Association Between H. Pylori Infection and Pathological Oral Manifestations
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ABSTRACT

Data from the literature are controversial regarding the presence of Helicobacter pylori (H. pylori) in dental plaque and its association with gastric infection. One of the possible mechanisms suggested for re-infection is the recolonization with H. pylori from dental plaque. The purpose of this review was to determine whether dental plaque, poor oral hygiene, and periodontal disease were risk factors for H. pylori infection.

Key words:
Helicobacter pylori
Gastric cancer
Oral manifestations
Gastroesophageal reflux disease

Introduction

Helicobacter pylori (H. pylori) infection represents one of the most common and medically prominent infections worldwide. Infection with this micro-aerobic, gram-negative bacterium has been considered as a causal factor in the development of peptic ulcer disease [1], chronic gastritis, gastric cancer, mucosa-associated lymphoid tissue (MALT) lymphoma and gastroesophageal reflux disease (GERD) [2]. H. pylori infection is common, however, the existence of extra gastric reservoirs and transmission routes remain controversial [3]. Because the oral cavity has been proposed as a reservoir for H. pylori, many

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studies were carried out to detect the presence of H. pylori in dental plaque and saliva [4]. The oral cavity has been implicated as a potential H. pylori reservoir, which may, therefore, be involved in the re-infection of the stomach following treatment of an H. pylori infection. H. pylori were present in the oral cavity with variable distribution between saliva and dental plaques, suggesting the existence of a reservoir for the species and a potential association with gastric re-infection [5]. Polat *et al*.[6] found significant evidence which suggests the potential role of H. pylori infection in the development of GERD, and they provided sufficient evidence to define the relationship between GERD and H. pylori infection. Gastroesophageal reflux (GER) is characterized by the rise of gastric contents into the esophagus and sometimes oral and nasal cavities [7]. GERD patients are at higher risk of developing dental erosion, acid reflux at the level of the oral cavity, in fact, can cause the dissolution of the tooth enamel, especially at the level of the palatal surfaces of the back teeth, with a reported prevalence of up to 42% [8].

Patients with gastritis are frequently positive for H. pylori in their stomachs (P<0.0001) and there is a statistically significant correlation between the presence of H. pylori in gastric biopsies and the oral cavity (P<0.0001) [9]. Data suggest a relationship between gastric infection and the presence of this bacterium in the oral cavity [10]. The typical manifestations can be considered as dental caries, dry mouth, feeling an oral acid/burning sensation, halitosis, and erythema of the palatal mucosa and uvula. For diagnosis, it is mandatory to exclude other causes, like dietary factors, drugs, poor oral hygiene, eating behavior disorders, genetic and racial factors. The esophageal pH monitoring and/or endoscopy are usually necessary just to confirm the diagnosis of GERD [11]. Although oral mucosal lesions may result from GERD by direct acid or acidic vapor contact in the oral cavity, there is a paucity of information on the effect of GERD on oral mucosal changes [12].

The severity of dental erosion due to GERD is related to the duration of disease, frequency of reflux, pH and type of acid, and the quality and quantity of saliva. However, if enamel demineralization is detected sufficiently early before the damage becomes irreversible, the enamel framework can be remineralized using oral regimes and preventative modifications in diet, behavior, or medication. Hence, the purpose of this review was to determine whether dental plaque, poor oral hygiene, and periodontal disease were the risk factors for H. pylori infection.

Materials and Methods

A systematic review was conducted in June 2015. All relevant studies published between January 2013 and December 2014 were identified and included in the systematic analysis. The engines used were Medline, EMBASE, Cochrane Library, Web of Science, Google Scholar, and Scopus databases for relevant studies. The research was carried out using the key words Helicobacter, Helicobacter pylori, and H. pylori in combination with dental plaque, periodontitis and oral hygiene. We also examined the bibliographies from identified studies, reviews, and gray literature.

Results

The results of these studies showed a wide variation and which seemed to depend at least in part on the method employed to detect the bacterium in the dental plaque. The investigators used several methods to detect the presence of the bacterium in the dental plaque and these included urease tests (rapid urease/CLO test), polymerase chain reaction (PCR), medium chain triglyceride (MCT), histology, culture, and immunoassays (Table 1).

