THE NEW ARMENIAN MEDICAL JOURNAL
Vol.5 (2011), No 3, p.41-45

METHODS AND MEANS OF HELICOBACTER PYLORI ERADICATION IN THE ORAL CAVITY

Mkrtchyan Z. G.

Chair of Therapeutic and Family Dentistry, Yerevan State Medical University, Yerevan, Armenia

Abstract

Various schemes of antihelicobacter therapy used for Helicobacter pylori (H. pylori) eradication in stomach and duodenum are unable to completely eliminate this microorganism in oral cavity. Thus, the problem of H. pylori re-infection of the lower parts of gastrointestinal tract and of the ulcer disease recurrence still exists. Therefore, elaboration of effective methods and means for antihelicobacter therapy of oral cavity is an actual problem for both dentists and gastroenterologists.

Our study included eradication therapy of H. pylori in oral cavity among 54 patients diagnosed with the method of PCR to have H. pylori in saliva and gingival fluid. Gingival bandages with Clarithromycin and spray containing MGO™400+ Manuka honey and New Zealand propolis were used as antihelicobacter means.

The selection of Clarithromycin is based on data suggesting that the eradication schemes containing Clarithromycin (Fromilid) have the highest antihelicobacter effectiveness in stomach and duodenum. Among other macrolides, Clarithromycin has the least suppressive concentration towards H. pylori and the resistance of the microbe to Clarithromycin is 13.8%, which is much lower than the critical level.

The antibacterial activity of Manuka honey and New Zealand propolis has been studied in details and has been scientifically proved. The antihelicobacter effectiveness of New Zealand Manuka honey is purely determined by its component, methylglyoxal (MGO), which shows high bactericide activity.

Both means used in the study manifested high effectiveness; however, considering high possibility of developing antibiotic resistance, the natural means is more preferable.

The study also showed that eradication therapy combined with local antihelicobacter treatment of oral cavity significantly increases the effectiveness of the latter decreasing the possibility of self-infection and re-infection at the same time.

Keywords: H. pylori, clarithromycin, propolis, MGO™400+ Manuka honey.

INTRODUCTION

Despite the existence of effective schemes of *Helicobacter pylori (H. pylori*) eradication in stomach, the problem of re-infection from the oral cavity and the recurrence of ulcer disease is still actual.

Studies among patients with peptic and duodenal ulcer showed that associated with *H. pylori* these diseases cause pathological modifications of parodontium tissues in 88-100% of patients [*Tsimbolistov A., Robakidze N., 2000; Arutyunov S. et al., 2005; Ivashkina V., Mayeva I., 2009*]. On the background of gastrointestinal tract diseases inflammatory-destructive modifications of parodontium have generalized nature and proceed much more actively [*Low D., Rite D., 2000; Miyabayashi H. et al., 2000; Tsimbolistov A., Robakidze N., 2005; Lepilin A., 2006*]. The studies also showed that among the patients with *H. pylori* combined with chronic gastritis and no *H. pylori* in the oral cavity, *H. pylori* eradication in stomach is detected in 92% of cases; no recurrences of the disease are observed during two years after treatment. On the other hand, eradication therapy of patients with *H. pylori*-associated gastritis and with *H. pylori* in the oral cavity is effective only in 52% of cases, while 35% of such patients suffered from recurrence of the diseases during the following two years [*Khavkin A., Blat S., 2007*]. In this regard, most of the researchers consider the possibility of existence of a permanent nidus for self-infec-

Address for Correspondence:
Yerevan State Medical University
5 Heratsi Street, 0025, Yerevan, Armenia
Tel.: (+374 93) 40 51 18
E-mail: armenk70@gmail.com

tion and re-infection even after effective *H. pylori* eradication in stomach [*Lepilin A., 2006; Ivashkina V., Mayeva I., 2009*].

The main scheme of the clinically practiced first-line eradication is the triple therapy: Proton Pump Inhibitor (PPI), Clarithromycin (Fromilid) and Amoxicillin or Metronidazole. The selection of Clarithromycin for the first-line anti-helicobacter therapy is based on its high bioavailability regardless the food intake, susceptibility and high level of acid resistance. Among the patients with ulcer disease, Clarithromycin shows synergism with PPIs in 91% of studied strains of *H. pylori* and effectively sanifies parodontium tissues, if contaminated by the microorganism. Among other macrolides, Clarithromycin has the lowest (0.03 *mcg/mL*) minimal suppressive concentration against *H. pylori* and high capability of penetrating into cells and generating in mucosa of the stomach and duodenum. It provides the highest level of eradication compared with any other antibiotics monotherapy. The scheme with Clarithromycin provides the highest level of *H. pylori* eradication: up to 95%. At present, the Clarithromycin resistance is 13.8%, which is much lower than the critical threshold. However, the traditional antihelicobacter therapy, as a rule, does not allow to completely eliminate *H. pylori* from the oral cavity [*McNulty C., Dent J., 1988; Low D., Rite D., 2000; Tsimbolistov A., Robakidze N., 2000*].

