

Helicobacter Pylori and Periodontal diseases: An update and proposal of a multidisciplinary clinical protocol

Sophie Marbaix¹, Assem Soueidan¹, Maya Romani², Guillaume Campard¹, Gilles Amador³, Zahi Badran¹

¹Department of Periodontology (Inserm U791/UIC Odontologie/CHU de Nantes), Faculty of Dental Surgery, Nantes, France

²Department of Family medicine, American University of Beirut-Medical Centre, Beirut, Lebanon

³Department of Dental public health, Faculty of Dental Surgery (CHU de Nantes), Nantes, France

Email: zahi.badran@univ-nantes.fr

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ABSTRACT

Helicobacter Pylori has been closely linked to chronic gastritis, peptic ulcers and increased risk of gastric carcinoma. Oral cavity, in particular dental plaque in periodontal pockets, may be a possible reservoir harboring *H. Pylori*, and may therefore be involved in the gastric reinfection by the bacterium, even after triple therapy regimen. This report is an update of scientific data showing the potential localization of *H. Pylori* in the oral cavity of periodontitis patients. A multidisciplinary clinical protocol combining full-mouth disinfection and triple therapy is also suggested. This protocol could permit to enhance oral *H. Pylori* eradication.

Keywords: Periodontal; Triple Therapy; Full-Mouth Disinfection

1. INTRODUCTION

Periodontal diseases are inflammatory chronic diseases affecting teeth supportive tissues, and have infectious bacterial etiology. It is initiated by oral bacterial biofilms developing on dental roots. Early stage of the disease is gingivitis, and is characterized by gingival inflammation (swelling, redness, bleeding...). Individually susceptible patients could develop Periodontitis, which implies alveolar bone loss and periodontal pockets formation around affected teeth (**Figure 1**). Periodontopathogenic bacteria (PB) are mainly anaerobic, Gram negative strains developing subgingivally in periodontal pockets. This subgingival environment is particularly favorable for the survival and proliferation of non-aerobic strains. Also, many locations in the oral cavity (OC), such as the dorsum of the tongue are oxygen-poor sites. *Helico-*



Figure 1. Periodontitis affecting teeth supportive tissues.

bacter Pylori (*HP*), as a gram-negative, microaerophilic, spiral-shaped bacterium; could find adequate conditions for colonization and proliferation in the OC. *HP* has been implicated in the etiology of gastritis and peptic ulcers. Its presence is also a risk factor for gastrointestinal cancers. Human infection by this pathogen could involve an oral route, and the OC is an anatomical region with a potential to harbor *HP*, in particular dental plaque (oral biofilm).

Thus, it seems conceivable that oral health status and different gingival clinical conditions may have an effect on the presence of *HP* in oral biofilms, hence influencing the process of *HP* gastric infection or reinfection [1,2].

Many reports found that *HP* could colonize the healthy OC or the subgingival periodontal pockets area. The latter could eventually serve as a bacterial reservoir. According to Savita *et al.* [3], subjects with periodontitis harbor a number of *HP* significantly higher than subjects without periodontitis. Also, reinfection of the gastrointestinal tract by *HP* from dental plaque could occur after proper eradication regimen. Triple therapy (TT) has been successfully used to eradicate gastric *HP*. TT is the most common first line treatment recommended for *H. Pylori*

eradication, it consists of a proton pump inhibitor (PPI) (lansoprazole 30 mg twice daily, omeprazole 20 mg twice daily, pantoprazole 40 mg twice daily, rabeprazole 20 mg twice daily) plus amoxicillin 1 gram twice daily and clarithromycin 500mg twice daily for 7 to 14 days. Metronidazole (500 mg twice daily) can be substituted for amoxicillin in penicillin-allergic patients. A longer duration of treatment (14 versus 7 days) may be more effective in curing infection, but this remains controversial. TT is currently considered the gold standard reaching an eradication rate up to 80% [1,4]. However, in many cases, *HP* is not completely eliminated after a single treatment, and the recurrence of the *HP* infection has been well-documented [5]. Therefore, the OC has been suspected to be a common source for reinfection of the stomach [2,6]. In fact, bacteria developing in biofilm configuration (such as in dental plaque) are much more resistant to antibiotics than freely circulating bacteria [7].

Full mouth disinfection (FMD) is a periodontal clinical protocol, combining mechanical antibacterial therapy (scaling/root planning of dental roots) and antiseptic regimen (chlorhexidine) to obtain PB eradication [8,9]. The mechanical debridement of all teeth is performed within 24 h, in order to eradicate rapidly PB present in dental biofilms, and thus preventing reinfection of treated sites. Also, the adjunction of a systemic antibiotic prescription to FMD (amoxicillin/metronidazole or azithromycin) has been found to successfully enhance clinical outcomes [10-12].

This article focuses on the specific association of periodontal status and oral *HP* in the published scientific literature. The rationale of considering periodontitis as a risk factor for *HP* infections/reinfection will also be discussed, with an emphasis on the eventual clinical implications of this assumption. Finally, we suggest the merging of both FMD and TT regimen, in order to enhance periodontal therapy outcome as well as eradication of *HP*.

