



# Influence of parental compliance on the effectiveness of treatment of chronic gastroduodenal pathology in children

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## Abstract

**Introduction:** The article focuses on the studies which point to particular difficulties in achieving compliance in pediatrics. A dangerous trend to escalate the number and doses of antibiotics in anti-*Helicobacter pylori* (HP) schemes, the dosage frequency and course duration of eradication therapy considerably complicates a patient's compliance to the treatment and contributes to a further growth of HP antibiotic resistance. In the treatment of children, the control of the outpatient therapy largely depends on the patient's parents.

**Materials and methods:** At the first stage of the study, 103 children with chronic gastroduodenal pathology associated with HP were examined. Diagnosis of the disease was based on the study of complaints, the anamnesis data, and the results of the endoscopic examination. All the patients underwent a course of anti-HP therapy in the outpatient setting. A degree of parental compliance to their child's therapy was determined in by a questionnaire, which had been developed by us, the families of the children suffering from chronic gastroduodenal pathology. At the second stage, 80 children suffering from peptic ulcer associated with HP were examined. HP was eradicated in the outpatients of both groups, using an anti-HP regimen: **omeprazole**, **clarithromycin**, and **amoxicillin** administered for 14 days. The influence of the measures to improve parental compliance carried out in tandem "doctor – pharmacist" in the families with children suffering from chronic gastroduodenal pathology was studied.

**Results and discussion:** A decrease in parental compliance was observed in more than 2/3 of the families with children suffering from chronic gastroduodenal pathology, associated with HP infection. A higher level of parental compliance was established in the families of children after the "compliance training". In the patients of this group, eradication of HP was achieved in 87.5% cases by using a traditional scheme: **omeprazole**, **clarithromycin**, and **amoxicillin** administered for 14 days.

**Conclusion:** It can be concluded that the level of parental compliance to an anti-HP therapy for their children is insufficient. In turn, conducting a "compliance training" in the tandem of "doctor – pharmacist" before starting the therapy is an important factor in increasing the level of parental compliance, which is reflected in increasing the effectiveness of the treatment. Strict adherence to the regimen and duration of administration of the prescribed drugs in children with ulcer allows achieving a high level of HP eradication – 95.2 %, even when using the traditional anti-HP regimen.

The eradication was achieved in 56.5 % of the children with partial parental compliance, and only in 6.7 % of the children with non-compliant parents.

## Keywords

chronic gastroduodenal pathology, *Helicobacter pylori*, parental compliance, children.

## Introduction

The chronic diseases of the stomach and the duodenum are the most common chronic inflammatory diseases of the gastrointestinal tract (GIT). To date, *Helicobacter pylori* (HP) infection is considered as the main cause of chronic gastroduodenal pathology (CGDP) and the formation of its most severe forms in patients of different age groups (Fasciana et al. 2019, Leja et al. 2019). Most aspects of HP eradication in pediatric practice remain unresolved. Anti-HP therapy is the main standard of treatment for patients with inflammatory and destructive processes of the stomach and the duodenum (Lee et al. 2013). However, in recent years, a number of problems associated with the development of HP resistance to the antibiotics, which are traditionally used to eradicate this microorganism, have arisen (Gressot et al. 2019, Megraud et al. 2013, Savoldi et al. 2018, Thung et al. 2016, Vianna et al. 2016).

According to the recommendations of Maastricht IV-V and the Kyoto Global Consensus on HP-associated gastritis and the National Guidelines to diagnose and treat acid-related and HP-associated diseases (VI Moscow Agreement), the use of high doses of proton pump inhibitors, an increase in the antibiotics course duration to 14 days, four-component sequential antibiotic regimens, and the use of fluoroquinolones are important ways to improve the effectiveness of anti-HP therapy in patients with CGDP (Malfertheiner et al. 2012, Malfertheiner et al. 2017, Sugano et al. 2015). However, these recommendations in pediatric practice remain difficult to implement due to the high frequency of side effects and little experience in using certain medicines in childhood. In addition, fluoroquinolones, widely used for HP eradication in adults, are contraindicated for use in pediatric practice.

A dangerous trend to escalate the number and doses of antibiotics used in anti-HP schemes, their dosage frequency and course duration of eradication therapy considerably complicates a patient's compliance to the treatment, reduces the quality of life, increases the frequency of side effects, which leads to reduced compliance and contributes to a further growth of HP resistance to antibiotics (Andreev and Kucherjavyj 2013, Cimmerman and Vologzhanina 2015, Kalach et al. 2015, Maev et al. 2013, O'Connor et al. 2009).

