Efficacy of Klatinol in eradication of *Helicobacter pylori* infection

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Although the epidemiology of Helicobacter pylori (*H. pylori*) infection has been changed significantly in recent years, and its prevalence is low enough in new affluent socio-economic cohorts, it still remains one of the most common infections in the world. The average prevalence of *H. pylori* worldwide is still being equal to approximately 50%, with the highest levels in the developing countries (80–90%) and lower levels in Western Europe (30–50%), North America (30–40%) and Australia (20%).

The clinical significance of *H. pylori* is defined by the fact that it's a major causal factor of gastroduodenal pathology (chronic gastritis, peptic ulcers, dyspepsia, gastric cancer, MALT-lymphoma of the stomach) and a number of extragastric disorders (unexplained iron-deficiency anemia, B_{12}-deficiency anemia, immune thrombocytopenia).

It should be stated that, despite the fact that *H. pylori* infection is a very common and serious problem, its therapy is low-optimized, empirically-prescribed in most cases and has worse results as compared with therapy of other more frequent infectious diseases. Although *H. pylori* bacterium is sensitive enough to wide range of antibiotics and antimicrobials, *H. pylori* infection itself is difficult to be treated. The effectiveness of many commonly recommended regimens of *H. pylori* therapy has been increasingly reduced due to the constantly increasing resistance of bacteria to many antimicrobial agents, especially metronidazole, clarithromycin, and fluoroquinolones. Moreover, the difficulties of treatment are associated with a very large number of *H. pylori* bacteria in the stomach, creating the "contamination effect", their ability to occupy different niches (e.g., intracellular ones or those in a thick layer of mucous gel of the stomach), the high rate of re-infection frequency in the

developing countries. In this regard, the regimens of *H. pylori* eradication treatment are constantly being changed and improved.

Currently, there are three main types of anti-*H. pylori* therapy — empirical therapy, individualized therapy and empirical therapy of salvation (Table 1).

Table 1

Recommended regimens of *H. pylori* treatment in 2014

Treatment	Drugs, dosage and duration
Empirical therapy	
Standard triple therapy upon clarithromycin-resistance in the region of <15%	Clarithromycin 500 mg + amoxicillin 1 g or metronidazole 500 mg (for those allergic to penicillins) + PPI — all b.i.d. for 10–14 days
Concomitant therapy	Amoxicillin 1 g + clarithromycin 500 mg and tinidazole 500 mg or metronidazole 500 mg + PPI — all b.i.d. for 10–14 days
Sequential therapy	Amoxycillin 1 g + PPI b.i.d. for 5 days, then clarithromycin 500 mg + tinidazole 500 mg or metronidazole 500 mg + IPP — all b.i.d. for the next 5 days (total 10 days)
Sequential -concomitant therapy	Amoxycillin 1 g + PPI b.i.d. for 7 days, then amoxicillin 1 g + clarithromycin 500 mg and tinidazole 500 mg or metronidazole 500 mg for the next 7 days (total 14 days)
Bismuth-containing quadruple therapy	Bismuth subcitrate (subsalicylate) + tetracycline hydrochloride 500 mg q.i.d. + metronidazole 500 mg or tinidazole 500 mg t.i.d. + PPI b.i.d. for 10–14 days
Individualized therapy	
Triple therapy upon known sensitivity of *H. pylori* to clarithromycin	Amoxicillin 1 g + clarithromycin 500 mg or tinidazole 500 mg or metronidazole 500 mg + PPI — all b.i.d. for 10–14 days
Fluoroquinolone therapy upon known sensitivity of *H. pylori* to fluoroquinolones	Fluoroquinolones (e.g., levofloxacin 500 mg od) + IPP + amoxicillin 1 g b.i.d. for 14 days
Empirical therapy of salvation	
Double PPI therapy in high doses	PPI + amoxicillin 500 mg — all q.i.d. every 6 hours for 14 days
Rifabutin-containing triple therapy	Rifabutin 150 mg + amoxicillin 1 g + PPI — all b.i.d. for 14 days

Empirical therapy, prescribed as a therapy of first or second line without determining the sensitivity of *H. pylori* to antibiotics, includes standard triple therapy, sequential therapy, concomitant therapy, sequential-concomitant therapy, and bismuth-containing quadruple therapy. Bismuth preparations are not used in the regimens of standard triple, consistent and concomitant therapy, these schemes

include four drugs: PPI, clarithromycin, metronidazole (or tinidazole), and amoxicillin.

Standard triple therapy on the basis of clarithromycin is still being the most widely used in Europe and the United States as the first-line therapy, although its effectiveness in many countries has declined steadily. In this regard, the Maastricht 4-2010 consensus strongly recommends selecting a first-line therapy on the basis of well-known clarithromycin-resistance in the country (region). In particular, if clarithromycin-resistance in a certain region doesn't exceed 15%, then, as before, it's recommended to prescribe the empirical standard clarithromycin-containing triple therapy (PPI + clarithromycin + amoxicillin or metronidazole in cases of allergy to penicillin) as the first line-therapy even without prior determination of the sensitivity, while the doses for all the drugs remain the same. An important conclusion of the consensus was that the extension of the standard triple therapy up to 10–14 days had increased the effectiveness of eradication by an average of 5%.