Recently, researchers resumed the studies on various natural products, in particular, different types of honey for their therapeutic use as effective antibacterial and wound healing means. Biochemical studies of various samples of honey indicated that darker samples of honey possess higher antioxidant features and Manuka honey is among those [*Al Somall N. et al., 1994;* Mavric E.*, 2008;* Marceau E.*,* Yaylayan V.*, 2009*].

The New Zealand bee Manuka honey is obtained from the plant Manuka (*Leptospermum scoparium*), its antibacterial active nature was studied in details and scientifically grounded. The high activity of honey towards numerous pathogenic bacteria was established as well as [*Al Somall N. et al., 1994; English H. et al., 2004*].

The researchers still study the bioactive characteristics, especially the bactericide potential of this particular type of honey. E. Mavric and co-workers based on results of their own laboratory examination confirmed that the antibacterial activity of the New Zealand Manuka honey is purely determined by its component, methylglyoxal ($MGO^{TM}400^{+}$), possessing high bactericide activity [*Mavric E. et al., 2008*].

The studies on activity of Manuka honey toward *H. pylori* were rather discrepant. Thus, a number of authors studying biopsy material revealed that Manuka honey brings to extermination of *H. pylori* in case of stomach ulcer disease [*Al Somall N. et al., 1994;* English H. *et al., 2004*]. However, other authors state that the effectiveness of honey in case of stomach disease is not determined by its active impact on *H. pylori* [*McGovern D. et al., 1999*].

Scientific publications on the effective use of Manuka honey in dentistry are also available. The application of this means brings to statistically significant decrease in dental plaque index and reduction of gum bleeding [*Miyabayashi H. et al., 2000;* English H. *et al., 2004*].

The purpose of this study was to comparatively characterize effectiveness of *H. pylori* eradication in the oral cavity with Clarithromycin and spray containing $MGO^{TM}400^{+}$ Manuka honey.

MATERIAL AND METHODS

The study involved 96 patients aged 18-65 (average age 41.5) with genetic markers of *H. pylori* in saliva and gingival fluid revealed with the method of polymerase chain reaction (PCR).

The patients were divided into 5 groups:

✓. Group I included patients with no complaints of gastrointestinal tract;

✓ Group II included patients with the diagnosis of peptic ulcer and duodenal ulcer diseases without eradication therapy;

✓ Group III consisted of patients with the diagnosis of peptic ulcer and duodenal ulcer diseases and examined immediately after the general course of eradication therapy conducted by a gastroenterologist;

✓ Group IV consisted of patients with the diagnosis of peptic ulcer and duodenal ulcer diseases; they were examined 1.5-2 months after the general course of eradication therapy;

✓ Group V included patients, who had not been diagnosed with peptic ulcer and duodenal ulcer diseases, but had complaints from gastrointestinal tract (pains in epigastric area, heartburn).

Among all patients, 54 persons with PCR-diagnosed *H. pylori* in the oral cavity were selected. The researchers conducted laboratory examination of the patients' parodontium tissues (probe of periodontal pockets to identify their depth, gingival hemorrhage, teeth mobility, Green-Vermillion oral hygiene index, papillae-marginal-alveolar index (PMA).

The selected patients were redistributed into two groups: C (eradication with Clarithromycin) and M (eradication with spray containing MGO™400⁺ Manuka honey).

Group C involved 27 patients, whose oral cavities, gingival and periodontal pockets were treated using gingival bandages with Clarithromycin for *H. pylori* eradication. The medication was mixed into paste with distilled water (250 *mg* of Clarithromycin + 0.2 *mL* of distilled water), located in the pocket with a turunda and covered with self-resorbable (bioresorbable) tape on the basis of polyvinyl alcohol for 30-40 minutes. The treatment duration was 10 days.

Group M also involved 27 patients, whose oral cavities were treated with Manuka honey spray for eradication of *H. pylori* as an antihelicobacter means. In this group the gums of patients were sprayed with "Manuka Health" spray (Figure 1) containing MGO™400⁺ Manuka honey, pure New Zealand propolis, lecithin, aniseed oil, clove oil, peppermint oil, aromatic oils, water. In order to prolong the impact of the spray, the gums were covered with self-resorbable tape on the basis of polyvinyl alcohol for 30-40 minutes. The course took 10 days.

Figure 1. *Spray containing MGO™400⁺ Manuka honey.*

Group II patients underwent antihelicobacter therapy of the oral cavities in parallel to general eradication therapy.

After the treatment course, examination of all patients was repeated to reveal genetic markers of H. *pylori* in saliva and gingival fluid with the method of PCR.

