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Considering Alternative and Complementary Therapies for H. pylori Treatment Versus Antibiotic Resistance at Zawia Clinics and Zawia Plasma Lab in Libya

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Abstract

Helicobacter pylori (H. pylori) is a resilient pathogen that may live for the rest of a person's life in their stomach. It causes persistent stomach inflammation. The typical treatment for *H. pylor*i infection is triple therapy, which includes a proton pump inhibitor, clarithromycin, and either amoxicillin or metronidazole. The study was conducted on two groups of patients that have *H. pylori* infection at some of Zawia Clinics and Plasma Lab in Zawia city in Libya. Each group consisted of 50 patients (different gender and age). The purpose of this study is to examine the function of a few well-known natural items that have been studied in clinical trials for preventing, modifying, or curing *H. pylori* infections. The goal of the study was to compare the efficacy of natural medicines with standard antibiotic therapy for *H. pylori* symptoms and the presence of the bacteria. The first step in this approach was to investigate the effects of medicinal herbs and natural products and probiotics . Finally, they were put to the test employing in vitro and in vivo *H. pylori* growth tests. The study results showed that 27 of the patients treated with antibiotics, anti-fungi, and Omeprazole (Triple therapy) still tested *H. pylori* positive, while only 14 of the patients treated with Alternative and Complementary Therapies tested positive. These results lead to the conclusion that complementary therapies were found to be more effective at treating *H. pylori* infection. It was discovered that 72% of bacteria were successfully eradicated by natural cures, compared to 46% by pharmacological treatments.

KEYWORDS: *H. pylori*, alternative therapy, antibiotic therapy,

الملخص

جرثومة المعدة *(هيليكوباكتر بيلوري)* هي بكتيريا مسببة للمرض قد تعيش لبقية حياة الشخص في معدته. تسبب التهابًا مستمرًا في المعدة . العلاج الشائع لعدوى جرثومة المعدة هو العلاج الثلاثي ، والذي يتضمن مثبط مضخة البروتون ، كلاريثروميسين ، وأموكسيسيلين أو ميترونيدازول. أجريت هذه الدراسة على مجموعتين من المرضى المصابين بعدوى جرثومة المعدة في بعض عيادات الزاوية ومعمل البلازما في مدينة الزاوية بليبيا. تتكون كل مجموعة من 50 مريض (جنس وعمر مختلفين). الغرض من هذه الدراسة هو فحص وظيفة عدد قليل من العناصر الطبيعية المعروفة التي تمت دراستها في التجارب السريرية للوقاية من عدوى جرثومة المعدة أو تعديلها أو علاجها. كان الهدف من الدراسة هو مقارنة فعالية الأدوية الطبيعية مع العلاج الشائع بالمضادات الحيوية لأعراض جرثومة المعدة ووجود البكتيريا. كانت الخطوة الأولى في هذا النهج هي دراسة تأثير الأعشاب الطبية والمنتجات الطبيعية والبروبيوتيك. أخيرًا ، تم اختبارهم باستخدام اختبارات النمو في المختبر وفي الجسم الحي. أظهرت نتائج الدراسة أن 27 من المرضى الذين عولجوا بالمضادات الحيوية ومضادات الفطريات والأوميبرازول (العلاج الثلاثي) ما زالوا مصابين بالبكتيريا *هيليكوباكتر بيلوري* ، في حين أن 14 فقط من المرضى الذين عولجوا بالعلاجات البديلة والتكميلية كانت إيجابية. أدت هذه النتائج إلى استنتاج مفاده أن العلاجات التكميلية كانت أكثر فعالية في علاج عدوى جرثومة المعدة. تم اكتشاف أن 72٪ من البكتيريا تم القضاء عليها بنجاح عن طريق العلاجات الطبيعية ، مقارنة بـ 46٪ عن طريق العلاجات الدوائية.

