H. pylori eradication with beta carotene, ascorbic acid and alllicin

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Summary: In this study, in vitro effectiveness of ascorbic acid (AA), beta carotene (BC) and alllicin in HP eradication were evaluated. 210 patients who are HP positive in biopsy were involved in this study. The patients randomised to seven treatment groups (each group consisting of 30 patients). The first group was given standard eradication treatment (lansaprazole 30 mg bid, claritromisin 500 mg bid, amoxicilline 1 g bid for 14 days). Second group received AA 1000 mg/day in addition to the standard treatment. Third group received only AA 1000 mg/day for 14 days. Fourth group was treated with standard regimen plus 120 mg/day BC. Fifth group was given only BC 120 mg/day for 14 days. Sixth group was given standard regimen and alllicin 4200 µg/day. Seventh group received only alllicin 1200 µg/day for 14 days. The eradication was achieved in 20 (66.6 %) in group I, 15 (50 %) in group II, 3 (10 %) in group III, 15 (50 %) in group IV, 0 (0 %) in group V, 7 (23.3 %) in group VI and 7 (23.3 %) in group VII. Alllicin seemed to be potentially effective agent for HP eradication but ascorbic acid, beta caroten was found to be ineffective.

Key words: Helicobacter pylori, Alllicin, Ascorbic Acid, Beta Carotene
sive gastritis and acute erosive gastritis. The eradication was described as histologically negative examination (grade 0).

**Results**

The patient characteristics and distribution of risk factors for gastritis were shown in table 1. There were no statistically significant differences between groups in age, alcohol intake, smoking, non steroidal antiinflammatory drug use and HP positivity.

At the end of the treatment, eradication was achieved in 20 patients (66.6 %) in group I, 15 patients (50 %) in group IV, 0 patients (0 %) in group V, 27 patients (90 %) in group VI and 7 patients (23.3 %) in group VII. The eradication rates were compared with standard treatment group. There was no statistically significant difference between group I and II, IV and VI, III and VII and were higher and the differences were statistically significant (p<0.001, p<0.001, p<0.01 respectively). In group III eradication rate was significantly low. No eradication was achieved in group V.

P: value for average points after treatment: Group I and II, IV >0.05, Group I and III, <0.001, Group I and VI, VII <0.01.

**Discussion**

Despite numerous studies on HP eradication there is not an accepted standard treatment regement yet. In most studies two or three antimicrobial agents in combination with proton pump inhibitors were shown to be most effective. In previous studies Allicin was used in combination with standard eradication regient and lansoprazol combination were shown to eradicate HP in 60 % - 96 % of cases and accepted as one of the most successful regiments (11,16). On the other hand emerging antibiotic resistance, high treatment costs and drugs side effect necessitates development of new treatment modalities. HP induces infiltration of the gastric mucosa by polymorphonuclear cells and macrophages, as well as T and B lymphocytes (2.6). Paradoxically, this strong immune/inflammatory response cannot clear the infection, and thus leaves the host prone to complications resulting from chronic inflammation. The attracted immune cells produce inflammatory mediators that include reactive oxygen species (ROS). These mediators impart oxidative stress on the cells in the immediate vicinity in the gastric epithelium (15). Normally, oxidative stress is neutralized by natural antioxidants as vitamin C, beta carotene (4). However, levels of this antioxidant in the gastric juice are decreased during HP infection (2.7,13,19,25). On the other hand vitamin C is shown to be bactericidal for HP in vitro. In a clinical study high dose vitamin C (5 g/day for four weeks) successfully eradicated eight of 27 patients (30 %) (10). In our study, vitamin C treatment for shorter period (14 days) with a lower dose (1 g/day) was effective in only three of (10%) 30 cases. Vitamin C appears to be not an agent powerful enough to be used in eradication alone. On the other hand addition of vitamin C to standard regimen did not improve the eradication rates contrary to our expectations.

Similar to vitamin C gastric juice beta-carotene concentration was shown to be markedly lower in patients infected with HP (10,20). Beta carotene was thought to act as a mucosal protector by scavenging the ROS (20). The authors did not encounter any previous clinical study that beta carotene had been used in HP treatment. In our study beta carotene treatment (120 mg/day for 14 days) – either alone or in combination with the standard regement – was disappointingly ineffective.