As it's known, we don't have any true picture of *H. pylori* clarithromycin-resistance in Ukraine because the special large-scale studies in this field have never been conducted in our country. Upon focusing on our nearest neighbor Russia, where clarithromycin-resistance is at the level of 8–10%, the situation in Ukraine still looks quite favorable, which is indirectly proved by the high efficiency of standard clarithromycin-containing regimens of triple therapy.

Our own experience of using the standard triple therapy on the basis of clarithromycin and confirming the eradication of *H. pylori* with the usage of ^{13}C-UBT, comprising annual treatment of 300–400 patients during the last 15 years, shows that the effectiveness of the standard triple therapy is still being sufficiently high, exceeding 80%.

It's our deep conviction that upon eradication it's better and much more convenient to use the combined drugs in the form of ready-made kits containing all the necessary components. These drugs are produced as finished combined blisters, each containing all the necessary components in recommended dosages, which allows significantly improve treatment compliance and, correspondingly, achieve the higher

levels of eradication. It's also crucial that the practitioner of primary care (e.g., family doctor) doesn't even have to memorize the dosages and names of certain drugs, since they're all specially packaged in the necessary combination and dosages. The cost of a course treatment with such drugs is usually much lower than the use of three separate products from different manufacturers.

In this context, we conducted a study on the effectiveness of the drug Klatinol (Synmedic Company, India), which is just such a combined drug. One package of Klatinol has 7 combined blisters, each of which is designed for daily intake twice a day and contains 30 mg of lansoprazole, 250 mg of clarithromycin, and 500 mg of tinidazole.

The main aim of study was to investigate the effectiveness of Klatinol in *H. pylori* eradication, depending on the duration of a course treatment (7 and 14 days).

For this purpose, we examined 60 patients (25 women, 35 men at the age of 29–65) with uncomplicated *H. pylori*-positive duodenal ulcers. The presence of ulcers was verified upon videoesophagogastroduodenoscopy with biopsy, the presence of *H. pylori* was confirmed by rapid urease test and ^{13}C-UBT in all the patients. None of them had had received anti-*H. pylori* therapy before.

Depending on the conducted treatment, using the computer method of random numbers, all the patients were randomized in a ratio of 1:1 into 2 groups. Patients of group 1 (30 patients) had triple therapy by Klatinol for 7 days; group 2 (30 patients) had the same triple therapy for 14 days.

The main criterion of efficacy was represented by the rate of *H. pylori* eradication (determined 4 weeks after the end of treatment according to the ^{13}C-UBT). Clinical efficacy (% of ulcer healing in 4 weeks) and the frequency of side effects were regarded as the secondary criteria determining the effectiveness.

57 patients (95%) fully completed treatment (29 patients of group 1 (96.7%) and 28 patients of group 2 (93.3%)). The reason for the early termination of treatment in 2 cases was the development of such an allergic reaction as nettle rash, in 1 case — self-termination of the treatment due to the development of mild side effects (bad

taste in mouth, nausea). Compliance of patients in both groups was good. The results obtained during the treatment are shown in Table 2.

Table 2

Efficacy of Klatinol depending on the duration of treatment

Treatment	**Rate of *H. pylori* *eradication*, n (%)**	**Rate of side effects, n (%)**	**Rate of complete healing of ulcers, n (%)**
Group 1, n=29	24 (82.8%)	13 (44.8%)	28 (96.6%)
Group 2, n=28	25 (89.3%)	16 (57.1%)*	28 (100%)

Note: * — the differences in comparison with other groups were significant at $p \leq 0,05$.

As it can be seen from these data, the rate of *H. pylori* eradication in both groups exceeded 80%, which is a requirement for effective eradication therapy, and increased with the prolongation of treatment (89.3% vs. 82.8%), although it was accompanied by the development of mild side effects in a larger number of patients. Almost all the patients noted healing of ulcers in 4 weeks.

The rate of side effects is presented in Table 3. As it can be seen from the data, the rate of side effects was significantly increased with the prolongation of treatment, although their character remained the same. The most common side effects of eradication therapy were: a change of taste, nausea, diarrhea, headache, and dry mouth. Any significant laboratory changes affecting the prolongation of therapy weren't identified.

Table 3

Rate of the most common side effects in both groups of patients

Side effect	**Group 1, *n (%)***	**Group 2, *n (%)***
Allergic reaction	1 (3.3%)	1 (3.3%)
Change of taste	5 (16.6%)	6 (20%)
Nausea	4 (13.3%)	5 (16.6%)
Diarrhea	2 (6.6%)	3 (10%)
Headache	1 (3.3%)	1 (3.3%)
Dry mouth	1 (3.3%)	2 (6.6%)

Total	14 (46.6%)	18 (60%)

Therefore, this study showed that the combined drug Klatinol was quite effective for the anti-*H. pylori* therapy and provided successful eradication in more than 80% of patients. The effectiveness of eradication therapy has been significantly increased with increasing duration of treatment (from 7 to 14 days), although it was accompanied by the appearance of mild side effects in a larger number of patients.

Taking the obtained results in consideration, 14-day course of standard triple therapy using the drug Klatinol can be recommended as the first-line eradication of *H. pylori.*

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Results of studying Klatinol efficacy in *H. pylori* eradication are presented in the article. The conclusion has been made that Klatinol is an effective drug for *H. pylori* eradication, its efficacy being increased upon the prolongation of treatment.