The researchers used MS Excel editing tools for data processing. They used the method of correlation analysis of the qualitative characteristics to calculate the association coefficient (r_a). The quantitative relation was evaluated based on the r_a significance (r_a = 0.7-0.99: statistically significant interrelation). Statistical significance of r_a was considered at $p \leq 0.05$.

RESULTS

In 96.3% of Group C patients genetic markers of *H. pylori* were absent after the treatment course involving local antihelicobacter therapy with the use of Clarithromycin gingival bandages (Figure 2 *a*).

In 92.6% of Group M patients *H. pylori* in oral cavity was absent after the 10-day local antihelicobacter therapy with the use of spray containing Manuka honey and propolis (Figure 2 *b*).

The study revealed non-significant difference (r_a=0.35; p>0.05) between the levels of eradication with the use of Clarithromycin and spray containing MGO™400⁺ Manuka honey as means for local antihelicobacter therapy.

At the same time the level of *H. pylori* eradication in the oral cavity among the patients with ulcer disease from Group II, who underwent combined course of general and local antihelicobacter therapy, was significantly higher than among the patients of Group III who had taken only general antihelicobacter therapy course (r_a=0.83; p<0.05). Thus, repeated PCR analysis of saliva and gingival fluid among the patients of Group II after the treatment course revealed absence of *H. py-*

lori in the oral cavity in 95.2% of cases (Figure 2 *c*) versus the patients of Group III, among whom the effectiveness of eradication was only 66.7% (Figure 2 *d*) immediately after the general eradication therapy course without local treatment.

Thus, both means used by us for local eradication of *H. pylori* in the oral cavity, Clarithrimycin and spray containing MGO^{TM}400^{+} Manuka honey, demonstrated high effectiveness.

Based on data of scientific publications allergic, toxic effects, disturbances in microecological balance of normal microflora and possibility of developing resistance to antihelicobacter treatment with antibiotics are observed; whereas, the use of a natural product, *Manuka honey*, is considered more promising as it allows to improve the level of *H. pylori* eradication in the oral cavity and avoid side effects.

Our study showed that combination of eradication therapies in patients with *H. pylori*-associated pathology of stomach and duodenum and with local treatment using antibacterial medication active towards *H. pylori* and professional hygiene of the oral cavity significantly increases the effectiveness of *H. pylori* eradication in the oral cavity decreasing the possibility of self-infection and re-infection.

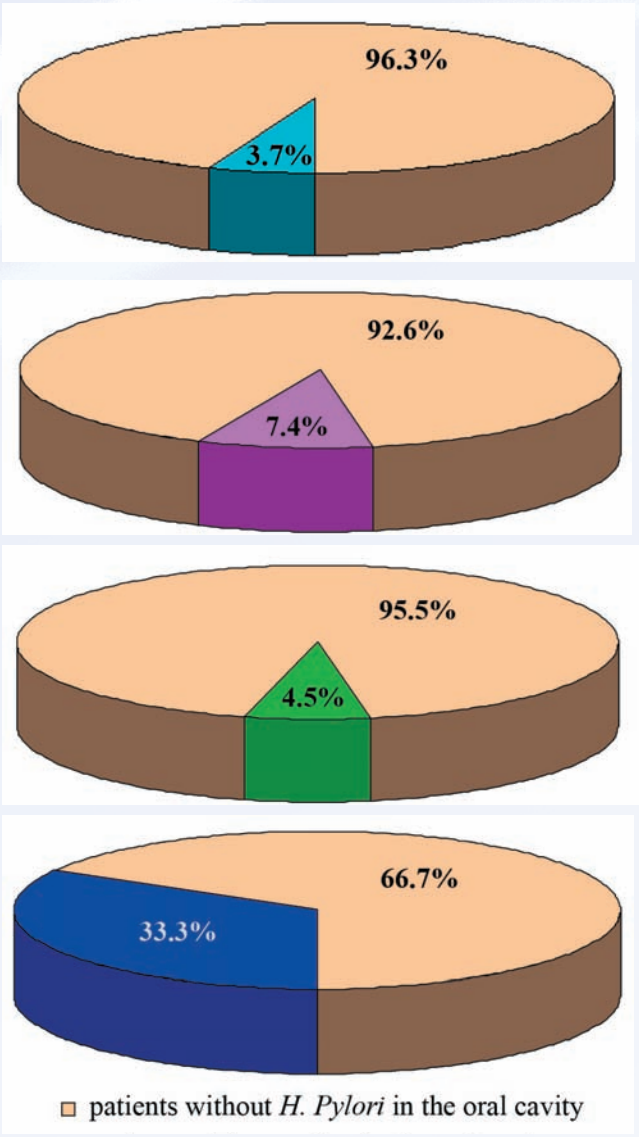

Figure 2. *Level of H. pylori eradication in the oral cavity*
a. *after local therapy with Clarithromycin.*
b. *after local therapy with Manuka honey.*
c. *after the combined local and general antihelicobacter therapy.*
d. *after general anti-helicobacter therapy.*

