

Effect Of Zataria Multiflora (Avishan-E-Shirazi) In Helicobacter Pylori Eradication

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Abstract:

Introduction: Drug resistance has increased the failure of H-pylori eradication therapy worldwide, therefore it is necessary to examine newer treatment regimens. This study was done to investigate the effect of Zataria multiflora with a quadruple Therapy on H-pylori eradication.

Method: This study was performed on 60 patients referred to Kosar Hospital where H-pylori infection was detected by upper endoscopy and rapid urease test. Patients were divided into two groups: Group A received amoxicillin 1gr, metronidazole 500mg, Bismuth 250mg, omeprazole 20mg twice daily and Zataria multiflora (5.5-6.5mg) three times daily. Group B (28 patients) were treated with the same diet without Zataria multiflora hc. Finally, H-pylori eradication was evaluated by the urea Breath test in both groups.

Result: H-pylori eradication was observed in 86.4% (22 patients) of group A and 92.9% (26 patients) of group B and there was no significant difference between the two groups.

Conclusion: The addition of Zataria multiflora was clearly not effective in eradicating H-pylori. However, the positive effects of this plant on the immune system and its indirect effects on reducing inflammation can be considered in future studies.

Keywords: Zataria Multiflora, Avishan-e-Shirazi, Helicobacter Pylori, Eradication, H-pylori.

1. INTRODUCTION

H-pylori is a gram-negative bacterium that is commonly associated with diseases of the upper gastrointestinal tract and its known effects on the stomach include Chronic gastritis, peptic ulcer, Gastric MALT Lymphoma, and gastric adenocarcinoma [1, 2]. Numerous therapeutic regimens have been used to eradicate this bacterium, which included a combination of antibiotics such as amoxicillin, metronidazole, clarithromycin, doxycycline, levofloxacin, and a PP I and bismuth and have been used as drug regimens 3 and 4. The reason for using combination diets is because the single-drug regimen has not been effective in eradicating bacteria. Recently, use of various diets such as rabeprazole and amoxicillin and other drug regimens using stronger doses has been used [3-5]. However, the results of Meta-analyzes have shown that the success rate of treatment in combination diets is lower than expected and between 15% and 25% of patients treated with first-line drugs have still Helicobacter pylori infection [6-8].

There are many studies in different parts of the world, all of which address the issue of drug resistance. The high prevalence of Helicobacter pylori in the world and its association with gastric cancer is a very important issue and shows the importance of eradicating this bacterium [9, 10]. But in many cases drug resistance has been the cause of reduced treatment success and effectiveness [11].

The use of herbal remedies is one of the safest and easiest treatments that have created the least resistance and less side effects in relation to *Helicobacter pylori* [12].

Currently, a lot of research has been done on medicinal plants with antimicrobial effects; one of the most effective plants in this field is thyme Shirazi. *Zataria multiflora boiss* is a genus of Labiatae. It's anti-inflammatory, antimicrobial and antioxidant effects have been well known. [13, 14]. The FDA has approved the essential oil of this plant for use as a safe food additive and can be used in the packaging of antimicrobial foods [15]. Tabak et al., showed that the thyme extract (*Zataria multiflora Boiss*) has an inhibitory effect on the growth and production of urease by H-pylori [16]. This property is considered to be related to thymol and Carvacrol in it [17]. In another study identified thyme in a laboratory study as an alternative treatment for controlling H-pylori [18].

Due to the failure of treatments to completely eradicate *Helicobacter pylori* as well as the growing drug resistance, this bacterium feels important to find new herbal medicines. Therefore, the present study was performed to investigate the combined diet of thyme along with the standard diet for eradication of *Helicobacter pylori*.

2. MATERIALS AND METHODS

Study Design

This study was a randomized clinical trial which was done on 60 patients' who were diagnosed with confirem endoscopy from July 2015 to March 2016 referral to the Kosar Hospital clinic in Iran. The study was approved by the ethics committee of Semnan University of Medical Sciences and all patients participated in the study with conscious consent.

Inclusion and Exclusion Criteria

Exclusion criteria was patients younger than 18 years, previous gastric surgery, pregnancy, lactation, major systemic diseases, non-complication, antibiotic use, bismuth, H2 antagonist receptor or PPI in the last 4 weeks, use of the nonsteroidal anti-inflammatory drug (NSAID) for two weeks before C-UBT, accompanied by other serious illnesses (decompensated liver cirrhosis, uremia, advanced gastric cancer, recent, myocardial infarction, chronic Renal failure), allergy was one of the treatments used in the 4-drug regimen and the unwillingness to continue the study.

Regimes, Biologic Samples and Data Collection

Patients were randomly divided into two groups of H-pylori eradication treatments for two weeks; group A (26 patients) received the H-pylori eradication diet as follows: amoxicillin 1 g, metronidazole 500 mg, bismuth 240 mg, omeprazole 20 mg two times a day and thyme Shirazi (5.5-6.5 mg each capsule north) three times a day. Group B patients (including 28 patients) received the same diet without thyme Shirazi. 4 patients were excluded from group A due to a lack of compliance and unwillingness to continue the study. Both groups received omeprazole for two weeks (20 mg once daily after antibiotic treatment). At the end of the 1 month recovery period, patients did not receive any treatment for 2 weeks. (To prevent any false-negative results in the UBT test), patients were then tested for UBT for H-pylori eradication. If the UBT test is negative, it means that the H-pylori have been eradicated. During treatment, patients were repeatedly referred to the regimen and were being reminded of how to use the medication correctly and the importance of treatment. Patient information including age, sex, and body mass index were collected.