1 Introduction

H. pylori is a Gram-negative bacterium that infects humans globally. Infection with *H. pylori* happens when the bacteria infect the stomach, and it is most common in childhood (Vaki, 2009). The stomach's protective lining is affected by *H. pylori*. According to the most recent estimates, *H. pylori* has invaded the stomachs of 4.4 billion individuals globally (Hooi *et al*, 2017). Urease is a bacterially generated enzyme. This enzyme also aids in the

reduction of acidity in stomach secretions (neutralizes them). As a result, the lining of the stomach is weakened. It causes persistent stomach inflammation, which can progress to major gastrointestinal disorders including peptic ulcers, gastric cancer, and even death. Because the stomach mucosa is thought to be *H. pylori's* primary habitat, its survival in an acidic environment is critical. *H. pylori* urease, which produces large quantities of ammonia (10–15 percent of total proteins by weight), allows bacteria to proliferate and survive by raising the pH of the environment (Ha *et al*, 2001). The bacteria infects over half of the world's population, with prevalence varying significantly depending on region, ethnicity, age, and socioeconomic variables (Guarner *et al*, 2011). Despite 30 years of experience treating *H. pylori* infections, the best treatment strategy for this illness has yet to be discovered (Gisbert and Calvet, 2011). As medication resistance and then multi-drug resistance grew increasingly common over time, various treatment regimens and rescue medicines were available (O'Connor *et al*, 2020). Antibiotic usage is linked to a rise in antimicrobial resistance, with resistance rates of popular antibiotics (clarithromycin, for example) used in *H. pylori* regimens reaching above 15% (Ganz et a,l 2005). Furthermore, clarithromycin-resistant *Helicobacter pylori* were placed on a high-priority list for novel medication development (Tacconelli *et al*, 2018).

In general, numerous worldwide guidelines for treating individuals with Helicobacter pylori infections recommend triple therapy as the first-line treatment. This therapy is taking a proton pump inhibitor (PPI), clarithromycin, and amoxicillin for 7 to 14 days (Megraud, 2004, Megraud & Lehours, 2007). However, because of a rise in clarithromycin resistance, *H. pylori* eradication therapies with this regimen achieve cure rates of less than 80% (Graham and Fischbach, 2010). For example, in one research, metronidazole resistance was found in 44% of patients, and clarithromycin resistance was recorded in 14% of cases, (Savarino *et al*, 2000), whereas resistance to the same medicines was observed in 49.4% and 10.8%, respectively, in another study (Wang *et al*, 2000). As a result, many treatment regimens (second-line treatments) have been recommended. Furthermore, eradication of

H. pylori is becoming more difficult due to new concerns such as metabolic alterations and changes in the gut flora following therapy. The World Health Organization (WHO) recently released a list of antimicrobial-resistant "priority pathogens," which cataloged 12 bacterial families that represent the greatest threat to human health (World Health Organization, 2017). The list was categorized into three priority levels: critical, high, and medium. *H. pylori* which are resistant to clarithromycin has been designated as a high-priority species.

Because there is currently no large-scale manufacture of an efficient *H. pylori* vaccine on the market (Talebi and Abadi, 2016), natural products should be considered as one of the effective methods to treat the infections caused by *H. pylori* (Wagenaar *et al*, 2005). It is a fact that many natural products are used in traditional medicine to treat bacterial infections. The first study on the anti-*H. pylori* action of plant products was only published eight years after its discovery (Cassel-Beraud *et al* , 1991*)*. Anti-*H. pylori* activity can be found in a variety of natural products. Urease inhibition, DNA damage, protein synthesis inhibition, and anti-inflammatory actions are some of the processes that these potentials work through. Some enzymes, such as dihydrofolate reductase and myeloperoxidase N-acetyltransferase, have anti-*H. pylori* properties. For many years, Boswellia sacra (B. sacra) or Frankincense has been used in traditional medicine to treat a variety of gastrointestinal ailments. In the Indian subcontinent and Africa, Boswellia carterii is abundantly dispersed. The oleo-gum resin known as frankincense or olibanum is extracted from deep incisions in the tree trunk by B. sacra. The gum exudates of Boswellia spp include multiple pentacyclic triterpenoid acids known as boswellic acids, which have been linked to a variety of biological functions. The plant's principal characteristic is its gum resin, from which essential oils may be extracted. Frankincense has a special position in traditional medicine as a remedy for a variety of ailments (dermatological, gastric, hepatic, rheumatoid arthritis, etc.) (Yasiry and Kiczorowska, 2016). Resin essential oils show antibacterial action against *Staphylococcus aureus, H. pylori, Escherichia coli,*

Proteus Vulgaris, and Candida albicans, among other bacterial and fungal pathogens (Camarda *et al*, 2007).