2. *HELICOBACTER PYLORI* AND PERIODONTAL DISEASES

2.1. *Helicobacter Pylori* in Periodontally Ill and Healthy Patients

Several studies have evaluated the correlation between the prevalence of *HP* and periodontal diseases. Conflicting results could be observed in the literature, this could be attributed to the diversity of the studied populations, sample collection methods, and the specificity of the methods used for *HP* detection [2,13]. Although it may affect the presence of *HP* in dental plaque, few studies have separately investigated supra and subgingival plaque, which corresponds to different microenvironments when availability of nutrients, oxygen and host mechanisms are considered [14].

Souto *et al.* [2] performed a full-mouth clinical ex-

amination (six sites per tooth) to determine periodontal health status and examined subjects with no history of gastric symptoms, their results showed a higher prevalence of *HP* in subgingival biofilm of subjects with periodontitis compared to individuals with periodontal health (50% versus 11% respectively), suggesting that periodontal pockets and inflammation may favor *HP* colonization. Another study by Riggio and Lennon [15] examined the presence of *H. Pylori* in subgingival plaque (sites with periodontal pocket depth ≥ 5 mm) of periodontitis patients with no symptoms of gastritis or peptic ulcer disease. This study found that 38% of subjects with deep periodontal pockets were positive for *HP*. Consequently, the authors concluded that subgingival plaque in individuals presenting periodontitis may function as a reservoir for *HP*.

Gebara *et al.* [14], found that more than 26% of *HP* was detected in the OC of periodontitis patients (all positive for gastric *HP*), periodontitis and gingivitis showed a high prevalence; however, no control group with healthy patients were included. Al Asqah *et al.* [13] found that periodontitis patients had a significantly higher percentage of *HP* in subgingival plaque samples in comparison to periodontally healthy controls (79% versus 43% respectively). Other studies failed to detect *HP* in the subgingival plaque [16,17] or found no association between periodontal status and the prevalence of the bacterium in OC [18].

2.2. Relation between Gastric Infection and Periodontal Disease

Umeda *et al.* [19] showed that more than 40 % of patients with history of gastritis or peptic ulcers had periodontal pockets (>4 mm). Bruce *et al.* (54) found that periodontal pockets ≥ 5 mm are associated with increased odds of *HP* seropositivity. Also, a large epidemiological investigation performed over 10,000 subjects [20], found a positive link between *HP associated* gastric infection and periodontal diseases. The latter may facilitate the *HP* oro-gastric transmission and colonization of the bacteria in the digestive tract. Also, periodontitis microenvironment conditions could be favorable for *HP* multiplication, thus increasing sufficiently to cause gastric infection [21,22].

On the other hand, many studies [23-25] failed to establish a positive correlation between periodontal disease and gastric infection.

3. TRIPLE THERAPY AND ORAL *HELICOBACTER PYLORI*

3.1. Effect of Triple Therapy on Oral *HP*

It is still unclear whether TT affects *HP* in dental plaque. Song *et al.* [26] found plaque samples negative for *HP*

only in patients who had recently been treated with TT. But many reports, found a persistent oral *HP* after TT [27-29]. More recently, a meta-analysis [30] confirmed the close relationship between *HP* infection in the OC and the stomach, and concluded that oral *HP* is more difficult to eradicate than gastric *HP* and it may be a source of reinfection. On the other hand, Umeda *et al.* [19] reported that subjects with periodontal pockets retained *HP* in the OC even after eradication of the bacterium from the stomach. Similarly, Gebara *et al.* [1] showed that 60% of subjects with periodontal disease were still positive for *HP* DNA in their OC, whereas only 10% were positive in the stomach after triple therapy. In a same way, Zarik *et al.* [5] revealed that 3 months after triple therapy in the group of participants who did not harbor *HP* in periodontal pockets, the eradication rate was 87.4%. In contrast, the group positive for *HP* in the subgingival plaque exhibited a significantly lower rate of eradication (47.6%). Also, polyantibiotic systemic therapy was considerably less efficient in the eradication of *HP* from periodontal pockets, compared with its elimination in the stomach (33% and 87% respectively).

3.2. Effect of Periodontal Therapy on Prevention of Gastric *Helicobacter Pylori* Recurrence

Few studies investigated the effect of periodontal therapy on eradication of gastric *HP*. Zarik *et al.* [5], evaluated the effectiveness of periodontal treatment and TT in achieving complete elimination of gastric *HP* infection. Participants positive for *HP* in the subgingival biofilm, who had undergone basic periodontal therapy and a TT regimen, showed a higher elimination rates compared to the group who underwent TT alone (77.3% and 47.6% respectively), thus suggesting that systemic antibiotic polytherapy alone is not as effective in preventing the reappearance of gastric *HP* in subjects positive for the oral form of *HP*. A meta-analysis [31] concluded that periodontal therapy reduces the relative risk of persistence of gastric *HP* by 63%. Similar results were found in a study with a two years follow-up [32].