Statistical Analysis

Data analysis was performed using the Shapiro-Wilk test, Chi-squared test, t-student as well as logistic regression. SPSS V.25 was used applied for statistical analysis. statistical significance was assessed at the 5% level.

3. RESULTS

The mean age in group A was 45.2 ± 13.1 and in group B, 35.1 ± 13.6 , where the difference between the two groups was clearly different and group A was clearly older ($p = 0.007$). Most patients in group

A (n = 14, 53.8%) and group B (n = 15, 53.6%) were female. There was no clear gender difference between the two groups (P = 0.984).

Table 1

		Patients		P value
		group A n (%)	group B n (%)	
Age (y)	30 >	5 (19.2%)	14 (50%)	0.067
	30-39	3 (11.5%)	3 (10.7%)	
	40-49	4 (15.4%)	5 (17.9%)	
	≥ 50	14 (53.8%)	6 (21.4%)	
Gender	Male	14 (53.8%)	15 (53.6%)	0.984
	Female	12 (46.2%)	13 (46.4%)	
BMI (mean ± SD)		24.1 ± 1.86	23.9 ± 1.72	0.845

There was no clear difference among BMI between the two groups. Table 1 shows the biographical information of patients including age, sex, and BMI. Data analysis after UBT testing showed that H-pylori eradication was performed in 22 patients in group A (86.4%) and 26 patients in group B (92.9%) and there was no clear difference between the two groups. (P = 0.135 and RR = 0.88) Table 2).

Table 2: The results of the H. pylori Eradication

H-pylori eradication	Patients		P value
	Regime A n (%)	Regime B n (%)	
+	22 (84.6%)	26 (92.9%)	0.135
-	4 (15.4%)	2 (7.1%)	

Since the groups were heterogeneous in terms of age and to investigate the simultaneous effect of the variables under study on H-pylori eradication, logistic regression analysis was performed. The final results showed that none of the variables mentioned had a clear effect on Hpylori eradication and H-pylori eradication did not differ significantly between the two groups.

4. DISCUSSION

The findings of this study showed that addition of thyme to four drugs omeprazole, amoxicillin, metronidazole, bismuth subcitrate in the eradication of Helicobacter pylori has no significant effect compared to standard diet. In similar studies, Alizadeh et al. Investigated the therapeutic effect of herbal medicines of thyme extract, safflower extract and thyme mix with a combination of ranitidine and metoclopramide in functional digestion. Thyme extract in 55.6%, savory extract in 53.3%, thyme mix in 42.2% and the combination of ranitidine-metoclopramide in 42.2% of patients completely improved the symptoms of the disease. The improvement of herbal treatment groups was not significant [19]. In another study, it was shown that the anti-helicobacterial effects of Zataria multiflora were similar to those of delalarithromycin [20].

However, in similar studies, positive results of thyme have been seen, so that the rate of eradication of Helicobacter pylori in the group with thyme was significantly higher than the two groups without thyme. In other words, the effectiveness of the treatment regimen was higher in the groups to which thyme was added to the drug regimen. However, in the group where thyme replaced metronidazole, it had the greatest effect on eradicating Helicobacter pylori compared to the other two treatment regimens [19]. In our study, thyme was used concomitantly with metronidazole, which may be the reason for the reduced effect of thyme. The fact that concomitant use of thyme and metronidazole reduces the effectiveness or non-response of thyme requires additional clinical trials with high sample size.

The present study showed that adding thyme to standard diet did not have a significant effect on eradicating *Helicobacter pylori*. But it did not have a negative effect and certainly adding plant extracts to the treatment regimen with antioxidant properties has a positive effect on immune system function. In similar studies where thyme has replaced metronidazole, eradication of *Helicobacter pylori* has occurred to a greater extent [20, 21]. In Sharifi et al.'s study, the effect of omeprazole, bismuth subcitrate, amoxicillin, metronidazole (OBAM) regimens was compared with that of omeprazole, bismuth subcitrate, amoxicillin, thyme (OBAT) in patients with *Helicobacter pylori*. Findings of this study showed that the treatment rate of *Helicobacter pylori* was 16% in OBAM group and 17.4% in OBAT group and no significant difference was observed between the two groups [21]. Although in this study the two treatment regimens had relatively similar results, the rate of complete cure was higher in the group in which thyme replaced metronidazole.

Therefore, due to the high prevalence of resistance to antibiotics, especially in third world countries, thyme can probably be recommended due to its favorable effectiveness in eradicating *Helicobacter pylori* and improving symptoms and side effects, and on the other hand due to high drug resistance to metronidazole. This plant can replace metronidazole and in case of using antibiotics, first an antibiotic susceptibility test (antibiogram) should be performed. And Then use antibiotics effective against *Helicobacter pylori*. However, it is necessary to conduct clinical trials with a large number of samples for these purposes.

One of the limitations of the present study was the multi-stage and long duration of treatment, which in some cases led to patients being excluded from the study due to incomplete use of the drug. The second limitation was the small sample size, which is suggested to be done in larger studies in subsequent studies.

5. CONCLUSION

The two treatment regimens had similar results, but due to the high prevalence of antibiotic resistance and the pronounced inhibitory effects of thyme on *Helicobacter pylori* in vitro, it is recommended that the possible effect of thyme eradicate this organism be combined with other treatment regimens. Since several other studies have shown that the replacement of metronidazole with thyme increases the rate of eradication, it is suggested that a randomized clinical trial with the aim of replacing metronidazole with thyme extract be studied in multidrug therapy.

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7. REFERENCES

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