrointestinal Disorders, KU Leuven, Leuven, Belgium †Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Instituto de Salud Carlos II, Madrid, Spain

Key Messages

- The exact role of the impaired mucosal integrity in the pathophysiology of gastro-esophageal reflux disease (GERD) is not yet elucidated and needs to be further explored.
- The aim of this review is to update the most recent findings on the putative pathophysiological mechanisms in GERD and specially focus on the role of esophageal mucosa integrity.
- Full-text articles were selected from searches of the PubMed database (1966 to present). Some relevant abstracts
 presented at international meetings were also included.
- Impaired mucosal integrity is present in patients with erosive and non-erosive reflux disease. Luminal (acid, bile acids, trypsin...) and endogenous factors such psychological stress can be involved.

Abstract

Background Gastro-esophageal reflux disease (GERD) is very prevalent and has a high burden on health security system costs. Nevertheless, pathophysiology is complex and not well-understood. Several mechanisms have been proposed: decreased salivation, impaired esophageal clearance, decreased lower esophageal sphincter pressure resting tone, presence of hiatal hernia, increased number of transient lower esophageal sphincter relaxations (TLESRs), increased acid, and pepsin secretion, pyloric incompetence provoking duodeno-gastro-esophageal reflux of bile acids and trypsin. Independent of the relevance of each mechanism, the ultimate phenomenon is that muco-

Address for Correspondence Ricard Farré, Translational Research Center for Gastrointestinal Disorders, Herestraat 49, box 701, Leuven 3000, Belgium. Tel: +32 16 330147; fax: +32 16 330723; e-mail: ricard.farre@med.kuleuven.be Received: 11 June 2013 Accepted for publication: 16 July 2013

sal epithelium is exposed for a longer time to agents as acid and pepsin or is in contact to luminal agents not commonly present in gastric refluxate as trypsin or bile acids. This leads to a visible damage of the epithelium (erosive esophagitis -EE) or impairing mucosal integrity without any sign of macroscopic alteration as occurs in non-erosive reflux disease (NERD). Luminal factors are not the only responsible for such impairment; more recent data indicate that endogenous factors may also play a role. Purpose This review will update the most recent findings on the putative pathophysiological mechanisms and specially will focus on the role of esophageal mucosal integrity in GERD. Methodologies used for the evaluation of mucosal integrity, its relevance in EE and NERD, its involvement in symptoms perception and the effect of luminal and endogenous factors will be discussed.

Keywords baseline impedance, gastro-esophageal reflux disease, luminal and endogenous factors, mucosal integrity, pathophysiology.

© 2013 John Wiley & Sons Ltd

Pediatr Drugs (2013) 15:19–27 DOI 10.1007/s40272-012-0004-2

THERAPY IN PRACTICE

Gastroesophageal Reflux Disease in Neonates and Infants

When and How to Treat

Steven J. Czinn · Samra Blanchard

Published online: 16 January 2013 © Springer International Publishing Switzerland 2013

Abstract Gastroesophageal reflux (GER) is defined as the involuntary retrograde passage of gastric contents into the esophagus with or without regurgitation or vomiting. It is a frequently experienced physiologic condition occurring several times a day, mostly postprandial and causes no symptoms. These infants are also called 'happy spitters'. GER disease (GERD) occurs when reflux of the gastric contents causes symptoms that affect the quality of life or pathologic complications, such as failure to thrive, feeding or sleeping problems, chronic respiratory disorders, esophagitis, hematemesis, apnea, and apparent life-threatening events.

About 70–85 % of infants have regurgitation within the first 2 months of life, and this resolves without intervention in 95 % of infants by 1 year of age. The predominant mechanism causing GERD is transient lower esophageal sphincter (LES) relaxation, which is defined as an abrupt decrease in LES pressure to the level of intragastric pressure, unrelated to swallowing and of relatively longer duration than the relaxation triggered by a swallow.

Regurgitation and vomiting are the most common symptoms of infant reflux. A thorough history and physical examination with attention to warning signals suggesting other causes is generally sufficient to establish a clinical diagnosis of uncomplicated infant GER. Choking, gagging, coughing with feedings or significant irritability can be

S. J. Czinn · S. Blanchard Department of Pediatrics, Division of Gastroenterology, University of Maryland School of Medicine, Baltimore, MD, USA

S. Blanchard (⊠) Pediatric Gastroenterology and Nutrition, University of Maryland Medical Center, 22 S. Greene Street, Room N5E70, Baltimore, MD 21201, USA e-mail: sblanchard@peds.umaryland.edu warning signs for GERD or other diagnoses. If there is forceful vomiting, laboratory and radiographic investigation (upper gastrointestinal series) are warranted to exclude other causes of vomiting. Irritability coupled with back arching in infants is thought to be a non-verbal equivalent of heartburn in older children. Other causes of irritability, including cow's milk protein allergy, neurologic disorders, constipation and infection, should be ruled out. The presentation of cow's milk protein allergy overlaps with GERD, and both conditions may co-exist in 42–58 % of infants. In these infants, symptoms decrease significantly within 2–4 weeks after elimination of cow's milk protein from the diet. For non-complicated reflux, no intervention is required for most infants.

Effective parental reassurance and education regarding regurgitation and lifestyle changes are usually sufficient to manage infant reflux. Sandifer syndrome, apnea and apparent life-threatening events are the extraesophageal manifestations of GERD in infants.

Pharmacotherapeutic agents used to treat GERD encompass antisecretory agents, antacids, surface barrier agents and prokinetics. Currently, North American Society for Pediatric Gasroenterology, Hepatology and Nutrition (NASPGHAN) and European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) practice guidelines concluded that there is insufficient evidence to justify the routine use of prokinetic agents. Esomeprazole (Nexium) is now approved in the US for short-term treatment of GERD with erosive esophagitis in infants aged from 1 to 12 months. Although Nissen fundoplication is now well established as a treatment option in selected cases of GERD in children, its role in neonates and young infants is unclear and is only reserved for selective infants who did not respond to medical therapy and have life-threatening complications of GERD.

∆ Adis

Drugs (2013) 73:1281-1295 DOI 10.1007/s40265-013-0101-8

REVIEW ARTICLE

Extra-Esophageal Manifestations of Gastroesophageal Reflux Disease: Diagnosis and Treatment

Christopher Hom · Michael F. Vaezi

Published online: 24 July 2013 © Springer International Publishing Switzerland 2013

Abstract Gastroesophageal reflux disease (GERD) is a common disease that is often diagnosed based on typical symptoms of heartburn and regurgitation. In addition to these more classic manifestations, GERD is increasingly associated with extra-esophageal symptoms, including chronic cough, asthma, laryngitis, and dental erosions. Due to the poor sensitivity of endoscopy and pH monitoring, and the poor specificity of laryngoscopy, empiric therapy with proton pump inhibitors (PPIs) is now considered the initial diagnostic step in patients suspected of having GERD-related symptoms. For those who improve with PPIs, GERD is the presumed etiology, but for those who remain unresponsive to such therapy, further diagnostic testing with impedance/pH monitoring may be necessary in order to exclude refractory acid or weakly acid reflux. In those with normal test results despite PPI therapy and continued symptoms, causes other than GERD may be pursued. Recent data suggest that in patients with extra-esophageal symptoms, objective findings of moderate-sized hiatal hernia and moderate reflux on pH testing may predict response to acid suppressive therapy. PPI-unresponsive patients usually have causes other than GERD for their extra-esophageal symptoms and continued PPI therapy in this group is not recommended.

1 Introduction

The Montreal Classification defines gastroesophageal reflux disease (GERD) as a condition that develops when

reflux of the stomach contents causes troublesome symptoms [1]. Its prevalence has been increasing worldwide, with Western Europe, North America, and South America having the highest prevalence rates of approximately 20-40 % [2-4]. GERD is most commonly accompanied by primary complaints of heartburn and regurgitation [1, 5-7], but extra-esophageal symptoms of GERD may also be present with reflux of gastric contents into the esophagus. For example, chronic cough, asthma, posterior laryngitis, and dental erosion are a few examples of extra-esophageal reflux (EER) disease (Fig. 1) [1, 8]. Non-cardiac chest pain (NCCP) was previously considered an extra-esophageal symptom; however, it is now grouped among the esophageal syndromes by the Montreal Classification [9]. A major obstacle in diagnosing the extra-esophageal symptoms of GERD is the possible absence of heartburn or regurgitation in 57-94 % of patients with otolaryngological complaints, 43-75 % of patients with chronic cough, and 40-60 % of asthmatic patients. GERD has become an important public health issue because of the significant healthcare costs associated with treating it. The annual direct cost of GERD management in the USA is cited at US\$971 per patient [10], with national expenditures ranging from US\$9.3 billion [11] to US\$12.1 billion [12]. Further, the cost of caring for patients with ERR in the USA is 5.6 times that of GERD at over US\$50 billion (Fig. 2) [3].

2 Pathophysiology

EER is a consequence of a proposed direct (aspiration) or indirect (vagally mediated) mechanism (Fig. 3) [1, 14–18]. The former is the result of direct exposure of the pharynx or larynx to gastric contents (e.g. acid, pepsin, and bile acids), causing a tracheal or bronchial cough reflex. The

C. Hom · M. F. Vaezi (🖂)

Division of Gastroenterology, Hepatology, and Nutrition, Center for Swallowing and Esophageal Disorders, Vanderbilt

University Medical Center, 1660 TVC, 1301-22nd Ave. South, Nashville, TN 37232-5280, USA

e-mail: Michael.vaezi@vanderbilt.edu



(JGHF

doi:10.1111/j.1440-1746.2011.06945.x

REVIEW

Oral manifestations of gastroesophageal reflux disease

Sarbin Ranjitkar, Roger J. Smales and John A. Kaidonis

School of Dentistry, The University of Adelaide, Adelaide, South Australia, Australia

Key words

collaborative management, dental erosion, gastroesophageal reflux disease, prevention.

Accepted for publication 18 September 2011.

Correspondence

Dr Sarbin Ranjitkar, School of Dentistry, The University of Adelaide, North Terrace, Adelaide, SA 5005, Australia. Email: sarbin.ranjitkar@adelaide.edu.au

Conflict of interest: None

Abstract

Numerous case-control and other studies involving confirmation of gastroesophageal reflux disease (GERD) by esophageal pH-metry and the assessment of dental erosions have shown significant associations between the two conditions in both adults and children. By contrast, when asked to vote on whether GERD may cause dental erosions, only 42% of physicians strongly agreed that such an association existed in adults, and just 12.5% strongly agreed for children, respectively in two global consensus reports. Part of this divergence between the perceptions of physicians and the findings of research publications may reflect a general lack of oral health education during medical training, and cursory oral examinations being made under less-than-ideal conditions. Adequate salivary secretions are essential for the protection of the teeth and the oropharyngeal and esophageal mucosa. The quantity and quality of the saliva require monitoring as many drugs, including several of the proton pump inhibitors (PPIs), can cause hyposalivation. In addition, PPIs do not always result in adequate acid suppression. Therefore, collaboration between physicians and dentists is strongly advocated to prevent or ameliorate possible adverse oral effects from both endogenous and exogenous acids, and to promote adequate saliva production in patients with GERD.

