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The Importance of Helicobacter Pylori in The Development of Iron Deficiency Anemia

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Abstract

The review article is devoted to the analysis of scientific and literary data published over the past 10 years on the problem of studying the role of Helicobacter Pylori in the development of iron deficiency anemia. Comparative data from domestic and foreign scientists on the mechanism of action of Helicobacter Pylori (HP) and the pathogenesis of resistant iron deficiency anemia are given. It has been determined that the development of iron deficiency anemia and HP infection is influenced by many mechanisms; therefore, in the treatment of this pathology, the prescription of anti-HP bacterial therapy with ferrotherapy, taking into account age characteristics and needs, is justified.

Keywords: *Iron Deficiency Anemia; Helicobacter Pylori; Chronic Gastroduodenal Pathology*

1. Introduction

The problem of diagnosing and timely initiation of treatment for iron deficiency anemia (IDA) has been and remains one of the pressing problems of modern medicine, and there is a lot of modern literature data on this topic. According to WHO (2013), IDA affects 500–600 million people worldwide and represents a major health problem, especially in developing countries [1]. One of the factors in the development of IDA is malnutrition, therefore, the bioavailability of dietary iron, as well as a high rate of chronic gastrointestinal diseases [2].

There is a lot of literature data linking the development of IDA with Helicobacter pylori (HP) infection of patients. By itself, the average prevalence of Helicobacter pylori worldwide is approximately 50%, with the highest detection rates in developing countries (80–90%) and lower in Western Europe (30–50%), North America (30–40%). %) and Australia (20%) [3]. Thus, according to R. A. Faizullina et al. (2014), the prevalence of HP infection with chronic gastroduodenal pathology (CGDP) in Kazan was in the confidence interval of 73.6% - 94.2% ($P<0.05$) , and in patients with CGD – 66% – 95% ($P<0.05$), which indicates a high prevalence of HP infection [6].

At the same time, as noted by D.V. Pechkurov and A.A. Romanova (2017), the peak of the clinical manifestation of HP infection comes in adolescence, when deep neuropsychic and endocrine-humoral changes are noted, causing the morphofunctional transformation of organs and systems, imposing increased adaptive demands on the adolescent's body [7].

However, there are a number of extragastric diseases associated with this pathogen, including several hematological diseases such as iron deficiency anemia (IDA), immune thrombocytopenia, and vitamin B12 deficiency [13, 14]. A wealth of evidence in the literature supports these associations, sufficient for them to be recognized in the latest Maastricht V/Florence European Study Group consensus report [15]. Thus, according to Sarah Cherian et al., (2008), HP infection can cause IDA in 81.8% of infected people [16]. As noted by Pacifico L et all. (2014), the clinical manifestation of HP infection in the form of Helicobacteriosis is a serious chronic infection associated with a diverse range of extragastric disorders, including iron deficiency anemia, chronic idiopathic thrombocytopenic purpura, growth retardation and diabetes mellitus [17]. The pathogenic mechanisms underlying the association between Helicobacter pylori and these hematological disorders are not clearly defined, but a number of studies have shown that good hematological responses are achieved after eradication therapy, confirming the central role of the bacterium in this process [15, 18]. In particular, N.V. Butorina et al. (2015) examined 156 children aged 9 to 17 years with gastroesophageal reflux disease, who underwent eradication

therapy. The effectiveness of treatment was assessed based on clinical data and the results of endoscopic examination with pH measurements, and it was concluded that anti-Helicobacter therapy has a more significant effect on the dynamics of clinical manifestations and especially endoscopic signs of esophageal damage [19].

And the logical opinion is supported by R. A. Fayzullina (2010), in her previous article [20], pointing out that Helicobacter pylori requires iron in order to maintain its existence, and H. pylori-positive patients have lower serum ferritin and iron levels compared with H. pylori-negative patients. Moreover, in patients with atrophic gastritis associated with HP infection, these indicators of the level of "iron" status were the lowest.

According to G. Sh. Isaeva and R. I. Valieva (2018), When cultivating H. pylori in vitro, this microorganism is very fastidious, requiring the presence of additional factors (vitamins, microelements) that enhance the growth of this microorganism, and a mandatory component of the medium is the addition of 510% blood. That is, for the growth of a microorganism, the presence of iron in red blood cells is important. The authors also point to the important role of an iron uptake regulator in H. pylori colonization, which regulates ion homeostasis, the oxidative response, and the flagellar mechanism. A number of other authors express a similar opinion [11].

There is an assumption by some authors [18] that the development of IDA in HP is associated with the high absorption of nutritional iron by HP bacteria, which use it as a growth factor. Another assumption is that the mechanism of development of IDA in helicobacteriosis involves sequestration of lactoferrin in the infected CO, especially in the cardiac and pyloric region, and neutrophils within the surface epithelium [18].

