Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.elsevier.com/locate/medici

Original Research Article

Pepsinogen testing for evaluation of the success of *Helicobacter pylori* eradication at 4 weeks after completion of therapy

Marcis Leja [a,b,c,*], *Sanita Lapina* [a,b], *Inese Polaka* [d], *Dace Rudzite* [a,b], *Ilona Vilkoite* [a,b], *Ilva Daugule* [a], *Anna Belkovets* [a,e], *Sergey Pimanov* [f], *Jelena Makarenko* [f], *Ivars Tolmanis* [c], *Aivars Lejnieks* [a,b,g], *Viesturs Boka* [a,b], *Ingrida Rumba-Rozenfelde* [a], *Uldis Vikmanis* [a]

[a] *Faculty of Medicine, University of Latvia, Riga, Latvia*
[b] *Riga East University Hospital, Riga, Latvia*
[c] *Digestive Diseases Centre GASTRO, Riga, Latvia*
[d] *Department of Modelling and Simulation, Riga Technical University, Riga, Latvia*
[e] *Institute of Internal Medicine, Siberian Branch, Russian Academy of Medical Sciences, Novosibirsk, Russia*
[f] *Department of Therapy No. 2, Vitebsk State Medical University, Vitebsk, Belarus*
[g] *Riga Stradins University, Riga, Latvia*

ARTICLE INFO

Article history:
Received 20 July 2013
Accepted 11 January 2014
Available online 5 June 2014

Keywords:
Pepsinogen
Gastrin-17
Eradication
Helicobacter pylori
Efficacy

ABSTRACT

Background and objective: Pepsinogen levels in plasma are increased by inflammation in the gastric mucosa, including inflammation resulting from *Helicobacter pylori* infection. A decrease in pepsinogen II level has been suggested as a reliable marker to confirm the successful eradication of infection. The aim of our study was to evaluate the potential role of pepsinogens I and II, gastrin-17 and *H. pylori* antibodies in confirming successful eradication.

Material and methods: Altogether 42 patients (25 women, 17 men), mean age 45 years (range 23–74), were enrolled. Pepsinogens I and II, gastrin-17 and *H. pylori* IgG antibodies were measured in plasma samples using an ELISA test (Biohit, Oyj., Finland) before the eradication and 4 weeks after completing the treatment. The success of eradication was determined by a urea breath test.

Results: Eradication was successful in 31 patients (74%) and unsuccessful in 11 patients (26%). Pepsinogen II decreased significantly in both the successful ($P = 0.029$) and unsuccessful ($P = 0.042$) eradication groups. Pepsinogen I decreased significantly in the successful ($P = 0.025$) but not the unsuccessful ($P = 0.29$) eradication group. The pepsinogen I/II ratio increased in the successful eradication group ($P = 0.0018$) but not in the group in which treatment failed ($P = 0.12$). There were no differences in gastrin-17 or *H. pylori* antibody values.

* *Corresponding author at*: Faculty of Medicine, University of Latvia, Riga East University Hospital, 6 Linezera, 1006 Riga, Latvia.
E-mail addresses: cei@latnet.lv, ras.zinatne@latnet.lv (M. Leja).

Peer review under the responsibility of the Lithuanian University of Health Sciences.

Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.medici.2014.05.001

Conclusions: A decrease in pepsinogen II levels cannot be used as a reliable marker for the successful eradication of *H. pylori* 4 weeks after the completion of treatment. The increase in pepsinogen I/II ratio reflects differences in pepsinogen production following the eradication irrespective of improvement in atrophy.

1. Introduction

The accuracy of diagnostic tests for *Helicobacter pylori* (*H. pylori*) is influenced by various conditions including the use of acidity-lowering agents and antibiotics, so the recommended tests for initial detection of the microorganism differ from the follow-up tests to confirm the success of eradication therapy. The ^{13}C urea-breath test (UBT) and laboratory-based monoclonal stool antigen test are considered the non-invasive tests of choice for follow-up [1]. According to Maastricht-IV recommendations, the time for testing the success of *H. pylori* eradication after the end of treatment should be at least 4 weeks and PPI should be stopped for 2 weeks before testing [1].