Introduction

There is relatively little information in general medical and gastroenterology literature regarding tooth erosion that may be associated with gastroesophageal reflux disease (GERD). This association is commonly observed by dentists, but is given very cursory mention or omitted entirely when describing extraesophageal (supra-esophageal) manifestations of GERD.¹⁻⁷

When 44 medical experts and family physicians from 18 countries voted in the World Congress of Gastroenterology presentation in Montreal on the statement that "The prevalence of dental erosions, especially on the lingual and palatal tooth surfaces, is increased in patients with GERD" (Extra-esophageal Syndromes: Established Associations, Statement #48), the result was a highgrade consensus agreement of 96%.⁸ However, only 42% of the consensus votes "agreed strongly" with the above statement, 35% "agreed with minor reservations," and 19% "agreed with major reservations." Just three selected clinical studies were quoted to support the statement.⁹⁻¹¹

Subsequently, when eight pediatric gastroenterologists using a revision of the original Montreal presentation protocol voted on the statement that "GERD may cause dental erosions in pediatric patients" (Extraesophgeal Syndromes: Definite Associations, Statement #53), the result was a low-grade consensus agreement of 100%.¹² But, only 12.5% of the votes "agreed strongly," 37.5% "agreed moderately," and 50% "just agreed." One systematic

review article¹³ and four other selected clinical articles^{14–17} were quoted to support the above statement. Dental erosion was only one of two extra-esophageal conditions considered to be definitely associated with GERD in pediatric patients, the other being Sandifer's syndrome (torticollis).¹²

In the two previous global consensus reports,812 the relatively low percentages of physicians' votes agreeing strongly that GERD may cause tooth erosion in both adults and children is possibly a reflection of a lack of oral health training. One random survey involving 611 graduating pediatric residents found that most received either no training or less than 3 h of oral health training, with only 14% spending clinical observation time with a dentist. A national survey of pediatricians also found that only 54% examined the teeth of more than half of their 0-3-year-old patients. Fewer than 25% of these pediatricians had received any oral health education at all during their career.19 In both surveys, most of the pediatricians stated that they should be trained to undertake basic oral health screenings. Compounding this problem, another questionnaire survey found that only three of 104 pediatricians were aware of tooth erosion caused by acidic pediatric medications.20 A recent review article concluded that, "the primary care physician and the gastroenterologist need to pay more attention to the often neglected oral examination."1

Tooth erosion is usually a slow process occurring over many years, and its subtle appearance is often not adequately observed during a cursory examination under less-than-ideal conditions. It is

Journal of Gastroenterology and Hepatology 27 (2012) 21–27

© 2011 Journal of Gastroenterology and Hepatology Foundation and Blackwell Publishing Asia Pty Ltd

Revista Română de Anatomie funcțională și clinică, macro- și microscopică și de Antropologie

Vol. XI - Nr. 3 - 2012

CLINICAL ANATOMY

DENTAL EROSION AND OTHER ORAL ANATOMICAL CHANGES CAUSED GASTROESOPHAGEAL REFLUX

Dorelia Lucia Călin¹, Mihaela Mitrea², L.L. Frâncu² "Gr. T. Popa" University of Medicine and Pharmacy, Iași 1. Discipline of Cariology and Restorative Odontotherapy 2. Discipline of Anatomy

DENTAL EROSION AND OTHER ORAL ANATOMICAL CHANGES CAUSED GASTROESO-PHAGEAL REFLUX (Abstract): Gastroesophageal reflux can cause oral pathological changes. Dental erosion is the predominant oral manifestation of the disease and allows the dentist to make the initial diagnosis. Undiagnosed erosion can cause devastating damage to the dentition over time. Patients were not aware of the underlying condition. The causes of erosion are difficult to define without a detailed history. Erosive lesions were present in various degrees in the same patient, maxillary teeth showing greater erosive lesions in comparison with the lower teeth. Dentists must be familiar with typical and atypical symptoms of the disease because they could be the first to suspect the presence of the disease by observing dental erosion that cannot be explained. The consequences of intrinsic erosion are often severe and require a complex restorative treatment to restore tooth tissue loss. **Key words** : GASTROESOPHAGEAL REFLUX, TOOTH ERO-SION, ORAL EFFECTS OF GASTROESOPHAGEAL REFLUX

Dental erosion or, more correctly, corrosion is defined as an irreversible loss of hard tissues of tooth produced by chemical or electrolytic processes of nonbacterial origin, in contrast to carious tooth damage (1, 2). Dental erosion is caused by the presence of acid of non-bacterial origin in the mouth.

Tooth enamel begins to dissolve at a pH of 5.5 (3). Hydrochloric acid in gastric juice produced by parietal cells of the stomach, has a very low pH, less than 2 and therefore, it can cause significant chemical erosion (4).

Dental erosion is caused by the presence of acids in the oral cavity that may be of intrinsic (endogenous), extrinsic (exogenous) origin or a combination them (5).

The term intrinsic erosion implies the presence of gastric acid in the oral cavity (6). Intrinsic sources of acid include chronic vomiting, persistent acid regurgitation, gastroesophageal reflux, rumination (7).

Acid reflux is defined as abnormal propulsion of stomach contents into the esophagus. Reflux occurs when the lower esophageal sphincter, which controls the flow of food and fluids between the stomach and esophagus, does not work properly. This sphincter is a ringshaped muscle, being the anatomical location of the gastroesophageal junction, and behaves like a valve allowing normal passage of food and liquids only in one direction : from the esophagus to the stomach.

Gastroesophageal reflux disease occurs when the lower esophageal sphincter relaxation occurs at the wrong time (the other time than the ingestion of food) and remains open for a long time. Normally the sphincter opens for a few seconds during swallowing. Sphincter relaxation produces decrease in pressure gradient between it and the stomach. The stomach content comes into contact with the cervical esophagus, pharynx and oral cavity.

The etiology of gastroesophageal reflux. The main factors that cause weakness or relaxation of lower esophageal sphincter are :

- *Lifestyle*: alcohol consumption, smoking, obesity,
- · Medication: beta-blockers, calcium chan-

Original Article

Incidence and Pattern of Dental Erosion in Gastroesophageal Reflux Disease Patients

Anupama Ramachandran, Sulthan Ibrahim Raja Khan¹, Nandinee Vaitheeswaran²

Department of Conservative Dentistry and Endodontics, Chettinad Dental College and Research Institute, ²Chettinad Dental College and Research Institute, Kanchipuram, Tamil Nadu, India, ¹Lecturer, Restorative Dentistry and Endodontics, King Saud Bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia Aim: Gastroesophageal reflux disease (GERD) is a very common condition whose consequences of are localized not only in the esophagus; extra-esophageal involvement has frequently been reported. The aim of the study is to examine the incidence and pattern of dental erosion in GERD patients. Methodology: A total of 50 patients were recruited in this study (control -25 and GERD -25). All participants diagnosed having GERD by the endoscopic examination by their gastroenterologist are included. The patients were examined for dental erosion and will be quantified using Basic erosive wear examination index. Results: The results showed that the incidence of dental erosion was 88% as compared to 32% in the control group which was found to be statistically significant.

KEYWORDS: Gastroesophageal disease, dental erosion, erosive index

INTRODUCTION

Dental erosion is defined as the loss of tooth structure through a physicochemical process of dissolution of hard dental tissue due to acid exposure in the oral cavity, without bacterial activity. The etiology of dental erosion is multifactorial. The causes may consist of extrinsic acids or intrinsic factors.^[11] The extrinsic factors include acidic foods, acidic beverages, sports drinks, and chewable Vitamin C tablets. Intrinsic factors are reported to be: regurgitation, recurrent stress-induced vomiting, certain psychosomatic disorders such as anorexia, bulimia, and rumination, and alcohol abuse,^[2] the most common being gastroesophageal reflux disease (GERD) with regurgitation of gastric acid into the oral cavity.

The mechanism of erosion begins as superficial demineralization of the enamel, which can cause dissolution of the subsurface layers and eventual loss of tooth structure. Any acid with a pH below the critical pH of dental enamel (5.5) can dissolve the hydroxyapatite crystals in enamel.^[3] The damaged dental surface is exposed to mechanical friction in connection with chewing, swallowing, or brushing, sometimes which may extend up to dentin/pulp.^[4] Erosion from gastric acids forms smooth lesions which typically appear as cupped occlusal/incisal and concave buccal/facial surfaces.^[5]

Access this article online		
Quick Response Code:		
	Website: www.jpbsonline.org	
	DOI: 10.4103/jpbs.JPBS_125_17	

GERD is defined as involuntary muscle relaxing of the lower esophageal sphincter (LES), which allows refluxed acid to move upward through the esophagus into the oral cavity.^[6] The acid produced in the stomach is used to digest food. Normally during food swallowing, the LES opens and allows the food and saliva to flow into the stomach and then it closes to its original position. However, in GERD, the sphincter does not close properly allowing the acid along with food to flow upward. The acid flowing up into the esophagus irritates and inflames the lining of the esophagus. The lining of esophageal is not strong as that of stomach to withstand the corrosive effects of acid; hence, a burning sensation is usually felt which may lead to complications as reflux esophagitis, hemorrhage, stricture, Barrett's esophagus, and adenocarcinoma.17

Extraesophageal manifestations possibly resulting from GERD include laryngeal, pharyngeal, respiratory, sinus, middle ear, and oral conditions. The effect of GERD on oral cavity can be extensive. Gastric acid usually reaches the oral cavity through the esophagus. Tooth erosion and

Address for correspondence: Dr. Anupama Ramachandran, Department of Conservative Dentistry and Endodontics, Chettinad Dental College and Research Institute, Rajiv Gandhi Salai, Kelambakkam, Kanchipuram - 603 103, Tamil Nadu, India. E-mail: dr.anupama@gmail.com

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Ramachandran A, Raja Khan SI, Vaitheeswaran N. Incidence and pattern of dental erosion in gastroesophageal reflux disease patients. J Pharm Bioall Sci 2017;9:S138-41.

138 🔪 © 2017 Journal of Pharmacy and Bioallied Sciences | Published by Wolters Kluwer - Medknow

DENTAL EROSION IN GASTRO-ESOPHAGEAL REFLUX DISEASE. A SYSTEMATIC REVIEW

ANDREI PICOS, MÂNDRA EUGENIA BADEA, DAN LUCIAN DUMITRASCU

Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

Abstract

The growing interest reflected in the studies on dental erosion is justified by the severe health problems it entails, i.e. esthetic, phonetic, masticatory disturbances and pulp complications. Most studies investigate the prevalence of dental erosion in adults and children, the severity of lesions and etiopathogenetic factors.

Background and aim. Dental erosions (DE) are one of the extraesophageal complications of gastroesophageal reflux disease (GERD). An increasing amount of papers shed light on this topic. We carried out a systematic review on the association between GERD and DE.

Methods. We studied the association between DE and GERD in adults and children. The search for published studies was performed in PubMed using search terms "dental erosion" and "gastro-esophageal reflux disease". References published since 2007 were included and a systematic review was carried out. Articles not assessing DE in GERD patients were excluded, and also case presentations and articles in languages of limited circulation. The prevalence of DE in patients with GERD, extrinsic and intrinsic etiological factors of DE and the severity of dental erosion lesions were analyzed.

Results. A total of 273 articles were found, 10 studies being retained for analysis. Correlations between DE and GERD, namely the prevalence and severity of dental erosion in GERD patients, were investigated. DE prevalence was between 10.6% -42%, median 25.5%. Mean values of DE prevalence were 48.81% in GERD patients, compared to 20.48% in non-GERD controls. Comparative values of DE frequency in adults with GERD was 38.96%, compared to 98.1% in children with GERD.

Conclusions. DE is a condition associated with GERD. DE prevalence is higher in GERD patients. Intrinsic pathogenetic factors with direct action on the hard dental tissues are GERD, while extrinsic factors are represented by diet. Among the patients diagnosed with GERD, youth under the age of 18 had a higher frequency compared to adults.