Recently, a case series of 9 patients [33], investigated whether full mouth ultrasonic debridement can eradicate persistent oral *HP* after TT. Periodontal debridement was able to eradicate *HP* from 88.3% of patients with gingivitis, while it failed in eradicating the bacteria from the OC of periodontitis group. Within the limits of this case series, a single session of oral hygiene instruction combined with full mouth periodontal debridement seemed to promote a positive effect in eradicating *HP* only from supragingival sites.

4. CLINICAL MULTIDISCIPLINARY MANAGEMENT PROPOSAL

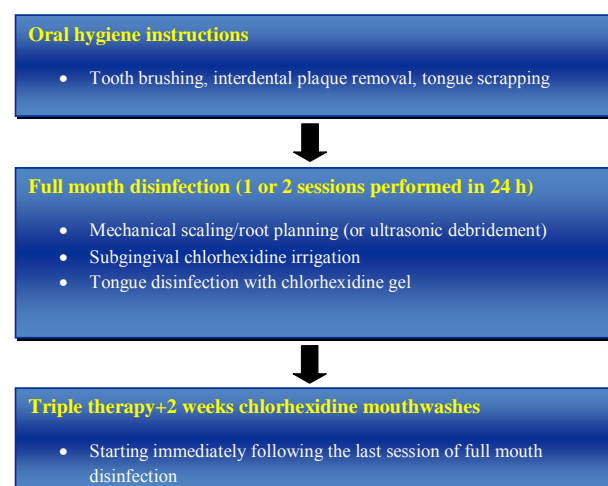
Actual consensus in Periodontology suggests that antibi-

otic regimen should be started immediately after mechanical periodontal treatment [34]. Thus, a complete elimination of calculus and disorganization of bacterial biofilms must be achieved prior to any antibiotic therapy in order to disrupt the biofilm configuration forming a barrier to antibiotic molecules. For periodontal treatment we suggest a full mouth disinfection (FMD) approach, as described in the periodontal literature [9]. The FMD consists of a total scaling/mechanical debridement of teeth root surfaces. An antiseptic irrigation of the pockets, the dorsum of the tongue and the tonsils is also performed [8]. The whole procedure should be finalized in one session (or two sessions within 24 h). Immediately after FMD, an antibiotic regimen (+ antiseptic chlorhexidine mouth-washes/oral gels) has been found to significantly enhance periodontal outcome [10]. A combination of amoxicillin/metronidazole is the most tested combination after FMD [11]. On the other hand, clarithromycin has shown an excellent availability in the gingival area [35]. Hence, the antibiotic regimen in TT could substitute periodontal prescription as soon as the mechanical treatment is accomplished. This approach could enhance PP and *HP* elimination (in the OC and the gastric tract). In fact, the antibiotics used to eradicate *HP* are also efficient against the anaerobic PB. Hence, the merging of the periodontal FMD protocol and the TT (**Figure 2**) permits to treat both pathologies in an optimal manner, and could significantly boost oral *HP* eradication.

For maintaining long-term results, routine dental/periodontal supportive therapy and daily oral hygiene procedures should be performed without interruption [6].

5. CONCLUSION

Although contradictory results are found in the scientific



Periodontal full mouth disinfection is immediately followed by triple therapy regimen and antiseptic regimen, in order to enhance the eradication of periodontopathogenic bacteria as well as oral/gastric *H. Pylori*.

Figure 2. Multidisciplinary clinical protocol.

literature, many reports have associated periodontal disease (periodontal pockets formation) to an increased prevalence of oral *HP*. Its bacterial load is increased by periodontal disease and periodontal pockets formation. The assumption that subgingival oral biofilm could act as a suitable reservoir for *HP* is plausible and supported by consistent evidence from preliminary clinical trials. The presence of oral *HP* in patients with periodontal disease (Periodontitis and gingivitis) may cause refractoriness of gastric infection to triple therapy alone [5,31].

The mechanisms that confer the ability of *HP* to escape systemic treatment are not well understood, but there is evidence indicating that biofilms provide defense from the host immunological response and the action of antimicrobials agents [36]. Hence, antimicrobials cannot be efficient if the biofilm is not mechanically disrupted [37] shortly prior to prescription. The subgingival dental biofilm is particularly suspected, due to the favorable micro-ecological conditions provided by the periodontal pockets. The biofilm is known to provide protection from the host's immunological response, and bacteria growing in biofilms exhibit high resistance to antimicrobial agents [5]. We therefore suggest a simple multidisciplinary clinical management protocol, merging the triple therapy to periodontal mechanical treatment and chemical antiseptic disinfection. A joint coordination between the periodontist and the gastroenterologist is a prerequisite for the success of this treatment regimen. Adopting this protocol has two objectives; treating periodontal disease and enhancing the efficacy of the anti *HP* therapy.

On the other hand, it should be considered that the efficacy of non-surgical treatment modalities is related to the pocket depth. Hence, surgical periodontal procedures like open flap debridement could be needed in some cases to eliminate deep bacterial biofilms potentially harboring *HP* [33]. To our knowledge, no research has been conducted in this field.

In conclusion, the efficacy of the combined proposed protocol should be investigated in future controlled, randomized clinical trials. If confirmed, it could be integrated in the standard clinical management of *HP* infections.

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