Today, control over the regular implementation of the appointments of the attending physician by the patient is the key to effective treatment of any disease, especially this is relevant in relation to chronic pathology.

Compliance is the conformity of the patient's behavior to the physician's recommendations, including medications, diet and/or lifestyle changes. Often, compliance is

viewed as the conscious cooperation of the physician and the patient, as well as the latter's family members, which is a prerequisite for any treatment, ensuring the effectiveness of the therapy (Danilov 2014). The patient's compliance with the therapy, his/her active participation in the treatment process, strict adherence to prescribed treatment regimens and diet therapy are of great importance for the treatment of chronic diseases and for a successful therapy (Naletov et al. 2018).

The problem of compliance among patients suffering from chronic pathology of the GIT is currently particularly relevant, as these diseases have chronic recurrent course, resulting in a significant decrease in the quality of the patient's life, to long-term limitations in diet and changing toilet habits, which has an impact on the psychological state of the patient, exacerbating the course of the disease, disappointing the patients in the therapy and discouraging the physicians (Beljakova 2014).

The results of the studies point to certain difficulties in achieving compliance in pediatrics. In the treatment of children, the control over the therapy in an outpatient setting largely depends on the patient's parents (Naletov et al. 2017).

The active inclusion of pharmacists (whose competence is to provide advice to the population and specialists on the use of medicines) in the activities aimed at improving the compliance of sick children and their parents, with overloaded physicians of the primary stage of medical care for children, may contribute to the optimization of the therapy.

## Materials and methods

At the first stage of the study, 103 children (young teens (12–14 years of age) and teenagers (15–17 years of age) with CGDP associated with HP (peptic ulcer, chronic gastroduodenitis) were examined at Donetsk City Children's Clinical Hospital No. 1 and Donetsk Medical Center "Gastro-line" to determine a degree of parental compliance to their children's therapy.

The diagnosis of CGDP was based on the study of complaints, anamnesis data, and results of the endoscopic examination.

All the patients underwent an outpatient course of anti-HP therapy. After the course, during a consultation with patients and their parents, an anonymous survey was conducted to determine the level of parental compliance by using a questionnaire, which had been developed for this study (Table 1).

**Table 1.** Questionnaire to determine the level of parental compliance.

№	Question	“Yes”	“No”
1	Have you ever forgotten to give your child the medicine?	0	1
2	Do you sometimes disregard your child’s medication intake time?	0	1
3	Do you skip taking the medicine if your child feels well?	0	1
4	If the child does not feel well after taking the medicine, do you skip the next dose?	0	1
5	May you refuse the next dose of the drug due to the child’s negative reaction to taking the medicine?	0	1
6	Can you independently replace the prescribed drug in your child’s treatment with a “more effective and safer” drug, in your opinion, without consulting the attending physician?	0	1

**Note:** 6 points – compliance, 4, 5 points – partial compliance, 3 or less points – non-compliance.

The questionnaire is highly valid (Cronbach test was over 0.8). Sensitivity = 92.8%, specificity = 82.4%, false-negative values = 7.2%, false-positive values = 17.6%.

At the second stage, 80 children (young teens (12–14 years of age) and teenagers (15–17 years of age)) suffering from peptic ulcer associated with HP were examined.

Diagnosis of HP infection was carried out by two methods (invasive and non-invasive). A Helpil test system was used for quick urease test with biopsy material (AMA Co Ltd., Russia). A Helik test system with indicator tubes was used for urease breath test (AMA Co Ltd., Russia). HP infection was determined if both methods provided positive results.

Before treatment, an anonymous questionnaire, which had been specially designed for this study, was conducted with the parents of the patients included in the study, determining the level of parental compliance.

Further, all the patients were divided into two groups: group 1 and group 2. There were 40 children in each group. HP was eradicated in the patients of both groups in outpatient setting, using an anti-HP regimen: **omeprazole**, **clarithromycin**, and **amoxicillin** administered for 14 days. This scheme is regulated by the *Federal Clinical Guidelines for the Provision of Medical Care to Children with Gastric Ulcer and Duodenal Ulcer Disease* (2016).

The patients of group 1 were prescribed a treatment during a consultation with a pediatric gastroenterologist at Donetsk City Children’s Clinical Hospital No. 1.