Keywords: dental erosion, gastroesophageal reflux, GERD, prevalence, intrinsic factors

Introduction

Dental erosion is defined as a loss of hard dental tissue by a chemical process without bacterial involvement [1]. In the last years this mechanism has been recognized as a major cause of tooth decay (TD) both in children and adults [2]. Differential diagnosis with other TD mechanisms

Manuscript received: 11.03.2018 Received in revised form: 09.04.2018 Accepted: 18.04.2018 Address for correspondence: mebadea@umfcluj.ro is difficult given the intricacy with attrition, abfraction, abrasion, and it is established based on the specific aspect of injury locations [3].

Early injuries may be barely visible to the dentist or patient when located in the enamel, being no major alterations in color or morphology; a detailed patient history, questions about diet, medication, diseases, is important for etiopathogenesis; medium and advanced lesions are recognized by the exposure of dentin as yellowish round islets at a lower level than the thin surrounding

Clujul Medical Vol. 91, No.4, 2018: 387-390



Revieu



Extra-Esophageal Presentation of Gastroesophageal Reflux Disease: 2020 Update

Marilena Durazzo ^{1,2,*}⁽⁰⁾, Giulia Lupi ^{1,2}, Francesca Cicerchia ^{1,2}, Arianna Ferro ^{1,2}, Federica Barutta ^{1,2}, Guglielmo Beccuti ^{1,2}⁽⁰⁾, Gabriella Gruden ^{1,2} and Rinaldo Pellicano ³⁽⁰⁾

- ¹ Department of Medical Sciences, University of Turin, C.so A.M. Dogliotti 14, 10126 Turin, Italy; giulia.lupi@unito.it (G.L.); fracice7@gmail.com (F.C.); arianna.ferro@unito.it (A.F.); federica.barutta@unito.it (F.B.); guglielmo.beccuti@unito.it (G.B.); gabriella.gruden@unito.it (G.G.)
- ² 3th Internal Medicine Unit, Città della Salute e della Scienza Hospital, C.so Bramante 88, 10126 Turin, Italy
- ³ Unit of Gastroenterology, Città della Salute e della Scienza Hospital, C.so Bramante 88, 10126 Turin, Italy; rinaldo_pellican@hotmail.com
- * Correspondence: marilena.durazzo@unito.it; Tel.: +39-0-116-708-4783

Received: 8 July 2020; Accepted: 5 August 2020; Published: 7 August 2020



Abstract: Gastroesophageal reflux disease (GERD) is defined by the presence of symptoms induced by the reflux of the stomach contents into the esophagus. Although clinical manifestations of GERD typically involve the esophagus, extra-esophageal manifestations are widespread and less known. In this review, we discuss extra-esophageal manifestations of GERD, focusing on clinical presentations, diagnosis, and treatment. Common extra-esophageal manifestations of GERD include chronic cough, asthma, laryngitis, dental erosions, and gingivitis. Extra-esophageal involvement can be present also when classic GERD symptoms are absent, making the diagnosis more challenging. Although available clinical studies are heterogeneous and frequently of low quality, a trial with proton pump inhibitors can be suggested as a first-line diagnostic strategy in case of suspected extra-esophageal manifestations of GERD.

Keywords: gastroesophageal reflux; cough; asthma; laryngo-pharyngeal reflux; chest pain; tooth erosions

1. Introduction

Gastroesophageal reflux disease (GERD) is a common gastrointestinal (GI) condition with a worldwide diffusion and high prevalence in Western countries. The 2006 Montreal consensus defined GERD as a condition that develops when the reflux of the stomach contents causes troublesome symptoms and/or complications into the esophagus [1]. Tissue damage related to GERD range from esophagitis to Barrett's esophagus and esophageal adenocarcinoma; troublesome symptoms attributable to reflux can be esophageal (heartburn, regurgitation) or extra-esophageal (EE) [2–5]. GERD can be further classified by the presence of erosions on endoscopic examination (Erosive Reflux Disease [ERD] and Nonerosive Reflux Disease [NERD]) [5].

GERD-related EE manifestations are frequent and represent a diagnostic and therapeutic challenge, being able to involve lungs, upper airways, and mouth, presenting with asthma, laryngitis, chronic cough, dental erosions, and non-cardiac chest pain (Figure 1).

J. Clin. Med. 2020, 9, 2559; doi:10.3390/jcm9082559

www.mdpi.com/journal/jcm

RESEARCH

Gastroesophageal Reflux Disease Symptom Screening in a Dental Setting

Anisha Raibrown, RDH, MSDH; Lori J. Giblin, RDH, MS; Linda D. Boyd, RDH, RD, EdD; Kristen Perry, RDH, MS

Abstract

Purpose: Gastroesophageal Reflux Disease (GERD) is a chronic health condition in which the symptoms often go unnoticed. Oral problems accompanying GERD may include non-specific burning sensation, mucosa ulceration and erosion, erythema of the soft/hard palate mucosa and uvula, loss of taste and either xerostomia or increased salivary flow with potential long-term complications such as difficulty swallowing, trouble breathing, esophagitis and potential development of esophageal adenocarcinoma (EAC). The purpose of this study was to assess the feasibility of using a GERD screening in the dental clinic setting to identify and refer patients.

Methods: This was a descriptive survey design utilizing a convenience sample of patients (n=227) from two dental hygiene clinics. Students and faculty were calibrated to administer a previously validated, GERD diagnostic screening questionnaire.

Results: The prevalence of GERD in the study population was 8.7%; with 10.1% of female reporting symptoms verses 7.0% of male. There were no statistically significant differences in the study population demographics and GERD prevalence.

Conclusion: Screening for GERD symptoms should be a routine procedure for oral health care providers, as is oral cancer screening. GERD screening has the potential to identify those at risk and enable referral to medical care in order to decrease the serious complications associated with GERD.

Keywords: GERD, screening, heartburn, complications, cancer, oral health

This manuscript supports the NDHRA priority area, **Client level: Oral health care** (new therapies and prevention modalities).

Introduction

The prevalence of GERD in the United States is estimated to be 18.1%-27.8% accounting for over 8.9 million primary care visits annually.^{1,2} GERD is a chronic or longer lasting form of gastroesophageal reflux.³ GERD occurs when the lower esophageal sphincter (LES), a group of muscles at the lower end of the esophagus, relaxes and allows the stomach's contents to flow up into the esophagus or beyond, into the oral cavity (including larynx) or lung.^{3,4} Gastric acid has a pH of 1.2 which can damage the tissue lining of the esophagus with repeated exposures.¹ A diagnosis of GERD is made using a combination of indicators including self-report of heartburn and regurgitation; endoscopy, or monitoring of reflux in an outpatient setting.³

GERD is common in a number of conditions including post-bariatric surgery, obesity, irritable bowel syndrome, developmental disorders, asthma, sleep apnea, obesity and pregnancy.^{5,6} Heartburn and regurgitation are typical symptoms of GERD, although some adults with GERD are asymptomatic.⁴

GERD symptoms may differ from person to person and range from mild to severe and can include a chronic dry cough, wheezing, asthma, recurrent pneumonia, sinusitis, nausea, vomiting, sore throat, chronic hoarseness or laryngitis, difficulty or painful swallowing, pain in the chest or the upper abdomen, dental erosion and oral malodor.^{3,4}

The symptoms are influenced by daily activities including diet, stressors and drugs, which can make the assessment of GERD symptoms at one point in time challenging.⁷ For individuals with disruptive GERD (daily symptoms) sleep may be disturbed and quality of life may be impacted resulting in missed work and/or reduced work productivity.³

Oral symptoms and complications associated with GERD may include non-specific burning sensation, mucosa ulceration and erosion, erythema of the soft/ hard palate mucosa and uvula, loss of taste and either xerostomia or increased salivary flow.^{1,8} Untreated or unmanaged GERD is capable of long-term complications such as dysphagia, difficulty breathing and esophagitis.⁴ Esophagitis is an irritation of the

44

THE JOURNAL OF DENTAL HYGIENE

Vol. 91 • No. 1 • February 2017

CHANGES INDUCED BY THE DECREASE OF SALIVARY PH ON THE HARDNESS OF THE DENTAL ENAMEL

PhD stud. Catrinel Stefania Petrovici³, Associate Professor Lucian Cristian Petcu¹, Lecturer Dr. Cristina Gabriela Puscasu¹, Lecturer Dr. Doru Florin Petrovici1, Lecturer Adina Petcu², Professor Dr. Ileana Ion³ *Corresponding author: Petcu Lucian Cristian ¹Faculty of Dental Medicine, Ovidius University Constanta, Romania ²Faculty of Pharmacy, Ovidius University Constanta, Romania

³Faculty of Medicine, Ovidius University Constanta, Romania

ABSTRACT

Introduction. The objective of this investigation is to pinpoint the influence of the salivary pH on the hardness of the dental enamel. Method. The study was realized using recently extracted 6 non-carious wisdom teeth, that were immersed in solutions of different pH (between 2.5 and 6.5) for 3 minutes, solutions that would simulate the pH of the oral cavity in patients with a potential condition of gastroesophageal reflux disease. The hardness of the enamel was tested using the Vickers method. Results show that there are no statistically significant differences (p> 0.05) between the average values of hardness of the specimens immersed in pH 5.5, 6.5 and control group specimens, while among all other specimens immersed in pH = 2.0 to 5.0 compared to the control group sample, there are statistically significant differences (p < 0.05).

Conclusion. The study highlighted the fact that lowering the pH value also entails a decrease in the dental enamel hardness, which is significantly depreciating.

Keywords: human enamel hardness, pH variation, gastroesophageal reflux disease, wisdom teeth, Vickers hardness test

INTRODUCTION

The main purpose of the present study is to highlight the changes that appear in the hardness of the dental enamel due to the low level of the salivary pH, situation that can often occur in patients with gastroesophageal reflux disease [1]. This condition most frequently develops in adult patients that over time become invalid, restricting their lives on a daily basis due to the appearance of gastritis, corrosive esophagitis or even gastric mucosa ulcerations and malignant lesions [2].