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**Results**

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To assess the efficiencies of drug therapies beyond the cases in which complete eradication has achieved we compared average points of HP colonisation grade before and after treatment in each group. The findings were given in Table 3. Rates of reduction in HP colonisation were similar to eradication rates in all groups. There were no additional adverse effects with the use of AA, BC and Allicin in combination with standard regimen. Monotherapy of these agents tolerated well also.

**Discussion**

Despite numerous studies on HP eradication there is not an accepted golden standard treatment regiment yet. In most studies two or three antimicrobial agents in combination with proton pump inhibitors were shown to be most effective. In previous studies, chloramphenicol, amoxicillin and metronidazole was shown to be effective, but the patients had to comply with the treatment for 14 days. We used Monotherapy of these agents tolerated well also, but on the other hand use of Allicin in combination with standard regimen significantly decreased the HP colonisation grade in group IV, 0 patients (0 %) in group V, 27 patients (90 %) in group VI and 7 patients (23.3 %) in group VII. The eradication rate was significantly low. No eradication was achieved in group V.

**Tab. 1:** Patients characteristic

| Group/Characteristic | Group I N=30 (%) | Group II N=30 (%) | Group III N=30 (%) | Group IV N=30 (%) | Group V N=30 (%) | Group VI N=30 (%) | Group VII N=30 (%) |
|----------------------|-----------------|------------------|-------------------|-----------------|-----------------|-----------------|------------------|
| Age (year)           | 38±10           | 40±10            | 39±10             | 41±10           | 38±10           | 37±10           | 40±13            |
| Sex (M/F)            | 18/12           | 16/14            | 18/12             | 16/16           | 16/14           | 15/15           | 16/14            |
| Smoking (+/-)        | 7/23            | 7/23             | 9/21              | 8/22            | 8/22            | 8/22            | 7/23             |
| Alcohol (+/-)        | 0/30            | 5/25             | 5/25              | 4/26            | 5/25            | 6/24            | 7/28             |

**F: Female**

M: Male

(+/-): used or not used

NSAID: Non Steroidal Anti Inflammatory Drugs. There was no statistically difference between the groups, P>0.05.

**Tab. 2:** At the end of the treatment eradication rates

| Group/Characteristic | Group I N=30 (%) | Group II N=30 (%) | Group III N=30 (%) | Group IV N=30 (%) | Group V N=30 (%) | Group VI N=30 (%) | Group VII N=30 (%) |
|----------------------|-----------------|------------------|-------------------|-----------------|-----------------|-----------------|------------------|
| Eradication (+)      | 20 (66.7)       | 15 (50)          | 3 (10)            | 15 (50)         | - (0)           | 27 (90)         | 7 (24.4)         |
| Eradication (-)      | 10 (33.3)       | 15 (50)          | 27 (90)           | 15 (50)         | 30 (100)        | 3 (10)          | 23 (76.6)        |

P: value for eradication rates: Group I and II, IV >0.05, Group I and III, <0.001, Group I and VI, VII <0.01.

**Tab. 3:** Density of HP colonisation before and after treatment

| Group/Characteristic | Group I N=30 (%) | Group II N=30 (%) | Group III N=30 (%) | Group IV N=30 (%) | Group V N=30 (%) | Group VI N=30 (%) | Group VII N=30 (%) |
|----------------------|-----------------|------------------|-------------------|-----------------|-----------------|-----------------|------------------|
| HP colonisation before treatment |                |                  |                   |                 |                 |                 |                  |
| 1 point              | 1               | 3                | 1                 | 4               | 1               | 5               |                  |
| 2 points             | 9               | 10               | 16                | 12              | 12              | 14              | 15               |
| 3 points             | 14              | 15               | 10                | 13              | 12              | 13              | 10               |
| 4 points             | 6               | 5                | 7                 | 6               | 5               | 6               | 5                |
| Aver.points          | 2.8             | 2.8              | 2.3               | 2.3             | 2.5             | 2.5             | 2.2              |

HP colonisation after treatment

| Group/Characteristic | Group I N=30 (%) | Group II N=30 (%) | Group III N=30 (%) | Group IV N=30 (%) | Group V N=30 (%) | Group VI N=30 (%) | Group VII N=30 (%) |
|----------------------|-----------------|------------------|-------------------|-----------------|-----------------|-----------------|------------------|
| Negative             | 23              | 22               | 2                 | 24              | -               | 29              | 3                |
| 1 point              | 7               | 8                | 10                | 6               | 4               | 22              |                  |
| 2 points             | 12              | 12               | 12                | 12              | 12              | 12              |                  |
| 3 points             | 7               | 7                | 7                 | 7               | 7               | 7               |                  |
| 4 points             | -               | -                | -                 | -               | -               | -               |                  |
| Aver.points          | 0.23            | 0.26             | 1.83              | 0.20            | 2.30            | 0.06            | 0.73             |

P values for average points before treatment: There was no statistically difference between the groups. P value for average points after treatment: Group I and II, IV >0.05, Group I and III, <0.001, Group I and VI, VII <0.01.

