ORIGINAL PAPER

Clinical-Therapeutic Correlations in Patients with Iron Deficiency and Helicobacter Pylori Infection

Decebal POPESCU[1], Dan ANDRONESCU[2], Petru Aurel BABES[3]

Abstract

Helicobacter pylori (H.pylori) infection is among the most common infections found in the human population. It is acquired during childhood and persists whole life if not treated. It is commonly found in the elderly, disadvantaged persons, people in general with poor socio-economic status. H.pylori infection may associate iron deficiency due to defective iron take-over from the diet. The objective of this study, on the causal relationship between H.pylori infection and iron deficiency with/without anaemia, was the evaluation of haematological parameters (haemoglobin, haematocrit, mean corpuscular volume, sideraemia, ferritin) in patients diagnosed with active H.pylori infection and iron deficiency. Out of 681 patients admitted during a period of 5 years in the Focşani Military Hospital with active H.pylori infection, 9.4% (64 patients) presented iron deficiency with/without anaemia, as a cause of H.pylori infection. Of these, 12 patients (18.75%) have normalized their hematological parameters 3 months after triple therapy. Another 25 patients (39.07%) with iron supplements associated, responded favorably to 6 months, more pronounced than the control group of 27 patients (42.18%) who received only iron preparations without triple therapy. The study highlights the need to investigate H.pylori infection in patients with iron deficiency with/without anemia. In this situation, eradication therapy is required.

Keywords: helicobacter pylori, iron deficiency, blood count, ferritin, gastric atrophy.

Rezumat

Infecția cu Helicobacter pylori (H.pylori) este printre cele mai frecvente infecții întâlnite la populația umană. Aceasta este dobândită în timpul copilăriei și persistă toată viața dacă nu este tratată. Este frecvent întâlnită la vârstnici, persoane defavorizate, în general cu stare socio-economică precară. Infecția cu H.pylori poate asocia deficit de fier din cauza preluării defectuoase a fierului din alimentație. Obiectivul acestui studiu, privind relația de cauzalitate dintre infecția H.pylori și deficitul de fier cu/fără anemie, a fost evaluarea parametrilor hematologici (hemoglobină, hematocrit, volum eritrocitar mediu, sideremie, feritină) la pacienții diagnosticați cu infecție activă H.pylori și deficit de fier. Din 681 pacienți internați într-o perioadă de 5 ani în Spitalul Militar Focșani cu infecție activă H.pylori, 9,4% (64 de pacienți) au prezentat carență de fier cu/fără anemie, considerându-se drept cauză infecția H.pylori. Din aceștia, 12 pacienți (18,75%) și-au normalizat parametrii hematologici la 3 luni după tripla terapie. Alți 25 de pacienți (39,07%), la care s-au asociat suplimente de fier, au răspuns favorabil la 6 luni, mai pronunțat decât lotul martor de 27 de pacienți (42,18%) care au primit doar preparate de fier fără triplă terapie. Studiul reliefează necesitatea investigării H.pylori la pacienții cu carență de fier cu/fără anemie. În această situație este necesară terapia de eradicare.

Cuvinte cheie: helicobacter pylori, deficit de fier, hemogramă, feritină, atrofie gastrică.

[1] Department of Internal Medicine, Emergency Military Hospital, Focsani, Romania
[2] „Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
[3] Faculty of Medicine and Pharmacy, University of Oradea, Romania

Corresponding author:
Decebal POPESCU, Department of Internal Medicine, Emergency Military Hospital, 3-5 Cezar Bolliac Street, Focsani, Romania.
E-mail: popescudecebal7@yahoo.com

INTRODUCTION

Helicobacter pylori is a spiral bacterium, gram negative, microaerobics, flagellated, with increased motility, causing one of the most common infections in humans[1,2].

Infection is acquired during childhood and persists for life if not treated.

The major risk factor for infection is the family socio-economic state[1].

Although it has decreased in frequency, the infection still remains high in the elders, disadvantaged people, immigrants and citizens of the african race[1,3,5].

Most of the infected people develop chronic active gastritis. The bacterium is located in the antrum and/or the entire stomach. In those with antrum location, the secretion of hydrochloric acid is preserved or increased, in which case the evolution is toward the duodenal ulcer or esophagitis secondary to gastro-oesophageal reflux[5].

In people with pangastric damage, gastric atrophy is produced and acid secretion decreases. These people develop hypo/achlorhydria and even vitamin B12 deficiency. In advanced cases, the chronic infection produces intestinal metaplasia and gastric adenocarcinoma[5].