Therefore, we aim to pinpoint the influence the acid-pH solutions (values between 2.5 - 6.5), similar to the mixture of the gastric acid reflux with the saliva in the oral cavity, on the hardness of the dental enamel of non-carious teeth that were extracted due to orthodontic treatment reasons from adult patients.

https://doi.org/10.5593/SWS.ISCSS.2019.3

409

Original Paper

Caries Research

Caries Res 2016:50:508-516 DOI: 10.1159/000448292

Received : March 3, 2016 Accepted after revision: July 3, 2016 Published online: September 10, 2016

Influence of Intrinsic Factors on **Erosive Tooth Wear in a Large-Scale Epidemiological Study**

Viivi Alaraudanjoki^{a, d} Marja-Liisa Laitala^a Leo Tjäderhane^{a, d, e} Paula Pesonen^{b, d} Adrian Lussi^g Jukka Ronkainen^{c, f} Vuokko Anttonen^{a, d}

^aResearch Unit of Oral Health Sciences, ^bInstitute of Health Sciences, and ^cCenter for Life Course Health Research, University of Oulu, and ^dMedical Research Center Oulu, Oulu University Hospital and University of Oulu, Oulu, eDepartment of Oral and Maxillofacial Diseases, University of Helsinki and Helsinki University Hospital, Helsinki, and ^fPrimary Health Care Center, Tornio, Finland; ^gDepartment of Preventive, Restorative and Pediatric Dentistry, University of Bern, Bern, Switzerland

Kev Words

Adult · Erosive wear · Intrinsic acid · Risk indicator

Abstract

Objective: To assess the influence of self-reported intrinsic factors [gastroesophageal reflux disease (GERD), long-term alcoholism, long-term heavy use of alcohol and multiple pregnancies] on erosive tooth wear in a middle-aged cohort sample. Materials and Methods: Of the total Northern Finland Birth Cohort (NFBC 1966), a convenience sample (n = 3,181) was invited for an oral health examination in 2012-2013, of which 1,962 participated, comprising the final study group. Erosive tooth wear was assessed by sextants using the Basic Erosive Wear Examination Index (BEWE, 0-18). Clinical data were supplemented by questionnaires conducted in 1997/1998 and 2012/2013. The participants were divided into severe (BEWE sum ≥9) and no-to-moderate (BEWE sum 0-8) erosive wear groups, and the logistic regression model was applied. Results: Selected intrinsic factors were quite rare in this cohort sample and explained only 5.9% of the difference in the prevalence and severity of erosive wear. Daily symptoms of GERD [odds ratio (OR) 3.8, confidence interval

KARGER

www.karger.com/c

© 2016 S. Karger AG, Basel 0008-6568/16/0505-0508\$39.50/0 E-Mail karger@karger.com

(CI) 1.2-12.0] and hyposalivation (OR 3.8, CI 1.2-11.8) were the strongest risk indicators for severe erosive wear. Additionally, variables associated with an elevated risk for severe erosive wear were diagnosed alcoholism at any point (OR 2.5, CI 0.7–9.7) and self-reported heavy use of alcohol in both questionnaires (OR 2.0, CI 0.6-6.2). Even low-dose long-term consumption of alcohol was associated with erosive wear. **Conclusions:** In this cohort sample, intrinsic factors such as GERD or alcoholism alone are relatively uncommon causes of erosive tooth wear. The role of long-term use of alcohol in the erosion process may be bigger than presumed.

© 2016 S. Karger AG, Basel

The chemical properties of intrinsic or extrinsic acids and the frequency of acidic challenges play an important role in the erosive tooth wear process [Lussi and Hellwig, 2014]. The most common general health condition, in which intrinsic acids may enter into the oral cavity, is gastroesophageal reflux disease (GERD); the prevalence in Europe has been reported to range between 12 and 24% [Ronkainen and Agreus, 2013]. The Montreal definition of GERD describes it as a condition that develops when

Viivi Alaraudanjoki Institute of Dentistry, University of Oulu PO Box 5281 FI-90014 Oulu (Finland) E-Mail viivi.alaraudanoki@oulu.fi

Wilder-Smith et al. BMC Gastroenterology (2017) 17:113 DOI 10.1186/s12876-017-0670-1

BMC Gastroenterology

RESEARCH ARTICLE



CrossMark

Longitudinal study of gastroesophageal reflux and erosive tooth wear

Clive H. Wilder-Smith^{1,2*}, Andrea Materna¹, Lukas Martig³ and Adrian Lussi²

Abstract

Background: Approximately 60% of patients presenting to dentists with erosive tooth wear have significant gastroesophageal reflux (GERD), despite minor reflux symptoms. No longitudinal studies of reflux-associated erosive tooth wear and of reflux characteristics have been reported to date.

The aim of this study was to characterize the longitudinal course of GERD and of associated erosive tooth wear, as well as factors predictive of its progression, in a large group of patients.

Methods: Seventy-two patients presenting to dentists with clinically significant erosive tooth wear and increased esophageal acid exposure by 24-h multichannel intraluminal pH-impedance measurement (MII-pH) were reassessed clinically and by MII-pH after 1 year treatment with esomeprazole 20 mg twice-daily. Predictive factors for erosive tooth wear were assessed by logistic regression.

Results: At follow-up, no further progression in erosive tooth wear was observed in 53 (74%) of patients. The percentage of time with a pH < 4, the number of acid reflux episodes and the percentage of proximal esophageal reflux off-PPI did not change significantly after one year, but the number of weakly acidic reflux episodes decreased significantly in the large subgroup without progression. None of the baseline demographic, clinical, endoscopic or esophageal acid exposure characteristics were significantly associated with progression of erosive tooth wear at follow-up.

Conclusions: In this longitudinal study in patients with erosive tooth wear and oligosymptomatic GERD receiving esomeprazole for one year, erosive tooth wear did not progress further in the majority of patients. Background acidic esophageal reflux exposure appeared stable over time, whereas weakly acidic exposure decreased significantly in patients without erosion progression. MII-pH measurements on-PPI and with healthy controls will be useful in the further elucidation of the causal role of reflux in erosive tooth wear.

Trial registration: ClinicalTrials.gov, retrospectively registered: NCT02087345.

Keywords: Dental erosion, Gastroesophageal reflux, GERD, Proton pump inhibitor, Esomeprazole, pH-impedance

Background

Dental erosion, the chemical dissolution of enamel without bacterial involvement, is considered an established complication of gastroesophageal reflux (GERD) [1]. It is caused by repeated episodes of exposure to acid and is influenced by chemical (e.g. salivary buffering effects, pH, fluoride,) and physical (temperature, flow rate) factors [2]. As dental erosion commonly occurs in

Full list of author information is available at the end of the article



conjunction with abrasive processes, it is now termed "erosive tooth wear" [3]. Advanced erosive tooth wear leads to functional compromise, oral symptoms and disfigurement. The reported prevalence erosive tooth wear varies between 17% and 68% in patients with symptomatic GERD and a recent study of erosive tooth wear revealed a prevalence of 29% in 3187 European adults aged 18–35 years without symptomatic GERD [4, 5]. Recently, characterisation of reflux by 24-h multichannel intraluminal pH-impedance measurements (MII-pH) and endoscopy in a large prospective cohort of oligosymptomatic patients presenting with erosive tooth wear to dentists was published, showing significant

© The Author(s). 2017 **Open Access** This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated

^{*} Correspondence: cws@braingut.com

¹Brain-Gut Research Group and Gastroenterology Group Practice, Bubenbergplatz 11, -3011 Bern, CH, Switzerland

Department of Preventive, Restorative and Pediatric Dentistry, University of Bern, Bern, Switzerland

BMJ Open Risk factors associated with oral manifestations and oral health impact of gastro-oesophageal reflux disease: a multicentre, cross-sectional study in Pakistan

Ibrahim Warsi,^{® 1} Javeria Ahmed,² Anjum Younus,³ Abdur Rasheed,⁴ Tayyab Saeed Akhtar,⁵ Qurrat UI Ain,⁶ Zohaib Khurshid⁷

To cite: Warsi I, Ahmed J, Younus A, et al. Risk factors associated with oral manifestations and oral health impact of gastrooesophageal reflux disease: a multicentre, cross-sectional study in Pakistan. BMJ Open 2019;9:e021458. doi:10.1136/ bmiooen-2017-021458

 Prepublication history for this paper is available online.
 To view these files, please visit the journal online (http://dx.doi. org/10.1136/bmjopen-2017-021458).

Received 4 March 2018 Revised 10 January 2019 Accepted 6 February 2019

Check for updates

© Author(s) (or their employer(s)) 2019. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

Correspondence to Dr Ibrahim Warsi; ibrahim.warsi@yahoo.com

ABSTRACT

Objective Gastro-oesophageal reflux disease (GORD) is a relatively common disorder and manifests with extraoesophageal symptoms, such as dental erosions (DE), cough, laryngitis, asthma, and oral soft- and hard-tissue pathologies. This study aimed (1) to identify oral soft and hard-tissue changes in patients with GORD and (2) to evaluate these oral changes as indices for assessing GORD and its severity.

Setting This cross-sectional study was conducted at four major tertiary care government hospitals, in two metropolitan cities of Pakistan.

Participants In total, 187 of 700 patients who underwent oesophago–gastro–duodenoscopy and having GORD were included in the study. Patients with GORD were divided according to the presence of DE into group A (with DE, chronic/severe GORD) and group B (without DE, mild GORD). Patients who were unconscious and had extremely limited mouth opening were excluded.

Primary and secondary outcome measures Abnormal conditions and lesions of the oral mucosa were recorded. The impact of oral hard and soft-tissue changes on the oral health-related quality of life was assessed using the Pakistani (Urdu) version of the validated Oral Health Impact Profile-14 (OHIP-14) instrument.

Results Oral submucous fibrosis (66.3%), ulceration (59.4%) and xerostomia (47.6%) were significantly more common in group A (p<0.05). The prevalence of GORD was 26.7%, within which the prevalence of DE was 35.3% Unhealthy dietary pattern, nausea/vomiting, oesophagitis, xerostomia, ulceration, gingivitis and angular cheilitis showed a statistically significant association with chronic GORD and DE. All subscales of OHIP-14 were positively correlated (p<0.05) in patients with GORD and DE, with notable impact on psychological discomfort (rs=0.30), physical disability (rs=0.29), psychological disability (rs=0.27) and functional limitation (rs=0.20). Conclusion Patients with GORD and DE presented with more severe oral manifestations than did those with GORD and no DE. We recommend timely dental checkups to assess the severity of both systemic and oral disease

Strengths and limitations of this study

- This study is the first of its kind to bridge the gap created by either lacking evidence or controversial literature on the effect of gastro-oesophageal reflux disorder (GORD) on oral soft-tissues.
- This study assessed oral health-related quality of life using Oral Health Impact Profile-14 instrument, the results of which highlight how oral health and systemic health are interlinked from a psychological and general well-being perspective.
- General practitioners and gastroenterologists are often the primary healthcare providers for patients with GORD, but while addressing their main gastroenterological concerns, the oral manifestations of these systemic conditions are often overlooked. This study highlights the need for dental referral in patients with upper gastrointestinal disorders (in this case GORD), which can have a marked effect on both systemic and oral health.
- Cross-sectional design of this study limits the ability to rule out confounders and establish causal–inference relationships. Hence, the study results are limited to correlation extent only. We recommend future researchers to assess the reported risk factors in a prospective study design, in order to understand the evolution of oral morbidities linked with the pathogenesis of GORD.

INTRODUCTION

Gastro-oesophageal reflux disease (GORD) is a common disorder, affecting approximately 10%–20% of the general population.¹ The Montreal consensus classifies GORD as an entity manifesting as oesophageal and extraoesophageal symptoms.² The oesophageal symptomatology includes regurgitation or burning retrosternal chest pain, reflux oesophagitis, strictures, Barrett's oesophagus and adenocarcinoma, and the extraoesophageal symptomatology comprises reflux,

BMJ

Warsi I, et al. BMJ Open 2019;9:e021458. doi:10.1136/bmjopen-2017-021458

PREVALENCE OF DENTAL EROSIONS IN GERD: A PILOT STUDY

ALINA M. PICOS¹, SIMINA POENAR¹, ALEXANDRA OPRIS², ALEXANDRA CHIRA², MARIUS BUD³, ANTONELA BERAR¹, ANDREI PICOS¹, DAN L. DUMITRASCU²

¹Department of Prosthetic Dentistry, Iuliu Hatieganu University of Medicine and Pharmacy Cluj-Napoca, Romania

²2nd Medical Dept. , Iuliu Hatieganu University of Medicine and Pharmacy Cluj-Napoca, Romania

³Department of Odontology, Iuliu Hatieganu University of Medicine and Pharmacy Cluj-Napoca, Romania

Abstract

Background. Dental erosions are determined by a mechanism involving increased oral acidity. Gastro-esophageal reflux disease (GERD) represents the pathological reflux of gastric content into the oral cavity, affecting the hard dental tissues integrity, with a major risk of advanced tooth wear.

Aim. This study aims to investigate the prevalence of dental erosions in GERD patients, in order to obtain a basis for therapeutic strategies and specific prophylactic measures.