The patients of group 2 were consulted by a pediatric gastroenterologist and pharmacist at Donetsk Medical Center “Gastro-line” before starting the therapy, with their parents present. During the 20-minute consultation, in order to increase the level of compliance, a ‘compliance training’ was conducted for the patient’s parents and the child. During the “training”, the doctor explained the causes and mechanisms of the disease, the need and expediency of strict adherence to a two-week course of anti-HP therapy with 2 antibiotics. In turn, the pharmacist during the “training” dwelled on the issues of the dosage regimen, potential side effects of the therapy, and the interaction of the components of the proposed medicine scheme, as well as the approximate possible cost of treatment; a medication diary was made to be filled in, specifying the daily order of medications on the scheme. Later, every three days, the pharmacist would call up with the patient’s parents and answer the questions they had about the order and regimen of taking the drugs.

The effectiveness of the eradication with the use of noninvasive respiratory urease test, the dynamics of clinical symptoms, and a level of parental compliance were determined in the children during the control visit 1 month after the treatment.

There was no statistically significant difference in age between the comparison groups ( $p > 0.05$ , Mann-Whitney U-test), and no statistically significant difference in sex distribution ( $p > 0.05$ , Mann-Whitney U-test).

The study met all the ethical requirements for scientific work, and was conducted with the permission of the ethics committee of the M. Gorky Donetsk National Medical University. Before the examination, all the parents were informed of the nature of the clinical study, the prescription of medicine and possible side effects. The studies were carried out after obtaining informed consents to participate in the studies from the parents / legal representatives of the child.

The STATISTICA 7 package was used for statistical analysis of the data. Comparisons of groups of quantitative data were carried out using one-factor analysis and multiple comparison methods: the Scheffe method (in the case of the normal distribution law); the Dann’s multiple comparison tests (in the case of the difference between the distribution law and the normal distribution law). The comparison of the mean qualitative data was performed, using a paired fraction comparison (Fisher’s angular transformation with Yates’ correction). In the case of multiple comparison of proportion, the Bonferroni correction was used. The tables show the average value of the indicator of the frequency of the feature manifestation (%) and its 95% confidence interval (95% CI).

## Results and discussion

At the first stage, in order to study parental compliance in families of children suffering from CGDP, an anonymous survey was conducted among the parents of the children receiving different schemes of HP eradication. When analyzing parental compliance in the families of children suffering from HP-associated CGDP, it was found that the majority of parents were not compliant with their children’s treatment. When using the developed questionnaire to assess a level of parental compliance, it was found that in the examined patients only in 31 (30.1 ± 4.5 %) families, the parents were compliant with the anti-HP therapy

**Table 2.** Assessment of the initial level of parental competence in the groups of patients.

Level of parental compliance	Group 1 (n = 40) abs. (% ± m%)	Group 2 (n = 40) abs. (% ± m%)	p-Fisher level
non-compliance	14 (35.0 ± 7.5 %)	13 (32.5 ± 7.4 %)	> 0.05
partial compliance	14 (35.0 ± 7.5 %)	14 (35.0 ± 7.5 %)	> 0.05
compliance	12 (30.0 ± 7.2 %)	13 (32.5 ± 7.4 %)	> 0.05

**Table 3.** Assessment of parental competence level in the groups of patients during the control physician visit.

Level of parental compliance	Group 1 (n = 40) abs. (% ± m%)	Group 2 (n = 40) abs. (% ± m%)	p-Fisher level
non-compliance	13 (32.5 ± 7.4 %)	2 (5.0 ± 3.4 %)	< 0.05
partial compliance	15 (37.5 ± 7.7 %)	8 (20.0 ± 6.3 %)	> 0.05
compliance	12 (30.0 ± 7.2 %)	30 (75.0 ± 6.8 %)	< 0.001

used in the treatment of their children. In these families, strict adherence to the regimen of drugs prescribed by a specialist to eradicate HP infection was observed. A decrease in parental compliance was observed in more than 2/3 of the surveyed families. Thus, in 34 (33.0 ± 4.6 %) cases, there was partial compliance of parents with the treatment received by their child, and in 38 (36.9 ± 4.8 %) – parents were non-compliant.

It was found that in 48 (46.6 ± 4.9 %) families of the children suffering from CGDP, the parents would forget about the drug taking schedule of the children. In some families, the parents tended to have their children skip drug taking in case of the child's negative reaction – 44 (42.7 ± 4.9 %) families, or if the patient got unwell after the previous drug-taking – 42 (40.8 ± 4.8 %) families. In 32 (31.1 ± 4.6 %) cases, the parents admitted their negligence as to the drug taking schedule. There was also an earlier completion of the anti-HP treatment after the general condition of the patient had improved – 15 (14.6 ± 3.5 %) cases. In 20 (19.4 ± 3.9 %) families, the parents could, without prior consultation with the attending physician, replace one or more components of the drug regimen with a medicine which they viewed as "more effective", or reduce the dose of the antibiotic.