The ginger rhizome (Zingiber officinale Roscoe, Zingiberaceae) is one of the most widely used medicinal herbs in the world. It has long been used as a treatment for a variety of disorders, including gastrointestinal issues such as burping, bloating, vomiting, indigestion, and constipation (Ebrahimzadeh *et al*, 2015). According to the findings of several research investigations, ginger administration appears to limit *H. pylori* growth and prevent stomach ulcers (Mahady *et al*, 2003 and Nostro *et al*, 2006). Through its many phenolic components (e.g., gingerol, shogaol, zingerone, and phenolic acids like gallic acid and cinnamic acid), ginger rhizome appears to have anti-*H. pylori* action. (Mahady *et al*, 2003) There are also some experimental and clinical studies of multi-herbal complexes containing ginger having anti-*H. pylori* effects. (Biglar *et al*, 2014 and Cwikla *et al*, 2001). Since ancient times, licorice (Glycyrrhiza glabra) has been used to relieve epigastric discomfort and repair gastric ulcers (Shibata, 2000) This herb's roots and rhizomes have been shown to have antioxidant, antibacterial, and antiviral properties. Licorice (sweet wood) extracted from the roots and stolons of the Glycyrrhiza species have anti-*H. pylori* effects (Nariman *et al*, 2009). They promote mucus membrane formation and may help with the symptoms of a peptic ulcer. Licorice acts against *H. pylori* and peptic ulcer disease (PUD). It inhibits DNA gyrase (a crucial enzyme for bacterial replication and transcription) and dihydrofolate reductase enzyme blockage of the *H. pylori*, and it has a repairing effect in PUD: secretin18 is a substance that has a protective mucosal action (Grimes, 2009 and Chatterji *et al*, 2001). Probiotics are microorganisms that provide the host with a variety of health benefits. (Eslami *et al*, 2020). Intestinal colonization with these microbes helps to keep the mucosal immune system healthy and prevents antibiotic-related adverse effects. (Eslami *et al*, 2019, 2020). Probiotics are used to treat a variety of ailments, including diarrhea and allergic responses (Collado *et al*, 2009). Some probiotics, especially Lactobacillus spp., have been demonstrated to have anti-*H. pylori* activity in vitro (Coconnier *et al*, 1998).Using probiotics as a complement to

standard antibiotic treatment enhances the eradication rate of *H. pylori* infection significantly compared to taking antibiotics alone (Eslami *et al*, 2019, Lesbros-Pantofickova *et al*, 2007). However, to our knowledge, no clinical investigation on the anti-H. pylori impact of natural herbs inpatients had been conducted in Zawia city in Libya, thus the purpose of this study was to assess the efficacy of natural herbs as a component of quadruple treatment for *H. pylori* eradication in dyspepsia patients.

2 Materials and methods

2.1 Subjects

The study, which involved two groups of patients with dyspepsia caused by *H. pylori*, was carried out at some of Zawia Clinics and Plasma Lab in Zawia city in Libya. Each group consisted of 50 patients (Total of 100 , 47 men and 53 women, with ages, ranging from 19 to 70 years) WHO had a positive result for *H. pylori* infection by both *H. pylori* stool antigen test (SAT), and *H. pylori* serum antibody test. The patients were randomly included in the research between October 2021 and May 2022. The first group received antibiotic medication for seven to ten days, while the second group received alternative treatment once or twice a day for ten days.

2.2 Tests Used to Confirm *H. pylori* Infection

Non-invasive (stool antigen, serum *H. pylori* antibodies) or invasive diagnostics (upper GI endoscopic examination with fast urease test and/or histopathology) were used to confirm *H. pylori* infection. The test is chosen independently for each patient by the physician while adhering to the customary, broad guidelines. An invasive technique was selected if the patient had clinical reasons for endoscopy. The non-invasive approach was chosen if there was no other need for endoscopy other than to diagnose *H. pylori* or if the patient refused.

2.3 H. pylori stool antigen test (HpSA) test.

Stool samples were prepared for testing by completely mixing them with a buffer solution supplied by: InTec Products, INC. Haicang, Xiamen, China. Three drops of the mixture were added to the sample well of the immunochromatography cassette after three

to ten minutes. After 10 minutes of incubation, the result was read. Monitoring the growth of the control's precipitation line on the strip proved the cassette's validity.