Methods. We incorporated a mandatory dental consultation in the therapeutic protocol of GERD patients. The study was carried out in a group of 60 patients with GERD. Dental examination of these patients revealed 21 cases showing visible dental erosions. The control group included 60 patients, without GERD, age and sex matched. All examinations were carried out in a tertiary center by the same team of dentists, instructed in dental erosion recognition and questionnaire administration.

Results. The dental erosion prevalence in patients with GERD was 35%. In the control group, erosions were 13% (OR: 3.6); 67% of patients with dental erosions were females and 33% were males. Middle age showed the highest risk for dental erosions, with peaks in the fourth and sixth decades.

Conclusions The risk of dental erosion was significantly higher in GERD patients as compared to the control group. The sex ratio shows a higher prevalence of erosion in females

Keywords: dental erosion, GERD

Introduction

The erosion of tooth structure is defined as a loss of dental hard tissue surface due to a chemical process of acid attack that does not involve bacterial factors (Fig 1). Exogenous factors are involved, related to the consumption of acidic foods and drinks, but also internal factors that decrease the pH in the oral cavity, which are common in gastro-esophageal pathology and hyperemesis [1].

Gastro-esophageal reflux disease (GERD) is a relatively common disorder, affecting daily approximately 7% of the adult population and 36% at least once a month [2]. GERD is caused by several mechanisms, mainly the abnormal pressure of the lower esophageal sphincter,

Accepted: 20.12.2013 Address for correspondence: ddumitrascu@umfcluj.ro pharynx or the oral cavity [2,3]. When a substance having a lower pH than 5.5, which is the critical pH for the enamel integrity, reaches the oral cavity, the crystals in the enamel hydroxyapatite can be dissolved. Gastric secretion has a pH between 0.8-2, with a great erosive potential [4]. Frequent exposure of teeth to this acid can cause

allowing the gastric fluid to enter into the esophagus and

even to reach the cervical portion of the esophagus, the

severe tooth wear (erosion). Dentists are often the first healthcare providers for guiding the diagnosis of GERD due to the identification of dental erosion that might be the first sign of disease [5,6].

The loss of tooth hard structure leads to: hypersensitivity to thermal, tactile or sweet stimuli, pain during chewing, loss of the vertical dimension of occlusion with esthetic consequences due to the decrease of the lower 1/3 of the face

344

Clujul Medical 2013 Vol. 86 - no. 4

Manuscript received: 08.12.2013

J Gastroenterol (2012) 47:412-420 DOI 10.1007/s00535-011-0515-6

ORIGINAL ARTICLE—ALIMENTARY TRACT

Oral symptoms including dental erosion in gastroesophageal reflux disease are associated with decreased salivary flow volume and swallowing function

Hiroo Yoshikawa · Kenji Furuta · Mayumi Ueno · Masayoshi Egawa · Aya Yoshino · Seiji Kondo · Yoshiki Nariai · Hiroaki Ishibashi · Yoshikazu Kinoshita · Joji Sekine

Received: 13 September 2011/Accepted: 31 October 2011/Published online: 27 December 2011 © Springer 2011

Abstract

Background This preliminary clinical study aimed to evaluate the effects of salivary flow volume and swallowing function on oral symptoms including dental erosion in gastroesophageal reflux disease (GERD).

Methods The subjects were 40 GERD patients and 30 (15 younger, 15 older) healthy controls. Detailed medical, dietary, and dental histories were obtained to identify individual behavioral habits potentially associated with dental erosion. Oral examination evaluated dental erosion and determined scores for the decayed, missing, filled (DMF) index, the papillary, marginal, attached (PMA) index for gingivitis, and the Simplified Oral Hygiene Index (OHI-S). Salivary flow volume and swallowing function were evaluated by the Saxon test and repetitive saliva swallowing test, respectively.

Results The DMF index and OHI-S scores differed significantly between all 3 groups. The PMA index was significantly different between the GERD group and the two control groups. The prevalence of dental erosion was 24.3% in the GERD group (0% in the control groups). No specific relationship was found between the incidence of

H. Yoshikawa \cdot M. Ueno \cdot M. Egawa \cdot A. Yoshino \cdot Y. Nariai \cdot H. Ishibashi \cdot J. Sekine (\boxtimes)

Department of Oral and Maxillofacial Surgery,

Shimane University Faculty of Medicine,

89-1 Enya-cho, Izumo, Shimane 693-8501, Japan e-mail: georges@med.shimane-u.ac.jp

K. Furuta · Y. Kinoshita

Department of Internal Medicine, Shimane University Faculty of Medicine, 89-1 Enya-cho, Izumo, Shimane 693-8501, Japan

S. Kondo

Department of Oral and Maxillofacial Surgery, Showa University, 2-1-1, Kitasenjyu, Tokyo 145-0062, Japan

Springer

dental erosion and dietary history or behavioral habits. The Saxon test results were significantly lower in the GERD group than in both the control groups. Frequency of swallowing was significantly lower and time to first swallow was significantly longer in the GERD group than in the two control groups.

Conclusions Oral symptoms in GERD are likely to be associated with impaired salivary flow volume or swallowing function. Treatment for the oral dryness induced by reduced salivary flow volume and rehabilitation for swallowing function could be indicated in patients with GERD.

Keywords Dental erosion · Gastroesophageal reflux disease · Salivary flow volume · Swallowing function · Age

Introduction

The global consensus definition and classification of gastroesophageal reflux disease (GERD) that was proposed by Vakil et al. [1] in 2006 brought about a conceptual change in the classification of GERD-related disease manifestations, presenting it as a set of syndromes. The manifestations of GERD were divided into esophageal and extraesophageal syndromes, with extraesophageal syndromes subclassified into established and proposed associations. One of the oral symptoms that can be caused by GERD is dental erosion, with reflux dental erosion syndrome being classed as an established association by Vakil et al. [1].

Dental erosion is defined as irreversible loss of dental hard tissue by a chemical process that does not involve bacteria [2, 3]. Dissolution of the mineralized tooth structure occurs upon contact with acids that are introduced into the oral cavity from intrinsic or extrinsic sources. Dental

CE

CASE-CONTROL STUDY

Dental Erosion in Children with Gastroesophageal Reflux Disease

Patricia Alves Drummond de Oliveira, BDS, MSc, PhD¹ • Saul Martins Paiva, BDS, MSc, PhD² • Mauro Henrique Nogueira Guimarães de Abreu, BDS, MSc, PhD³ Sheyla Márcia Auad, BDS, MSc, PhD⁴

Abstract: *Purpose:* The purpose of this study was to investigate the impact of gastroesophageal reflux disease (GERD) on dental erosion (DE) in children and analyze the association between dental erosion and diet, oral hygiene, and sociodemographic characteristics. **Methods:** This casecontrol study encompassed 43 two- to 14-year-olds diagnosed positive for GERD by the 24-hour pH monitoring, paired by age group with 136 healthy controls, in Belo Horizonte, Minas Gerois, Brazil. DE was assessed by one collibrated examiner using the O'Sullivan index. A questionnaire was self-administered by parents collecting information regarding sociodemographics, oral hygiene, and dietary habits. Dental erosion experience was compared between the groups, and a stratified analysis was performed (P<0.05). **Results:** Dental erosion was diagnosed in 10.6 percent (w equals 19) of all the children; 25.6 percent (w equals 11) of GERD children and 5.9 percent (w equals eight) of children without GERD, P=0.001). Dental erosion was not associated with dietary consumption or sociodemographic characteristics in both groups (P≥0.05). Children who used adult toothpaste had a 5.79 higher chance of having dental erosion in the group with GERD. **Conclusion:** Children diagnosed with gastroesophageal reflux disease were at an increased risk of having dental erosion were compared to healthy subjects; among the GERD children, dental erosion was associated with the use of adult toothpaste. (Pediatr Dent 2016;38(3):246-50) Received October 23, 2015 | Last Revision March 11, 2016 | Accepted March 13, 2016

KEYWORDS: DENTAL EROSION, CHILDREN, GASTROESOPHAGEAL REFLUX, CASE CONTROL

Gastroesophageal reflux disease (GERD) is a common condition that develops when the stomach reflux causes troublesome symptoms and complications. The manifestations of GERD are divided into esophageal (such as regurgitation and heart-burn) and extraesophageal (like dental erosion).^{1,2} Dental erosion (DE) is the irreversible loss of dental hard tissue due to an acid dissolution process that does not involve acids of bacterial origin. It is a progressive condition that could result in significant damage to the dentition and the need for complex treatment.3 The source of acids can be endogenous (regurgitation and vomiting) and/or exogenous (dietary, medicinal, and occupational) origins.4 GERD patients are at risk of developing dental erosion due to intrinsic acid exposure. The clinical signs of dental erosion caused by intrinsic acid may be modulated by the tongue, which forces the regurgitated acid along the palatal and occlusal surfaces of the teeth.⁵ Some patients are considered silent refluxers, with no symptoms indicating the presence of GERD. The presence of dental erosion could be a clinical sign that reflux is occurring, thus assisting in the diagnosis of gastroesophageal reflux disease.33

The association of dental erosion and GERD is stronger than may be perceived by physicians. It is important to detect and treat chronic acid reflux in children to prevent long-term tooth damage associated with GERD. Dentists could be the first health care professionals to diagnose a systemic disease through its oral manifestations.⁴

There is relatively little information in the general medical and gastroenterology literature regarding dental erosion and GERD.^{4.6} Despite the growing interest in epidemiological studies investigating DE in children in developed and developing countries, information is still scarce.^{7.8} Few studies have investigated the site specificity of dental erosion.³ Some studies have evaluated the occurrence of DE in GERD children compared with a control group of healthy children, showing that GERD patients had a higher prevalence of DE.⁶⁹⁻¹¹ Since DE is a progressive condition, early diagnosis and identification of the risk factors is increasingly important to establish preventive measures, especially in GERD patients.^{3,0} To the best of our knowledge, this is the first Brazilian study that has examined children who were positively diagnosed for GERD via 24-hour pH monitoring and compared their findings of dental erosion to children without GERD within the same age group.

The purpose of this case-control study was to analyse the impact of gastroesophageal reflux disease in dental erosion experience in children as well as possible factors associated with dental erosion, such as dietary habits, oral hygiene, and socio-demographic indicators.

Methods

This case-control study was approved by the Human Research Ethics Committee of the Federal University of Minas Gerais, Belo Horizonte, Minas Gerais, Brazil, and by the University Hospital Board of Ethics Research, Belo Horizonte, Minas Gerais, Brazil. Informed consent forms were obtained from the parents.

Sample selection criteria. The sample size was calculated based on the results found in a previous study, with 76 percent of DE in GERD children and 24 percent in children without GERD.⁹ The power of the test was 99.9 percent, and the 95 percent confidence interval (CI) was 95%. A total of 151 children were diagnosed positively via 24-hour pH monitoring at the University Hospital of the Federal University of Minas Gerais from May 2006 to January 2011. The 24-hour pH

¹Dr. Oliveira is a researcher, ²Dr. Paiva is a full professor and ⁴Dr. Auad is an associate professor, Department of Pediatrie Dentistry and Orthodontics, and ³Dr. Abreau is an associate professor, Department of Community and Preventive Dentistry, all in the Faculty of Dentistry, Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais, Brazil.

