The Results of *Helicobacter Pylori* Eradication on Repeated Bleeding in Patients with Stomach Ulcer

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**ABSTRACT**

The triple therapy of *Helicobacter pylori* eradication prevents repeated bleeding from stomach ulcer. The aim of this one-way blind prospective study was to evaluate the efficiency of the two-week triple therapy for *Helicobacter pylori* eradication in preventing renewed bleeding in patients with stomach ulcer within one year. This research included 60 hospitalized patients with bleeding stomach ulcer and positive *Helicobacter pylori* infection, 34 men and 26 women (average age 59.7 years). The patients were given therapeutic scheme of omeprazol – amoxicillin – metrodinazol (OAM) eradication for 14 days. Eradication of *H. pylori* infection was defined as lack of proof of the infection one month or several months after therapy suspension. By applying triple OAM therapy within two weeks the eradication was successful in 72%. In the group of 17 *H. pylori* positive patients there were 8 patients (47.6%) with repeated stomach ulcer and 3 patients (18%) with bleeding. Within the group of 43 *H. pylori* negative patients there were only 2 patients (4.65%) with repeated stomach ulcer and 1 patient (2%) with bleeding, during the observed period of 12 months. This research confirms the hypothesis about the necessity of eradication of *Helicobacter pylori* infection in patients with bleeding stomach ulcer as prevention of repeated bleeding.

**Key words:** *Helicobacter pylori*, bleeding, stomach ulcer

**Introduction**

*Helicobacter pylori* colonizes surface of the stomach mucous membrane and is one of the most important etiologic factors, which cause the chronic gastritis B and ulcer disease. It has been identified as first class carcinogen according to World Health Organization because of being involved with the development of adenocarcinoma of stomach and MALT lymphoma.

Prevalence of *H. pylori* infection in bleeding from duodenal ulcer is 97% and in bleeding from stomach ulcer 84%¹. Before the role of *H. pylori* in the pathogenesis of ulcer disease has been recognized, patients were usually given half the doses of the *H₂* blockers maintaining therapy after the first episode of bleeding. Research of the half doses of maintaining therapy with *H₂* blocker at night showed great reduce of recidivism of duodenal ulcer for 20–25%, in distinction from placebo where 60–90% of recidivism has been traced. The recidivism of gastric ulcer and its response to half of the maintaining therapy *H₂* blocker at night is similar to duodenal ulcer. The annual recidivism of gastric ulcer on the maintaining therapy is reduced to 10–30% in distinction from placebo where there is recidivism between 30 and 80%²³.

According to the already mentioned Spanish study¹, *H. pylori* eradication therapy is a choice therapy in preventing of recidivism of bleeding duodenal ulcer. During 12 months of research there was no trace of any recidivism of bleeding without giving the maintaining anti-secretory therapy. The annual recidivism of gastric ulcer on the maintaining therapy is reduced to 10–30% in distinction from placebo where there is recidivism between 30 and 80%²³.

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H₂ blocker therapy³. Gastric ulcer recidivism has been traced after the successful eradication of H. pylori only with 2.3% of patients in the period of one year³. There is better efficiency in preventing duodenal bleeding with dual eradication therapy by antibiotics and PPI, rather than PPI and H₂ blocker in monotherapy). In the period of 27 months it has not been traced any recidivism bleeding from duodenal or gastric ulcer after successfully applied triple or quadruple eradication therapy of H. pylori⁶.

So we came to the question whether to prevent and postpone the recidivism of ulcer bleeding by expensive and long lasting maintaining therapy with H₂ blocker or to make eradication of H. pylori with the following blocker treatment of proton pump without maintaining therapy or to combine both.

**Materials and methods**

60 hospitalized patients with bleeding stomach ulcer and combined H. pylori infection were involved in this research. The existence of stomach ulcer and accompanying bleeding was found through endoscopy and presence of H. pylori infection through biopic ureasis test and histology. The bleeding was stopped endoscopically, by injection sclerosant technique with 1% Polidocanol. The patients were acquainted with the medicines they were given. After 14 days of treatment 4–6 biopsies were taken from the edge of the ulcer to eliminate the malignancy. Patients with difficult respiratory, cardiovascular, renal or liver diseases, patients on long lasting drug therapies (especially nonsteroid antireumatics), psychiatric patients, pregnant and breastfeeding women and patients with already operated abdomen were not involved in this research.

The bleedings were categorized according to Forrest’s classification. The patients were given, apart from endoscopic homeostasis and antishock therapy, ranitidine 4 x 100 mg i.v. during three to four days depending on stopping of bleeding and transition to peroral feeding. After transition to peroral therapy the patients were given omeprazol 40 mg in the morning before taking meal.