Discussion

H. pylori infection remains one of the most important public health problems in the biomedical literature worldwide and represents the most prevalent chronic bacterial disease. It affects more than half of the world's population, with a distribution related to the degree of economic development in each country [52]. Table 2 shows the prevalence of H. pylori in dental plaque in various studies ranging from 0%-100% [13-51]. This wide variation in results may be explained by several factors, such as characteristics of sample population, different sampling procedures, and differing methodologies used to detect the microorganism in dental plaque. Data generated from these studies show that the microorganism can be reliably detected in plaque samples, especially when using PCR techniques. Some investigators believed that the occurrence of H. pylori in dental plaque was significant, in terms of management of H. pylori-associated gastric disease, others held that the microorganism was present only transiently in the oral cavity [27, 43]. Compared with studies on dental plaque, there are fewer reports on the prevalence of H. pylori in saliva. The detection rates of H. pylori from saliva were less than those from dental plaque. This may be due to the fact that, while dental plaque, being a biofilm, allows the bacteria to adhere to solid surfaces, the constant flow of saliva may contribute to a reduction in bacterial load, making detection difficult. It is not

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Table 1 H. Pylori Detection in Dental Plaque and Saliva

References	Sample	Diagnostic method	Patient profile	H. pylori detection rate[*n*(%)]
Krajden *et al.*[13]	Pq	MCT	Dys	1/71 (1.4)
Shames *et al.* [14]	Pq/Sa	MCT, REA	Dys	Pq: 1/29 (3.4) Sal: 0/29 (0.0)
Majmudar *et al.* [15]	Pq	MCT	Dys	40/40 (100.0)
Desai *et al.* [16]	Pq	RUT	Dys	Gc: 0/24 (0.0)
D'Alessandro *et al.* [17]	Pq	MCT, Giemsa, RUT	Dys	16/20 (80.0)
Nguyen *et al.*[18]	Pq	RT-PCR (16S rRNA)	Dys	18/25 (72.0)
Bernander *et al.* [19]	Pq	MCT	Dys	0/94 (0.0)
Mapstone *et al.* [20]	Pq/Sal	PCR	Dys	Pq: 3/13 (23.0) Sal: 2/13 (15.4)
Von Recklinghausen *et al.* [21]	Pq	MCT, RUT	Dys	0/55 (0.0)
Li *et al.* [22]	Sal	PCR (860-bp DNA)	Dys	30/40 (75.0)
Hardo *et al.* [23]	Pq	MCT, N-PCR (16S rRNA)	Dys	1/62 (1.6)
Cammarota *et al.* [24]	Pq	Giemsa: PCR (ureA), RUT	Dys	0/31 (0.0)
Luman *et al.* [25]	Pq/Sal	MCT	Dys	Pq/Sal: 0/120 (0.0)
Pustorino *et al.* [26]	Pq	MCT	Dys	5/83 (6.0)
Pytko-Polonczyk *et al.* [27]	Pq/Sal	RUT, -UBT	100 Dys 50 DU	Post-triple H. pylori ET DU Gc: 1/30 (3.3)
Cheng *et al.* [28]	Pq	MCT, RUT	Dys	MCT: 1/122 (0.8) RUT: 71/122 (58.2)
Oshowo *et al.* [29]	Pq/Sal	MTC, Giemsa, RUT, REA	Dys	EGB: 116/116 (100.0)
Améndola *et al.* [30]	Pq	MCT	Dys	1/20 (5.0)
Mattana *et al.* [31]	Pq	MCT	Dys	1/62 (1.6)
Song et al.[32]	Pq	N-PCR1	Dys	41/42 (97.6)
Doré-Davin *et al.* [33]	Pq/Sal	N-PCR (16S rRNA-ureC), UBT	DU	9/22 (40.9)
Kim *et al.* [34]	Pq/Sal	MCT, Giemsa, PCR1, RUT	Dys	Gc: 29/46 (63.0) Pq: 2/29 (6.9) Sal: 4/29 (13.8)
Ozdemir *et al.* [35]	Pq	RUT	Dys	Pq: 63/81 (77.8)
Suk *et al.* [36]	Pq	RUT	Dys	Pq: 28/65 (43.1)
Wang *et al.* [37]	Sal	PCR-Sequence (cagA-vacA)	Gtis, DU	More than one H. pylori strain in Gc and Sal, in same patient
Berroteran *et al.* [38]	EGB	PCR (urease gene cluster)	32 Dys	Gc: 24/32 (75.0)
Gürbüz *et al.* [39]	Pq	RUT	Dys	Pq: 68/75 (90.1)
Nasrolahei *et al.* [40]	Pq	MCT, PCR1, RUT	Dys	$P>0.05$
Siddiq *et al.* [41]	EGB	Giemsa, 13-UBT	Dys	Gc: 32/52 (61.5) Pq: 48/52 (92.3)
Czesnikiewicz-Guzik *et al.* [42]	Pq/Sal	MCT, 13-UBT	Dys	Gc: 51/100 (51.0) Pq-Sal: 54/100 (54.0), $P>0.05$
Kignel *et al.* [43]	Pq/Sal	PCR	Dys	Pq-Sal: 1/20 (5.0)
Chitsazi *et al.* [44]	Pq	RUT	Dys	Gc H. pylori: 16/44 (36.4)
De Sousa *et al.* [45]	Pq/Sal	MCT, Giemsa, RUT	Dys	Pq/Sal (RUT): 0/147 (0.0)
Sudhakar *et al.* [46]	Pq	MCT, RUT	50 Dys 25 control	Pq MCT: 5/50 (10.0) Pq RUT: 37/50 (74.0)
Silva *et al.* [47]	Pq/Sal	PCR (vacA)	Dys	Gc: 30/62 (48.4) Pq: 11/30 (36.7) Sal: 16/30 (53.3)
Medina *et al.* [48]	Pq	PCR (ureA)	Dys	Pq/Sal: 15/43 (34.9)
Assumpção *et al.* [49]	EGB	PCR (cagA-vacA), Giemsa, RUT	Dys	Gc PCR: 95/99 (96.0) Gc Giemsa: 39/99 (39.4) Gc RUT: 47/99 (47.5) Pq PCR: 71/99 (71.7) Pq RUT: 48/99 (48.5)
Navabi *et al.* [50]	MAS	MAS MCT, PCR, RUT	Dys	925/1861 (49.7)
Zou *et al.* [51]	MAS	MCT, PCR, RUT	Dys	490/1088 (45.0)