Correspond with Dr. Oliveira at patricia_drummond@vahoo.com

Gut and Liver, Vol. 7, No. 3, May 2013, pp. 278-281

equately to changes in abdominal pressure.1 Gastroesophageal

reflux disease (GERD) is a chronic form of acid reflux which allows refluxed acid to move upward through the esophagus into

oropharynx produce symptoms or complications.2 Studies show

GERD is common and may be overlooked in infants and children. For example, GERD can present as repeated regurgitation,

nausea, heartburn, coughing, laryngitis, or respiratory problems

like wheezing, asthma, or pneumonia. Infants and young chil-

dren may demonstrate irritability or arching of the back, often

during or immediately after feedings. Infants with GERD may

refuse to feed and experience poor growth.3 Esophageal compli-

cations of GERD are reflux esophagitis, hemorrhage, stricture,

Barrett's esophagus, and adenocarcinoma.4 Dental erosion as

extra esophageal manifestations of GERD has been reported with varying prevalences in the population and may be as high

as 42%.⁵ Some studies in children and adolescents with GERD, reported the high occurrence of dental erosions with enamel

loss in facial, occlusal, and lingual surfaces.6 Also an increased

risk of dental caries was reported in children with GERD.7 On

the other hand, a large case control study found no significant associations between GERD and either dental erosion or tooth

sensitivity, but significant associations between GERD, xerosto-

mia, oral acid/burning sensation, subjective halitosis, ervthema

of the palatal mucosa and uvula⁸ where reported. Strong associations have been reported between GERD, asthma⁴ and between asthma and tooth erosion.⁹ The prevalence of dental erosions

due to GERD has not been clearly reported and there are a few

studies to evaluate the efficacy of GERD treatment for prevention of these dental erosions.¹⁰ The first randomized clinical trial

to demonstrate quantitatively suppression of tooth erosion after

treatment with a proton pump inhibitor has recently been pub-

lished.11 We evaluated whether any presence of specific type of

erosions could be a key to search for GERD and require referral

Gastroesophageal Reflux Disease and Tooth Erosion: A Cross-Sectional Observational Study

Fatemeh Farahmand*, Mozhgan Sabbaghian*, Sharareh Ghodousi[†], Nasila Seddighoraee[†], and Mahdi Abbasi[‡]

Departments of *Gastroenterology, 'Pedodontics, Children's Medical Center Hospital, Tehran University of Medical Science, and [†]Department of Restorative Dentistry, Tehran University of Medical Science, Tehran, Iran

Background/Aims: Gastroesophageal reflux disease (GERD) is common in children. Recurrent exposure to gastric acid in GERD may contribute to tooth erosion. Methods: In this prospective study, 54 GERD patients qualified according to endoscopy, pH-metry, and the GERD questionnaire and 58 healthy controls qualified by the GERD questionnaire were assessed. Two groups underwent dental evaluations for the presence, severity, and patterns of erosion and for the stage of dentition using a Tooth Wear Index. The health care providers who performed the dental exams did not know which children had been diagnosed with GERD. Results: A total of 112 children, 3 to 12 years old were enrolled in the study, and 53 of 54 (98.1%) GERD patients and 11 of 58 (19.0%) controls had dental erosions (p<0.0001). In GERD patients, the posterior occlusal surfaces of milk teeth were more affected (p<0.0001). There was no correlation between GERD and the affected surfaces in permanent teeth, nor in the patterns or erosion grades (localized or general). In both groups, milk teeth had more erosions than permanent teeth, but the difference was not statistically significant. Conclusions: According to this study, there is a positive correlation between GERD and dental erosion. Posterior occlusal surface erosions in milk teeth could indicate GERD. (Gut Liver 2013:7:278-281)

Key Words: Gastroesophageal reflux; Tooth erosion; Child

INTRODUCTION

Gastroesophageal reflux (GER) is a normal physiologic process that occurs in healthy infants, children and adults. Reflux occurs when there are episodes of transient relaxations of the lower esophageal sphincter or when the sphincter tone adapts inad-

Correspondence to: Mozhgan Sabbaghian

Department of Gastroenterology, Children's Medical Center Hospital, Tehran University of Medical Science, Keshavarz Boulevard, Tehran 1419854451, Iran

pISSN 1976-2283 eISSN 2005-1212 http://dx.doi.org/10.5009/gnl.2013.7.3.278

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/3.0) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Tel: +98-21-6692-0981, Fax: +98-21-6693-0024, E-mail: mozhgan_sabbaghian@yahoo.com

Received on January 3, 2012. Revised on August 5, 2012. Accepted on August 20, 2012. Published online on April 9, 2013.

Watanabe et al. BMC Gastroenterology (2017) 17:92 DOI 10.1186/s12876-017-0650-5

BMC Gastroenterology

RESEARCH ARTICLE

Open Access

Oral soft tissue disorders are associated with gastroesophageal reflux disease: retrospective study

Masaaki Watanabe¹, Eiji Nakatani², Hiroo Yoshikawa¹, Takahiro Kanno¹, Yoshiki Nariai³, Aya Yoshino¹, Michael Vieth⁴, Yoshikazu Kinoshita⁵ and Joji Sekine^{1*}

Abstract

Background: Dental erosion (DE), one of oral hard tissue diseases, is one of the extraoesophageal symptoms defined as the Montreal Definition and Classification of gastroesophageal reflux disease (GERD). However, no study evaluated the relationship between GERD and oral soft tissues. We hypothesized that oral soft tissue disorders (OSTDs) would be related to GERD. The study aimed to investigate the association OSTDs and GERD.

Methods: GERD patients (105 cases), older and younger controls (25 cases each) were retrospectively examined for oral symptoms, salivary flow volume (Saxon test), swallowing function (repetitive saliva swallowing test [RSST]), teeth (decayed, missing, and filled [DMF] indices), and soft tissues (as evaluation of OSTDs, gingivitis; papillary, marginal, and attached [PMA] gingival indexes, simplified oral hygiene indices [OHI-S], and inflammatory oral mucosal regions). Clinical histories, which included body mass index [BMI], the existence of alcohol and tobacco use, and bruxism, were also investigated. A *P* value of <0.05 was defined as statistically significant.

Results: GERD patients, older and younger controls participated and aged 66.4 ± 13.0 , 68.3 ± 8.2 and 28.7 ± 2.6 years old, respectively. The most common oral symptom in the GERD patients was oral dryness. Salivary flow volume and swallowing function in the GERD patients were significantly lower than in either of the controls (all P < 0.05). Inflammatory oral mucosal regions were found only in the GERD patients. The DMF indices, as a measure of dental caries, in the GERD patients were higher than in the younger controls (P < 0.001), but lower than in the older controls (P = 0.033). The PMA gingival indexes, as a measurement for gingival inflammation, and OHI-S, as a measure for oral hygiene, in the GERD patients were significantly higher than in either of the controls (all P < 0.05). Though no significant differences in BMI, the existence of alcohol and tobacco use were found, bruxism, as an exacerbation factor of periodontal disease, in the GERD patients was significantly more frequent than in either control group (P = 0.041).

Conclusions: OSTDs were associated with GERD, which was similar to the association between DE and GERD.

Keywords: Dental erosion, Gastroesophageal reflux disease, Gingivitis, Inflammatory oral mucosal regions, Oral soft tissue disorders, Salivary flow volume, Swallowing function

¹Department of Oral and Maxillofacial Surgery, Shimane University Faculty of Medicine, 89-1 Enya-cho, Izumo, Shimane 693-8501, Japan Full list of author information is available at the end of the article



© The Author(s). 2017 **Open Access** This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated.

^{*} Correspondence: georges@med.shimane-u.ac.jp

Received: 20 October 2018 Revised: 11 April 2019 Accepted: 25 April 2019 DOI: 10.1111/joor.12807

REVIEW

REHABILITATION WILEY

Associations between tooth wear and dental sleep disorders: A narrative overview

Peter Wetselaar¹ Daniele Manfredini² Jari Ahlberg³ Anders Johansson⁴ Ghizlane Aarab¹ | Chryssa E. Papagianni¹ | Marisol Reyes Sevilla¹ | Michail Koutris¹ | Frank Lobbezoo¹

¹Department of Orofacial Pain and Dysfunction, Academic Centre for Dentistry Amsterdam (ACTA), University of Amsterdam and Vrije Universiteit Amsterdam, Amsterdam, The Netherlands ²School of Dentistry, University of Padova, Padova, Italy

³Department of Oral and Maxillofacial Diseases, Faculty of Medicine, University of Helsinki, Helsinki, Finland

⁴Departement of Clinical Dentistry-Prosthodontics, Faculty of Medicine, University of Bergen, Bergen, Norway

Correspondence

Peter Wetselaar, Department of Orofacial Pain and Dysfunction, Academic Centre for Dentistry Amsterdam (ACTA), Gustav Mahlerlaan 3004, 1081 LA Amsterdam, The Netherlands.

Email: p.wetselaar@acta.nl

Abstract

Objectives: Tooth wear is a common finding in adult patients with dental sleep disorders. The aim of this paper was to review the literature on the possible associations between tooth wear and the following dental sleep disorders: sleep-related oro-facial pain, oral moistening disorders, gastroesophageal reflux disease (GERD), obstructive sleep apnoea syndrome (OSAS) and sleep bruxism.

Methods: A PubMed search was performed on 1 June 2018 using MeSH terms in the following query: Tooth Wear AND (Facial Pain OR Temporomandibular Joint Disorders OR Xerostomia OR Sialorrhea OR Gastroesophageal Reflux OR Sleep Apnea Syndrome OR Sleep Bruxism).

Results: The query yielded 706 reports on tooth wear and the mentioned dental sleep disorders. Several associations between tooth wear and the dental sleep disorders were suggested in the literature. It could be concluded that: (a) tooth wear is associated with dental pain and/or hypersensitivity; (b) oral dryness is associated with tooth wear, oro-facial pain and sleep bruxism; (c) GERD is associated with tooth wear, oro-facial pain, oral dryness, OSAS and sleep bruxism; (d) OSAS is associated with oral dryness, GERD and sleep bruxism; and (e) sleep bruxism is associated with tooth wear.

Conclusions: Tooth wear is associated with the dental sleep disorders oro-facial pain, oral dryness, GERD and sleep bruxism. The dental sleep disorders are interlinked with each other, which leads to indirect associations as well, and makes the consequences of each single condition difficult to disentangle. Knowledge of these associations is clinically relevant, but more research is needed to confirm their validity.

KEYWORDS

adult, gastroesophageal reflux disease, hypersalivation, hyposalivation, oral moistening disorders, oro-facial pain, ptyalism, sialorrhea, sleep apnoea, sleep bruxism, tooth wear, xerostomia

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made. © 2019 The Authors, Journal of Oral Rehabilitation Published by John Wiley & Sons Ltd

J Oral Rehabil. 2019;46:765-775.

wileyonlinelibrary.com/journal/joor 765





Associations among Bruxism, Gastroesophageal Reflux Disease, and Tooth Wear

Yuanyuan Li 1 , Fan Yu 1 , Lina Niu 1 , Wei Hu 1,2 , Yong Long 1,3 , Franklin R. Tay 4,* and Jihua Chen 1,*

- ¹ State Key Laboratory of Military Stomatology & National Clinical Research Center for Oral Diseases & Shaanxi Key Laboratory of Oral Diseases, Department of Prosthodontics, School of Stomatology, The Fourth Military Medical University, Xi'an 710032, Shaanxi, China; YuanyuanLi_1@163.com (Y.L.); fan81811@163.com (F.Y.); niulina831013@126.com (L.N.); weihuta21@163.com (W.H.); longyong@fmmu.edu.cn (Y.L.)
- ² Department of Immunology, The Fourth Military Medical University, Xi'an 710032, Shaanxi, China
- ³ Department of Epidemiology, School of Public Health, The Fourth Military Medical University, Xi'an 710032, Shaanxi, China
- ⁴ Department of Endodontics, The Dental College of Georgia, Augusta University, 1430, John Wesley Gilbert Drive, Augusta, GA 30912-1129, USA
- * Correspondence: ftay@augusta.edu (F.R.T.); jhchen@fmmu.edu.cn (J.C.); Tel.: +1-706-721-2606 (F.R.T.); +86-29-8477-6329 (J.C.)

