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Helicobacter pylori, an odontological point of view

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Abstract
Introduction: Helicobacter pylori favors the formation of gastric ulcers, gastric carcinoma, MALT lymphoma, and is related to costly treatment, bacterial resistance and other adverse effects.
Objective: To analyze the literature on the importance of H. pylori in dentistry, particularly its epidemiology, diagnostic methods, oral manifestations, treatment and the use of probiotics.
Methodology: Current literature review carried out using the following databases: Pubmed and SCOPUS. The keywords used were Helicobacter pylori, diagnosis, treatment, dentistry, probiotics.
Results: Epidemiology: It is up to 90% in developing countries, while the annual recurrence rate is much higher than in developed countries. Recurrence may occur by recrudescence or reinfection. Diagnosis: Methods include urea breath test, stool antigen test, serology and molecular methods. The preferred method is the rapid urease test of human biopsies. Oral manifestations: It has been associated with oral pathologies, including gingivitis/periodontal disease, aphthous stomatitis and oral cancer. Treatment: Standard triple therapy combines amoxicillin (1g twice daily) and clarithromycin (500mg twice daily) or metronidazole (500mg twice daily). Use of probiotics: significantly helps in repairing the intestinal microbiota affected by antibiotics, helping to decrease side effects.
Conclusion: H. pylori infection represents a risk factor for the organism and antibiotic resistance complicates its eradication, an early diagnosis should be made to prevent adverse effects.

Keywords: Helicobacter pylori, diagnosis, treatment, dentistry, probiotics

1. Introduction
The presence of Helicobacter pilory favors the formation of gastric ulcers, gastric carcinoma, MALT lymphoma and is associated with costly treatment, bacterial resistance and other adverse effects. It was first described in 1984 and represented a breakthrough for gastroenterology [1].
It is a Gram-negative bacterium with a high virulence factor and is able to colonize the gastric mucosa [2]. During the last few years it was stipulated that anyone infected with H. pylori should be treated immediately to eradicate the pathogen [3]. Different recent studies indicate that H. pylori can also be found in the oral cavity, as this is the route of entry for microorganisms that colonize the digestive tract and are able to survive the acidic pH of the stomach [4]. In the oral cavity, H. pylori can be found in saliva, dentin caries, subgingival dentobacterial plaque, in cases of chronic periodontitis and on the tongue [5]. This microorganism generally occurs during childhood and is known to be transmitted from mother to child, since its presence is normally found in the microflora of adults [6]. It has been shown that there is a direct relationship between chronic gastritis caused by H. pylori and poor periodontal health [7].
Nowadays, it is important for the dental surgeon to develop a broad knowledge of the pathogens present in the oral cavity and their relationship with the other systems of the organism. Because numerous studies have shown that the H. pilory infection represents a latent risk for the health of the periodontium, it is essential to be informed in order to maintain a vigilant behavior in the dental office. The objective of this work was to analyze the literature on the importance of Helicobacter pylori in dentistry, its etiology, diagnostic methods, oral

manifestations, treatment, and probiotics as a therapeutic alternative.

2. Materials and methods

Articles on the subject published through the PubMed, SCOPUS and Google Scholar databases were analyzed, with emphasis on the last 5 years. The quality of the articles was evaluated using PRISMA guidelines, i.e., identification, review, choice and inclusion. The quality of the reviews was assessed using the measurement tool for evaluating systematic reviews (AMSTAR-2). The search was performed using Boolean logical operators AND, OR and NOT. It was realized with the words "Helicobacter pylori", "etiology", "diagnostic methods", "oral manifestations", "treatment", "probiotics". The keywords were used individually, as well as each of them related to each other.

3. Results & Discussion

3.1 Epidemiology

Helicobacter pylori is a gram-negative bacterium that affects around 4.4 billion people worldwide. Its prevalence may vary by geographic area and is influenced by several factors [8]. The prevalence of H. pylori is up to 90% in developing countries, while the annual recurrence rate is much higher than in developed countries. Because of this, it is recognized that the influencing factors are living conditions, the state of hygiene and the industrialization of society [9].

The majority of infections are acquired in early childhood with the highest prevalence in Africa and Asia [10]. In Africa, 79.1% is predominant, followed by Latin America and the Caribbean with 63.4%, Asia with 54.7%, followed by North America with 37.1% and the lowest in Oceania with 24.4% [11]. In Mexico, the presence of H. pylori can be observed in 20% of one-year-old children, 50% in 10-year-old children and in adults between 25-30 years of age it is a frequent bacterium due to recurrent gastrointestinal infections [12].