H.pylori infection is associated with iron deficiency due to an iron disturbed take-over from the diet. Concomitantly, this infection can favor the loss of iron through gastritis, peptic ulcerous disease[5].

A diet that provides iron sources contains: red meat, chicken, fish. It contains hemic iron.

The sources of non-hemic iron are: green vegetables, lentils, beans, pods. A normal diet should contain 5 mg of iron at a 1000 calories intake. Following the intake of dietary iron, 10-20% hemic and nonhemic iron is absorbed daily and 1 mg of iron is lost through the intestinal mucosa in the same time frame[4].

We recall that iron is an essential component of the hemoglobin molecule and is also necessary for the synthesis of DNA and cellular transport.

The objective of this study on the causal relationship between H.pylori infection and iron deficiency with or without anaemia was to assess certain biological parameters (blood count, iron and ferritin) in patients with active H.pylori infection and iron deficiency, patients monitored and treated with triple therapy as shown below.

MATERIALS AND METHODS

In the study conducted between June 2014-August 2019, 93 patients were enrolled with H.pylori infection and iron deficiency with/without anemia. They were selected from a larger group of 942 patients, over 18 years, with H.pylori antibodies in serum, determined using rapid immunochromatographic qualitative tests (Helicobacter P Antibody Test Artron). All 942 positive serological patients have been tested for H.pylori antigen in stool using rapid immunochromatographic tests (Laboquick Helicobacter Pylori Antigen Test) to highlight active infection. Following this step, 681 patients remain confirmed with H.pylori antigen in stool, 72.3% respectively of the 942 patients with anti-antibody H.pylori.

Out of all patients with active infection, 93 patients had iron deficiency with/without anemia have resulted, highlighted by hemoglobin (Hb) between 8.1-13.01 g / dL in 59 patients with anemia, while 34 of them were only in a deficit of iron without anemia, with iron between 19-49 mg/dL and ferritin between 24-50 μg/L.

These 93 patients with iron deficiency with/without anemia have been asymptomatic or showed symptoms and clinical signs encountered in most anemia (headache, fatigability, asthenia, dyspnoea exertional, palpitation, pallid skin and mucous membranes, angular stomatitis, glossitis, burns of the tongue, dysphagia , trophic hair disorders)[4].

Patients with Hb ≤ 8g/ dL were excluded from the study. The 93 patients with iron deficiency with/without anemia have benefited from gastroscopy and rapid endoscopic test of urease has been carried out from two fragments of the gastric mucosa (the antrum and the stomach body).

All 93 patients have been matched between a positive endoscopic test of urease, the presence of H.pylori antigen in stool and H.pylori antibodies in serum.

We have followed five parameters for the patients being analyzed: hemoglobin, hematocrit, mean corpuscular volume, iron and ferritin which were decisive for statistical analysis. These parameters have been evaluated at enrolling, 3 months and 6 months after the triple therapy.

The peripheral blood smear highlighted anisocytoses, poikilocytosis and the presence of anulocytes. in many situations.

After gastroscopies and colonoscopies, 29 patients with specific conditions for installation of iron de-

ficiency were excluded (proliferative processes of the gastrointestinal tract, gastro-duodenal ulceration, drug injuries, celiac disease, etc)

In this way, 64 patients remained in the study; of these, 37 patients have been treated with triple H.pylori eradication therapy and/or iron supplements, constituting the study group, and the remaining 27 patients, which didn't take the triple therapy for various reasons, it constituted the control group.

The triple therapy used was chosen and represented by the following classes of drugs depending on the tolerance, the adhesion, resistance or adverse effects of antibiotics which have required switching treatment schedule: proton pump inhibitors (pantoprazole/esomeprazole), penicillins/fluroquinolone (amoxicillin/levofloxacin), macrolide/nitroimidazole (clarithromycin/metronidazole), for a period of 10-14 days.

Of the 37 patients who received the triple therapy, 12 patients have responded spectacularly to the treatment administered, without the need for iron supplements. The remaining 25 patients, non-responders at 3 months after treatment, they subsequently required iron therapy.

Table 1 shows average and standard deviations for haematological parameters in the lot that required the triple therapy and iron supplements compared to the control group, and the statistical equities and differences between the stated lots are expressed by Fisher tests, whose results are given in Table 2.