CONCLUSION

The following conclusions could be drawn based on results of the conducted study:

1. *H. pylori* serve as a background factor for the formation of inflammatory diseases of parodontium initiating development of active gastritis and ulcer disease, which have close pathogenetic connection with gingivitis and periodontitis.
2. Peptic and duodenal ulcer disease is associated with inflammatory modifications in parodontium tissues.
3. If patients with peptic and duodenal ulcer diseases have *H. pylori* infection in their oral cavity, the lesion of parodontium tissues has more generalized character and heavy course.
4. After the general eradication therapy course, slight improvement in parodontium tissues is detected; this is an evidence of the necessity for oral cavity sanitation with the aim to improve the hygienic condition, as well as to facilitate local antihelicobacter treatment.
5. The spray containing MGO^{TM}400^{+} Manuka honey and gingival bandages with Clarithromycin display high antihelicobacter effectiveness used in oral cavity as local eradication therapy.
6. The combination of general eradication therapy of patients with *H. pylori*-associated pathologies in gastrointestinal tract and diseases of parodontium with local treatment using *H. pylori*-active antibacterial medication increases *H. pylori* eradication effectiveness in oral cavity and decreases the possibility of self-infection and re-infection.

REFERENCES

1. *Al Somall N., Coley K., Molan P., Hancock B.* Susceptibility of Helicobacter pylori to the antibacterial activity of manuka honey. J. of the Royal Society of Medicine. 1994; 87: 9-12.
2. *Arutyunov S.D., Mayeva I.V., Romanenko N.V. et al.* [Peculiarities of Parodontium Tissues of Patients with Duodenal Ulcer Disease Associated with Helicobacter Pylori] [published in Russian]. Periodontology. 2005; 3: 30-33.
3. English H., Pack A., Molan P. The effects of manuka honey on plaque and gingivitis: a pilot study. J. Int. Acad. Periodontol. 2004; 6(2): 63-67.
4. *Ivashkina V.T., Mayeva I.V.* [Antihelicobacter Therapy: Today and Tomorrow] [published in Russian]. Meditsinski Vestnik (Medical Bulletin). 2009; 31: 500.
5. *Khavkin A.I., Blat S.F.* [Role of Probiotic Therapy for Children with H. pylori Infection] [published in Russian]. Detskie infekcii (Pediatric Infections Journal). 2007; 4: 53-58.
6. *Lepilin A.V.* [Impact of Complex Helicobacter pylori Eradication on Dental Status of Patients with Duodenal Ulcer Disease] [published in Russian]. Rossijski Stom. Zhurnal (Russian Dental Journal). 2006; 2: 27-29.
7. *Low D.E., Rite D.D.* [Maintenance of Resistance][published in Russian]. Clinical Antibiotic Therapy. 2000; 2: 28-30.
8. Marceau E., Yaylayan V. Profiling of alpha-dicarbonyl content of commercial honeys from different botanical origins: identification of 3,4-dideoxyglucoson-3-ene (3,4-DGE) and related compounds. J. Agric. Food Chem. 2009; 22: 10837-10844.
9. Mavric E., Wittmann S., Barth G., Henle T. Identification and quantification of methylglyoxal as the dominant antibacterial constituent of Manuka (Leptospermum scoparium) honeys from New Zealand. Mol. Nutr. Food Res. 2008; 52(4): 483-489.
10. *McGovern D., Abbas S., Vivian G., Dalton H.* Manuka honey against Helicobacter pylori. J. of the Royal Society of Medicine. 1999; 92: 439.
11. *McNulty C.A.M., Dent J.C.* Susceptibility of Campylobacter pylori to twenty-one antimicrobal agents. Eur. J. Clin. Microbiol. Infect. Dis. 1988; 7: 566-569.
12. *Miyabayashi H., Furihata K., Shimizu T. et al.* Influence of oral Helicobacter pylori on the success of eradication therapy against gastric Helicobacter pylori. Helicobacter. 2000; 5(1): 30-37.
13. *Tsimbolistov A.V., Robakidze N.S.* [Parodontic Status of Helicobacter pylori-infected Patients with Ulcer Disease] [published in Russian]. In: Materials of IV Congress of Dental Associations of Russia. Moscow. 2000. 255-257.
14. *Tsimbolistov A.V., Robakidze N.S.* [Pathophysiologic Aspects of Combined Pathology Development in Oral Cavity and Gastrointestinal Tract] [published in Russian]. Stomatology for al. 2005; 1: 28-34.