After the infection had been confirmed the eradication was done with omeprazol 40 mg in the morning before taking meal, with amoxicilin 2 x 1000 mg during 14 days and metronidazol 3 x 500 mg also during 14 days. After this therapy, the patients were given omeprazol 20 mg in the morning before meal until the ulcer was improved (healed). The control endoscopic examinations were done 1, 6 and 12 months after the ulcer was improved (healed) or after the symptoms had occurred. None of the patients was given the maintaining therapy.

Eradication of H. pylori infection was defined as lack of proof through biopic urease test and histology one month or several months after the therapy has been stopped.

Endoscopes (Olympus GIF Q10) and biopic forceps (Olympus FB 24K) were sterilized with 2% glutaralde-hid between the examinations. Four biopic samples were taken (2 from stomach antrum within 4 cm from pylorus and 2 from stomach corpus). Two samples for histology and 2 samples for urease test were taken. The statistic analysis was made by t-test proportions

\[
(t) = \text{Sqrt}(N_1+N_2(N_1+N_2)*p_1–p_2/Sqrt(p_1q)\),
\]

\[
p = (p_1^n1+p_2^n2)/(N_1+N_2), q=1–p.
\]

**Results**

60 patients with bleeding stomach ulcer and positive H. pylori infection were involved in this research. It could be seen in Table 1 that the average age of patients was 59.7 years. During the first endoscopic examination and sclerosation, the biggest percentage of patients (56.66%) was in the second group of Forrest’s classification of bleeding activities, 31.66% in the IB group and 11.66% in IA group (Table 2).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Characteristics of the patients with the bleeding stomach ulcer</th>
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<tbody>
<tr>
<td>Number of patients</td>
<td>60</td>
</tr>
<tr>
<td>Proportion men:women</td>
<td>32:26</td>
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<tr>
<td>Average age in years</td>
<td>59.7</td>
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</tbody>
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**Table 2**

<table>
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<th>Forrest’s classification</th>
<th>N (%)</th>
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<tr>
<td>IA</td>
<td>7 (11.66)</td>
</tr>
<tr>
<td>IB</td>
<td>19 (31.66)</td>
</tr>
<tr>
<td>II</td>
<td>34 (56.66)</td>
</tr>
</tbody>
</table>

After H. pylori status has been determined and eradication therapy given, endoscopic examination was performed in intervals of 1, 6 or 12 months during the period from the beginning of 1998 till the end of 2000. The period was lengthened because some new patients were involved. It was not possible to make contacts with some of the patients for the necessary examination.

The eradication through triple therapy with omeprazol 40 mg in the morning before taking the meal, amoxicilin 2 x 1000 mg a day and metro-nidazol 3 x 500 mg during 14 days (OAM) was 72% successful.

During 12 months of this research 8 ulcer recidives (out of 17 patients with H. pylori infection) were identified, and 2 out of 43 patients with successful eradication H. pylori (Table 3). The repeated bleeding was traced in 3 out of 17 patients with H. pylori infection, and only in 1 out of 43 patients with negative H. pylori status. There is a significant statistical difference in ulcer recidivism...


**TABLE 3**

<table>
<thead>
<tr>
<th>H. pylori infection</th>
<th>H. pylori positive patients</th>
<th>H. pylori negative patients</th>
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</thead>
<tbody>
<tr>
<td>Ulcer recidivum N (%)</td>
<td>8/17 (47.05%)</td>
<td>2/43 (4.6%)</td>
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**TABLE 4**

<table>
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<th>H. pylori infection</th>
<th>H. pylori positive patients</th>
<th>H. pylori negative patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding recidivum N (%)</td>
<td>3/17 (18%)</td>
<td>1/43 (2%)</td>
</tr>
</tbody>
</table>

between the patients with positive and negative H. pylori status (p<0.001) (Table 4). There is also great statistical difference in renewed bleeding between the group with positive and negative H. pylori status during 12 months of observation (p=0.03).