Table 1. The mean and standard deviations for haematological parameters

	Treatment for H.pylori	Sample volume	Mean	Standard deviation
Initial Hb	N	27	10.7748	1.68943
	Y	25	11.2552	2.06970
Hb after_treatment	N	27	13.0344	1.25648
	Y	25	13.5828	1.24544
Initial HCT	N	27	32.0278	4.94827
	Y	25	34.3676	5.24135
HCT after_treatment	N	27	38.0752	3.90122
	Y	25	42.3144	3.22162
Initial MCV	N	27	74.9226	6.10605
	Y	25	73.2416	10.25211
MCV after_treatment	N	27	84.3385	4.15527
	Y	25	89.0760	5.69958
Initial iron	N	27	41.519	10.1919
	Y	25	29.680	11.2906
Iron after_treatment	N	27	97.852	22.7912
	Y	25	107.200	17.7294
Initial ferritin	N	27	33.852	12.8024
	Y	25	32.920	9.3716
Ferritin after_treatment	N	27	123.667	33.0908
	Y	25	140.720	34.7797

N-no; Y-yes; Hb-hemoglobin; HCT-haematocrit; MCV- mean corpuscular volume

Table 1. Statistical analysis of haematological parameters (Fisher tests) before and after treatment

		Sum of square	df	F	p-value
Initial Hb	Between groups	2.996	1	.846	.362
	In groups	177.016	50		
	Total	180.011	51		
Hb after_treatment	Between groups	3.903	1	2.493	.121
	In groups	78.274	50		
	Total	82.177	51		
Initial HCT	Between groups	71.067	1	2.742	.104
	In groups	1295.943	50		
	Total	1367.010	51		
HCT after_treatment	Between groups	233.277	1	18.089	.000
	In groups	644.799	50		
	Total	878.076	51		
Initial MCV	Between groups	36.680	1	.525	.472
	In groups	3491.920	50		
	Total	3528.601	51		
MCV after_treatment	Between groups	291.337	1	11.857	.001
	In groups	1228.569	50		
	Total	1519.906	51		
Initial iron	Between groups	1819.262	1	15.792	.000
	In groups	5760.181	50		
	Total	7579.442	51		
Iron after_treatment	Between groups	1134.362	1	2.695	.107
	In groups	21049.407	50		
	Total	22183.769	51		
Initial ferritin	Between groups	11.272	1	.088	.767
	In groups	6369.247	50		
	Total	6380.519	51		
Ferritin after_treatment	Between groups	3775.018	1	3.283	.076
	In groups	57501.040	50		
	Total	61276.058	51		

Hb-hemoglobin; HCT-haematocrit; MCV- mean corpuscular volume

Starting from the fact that the null hypothesis is associated with equality between the averages, and the alternative hypothesis, with statistically significant differences between the averages, applying the Fisher tests gives us the following results:

- initially, in the case of the indicators Hb, HCT, MCV and ferritin at the level of the two lots, there are no statistically significant differences between their averages level (p-value is greater than 0,05);
- for the iron indicator, there are significant statistical differences at admission in the the averages of the two lots (p-value = 0.000) in the sense that the patients in the study group have a lower average of the iron indicator lower than that in the control lot (29.68 μg/ dL for those in the study group compared 41.519 mg/dL for those in the control group, as shown in Table 1;
- according to the Fisher tests, at 3 months of treatment with iron medication, the level of statistical significance shows us statistically significant differences for the mean levels of HCT, MCV and ferritin, well highlighted in Table 3.

Table 1. Mean level of HCT, MCV and ferritin at 3 months of treatment

Treatment for H.pylori	HCT %	MCV fl	Ferritin µg/L
Y	42.3144	89.0760	140.720
N	38.0752	84.3385	123.667

N-no; Y-yes; HCT-haematocrit; MCV- mean corpuscular volume

We can notice that the patients with H.pylori infection and iron deficiency with/without anemia who have received both classes of medication, have shown better results in hematological indicators (HCT, MCV and ferritin), and in the case of iron, if initially there were significant differences between the means of the two lots, at the end of the 3 month period, they are no longer detected.

It can therefore be stated that the treatment of H. pylori has a beneficial effect on iron by associating iron preparations to the eradication treatment.

In the case of Hb, we did not find any differences of statistical significance between the mean of the study and control lot, neither in enrollment, nor in the application treatment.

Statistical analysis indicates that H.pylori therapy associated with the treatment for iron deficiency, provides better results in HCT, MCV,ferritin and iron remediation.

RESULTS

After exclusion of patients with iron deficiency with/without anemia for other reason than H.pylori infection, 64 patients have remained in the study and have been divide into two lots:

- research group (37 patients) who received anti-H. pylori treatment;
- control group (27 patients) without anti-H.pylori therapy.