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and serological examinations (anti-gliadine, anti-endomysium) were done. Disaccharides are absorbed paracellularly via tight junctions. If the small mucosa is damaged, transcellular absorption decreases and paracellular absorption increases due to adaptation to worsening absorption.

30 patients (7 males, 23 females) aged 39 ± 13 years with non-specific gastrointestinal problems served as controls (Table 1).

Patients with untreated celiac disease show villous atrophy and serum in patients with gastritis and ulcer: does Helicobacter pylori infection affect the mucosal levels? Int J Cancer 2000;87:133-40.

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Summary:
The aim of study was to measure gut permeability in patients with untreated celiac disease and during treatment with a gluten-free diet. The test suitable for the diagnosis of celiac disease and monitoring of compliance to a gluten-free diet in these patients.

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Original Article

Original article

And monitoring of compliance of a gluten-free diet (GUT PERMEABILITY IN CELIAC DISEASE)

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Summary: Background & Aim: Celiac disease is an autoimmune disease with the damage of the intestinal barrier. The aim of study was to measure gut permeability in patients with untreated celiac disease and during treatment with a gluten free diet. Methods: 30 patients with celiac disease before and during treatment with gluten-free diet were investigated. 30 patients without organic damage of the gastrointestinal tract served as control. Small bowel permeability was measured using lactulose/mannitol and lactulose/D-xylose ratios. The saccharides were examined in the 5 hours collected urine using capillary gas chromatography. Results: Small bowel permeability (indices lactulose/mannitol and/or lactulose/xylose) increased significantly in patients with untreated celiac disease. 23 patients were followed up before and during treatment with a gluten-free diet 2.6 months after beginning of this treatment and small bowel permeability (measured as indices lactulose/mannitol and/or lactulose/xylose) significantly decreased. Conclusion: Small bowel permeability test is a non-invasive test suitable for the diagnosis of celiac disease and monitoring of compliance to a gluten-free diet in these patients.

Key words: Gut permeability, Lactulose, Mannitol, D-Xylose, Celiac disease, Gluten-free diet

INTRODUCTION

Celiac disease is an autoimmune disease with presence of antibodies against gluten causing damage to enterocytes and villous atrophy in sensitive patients (1). Celiac disease is a suitable model of gut barrier damage with an increase of small bowel permeability (2). There are two theories explaining the increase of small bowel permeability in villous atrophy (2). One theory differentiates the various ways of absorption of saccharides according to molecular size: the monosaccharides (e.g. mannitol, L-thamnose) are absorbed passively via enterocytes (passive transcellular absorption); other monosaccharides (D-xylose) are absorbed by facilitated diffusion (active transport after concentration); glucose, amino acids and dipeptides are absorbed by active, carrier mediated transport, which is Na\(^+\)/K\(^+\)-ATPase dependent. Disaccharides are absorbed paracellularly via tight junctions. If the small mucosa is damaged, transcellular absorption decreases and paracellular absorption increases due to adaptation to worsening absorption.

According to the second theory both monosaccharides and disaccharides are absorbed paracellularly via tight junctions, monosaccharides on villous tips and disaccharides in crypts and absorption of disaccharides is relatively higher (2,9,12).

Abbreviations:
- DTPA - Diethyl-triamino-propionic acid
- EDTA - Ethylen-diamino-tetraacetic acid
- LA/MA - Index lactulose/mannitol
- LA/XY - Index lactulose/D-xylose
- NSAID - Non-steroidal anti-inflammatory drug
- SD - Standard deviation

Patients

30 patients (7 males, 23 females) aged 39 ± 13 years with celiac disease were included in the study; 30 patients (8 males, 22 females) aged 38 ± 12 years with non-specific gastrointestinal problems served as controls (Table 1). Diagnosis of celiac disease was made using histological and serological examinations (anti-gliadine, anti-endomysium...