Notes: Asym: Asymptomatic subject; Bs: Biopsy; DU: Duodenal ulcer; Dys: Dyspepsia; EGB: Endoscopic gastric biopsy; Gc: Gastric; Gtis: Gastritis; GU: Gastric ulcer; H. pylori ET: Helicobacter pylori eradication therapy; MAS: Meta-analysis study; MCT: Microbial culture techniques; N: Nested; OR: Odds ratio; OS: Oral swab; PCR: Polymerase chain reaction; Pq: Plaque; PS-P: Periodontal status; Ptis: Periodontitis; REA: Restriction endonuclease analysis; RT: Reverse transcription; RUT: Rapid urease test; Sal: Saliva; SBlot: Southern-blotting; SB-P: Subgingival plaque; Ser: Serology; SP-P: Supragingival plaque; TBF: Tooth brushing frequency; Tg: Tongue; 13-UBT: 13C-urea breath test.

Table 2 Relationship of Clinical Symptoms and Frequency of H. Pylori Detected in Dental Plaque and Gastric Biopsy's Dyspeptic Patients[*n*(%)]

Clinical symptoms	Dental plaque culture	PCR urease C	Gastric biopsy culture
Epigastric pain without nocturnal awakening while patient is hungry (n =82)	34 (40.5)	62 (72.6)	30 (36.6)
Epigastric pain with nocturnal awakening while patient is hungry (n =18)	15 (83.3)	15 (83.3)	16 (88.8)
Bloating after meal without nocturnal awakening (n=61)	39 (63.9)	55 (90.1)	34 (55.7)
Bloating after meal with nocturnal awakening (n=9)	5 (55.5)	6 (66.6)	6 (66.6)
Reflux without nocturnal awakening (n=31)	15 (48.4)	24 (77.4)	15 (48.4)
Reflux with nocturnal awakening (n=8)	6 (75.0)	7 (87.5)	6 (75.0)
Previously infected with H. PYLORI and cured (n=24)	18 (75.0)	24 (100.0)	13 (54.2)

yet clear whether the presence of the microorganism in the oral cavity represents long-term colonization or whether its presence is transient due to either gastric reflux or because it is in route to the stomach. While some authors maintain that H. pylori may be a normal commensal organism in the oral cavity with no relation to gastric infection, others, based on detection of H. pylori from dental plaque and saliva of patients with and without H. pylori infection, have suggested that the oral cavity may be a permanent reservoir of the organism, acting both as source of re-infection and a route of transmission [40, 41, 44-47].