Although follow-up testing to evaluate the success of eradication is recommended, these recommendations are quite often not followed in routine practice [2]; one reason for this could be the unavailability of the tests in particular locations. Therefore new non-invasive tests to confirm the success of eradication would be useful.

Earlier research suggested the detection of *H. pylori* antibody in serum/plasma for judging the success of eradication [3–5], but in a large proportion of patients the antibody levels remain high for a substantial period even after successful eradication [6,7]. In addition, simple comparison between the initial and follow-up sample results may be not reliable owing to daily variations in the results if comprehensive methods to quantify the antibody are not used or the samples are not run in pairs. Therefore, the existing guidelines do not recommend serology tests for follow-up [1].

Most of the diagnostic tests for *H. pylori* (UBT, stool antigen test, biopsy-based tests) are dependent on the density of the microorganisms in the stomach mucosa, so a decrease in that density following therapy with antibiotics and/or proton pump inhibitors could lead to a false-negative result [2,8]. Therefore, a test independent of the density of *H. pylori* would be of particular interest. Pepsinogens (Pgs) are inactive pepsin precursors; the clinically relevant Pgs in humans are pepsinogen I (PgI) and pepsinogen II (PgII). PgI is synthesized by the chief cells and neck cells of the gastric corpus, while PgII is also synthesized in the cardiac, pyloric and Brunner gland cells in the proximal duodenum [9]. Active inflammation caused by *H. pylori* increases the blood levels of Pgs [10,11]. Atrophy of the corpus part is related to decreased PgI levels [11,12]; the ratio between PgI and PgII (PgI/PgII) is considered a better marker for corpus atrophy [13–15].

Gatta et al. recently suggested that the PgII level 8 weeks after eradication therapy is a reliable marker of successful eradication [9]. The cut-off value they used (22.7% decrease) resulted in 100% sensitivity and 96.6% specificity for detecting the success of eradication, while the other markers they evaluated (PgI, gastrin-17) did not give acceptable results. However, the authors acknowledged the need for additional studies to test their hypothesis that measuring the PgII level constitutes a method for determining whether eradication has been successful.

The objective of the present work was to evaluate changes in PgI, PgII and PgI/PgII as well as gastrin-17 (G-17) and *H. pylori* IgG antibody levels at 4 weeks after the completion of *H. pylori* eradication compared to the levels at baseline, and to evaluate the potential of these parameters as markers for the success of eradication.

2. Material and methods

Adult patients with upper gastrointestinal complaints referred for upper endoscopy were prospectively invited to participate in the study; patients having failed 1st line eradication therapy beforehand were excluded. Upper endoscopy was performed at the time of inclusion. Blood samples for detection of biomarkers were drawn prior to the endoscopy. Biopsy samples were taken during the initial endoscopy and analyzed according to the updated Sydney classification [16]. The presence of *H. pylori* was evaluated by histology at inclusion. All the slides were stained with hematoxylin and eosin as well as Giemsa (the latter was used to evaluate the presence or absence of *H. pylori* infection).

Standard eradication therapy was offered to *H. pylori*-infected individuals in whom this treatment was clinically indicated, consisting of lansoprazole (30 mg), clarithromycin (500 mg), amoxicillin (1000 mg), all BID for 7 days.

The success of eradication was determined by UBT 4 weeks after the completion of treatment; the use of proton pump inhibitors was not allowed during this period. Another blood sample for biomarker detection was withdrawn prior to the UBT. Only those patients who complied with the protocol were included in the analysis.

For the laboratory work-up, plasma samples were taken during a fasting state and before the follow-up UBT. The samples were frozen immediately and kept frozen at −80 °C pending tests. The initial and the follow-up plasma samples were tested at the same run and on the same test-plate. Biohit, Oyj. (Finland) reagents were used to test for PgI, PgII, G-17 and *H. pylori* IgG using the methods recommended by the manufacturer.

All patients gave a signed informed consent and the study was approved by the Ethics Committee of the Institute for