The results obtained at the first stage of the study indicate that in most cases the parents do not strictly comply with the prescriptions of the attending physician in relation to the eradication therapy. This actually prevents the patient from receiving a full course of therapy, which can subsequently affect the effectiveness of HP eradication. So it is necessary to find ways to increase parental compliance in relation to their children's therapy. In the conditions of heavily loaded doctors of polyclinics and hospitals, the work of the pharmacist may be an effective way to increase parental compliance.

At the second stage of the study, the effectiveness of the measures developed for this study – in tandem "doctor-pharmacist" to increase the level of parental compliance in order to improve the effectiveness of the treatment of children suffering from peptic ulcer disease (eradication of HP, relief of the main clinical symptoms).

It was found that the initial level of parental compliance in the comparison groups had no statistically significant differences ( $p > 0.05$ ) (Table 2).

After a two-week course of anti-HP therapy, the impact of the "compliance training" on the increased adherence of the parents of the children suffering from HP-associated CGDP was analyzed. The level of significance of differences in the distribution of parental compliance in the families of the examined patients was statistically significant –  $p < 0.001$  (Table 3).

In group 2, the patients whose parents were compliant with their children's course of eradication therapy prevailed – 30 (75.0 ± 6.8 %). In group 1, the level of parental compliance did not have a statistically significant ( $p > 0.05$ ) difference from the baseline. This positive dynamics of compliance in patients of group 2 seems to result from the "compliance training" conducted with the parents of the patients of this group before the start of the anti-HP therapy.

When studying the effectiveness of HP infection eradication, statistically significant differences in this indicator were established between the comparison groups ( $p < 0.001$ ). In the patients of group 1, HP eradication was achieved in 47.5 % of cases. In the patients of group 2, eradication of HP was achieved in 87.5 % cases ( $p < 0.001$ ).

There were significant differences between the effects of parental compliance on the effectiveness of HP infection eradication among the patients of both groups ( $p < 0.001$ ). The most effective eradication of HP infection was observed among the patients whose parents were committed to the treatment (42 children in both groups) – 95.2 % (95% CI 86.5 % – 99.6 %), which exceeds the minimum permissible level of eradication of 80–90 % when applying anti-HP regimens recommended by The International and National Guidelines. At the same time, this level of eradication was statistically significantly higher ( $p < 0.001$ ) relative to that in the patients with partial parental compliance (23 children in both groups) – 56.5 % (95% CI 35.1 % – 6.7 %), and the children with non-compliant parents (23 children in both groups) – 6.7 % (95% CI 0.0 % – 26.3 %),  $p = 0.002$ .

The results indicate that strict parental control over the prescriptions of the attending physician in relation to their child's therapy allows for a high level of HP eradication without the use of aggressive eradication schemes.

Further, the dynamics of clinical syndromes of CGDP (pain and dyspeptic syndromes) was studied in the comparison groups.

Among the patients of group 1, against the background of the anti-HP therapy course, 37.5% (95% CI 22.9% – 53.4%) of patients complained of the abdominal pain. In group 2, these complaints were detected during a control physician visit in 17.5% (95% CI 7.2% – 31.1%) children.

When studying the dynamics of dyspeptic syndrome against the background of the treatment, it was found that dyspeptic syndrome persisted in 35.0% (95% CI 20.8% – 50.8%) of the patients of group 1 at the control physician visit. These complaints were detected during a control visit in 10.0% (95% CI 2.6% – 21.5%) of the patients of group 2. The difference in indicators is at the level of  $p = 0.05$ .

The obtained results indicate that parents' strict adherence to the prescribed therapy regimen for their children makes it possible, against the background of effective eradication of HP, to achieve relief of the main clinical syndromes of the disease in a shorter time.

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## Conclusions

Thus, it was found that the level of parental compliance to anti-HP therapy for their children is insufficient. In most cases, parents do not fully comply with the prescribed treatment regimen, which is the reason for the incomplete course of eradication therapy recommended by the attending physician. In turn, conducting a “compliance training” in the tandem of “doctor – pharmacist” before starting the therapy is an important factor in increasing the level of parental compliance in patients with CGDP, which is reflected in increasing the effectiveness of the treatment. Strict adherence to the regimen and duration of administration of the prescribed drugs in children with ulcer disease allows achieving a high level of HP eradication even when using the traditional anti-HP regimen.

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