Dental plaque

The bacterial plaque or oral biofilm is a translucent film, mixing a biotic array (bacteria and fungi) and inter- or extracellular matrix (organic compounds and minerals), which adheres to the dental surfaces, gingival and oral epithelium, prostheses and restorations, but it is not deletable with simple rinsing. It has a variable composition depending on the location and ripening time. When located in dental and periodontal surfaces, the biofilm is immediately responsible for both dental caries and periodontal disease [14-17, 46, 53]. It is recommended that proper oral hygiene is required to remove H. pylori from dental plaque.

Intestinal microbiota

The human gut harbours about 100 trillion bacteria and more than 500 different species are present in the colon. A well balanced gut microbiota promotes the health of colocytes through the production of important compounds and the correct modulation of the immune system. Qualitative and quantitative modifications in the bacterial composition are responsible of changes in the biochemistry and in the cell cycle of colocytes. An altered microbiota, termed dysbiosis, could lead to altered immune functions and increased risk of disease. The current re-evaluation of the intestinal microbiota and its importance in health and disease has also brought up to light the potential of probiotics for its maintenance within healthy limits. It is becoming clear that imbalances in the subpopulations of the microbiota can lead to disease, so there is a need to develop means for restoring the balance. The wise use of probiotics might be one of those means. It is also increasingly clear that the microbiota interacts with the host, particularly with the intestinal mucosa, its cells, and molecules [54-56].

Effect of H. pylori on GERD

It has been documented that H. pylori is an important human pathogen that causes chronic gastritis and is associated with the development of peptic ulcer disease and gastric malignancies [6, 57-58]. Dentists are often the first healthcare professionals to diagnose a systemic disease through observation of its oral manifestations. One such disease is GERD, which may be evidenced by dental erosion. GERD is defined as involuntary muscle relaxing of the lower esophageal sphincter, which allows refluxed acid to move upward through the esophagus into the oral cavity. Acid reflux at the level of the oral cavity, in fact, can cause the dissolution of the tooth enamel, especially at the level of the palatal surfaces of the back teeth. The typical manifestations of GERD include dental caries, dry mouth, feeling of oral acid/burning sensation, halitosis, erythema of the palatal mucosa and uvula. For diagnosis, it is mandatory exclude other causes, like dietary factors, drugs, poor oral hygiene, eating behavior disorders, genetic and racial factors. The esophageal pH monitoring and/or endoscopy are usually necessary just to confirm the diagnosis of GERD. In addition, it was shown that GERD was an independent risk factor for chronic periodontitis regardless of the established risk factors of chronic periodontitis such as dental caries, tobacco use, and a history of drug use. However, H. pylori infections are particularly difficult to eradicate. To control the infection there is need to know about the routes of entry and the various reservoirs including modes of transmission like oro-oral, feco-oral, and spread by water and through food have also been implicated.

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Conclusion

Dental plaque has been implicated as a possible source and route of transmission of H. pylori, a major etiologic factor in the development of gastritis and peptic ulcer disease. In fact, there is sufficient evidence on the presence of H. pylori in the subgingival oral biofilm which could act as a reservoir for harboring H. pylori, leading to gastric re-infection. However, variation in results may be explained by several factors, such as characteristics of the sample population, differing sampling procedures, and differing methodologies used to detect the microorganism in dental plaque. While some investigators believed that the occurrence of H. pylori in dental plaque was significant in terms of management of H. pylori-associated gastric disease, others held that the microorganism was present only transiently in the oral cavity. Moreover, significant evidence suggests the potential role of H. pylori infection in the development of GERD, and provides sufficient evidence to define the relationship between GERD and H. pylori infection. Actually, numerous laboratory and mainly case-control and observational clinical studies in adults and children, have shown a clear though variable relationship between GERD and tooth erosion [59-61]. However, further randomized clinical trials are required to demonstrate that the progression of dental erosion reduces or ceases following gastric acid suppression therapy in patients with confirmed GERD. Mouthrinse treatment alone or combined with periodontal treatment can, to some extent, reduce the prevalence of oral H. pylori and improve the eradication rate of gastric H. pylori.

Declaration

The authors of this manuscript declare that they have no conflict of interest.

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