**Discussion**

The real history of the peptic ulcer of patients who were not operated was settled down in 50th and 60th years of the previous century. Renewed bleeding was traced in 19.5–46% of the patients with one previous bleeding and in 23.5–62% of the patients with two previous bleedings. Besides this tendency of bigger bleeding, the risk is not lessened by continuous observation. The more update research shows that 13–16% of the patients with two previous bleedings will bleed once again9–11. Surgery could lessen the percentage of recidivism. The possibility of therapy with H2 antagonists in long-lasting therapy of ulcer with bleeding complications is an integral part of the pathogenesis of ulcer disease and at stake of acute and chronically morbidity. That is why it has been looked for nonsurgical alternatives in long-lasting therapy of ulcer with bleeding complications. The possibility of therapy with H2 antagonists occurred in order to lessen the percentage of renewed ulcer bleeding12–14. This therapy must be given once a day, because the ulcer recidivism comes back to placebo effects if the therapy is intermittent or stopped. During three years of observation, Penston and Wormsley13 have retrospectively found bleeding from ulcer in 1.3% of the patients on long-term maintaining therapy with antagonist to H2 receptors, in comparison to 15.2% of those on placebo. In the second multicentrical, random and control study with 65 patients with endoscopically confirmed bleeding from the duodenal ulcer, the renewed bleeding was traced in 3 out of 32 (9.3%) patients who were given ranitidine, unlike 12 out of 33 (36.4%) patients who were given placebo12. The disadvantages of longterm maintaining therapy with H2 receptors blockers include high price, need for the longterm cooperation, possible side–effects and interaction with other medications.

Based on great number of research, which proved that eradication H. pylori infection lessens the percentage of ulcer recidivum15–20, it is supposed that the number of ulcer complications will lessen. The previous work of Graham from 1993, Labenz from 1994, Jaspersen and Rokkas from 1995 showed the benefit of the eradication therapy for patients with bleeding duodenal and stomach ulcer as bleeding prevention by patients who became H. pylori negative through the certain period of observation21–24. The same facts could be found in more recent works1–5. It is difficult to compare these studies with ours because there are different therapy eradication schemes and the patients included were with duodenal and stomach ulcer. However, it was important to note the renewed bleeding in the group of H. pylori positive and negative patients. In distinction from our study, the mentioned authors and co-workers had the bigger percentage of eradication of H. pylori (80%), whereas our research identified 72% of the patients eradicated from H. pylori, what is probably due to resistance to metronidazol therapy in our subpopulation. One more possible reason for smaller eradication percentage is poor cooperation of patients during classical triple 14 days OAM therapy, because older persons were involved. Ulcer recidivism occurred within H. pylori positive group in 47% of the cases and in the H. pylori negative group in 4.6%, and there is not a big difference when comparing to the already mentioned studies. During 12 months of observation the renewed bleeding was traced in 18% within H. pylori positive patients and in 2% within H. pylori negative group. The already mentioned authors did not find any renewed bleeding within the group of H. pylori negative patients during the period of observation, and 19–46% within the H. pylori positive group.

Our results confirm the hypothesis that H. pylori is an integral part of the pathogenesis of ulcer disease and its eradication results with prevention of renewed ulcer thus ulcer complications, as well.

**REFERENCES**


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UTJECAJ ERADIKACIJE INFEKCIJE S HELICOBACTER PYLORI NA RECIDIV KRVARENJA KOD BOLESNIKA S ŽELUČANIM VRIJEDOM

S A Z E T A K

Trojna terapija eradikacije Helicobacter pylori prevenira recidiv krvarenja iz želučanog vrijeda. Cilj ove jednostroko slijepe prospektivne studije bio je evaluirati efikasnost trojne dvojedne terapije eradikacije H. pylori u prevenciji ponovljenog krvarenja kod bolesnika s želučanim vrijedom, u trajanju od 1 godine. U ispitivanje je uključeno 60 hospitaliziranih bolesnika s krvarenjem želučanim vrijedom i pozitivnom Helicobacter pylori infekcijom, 34 muškarca i 26 žena prosječne starosti 59,7 godina. Bolesnici su dobivali terapijsku shemu eradikacije omeprazol-amoxicilin-metronidazol (OAM) kroz 14 dana. Eradikacija H. pylori infekcije definirala se kao nedostatak dokaza infekcije biotički ureaza testom i histologijom, jedan ili više mjeseci nakon prestanka davanja terapije. Primijenjenom trojnom terapijom OAM kroz dva tjedna uspješnost eradikacije je bila 72%. U grupi od 17 bolesnika koji su bili H. pylori pozitivni, bilo je 8 bolesnika (47,06%) s recidivom želučanog ulkusa i 3 bolesnika (18%) s krvarenjem, a u grupi od 43 bolesnika s negativnim H. pylori statusom samo 2 bolesnika (4,65%) s recidivom želučanog ulkusa samo 1 bolesnik (2%) s krvarenjem, tijekom praćenja od 12 mjeseci. Ovo ispitivanje potvrđuje hipotezu o potrebi primjene terapije eradikacije u bolesnika s krvarećim želučanim vrijedom u svrhu prevencije ponovljenog krvarenja.