The infection can be acquired by oral-oral or fecal-oral transmission, and the pathogen has various mechanisms that facilitate its ability to move, adhere and manipulate the gastric microenvironment, making colonization of an organ with a highly acidic lumen possible [9]. In Arctic countries where the prevalence of H. pylori exceeds 60%, treatment of individuals with H. pylori infection should be limited to only those cases where there is strong evidence of direct benefit in reducing morbidity and mortality [13]. Recurrence can occur by recrudescence or reinfection [14]. Consequently, these data can be used to support regional initiatives to prevent and eradicate H. pylori, with the goal of reducing complications of H. pylori [7]. Infected individuals develop antibodies to H. pylori that persist for up to 6 months after eradication [10].

H. pylori is most prevalent in underdeveloped countries. It can be found in adults and children as part of their normal microbiota. It is important to prevent it through campaigns to improve hygiene conditions and avoid its transmission.

3.2 Diagnostic Methods

H. pylori infection is usually acquired during childhood; infected individuals generally remain asymptomatic, but about 30% of individuals may develop mild to severe gastrointestinal disease [14]. The question of whether the bacterium is acquired early or later in life is a key point in analyzing such effects, as H. pylori has been reported to co-evolve with its host, shaping the immune system and, consequently, the microbiome [15]. The potential effects of H. pylori outside the stomach are neurological, dermatological, hematological, ocular, cardiovascular, metabolic, allergic and hepatobiliary diseases [9]. The risk of developing cardiovascular disorders, such as atherosclerosis, is also influenced by infection. It can also lead to increased insulin resistance, increased risk of diabetes mellitus among infected individuals [16].

Accurate diagnosis of H. pylori infection is mandatory for the treatment of many gastroduodenal diseases, such as chronic gastritis, gastric ulcer, duodenal ulcer and increased risk of gastric cancer [17]. Diagnostic methods include urea breath test, stool antigen test, serology and molecular methods. The preferred method for rapid diagnosis of H. pylori is the rapid urease test (RUT) of human biopsies, which is based on the high activity of the urease enzyme present in H. pylori [18]. There are also invasive methods such as endoscopic imaging, rapid urease testing, histology, culture and molecular methods [19]. The urea breath test and stool antigen test, among the non-invasive tests, are the best methods for detecting active infection. Anti-HP antibodies are not recommended in the low prevalence population, moreover, they cannot reveal an ongoing infection, but only prove a contact with the bacteria [20]. The sensitivity of serological tests is high but the specificity is relatively low [21]. To increase the level of reliability in association with diagnostic tools for detecting H. pylori, several techniques should be applied at the same time as a multiple diagnostic technique [22].

The major known method for diagnosis is the RUT of human biopsies. Both invasive methods such as endoscopic imaging and non-invasive methods such as the urea breath test are useful to identify whether there is an active infection.

3.3 Oral Manifestations

H. pylori is found in the oral cavity, in saliva, the supragingival plaque, dentin caries, the subgingival plaque in chronic periodontitis, infected root canal and tongue coating [6]. Host factors are reflected in polymorphisms in host genes governing the inflammatory response that also influence the risk of a specific clinical disease [23].

At least 400 different bacterial species are found in dental plaque and form a biofilm in which organisms are associated with each other and embedded in an exopolymeric matrix formed of salivary polymers and microbial extracellular products [24]. In an individual, more than one strain of H. pylori may exist in the dental plaque. The prevalence of H. pylori and the detection of some gastrointestinal diseases associated with vacA / cagA genotypes in the oral cavity could be related to the progression of gingivitis [12].

H. pylori may be involved in the formation of periodontal pockets, as well as Campylobacter species, which are the main microaerobic periodontopathic bacteria. Periodontal pockets with low oxygen concentrations may serve as reservoirs for H. pylori [25]. Patients infected with H. pylori have worse periodontal parameters than uninfected individuals, suggesting that infection correlates with disease progression [15].

Oral H. pylori infection has been linked to oral pathologies, including gingivitis/periodontal disease, aphthous stomatitis and oral cancer [26]. H. pylori is transmitted from caries to the root canal, where colonization has occurred in the dental pulp. Caries is difficult to clean with a toothbrush and the microbial flora does not change, which constitutes a suitable reservoir for H. pylori colonization [27].

It has been shown that H. pylori strains associated with reinfection of the stomach were similar to those present in the oral cavity [28]. H. pylori may be present in the oral cavity

together with specific periodontopathic bacterial species such as Porphyromonas gingivalis, although its interaction with these bacteria is unclear [29].