Received: 7 October 2018; Accepted: 3 November 2018; Published: 6 November 2018



Abstract: The relationship between bruxism and tooth wear is contentious in the literature. The pathophysiological processes of tooth wear may be complicated by the relationship between bruxism and gastroesophageal reflux disease (GERD). The objective of this study was to evaluate the associations among bruxism, GERD, and tooth wear. Two complementary studies were performed: a case-control study to verify the linkage between GERD and bruxism and a cross-sectional study on the same cohort to establish the connection between GERD and tooth wear in bruxism patients. A cohort of 363 consecutive bruxism patients and 363 matched control participants were recruited. Gastroesophageal reflux disease was diagnosed in accordance with the Montreal criteria. Tooth wear was scored based on the index recommended by Smith and Knight. Logistic regression analyses were performed. After adjustment, GERD was identified as a risk factor of bruxism. Bruxism with reflux symptoms for extensive time-periods was associated with severe tooth wear for the whole dentition (odds ratio, 4.70, 95% confidence interval, 2.04–10.83). Increased odds ratios for severe tooth wear were also found in all tooth locations and palatal/lingual and occlusal/incisal surfaces of bruxism patients with GERD for extensive time-periods. In conclusion, strong associations were identified among bruxism, GERD, and tooth wear.

Keywords: tooth attrition; tooth erosion; bruxism; gastroesophageal reflux

1. Introduction

Tooth wear involves at least three courses of action: attrition (wear produced by tooth-tooth contact), erosion (chemical wear caused by acids), and abrasion (wear through tooth-material interaction) [1]. Abfraction is another possible theory that involves occlusal stress in the creation of non-carious cervical lesions [2].

Dentists generally ascribe occlusal wear to attrition [1]. Attrition also leads to wear of palatal/lingual and buccal/labial surfaces, especially with malocclusions [1]. Pathological attrition of occlusal surfaces is commonly associated with bruxism [1]. However, not all studies support the relationship between bruxism and tooth wear [3]. Tooth erosion is a distinctive manifestation of

J. Clin. Med. 2018, 7, 417; doi:10.3390/jcm7110417

www.mdpi.com/journal/jcm

doi: 10.1111/ped.12201

PEDIATRICS INTERNATIONAL

Pediatrics International (2014) 56, 24-30

Original Article

Association of problem behavior with sleep problems and gastroesophageal reflux symptoms

Katsuyoshi Sakaguchi,¹ Takakazu Yagi,² Aya Maeda,¹ Kunihiro Nagayama,¹ Sawako Uehara,¹ Yoko Saito-Sakoguchi,¹ Kyoko Kanematsu¹ and Shouichi Miyawaki¹

¹Department of Orthodontics, Field of Developmental Medicine, Health Research Course, Graduate School of Medical and Dental Sciences and ²Department of Orthodontics, Kagoshima University Hospital, Kagoshima University, Kagoshima, Japan

Abstract Background: There are few large-scale epidemiologic studies examining the associations between sleep problems, gastroesophageal reflux disease (GERD) symptoms, lifestyle and food habits and problem behaviors (PB) in adolescents. The aim of this study was to evaluate the associations among these factors in Japanese adolescents.

Methods: A cross-sectional survey of 1840 junior high school students was carried out using questionnaires. The subjects were classified into PB or normal behavior (NB) groups using the Pediatric Symptom Checklist (PSC). The scores of the sleep-related factors, sleep bruxism, lifestyle and food habits, and GERD symptoms were compared. Logistic regression analysis was used to determine the factors related to PB.

Results: Mean subject age was 13.3 ± 1.8 years. The PB group had significantly longer sleep latency and higher GERD symptom score (P < 0.001). Furthermore, the PB group was significantly more likely to experience absence of the mother at dinner time, skip breakfast, and have <30 min of conversation among family at dinner time. The PB group had significantly higher frequencies of sleep bruxism, difficulty falling asleep within 30 min, nightmares, feeling of low sleep quality, daytime somnolence, and daytime lack of motivation. Feelings of low sleep quality had the strongest association with PB, with an adjusted odds ratio of 12.88 (95% confidence interval: 8.99–18.46).

Conclusions: PB in adolescents are associated with sleep problems, including sleep bruxism, as well as lifestyle and food habits and GERD symptoms.

Key words behavioral symptom, gastroesophageal reflux disease, psychology, sleep bruxism, sleep problem.

Psychological problems are known to be common among adolescents. Epidemiologic studies have demonstrated high prevalence rates of psychological problems in US adolescents.¹ In Japan, the prevalence of psychological problems in adolescents is increasing, and has been associated with problem behaviors (PB).² For example, in 2009, the Ministry of Education, Culture, Sports, Science and Technology of Japan issued a press release detailing a rise in severe PB in recent years, with incidents of juvenile violence and bullying. Additionally, concurrent PB such as school performance, school absenteeism, risk-taking behavior, injury, and impaired social functioning in children are associated with sleep problems.³⁴ In particular, sleep bruxism in children is associated with an increased incidence of attention–behavior problems, which may be associated with higher arousal.⁵

Received 29 January 2013; revised 29 July 2013; accepted 2 August 2013.

© 2013 The Authors Pediatrics International © 2013 Japan Pediatric Society Furthermore, sleep bruxism is significantly associated with chronic stress.⁶ Some reviews reported an association between emotional state and sleep, and that the association would be bidirectional.^{7,8}

Gastroesophageal reflux disease (GERD) impairs daytime and nocturnal functioning. In the USA, at least 20% of adults experience heartburn once a week.⁹ According to the American Gastroenterological Association, 79% of adult respondents in a survey reported experiencing heartburn at night, and the majority reported that night-time heartburn resulted in sleeping difficulties and impaired daytime functioning.¹⁰ Past research suggested that sleep quality is related to the severity of reflux during sleep, and adult patients with night-time heartburn and sleep complaints have greater acid contact times.¹¹ That study also noted that poor sleep occurred on the following day after esophageal acid exposure.

To date, the literature focusing on the prevalence and symptoms of GERD in adolescents is scarce. Based on questionnaire reports in the USA, the prevalence of symptoms of heartburn and acid regurgitation in children is 1.8–8.2%.¹² In the UK, the incidence of GERD in children is 0.84 per 1000 persons/year.¹³ Prevalence and symptom complexes vary according to geography

Correspondence: Shouichi Miyawaki, DDS PhD, Department of Orthodontics, Field of Developmental Medicine, Health Research Course, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima 890-8544, Japan. Email: miyawaki@dent .kagoshima-u.ac.jp

Revista Română de Anatomie funcțională și clinică, macro- și microscopică și de Antropologie

Vol. XVI - Nr. 4 - 2017

SEVERE DENTAL WEAR CAUSED BY ASSOCIATION BETWEEN NOCTURNAL BRUXISM AND GASTROESOPHAGEAL REFLUX : OVERVIEW ON THE CLINICAL AND SCIENTIFIC ASPECTS

Dorelia Lucia Călin

"Grigore T. Popa" University of Medicine şi Pharmacy, Iaşi Discipline of Cariology and Restorative Odontotherapy

SEVERE DENTAL WEAR CAUSED BY ASSOCIATION BETWEEN NOCTURNAL BRUXISM AND GASTROESOPHAGEAL REFLUX: OVERVIEW ON THE CLINICAL AND SCIEN-TIFIC ASPECTS (Abstract): Dentists are often the first health professionals to diagnose systemic illnesses by observing their oral manifestations. Nocturnal bruxism may be secondary to gastro-esophageal nocturnal reflux, and patients with reflux often have excessive tooth wear, which is also a feature of nocturnal bruxism. The purpose of this article is to focus on the detrimental effects on teeth caused by the association between gastro-oesophageal reflux and night bruxism, recommending dentists to identify manifestations of systemic affections in the oral cavity through their distinctive features. Early diagnosis can improve the physical well-being of patients and may reduce teeth wear. The dental complications found in these patients present a number of clinical challenges to restore the functional and aesthetic disorders of these patients. **Keywords** : SEVERE DENTAL WEAR, NOCTURNAL BRUXISM, GASTROESOPHAGEAL REFLUX

INTRODUCTION

Considering the physiology of both nocturnal bruxism and gastro-oesophageal reflux, it is possible that these conditions occur simultaneously in some people. Randomized clinical trials have established a very important relationship between nocturnal bruxism and experimental intrasophageal acidity (1) and between nocturnal bruxism and physiological gastroesophageal reflux episodes (2). It has been suggested that nocturnal bruxism may be secondary to gastro-esophageal nocturnal reflux (2), and patients with reflux often have excessive teeth wear, which is also a feature of nocturnal bruxism (3). In patients with primary nocturnal bruxism, the association with gastroesophageal reflux may enhance the activity of grinding and/ or clenching, transforming it into an even more severe.

Etiological Factors

Psychological factors, in particular stress, have been implicated in the initiation and maintenance of both gastro-oesophageal reflux (4) and nocturnal bruxism to. Bruxism is characterized by the stereotypical rhythmic movement of the masticatory muscles and leading to the teeth grinding and clamping (5). It is frequently aggravated by stress, sleep disturbances, gastrooesophageal reflux and medication (6,7).

Nocturnal bruxism has been associated with excitatory response (8) and has been reported to overlap with gastroesophageal reflux in many patients (7). Studies have shown a positive correlation between sleep disturbances during sleep and tooth wear (9,10). Various factors, such as the occlusal interference (11), medication, sleep disorders, stress, anxiety (12) and the acidity of the esophagus (1,2) may be involved in the mechanisms of nocturnal bruxism. Emotions or stress can affect acid secretion and gastric motility, which are typical manifestations of gastro-esophageal reflux (13).

Dental anatomical changes caused by severe wear

Some of the consequences of nocturnal bruxism are oro-facial pain, temporomandibular disorders, tooth fractures and restorations, and



RESEARCH ARTICLE

The frequency of dental caries in adult patients with gastroesophageal reflux disease

Sîmpălean DS^{*}, Ghiga Dana, Petrișor M, Mărușteri M, Bacârea V, Bățagă Simona

University of Medicine and Pharmacy of Tirgu Mureş, România

Introduction. The aim of the study was to evaluate the frequency of dental caries in adults patients with gastroesophageal reflux disease. Material and method. A cross-sectional study was performed between November 2013 and October 2014. All subjects who agreed to participate to the study were asked to complete a questionnaire regarding personal information, oral hygiene and dental evaluation. The individuals with complete false teeth (superior and inferior removable prosthetic devices) were excluded from the study. The study included 134 people divided in two groups, based on upper gastrointestinal endoscopy: a group with gastroesophageal reflux disease (71), and a control group (63). Dental evaluation was performed by a dentist blind to the diagnosis of the subjects. Dental caries were evaluated by applying the decayed, missing, and filled teeth index (DMFT index). The statistical significance was defined as p<0.05. **Results**. From 71 subjects included in GERD group, 33 (46.48%) were males and 38 females (53.52%) with a mean age of 44.99±11.19 (42, 59.15%) from rura area and 29, 40.85%, from rural area). In the control group we included 28 (44.44%) males and 35 (55.56%) females (mean age 43.84±9.48) and 29 (46.03%) subjects were from urban area and 34 (53.97%) from rural area. DMFT index in GERD group was 19.49±4.28 and in control group term 18.16±4.54 (p<0.05). **Conclusions**. The present study showed that there is no difference between GERD and control group, regarding the frequency of dental caries.