2.4 H. pylori serum antibody test.

The same manufacturer's immunochromatography cassettes were utilized for evaluating antibodies. Two drops of the supplied buffer were added to one drop of the serum sample, which was then allowed to migrate for 10 minutes before the results were read. By keeping an eye on the formation of the precipitation line in the control region on the strip, the authenticity of the cassettes was verified.

2.5 Treatment Regimens for Eradication

The infected patients were randomized into two groups (see figure1), each group received different sequential eradication therapy. The first group contained 50 patients (23 men and 27 women) who received Triple therapy: conventional clarithromycin tablet 500mg twice a day for 10 days, Flagyl tablet 500mg three times a day for 7 days, and Omeprazole tablet 40 mg once a day for 30 days .

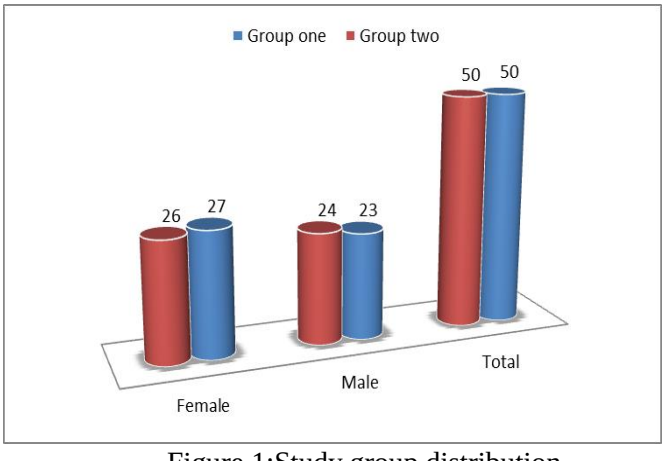

Figure.1:Study group distribution.

The second group contained 50 patients (24 men and 26 women) who received alternative and complementary therapies: a tablespoon of Boswellia sacra or Frankincense is submerged and

soaked in 300 ml of pure water for 8 hours, then a spoonful of the soaked Boswellia sacra suspension is added to a spoonful of grated ginger and a spoonful of licorice then mixed. Finally, a tablespoon of honey was added to the previous mixture. The final mixture is given to the patients to be taken twice a day, once on an empty stomach, and once before going to sleep for 21 days. This procedure will be repeated daily for the whole session period.

The number of each study group compared to the total number is presented in figure one. Eradication was evaluated via antibody test and stool antigen test performed 6 weeks after the completion of treatment.

3 Results

Using both the *H. pylori* SAT and the *H. pylori* serum antibody test, 41 patients (or 41%) of the total 100 patients following treatments had positive for *H. pylori* infection. Among *H. pylori* ulcer patients, the highest detection rates of the bacterium (27 patient) were recorded in group 1 (Triple therapy), while (14 patient) of the case was recorded in group 2(Alternative and Complementary Therapies) (Table.1 & Figure.1). The effectiveness of various treatments across a range of patient categories is displayed in (Table1 & Figure 2). comparison compared to triple medication, alternative, and complementary therapies dramatically improved *H. pylori* eradication.

Table 1: *H. pylori* stool antigen test (HpSA) and *H. pylori* serum antibody test results four weeks after both treatments.

Group name	Male		Female		Total	
	+ve	-ve	+ve	-ve	+ve	-ve
Group1	13	10	14	13	27	23
Group 2	6	18	8	18	14	36