From the point of view of pathology, within the research group, 21 patients (57%) showed iron deficit anemia with a Hb average of 10,65 g/dL and 16 patients (43%) showed only iron deficiency, the iron average being 37,44 µg/dl. In 12 patients out of the 37 we have seen a normalization of hematological parameters at 3 months since the triple therapy, while the remaining 25 patients needed iron preparations.

After triple therapy treatment against H.pylori, we can conclude that out of the 37 patients in the study group, 12 patients showed the normalization of hematological parameters at both 3 months and 6 months, in the remaining 25 patients a normalization of hematological parameters is made only after the addition, at 3 months after the eradication treatment, of iron medication with normalization of the hematological constants mentioned at 6 months.

DISCUSSION

Of the 681 patients H.pylori positive studied, about 6% had iron deficiency with/without anemia by H.pylori infection.

After the distribution of the number of positive H. pylori patients included in the study according to the Hb value, the largest share was presented by patients with moderate anemia (Hb between 10-11 g/dL and HCT between 32.1 and 34%).

In approximately 32% of the patients included in the study, we witnessed the normalization of hematological parameters at 3 months after the triple eradication therapy without the association of iron preparations; the remaining 68% required the addition of iron preparations.

The triple therapy used more classes of medication that were chosen according to tolerance, adhesion, resistance and adverse effects. Proton pump inhibitors (pantoprazole/esomeprazole), penicillins/fluroquinolone (amoxicillin/levofloxacin), macrolide/nitroimidazole (clarithromycin/metronidazole) have been used, for a period of 10-14 days.

Control of H.pylori eradication was checked 5-6 weeks after the end of the treatment by the absence of fecal H.pylori antigen, and the following hematological parameters were evaluated at 3 and 6 months: Hb, HCT, MCV, iron and ferritin.

The response of these parameters to the eradication of H.pylori without the addition of iron preparations has been evaluated both 3 and 6 months after the successful completion of the anti H.pylori therapy.

Therefore:

- out of the 37 patients in the research lot treated with the triple therapy, 12 patients (32%) responded to the medication, with hematological parameters normalized at 3 months;
- 25 patients (68%) without favorable results at 3 months, normalized their hematological parame-

ters 3 months later associating therapy with iron preparations.

This lot was compared to the 27 patients H.pylori positive and iron deficiency with/without anemia which for various reasons did not receive the triple therapy and which constitutes the control group.

The results highlight the role of H.pylori infection in the etiology of the iron deficiency anemia as well as in iron deficiency without anemia in which other etiological causes have been eliminated.

The eradication of H.pylori in patients with iron deficiency with/without anemia, which was also associated with iron supplements, led to an even better response compared to those who did not receive eradication therapy.

CONCLUSIONS

- **the causal role of the H.pylori infection**; out of the 681 patients admitted between June 2014 and August 2019 at the Focsani Military Hospital with active H.pylori infection, 9,4% (64 patients) showed iron deficiency with/without anemia, as the cause of H.pylori infection;
- **H.pylori eradication effect**; the 9,4% of patients were divided into 3 sublots:
- **18,75%** (12 patients) in which the triple therapy had favorable effects on the studied parameters (Hb, HCT, MCV, iron and ferritin) 3 months after the start of treatment;
- **39,07%** (25 patients) with iron supplements also associated, with a favorable response at 6 months more intense than those in the third sub-lot of 27 patients (42,18%) who only received iron preparations without anti H.pylori treatment;
- **the need to investigate for H.pylori infection of those with iron deficiency with/without anemia**; if an infection is active, patients must receive eradication therapy associated with iron preparations or not.

Compliance with ethics requirements: The authors declare no conflict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.

References

1. Sleisenger and Fordtran's. (2010) Gastrointestinal and Liver Disease. Pathophysiology/Diagnosis/Management Ninth Edition: 833-835
2. Antonietta Gerarda Gravina, Rocco Maurizio Zagari, Cristiana De Musis, Lorenzo Romano, Carmelina Loguercio and Marco Romano. (2018) Helicobacter pylori and extragastric diseases: A review. World J Gastroenterol. 24(29): 3204–3221. doi: 10.3748/wjg.v24.i29.3204
3. Barbara Braden. (2012) Diagnosis of Helicobacter pylori infection. BMJ . 344 doi: https://doi.org/10.1136/bmj.e828
4. Patrick C. Alguire Hematology and Oncology ACP / MKSAP 18, available until July 31, 2021: 19-21, 31-32.
5. Canan Avunduk. (2008) Manual of Gastroenterology: Diagnosis and Therapy. Lippincott Williams & Wilkins Fourth edition.: 169-172