Key words: oral manifestations, dental caries, gastroesophageal reflux

Received: 10 December 2014 / Accepted: 3 May 2015

Introduction

Gastroesophageal reflux is a physiological process, which consists in an effortless retrograde movement of the gastric contents to the esophagus (1). The gastroesophageal reflux disease (GERD) is a common chronic disease (2,3), with a high prevalence (4) and an increasing incidence (5). GERD occurs when the amount of gastric reflux into the esophagus is above the normal range, causing various symptoms, which can involve esophageal mucosal injury (esophagitis) (5,6). Regurgitation, pyrosis (heartburn), which can be reported in the presence or absence of regurgitation, retrosternal pain, dysphagia, sour taste and odynophagia, are considered typical manifestation of GERD (7, 8). Oral manifestations that may occur in patients with gastroesophageal reflux disease include periodic hypersalivation, xerostomia (dry mouth syndrome), burning sensation, halitosis, and dental erosions. A certain pattern of erosion was observed in patients affected by this disease: they appeared more frequently on the occlusal surfaces of posterior mandibular teeth and lingual surfaces of the anterior maxillary teeth (10).

Dental caries are represented by tooth hard tissue demineralization and destruction, caused by bacteria and acid. During a day, the enamel demineralizes and remineralizes many times. When this balance is disrupted and demineralization exceeds remineralization, the caries progress. In our country, dental caries occur frequently from an early age. The pathogenesis implies both internal and external factors.

Dental caries can have serious and long term complications, which is why they have to be treated properly, but most important they should be prevented.

The aim of the study was to evaluate the frequency of dental caries, in adult patients with gastroesophageal reflux disease.

Material and method

A cross-sectional study was performed, conducted between November 2013 and October 2014. During the study period all individuals with ages between 20 and 80 years old, who were hospitalized to the Gastroenterology clinic of the Emergency County Clinical Hospital, were evaluated. All subjects who agreed to participate in the study were asked to fill in a questionnaire regarding personal information, oral hygiene and dental evaluation.

Besides personal information, the questionnaire contained 7 questions, 5 questions concerning oral hygiene (fig. 1) and 2 questions referring to dental evaluation (Fig. 2). Regarding oral hygiene, we obtained information on the frequency of teeth brushing, the oral care products used and how often the respondent visits a dentist.

Concerning dental evaluation, we were interested if the respondent complained regarding the dental status and dental treatments.

After filling in the questionnaire, there were excluded from the study the individuals with complete false teeth (superior and inferior removable prosthetic devices). We

^{*} Correspondence to: Dan Ştefan Sîmpälean

E-mail: dansampalean@gmail.com



pewinternet.org/2013/01/28/mainreport-8/

- 14 Varnfield M, Karunanithi M, Lee CK, Honeyman E, Arnold D, Ding H et al. Smartphone-based home care model improved use of cardiac rehabilitation in postmyocardial infarction patients: results from a randomised controlled trial. Heart 2014; 100: 1770–9.
- 15 Clark RA, Conway A, Poulsen V, Keech W, Tirimacco R, Tideman P. Alternative models of cardiac rehabilitation: a systematic review. *Eur J Prev Cardiol* 2015; 22: 35–74.
- 16 Ganesan AN, Louise J, Horsfall M, Bilsborough SA, Hendriks J, McGavigan AD. International mobile health intervention on physical activity, sitting, and weight: the stepathlon cardiovascular health study. J Am Coll Cardiol 2016; 67: 2453–63.
- 17 Finkelstein EA, Haaland BA, Bilger M, Sahasranaman A, Sloan RA,

Nang EEK et al. Effectiveness of activity trackers with and without incentives to increase physical activity (TRIPPA): a randomised controlled trial. Lancet Diabetes Endocrinol 2016; 4: 983–95

- 18 Parthiban N, Esterman A, Mahajan R, Twomey DJ, Pathak RK, Lau DH et al. Remote monitoring of implantable cardioverter-defibrillators: a systematic review and meta-analysis of clinical outcomes. J Am Coll Cardiol 2015; 65: 2591–600.
- 19 Catanzariti D, Lunat M, Landolina M, Zanotto G, Lonardi G, Iacopino S et al. Monitoring intrathoracic impedance with an implantable defibrillator reduces hospitalizations in patients with heart failure. *Pacing Clin Electrophysiol* 2009; **32**: 363–70.
- 20 Adamson PB, Abraham WT, Bourge RC, Stevenson LW, Yadav J. CardioMEMS heart sensor allows monitoring of pressures to improve outcomes in NYHA class III heart failure

patients (CHAMPION) trial: impact of hemodynamic guided care on patients with preserved ejection fraction. J Card Fail 2010; 16: 913.

- 21 Miller AS, Cafazzo JA, Seto E. A game plan: gamification design principle in mHealth applications for chronic disease management. *Health Inform J* 2016; 22: 184–93.
- 22 Sunyaev A, Dehling T, Taylor PL, Mandl KD. Availability and quality of mobile health app privacy policies. J Am Med Inform Assoc 2015; 22: e28–33.
- 23 Xu W, Liu Y. mHealthApps: a repository and database of mobile health apps. JMIR Mhealth Uhealth 2015; 3: e28.
- 24 Stoyanov SR, Hides L, Kavanagh DJ, Zelenko O, Tjondronegoro D, Mani M. Mobile app rating scale: a new tool for assessing the quality of health mobile apps. J Med Internet Res 2015; 3: e27.
- 25 Hayden E. Mobile-phone health apps deliver data bounty. Nat Int Weekly J Sci 2016; 531: 422–3.

REVIEW

Dental complications of gastro-oesophageal reflux disease: guidance for physicians

Robert J. Lee,¹ Amin Aminian² and Paul Brunton¹

¹Faculty of Dentistry, Sir John Walsh Research Institute, University of Otago, Dunedin, New Zealand, and ²University of Manchester, Wilmslow, Cheshire, UK

Key words

gastro-oesophgeal reflux, intrinsic dental erosion, diagnosis, dentistry, intra-oral.

Correspondence

Paul Brunton, Faculty of Dentistry, University of Otago, 310 Great King Street, Dunedin 9054, New Zealand. Email: paul.brunton@otago.ac.nz

Received 20 May 2016; accepted 30 August 2016.

doi:10.1111/imj.13249

Abstract

There is potential for gastro-oesophageal reflux disease (GORD) to be under-diagnosed by physicians. A quick, focused examination, requiring no special equipment, of a patients' dentition can assist in making a more accurate diagnosis where GORD is suspected. Guidance is provided for physicians as to what intra-oral signs are suggestive of intrinsic dental erosion, which is a clinical feature of GORD and its associated conditions. Use of this information will, it is suggested, improve outcomes for patients where GORD is suspected.

Funding: None. Conflict of interest: None.

© 2016 Royal Australasian College of Physicians

619

THE INFLUENCE OF GASTROESOPHAGEAL REFLUX IN ORAL CAVITY

MARIA VITÓRIA **JANKOVITZ**¹, HENRIQUE DA GRAÇA **PINTO**², ROGÉRIO JARDIM **CALDAS**³, CARLA CRISTINA NEVES **BARBOSA**³, OSWALDO LUIZ CECILIO **BARBOSA**^{3*}

1. Undergraduate student, Dentistry Course, University of Vassouras; 2. Dental Surgeon. 3. Professor of the Dentistry Course, University of Vassouras.

* Lúcio Mendonça St, 24/705, Downtown, Barra do Piraí, Rio de Janeiro, Brazil. ZIP CODE: 27115-010. oswaldolcbarbosa@hotmail.com

Received: 04/02/2019. Accept: 04/30/2019

ABSTRACT

The gastroesophageal reflux disease (GERD) occurs from a failure of the esophageal valve, not having a single cause for this problem, but a series of factors that hinder the correct functioning of the valve, among which stand out: eating habits, smoking, some medications, which modify the stomach structure, compression of the abdominal cavity, obesity and pregnancy. This is due to the mechanisms involved in its pathophysiology, which once in contact with the oral cavity cause among others, dental erosion and canker sores. The objective of this study was to evaluate, through a literature review, how the gastroesophageal reflux disease influences patients' quality of life and their interference in the daily practice of the dental surgeon. In conclusion, the GERD interferes directly with patients' quality of life and with the daily practice of the dentist.

KEYWORDS: Oral cavity, gastroesophageal reflux disease, oral diseases.

1. INTRODUCTION

Gastroesophageal Reflux Disease (GERD) is a chronic condition resulting from failure of the esophageal valve, also called the cardiac valve, where its relaxation in the lower portion causes a return of inappropriate content to the esophagus and adjacent organs. The esophagus has in its histological constitution mucosa is similar to the mouth^{1,2}.

In cases of valve failure, the return of a stomach acid material not suitable for the esophageal mucosa, causing it to attack and causing lesions. The return of acid can reach the mouth causing various symptoms such as: burning, burning and discomfort¹.

The gastroesophageal reflux disease has multiple factors involved in its pathophysiology, the main one is the return of stomach acid through relaxation of the lower sphincter of the esophagus to the oral cavity, in this, the mucosa and hard tissues can be affected. The main intercurrences in the oral cavity are dental erosion and aphtha³.

Dental erosion is characterized by irreversible and progressive loss of dental hard tissue through a chemical process without bacterial action. Considered multifactorial erosion may have extrinsic sources such as dietary habits and lifestyle and intrinsic as systemic diseases⁴.

Aphtha (or APHTAE) was the term used by

Hippocrates (460-370 BC), the father of medicine, to identify oral disorders, later extending to any mucosal ulceration. Aphtha sores are classified into three types: Smaller (or Mickulicz), Greater (or Sutton's) and Hepetiformes^{5,6}.

Contact of the gastric juice of the larynx and pharynx causes inflammation and edema even with little exposure. The histology of the distal esophagus should complement the upper digestive endoscopy⁷. Histologically, the replacement of the typical stratified squamous esophageal epithelium with columnar epithelium with goblet cells, where it is believed that the appearance of columnar epithelium covering the distal esophagus is a restorative response, but that the addition of duodenal content to acid reflux is responsible by the appearance of intestinal cells and, consequently, of premalignant potential⁸.

The diagnosis through detailed anamnesis is important since several patients do not present symptomatology. This phase of absence of symptoms has a lot of relevance for dental surgeons, since the patients present with ulcerous lesion in the buccal mucosa. When the patient has symptoms, he reports the following symptoms: heartburn (or heartburn) and acid regurgitation, where the intensity, duration, triggers and improvement need to be evaluated. It is associated with imaging exams, such as: upper digestive endoscopy, prolonged esophageal pHmetry, contrast radiological study of the esophagus, esophageal manometry and esophageal impedanciometry; help to define the diagnostic hypothesis⁹.

The clinical treatment provides relief of symptoms, healing of lesions and prevention of relapses and complications, minimizing the aggressive potential of the acid content. Behavioral measures should be used in the treatment, among them we can mention: moderate the intake of fatty foods, citrus fruits, coffee, alcoholic beverages, among others, raise the bed head (15 cm), smoking cessation, slimming and special care for medicines that cause aggression of the mucosa as the antihypertensive beta-adrenergic agonists and calcium channel blockers⁹.

With respect to the pharmacological measures we can mention the intake of antacids based on calcium hydroxide, magnesium and aluminum, others as medications that accelerate gastric emptying, and still inhibitors of the proton pump⁹.

BJSCR (ISSN online: 2317-4404)

Openly accessible at http://www.mastereditora.com.br/bjscr