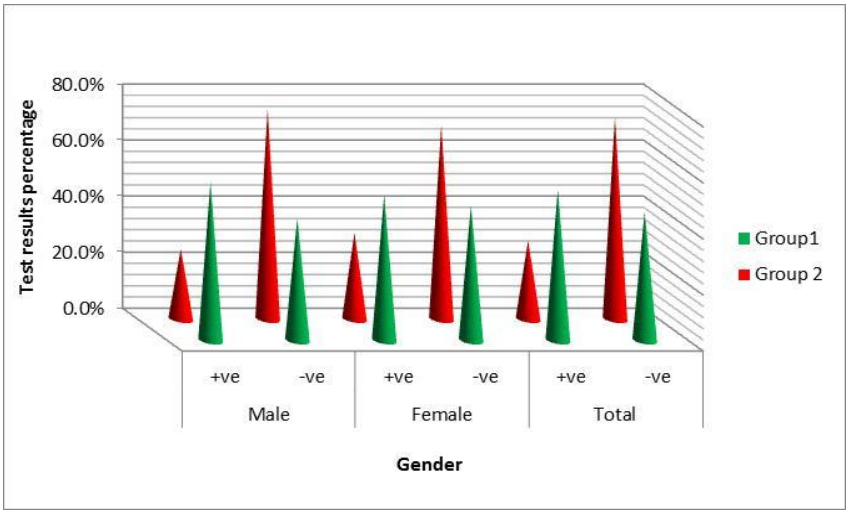

Figure .2: Percentage for each group and the total results.

Of the 23 males in group 1, 13 % tested positive for *H.* pylori, whereas 6 % of the 24 males in group 2 tested positive for *H. pylori*. Out of 27 females in Group 1 of this study, 14 % tested positive for *H. pylori*, while only 8 % tested positive for *H. pylori* in Group 2 of this study, with the rest tested negative (Table 1 & Figure 2). *H. pylori* eradication rates for group 1 were 46 %, and 72 % in group 2 (Figure 2). When Alternative and Complementary Therapies (group 2) were assessed for their efficacy in curing *H. pylori* infection, 21-day sequential treatment was superior to triple therapy (group 1). Over 90% of patients successfully took all prescribed drugs, and compliance was similar across all groups.

4 Discussion

The necessity for the development of novel and secure treatment methods for *H. pylori* infection and the consequent gastroduodenal illness is highlighted by the increased frequency of *H. pylori* antibiotic resistance. Because of the very unusual traits of the organism, its habitat, and the low pH of the stomach, not all medicines and plant materials that are effective against *H. pylori* in vitro can be utilized to treat the infection in humans. (Liou *et al*,2020) The few antibiotics used in the eradication of *H. pylori*

(clarithromycin, amoxicillin, metronidazole, levofloxacin, tetracycline, and rifabutin), and rising antibiotic resistance is a serious clinical issue. Based on the most recent data, it is critical to developing local reports on alternative and complementary treatment effectiveness to assist clinicians in determining the best course of action for a specific group. Results of this study showed that using natural herbs in eradicating *H. pylori* was more effective than the usual triple regimen based on clarithromycin. By performing a quick review of some previous studies that investigated the success percentage of the Triple therapy against *H. pylori* infection, it was noticed that the effectiveness of this treatment has declined over time due to the rising of clarithromycin resistance. For many years, triple therapy for 7–10 days, has shown a success rate of up to 90% (Malfertheiner *et al*, 1997). The success percentage of this therapy has declined to 30% in Italy and varies from 26% to 46% in Poland (Thung *et al*, 2016). Africa's total level of clarithromycin resistance was nearly the same as that of North America (30.8%) and Portuguese (42.3%) (Hyasinta *et al*, 2018). The reported resistance, however, was much higher than that recorded in various regions of Europe and South America (0–8%) (Ghotaslou *et al*, 2015) and Middle Eastern nations (0–8%) (Megraud, 2004 and Hunt, *et al*, 2011). Therefore, This study's resistance rate was equally high, at 27%.

Research into plant materials as alternate sources of antimicrobials has grown during the past several years. Although several herbs are efficient in getting rid of *H. pylori*, this study shows that 28% of people might develop resistance to them. The plants utilized and proved to be efficient in this study are frequently consumed by people. Our findings show that natural herbs (group 2) successfully eliminated (72%) *H. pylori*.

5 Conclusions

Antibiotic resistance in bacteria is currently a major issue due to its frequency and development. In line with this, *H. pylori* antibiotic eradication success rates have been dropping internationally in recent years.

In our research, we discovered a well-tolerated, non-prescribed mixture that was successful in eradicating H pylori and enhancing general digestive symptoms. Combined nonprescription therapy based on an over-the-counter approach may be useful in getting rid of some strains of H pylori. This therapy deserves more investigation. This paper showed a comparison between natural herbal remedies and drug treatments, and it found that natural remedies successfully eliminated bacteria by 72%, while drug treatments eliminated only 46% of the bacteria.

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