We can now associate reinfection of the stomach due to the presence of H. pylori in the oral cavity and can be found in oral pathologies, including gingivitis/periodontal disease, aphthous stomatitis and oral cancer.

3.4 Treatment

There is currently no universally accepted regimen for the treatment of H. pylori infection. The goal of therapeutics will be regressive symptomatology and healing of the gastric mucosa [30]. H. pylori is adapted to the human stomach environment by possessing several virulence genes that allow bacterial survival in the acidic environment, movement into the gastric epithelium and binding to gastric epithelial cells [31]. Urease is produced by H. pylori, which results in the generation of ammonia to neutralize the acidic condition and binds to gastric epithelial cells through outer membrane proteins [23].

The antibiotics effective and generally used against H. pylori are mainly the following five: amoxicillin, clarithromycin, metronidazole, tetracycline and quinolones [32]. The standard triple therapy is so far the most widely used method and combines amoxicillin (1g twice daily) and clarithromycin (500mg twice daily) or metronidazole (500mg twice daily), is the recommended first-line therapy for H. pylori infection19. Unfortunately, this combination seems to have lost efficacy during the last decade mainly due to clarithromycin resistance [33].

A 10-day tetracycline-levofloxacin quadruple therapy consisting of a proton pump inhibitor, bismuth, tetracycline and levofloxacin has been developed and achieves a markedly higher eradication rate compared to levofloxacin-amoxicillin triple therapy [34].

Infections caused by this parasite have a high rate of drug resistance and an important factor would be adherence to antibiotic therapy, which is the reason for the onset of resistance, as it could stimulate the selection of resistant mutants [30]. If antimicrobial sensitivity data are not available, empirical therapy (such as rifabutin- or furazolidone-based therapies) can be used to terminate H. pylori infection [35].

It has been described that the appropriate strategy for the treatment of this infection should use several therapies that, if used consecutively, achieve as close to a 100% cure rate as possible [36]. In the event of H. pylori therapy failure, we should not re-administer any of the antibiotics against which H. pylori is likely to have become resistant [17].

Due to the resistance of H. pylori to antibiotic therapy, different strategies combining several types of antibiotics are needed to eradicate H. pylori. The most commonly used are: amoxicillin, clarithromycin, metronidazole, tetracycline and quinolones.

3.5 Probiotics as a therapeutic alternative

Nowadays, probiotics have proven to be effective when used preventively and as a therapeutic alternative in the presence of gastrointestinal infections caused by H. pylori [37]. They are defined as factors derived from microorganisms that stimulate the proliferation of beneficial bacteria and are used for the treatment of various gastrointestinal diseases [38].

Among the benefits of incorporating probiotics in the face of infections by this parasite, they are associated with the production of substance, strengthening of the gastric mucosa and regulation of the immune system [39]. The use of probiotics prior to eradication treatment and during the entire eradication treatment, as well as the use of probiotics for more than 2 weeks, demonstrates better eradication effects [40].

Probiotics alone can eradicate H. pylori by 14%. This is an unsatisfactory rate; however, considering that this percentage is considerably higher than that of placebo, it indicates that the direct antibacterial action of probiotics against H. pylori is consistent [41]. Saccharomyces boulardii is effective in reducing the side effects of eradication therapy. The addition of this probiotic to CLR and AMX-based triple therapy for 4 weeks achieved an eradication rate of 85.4% compared to 80% in the absence of probiotic [42].

Antagonism of probiotics against H. pylori is achieved through a number of direct or indirect interactions, including secretion of antibacterial substances, competitive inhibition, mucosal barrier enhancement and regulation of immunity [43]. Treatment results are contradictory due to species, doses and duration of administration [21].

Its use is controversial in the literature; a study in 2020 showed that including probiotic supplements did not improve the efficacy or tolerance of the treatment [17]. However, there are studies that show that their use significantly helps in the repair of the intestinal microbiota affected by antibiotics, helping to reduce side effects and favoring adherence to treatment by patients [44].

The benefits of the use of probiotics are to avoid the side effects of antibiotic therapy and to favor adherence to treatment. They are not recommended for use as the only therapy due to their low percentage of H. pilory eradication.

4. Conclusions

It is important to diagnose H. pilory in early stages to avoid the development of serious complications, because it is a bacterium difficult to eradicate due to bacterial resistance and because its main risk factors for contracting it are living conditions, the state of hygiene and the industrialization of society, it can be very difficult to prevent it. Currently, the use of probiotics is recommended to improve adherence to treatment and guarantee better therapeutic results.

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