R. A. Faizullina (2010), pointing out that Helicobacter pylori is a virulent agent that absorbs and uses a significant amount of iron for its vital activity, like other gram-negative bacteria, enter into complex competitive relationships for iron. For this, a siderophore of the phenolate or hydroxomate type synthesized by it is used, which is subsequently combined with ferrate of siderophiles, followed by extraction of iron from the cell surface. Direct lysis of cells is possible under the influence of urease and mucinase produced by NR with the extraction of iron from the macroorganism (human), digestion of hemoglobin and assimilation (assimilation) of heme with the formation of siderophores, allowing the extraction of iron from the macroorganism [20].

One of the possible explanations for the connection between the causes of IDA development in HP and infection is the loss of iron during bleeding from the gastrointestinal tract. However, several case reports and case series have been described in which no bleeding lesions were found during endoscopy with IDA due to HP gastritis. Testing for fecal occult blood was negative, and anti-HP treatment was associated with resolution of IDA [19].

In studies by El Demerdash DM et al., (2018), which were conducted among children with HP associated IDA, no signs of bleeding from the gastric and duodenal mucosa were observed, and a fecal occult blood test was negative [20]. Another version of the relationship between HP and IDA is the development of HP gastritis, which leads to impaired secretion of gastric acid and absorption of nutritional iron [17]. Changes in iron valency directly depend on hydrochloric acid and pH of gastric juice [12]. These results suggest that decreased acid secretion was a consequence of HP infection, with subsequent inflammation of the mucus and deterioration of acid secretion function. A number of studies have determined a direct correlation between HP and a decrease in the secretion of hydrochloric acid (hypochlorhydria pH>4), against the background of a significant decrease in the amount of serological iron and transferrin saturation [3]. Considering that these children did not have atrophy of the gastric mucosa, it is possible that HP could cause hypochlorhydria through an increase in gastric interleukin (IL)-1β and tumor necrosis factor (TNF)-α, which inhibit acid secretion, causing parietal cell apoptosis [4].

Tsay FW, Hsu PI., (2018), there are several mechanisms of connection between Helicobacter pylori and IDA. First, increased iron loss may be associated with hemorrhagic gastritis, peptic ulcers and gastric adenocarcinoma. Secondly, Helicobacter pylori CagA is involved in obtaining iron from interstitial holotransferrin, and the uptake of iron by Helicobacter pylori is enhanced by bacterial growth. Third, antral gastritis caused by Helicobacter pylori may reduce acid secretion due to gland atrophy and lead to decreased absorption of dietary iron [2]. At the same time, according to Camacho-Gomez SM. et al., (2018), with HP infection against the background of gastric intestinal metaplasia (GIM), the clinical picture of IDA is detected. However, the association of GIM and adenoma/dysplasia and carcinoma is rarely observed, primarily because the time required for their development takes a person into adulthood [4].

To summarize the above data, we can note several hypotheses for the pathogenesis of the development of IDA during HP infection, which was more specifically described by S. Yu. Tereshchenko and I. A. Olkhovsky (2014), [12]: Enhanced uptake of free iron by Helicobacter pylori (nutritional), as well as in the form of lactoferrin, with the subsequent "sequestration" of iron and its enhanced removal from the circulation due to the rapid reproduction and renewal of the intragastric HP pool. This condition contributes to an imbalance between iron supply and the need for it;

HP-mediated change in the synthesis of hepcidin (a protein that plays a leading role in the mechanisms of iron absorption) in hepatocytes;

Competitive binding of iron, ascorbic acid and other vitamins by Helicobacter pylori as necessary bacterial growth factors;

Due to an increase in intragastric pH during helicobacteriosis, inflammation of the duodenal mucosa and stomach develops with the development of iron malabsorption;

Anemia associated with poorly diagnosed micro-losses of blood through the gastrointestinal tract.

Redistribution anemia of chronic inflammation associated with activation of liver and spleen macrophages.

An early study examining the effectiveness of ferrotherapy for HP infection in a randomized controlled trial using placebo was conducted among 43 Korean children and adolescents with IDA who had previously undergone gastroduodenal endoscopy, confirming CGDP. In a study conducted over 8 weeks, at the end of the first two weeks of HP treatment, a significant increase in hemoglobin was noted in relation to children who received only ferrotherapy. Similar results were obtained in alternative studies [15]. In particular, Franceschi F et al., (2019), in their article, refer to data that shows the results of a study of 105 patients with IDA and 70 controls matched by age and gender, where a high rate of HP infection was diagnosed in patients with refractory IDA (61.5%) with a positive correlation with the mean corpuscular value (MCV; P=0.046). In addition, they observed a significant correlation between the administration of eradication therapy and ferrotherapy, followed by an increase in hemoglobin (P<0.001), MCV (P<0.001), serum iron (P<0.001) and ferritin levels (P<0.001), [16].

A double-blind randomized study performed by Cardenas VM et al., (2011), in El Paso, Texas, showed that after anti-HP therapy there was a threefold increase in serum iron (SF) relative to baseline and relative to patients who did not receive appropriate treatment [19].

At the same time, O.V. Magnitskaya et al. (2014), having studied the effectiveness of combined anti-HP therapy in 132 children from 2 to 16 years old (according to ESPGHAN/NASPGHAN, 2010), and adults (n=94, according to provisions of the IV Maastricht Agreement) living in Volgograd, noted the positive effect of this therapy on the clinical manifestation of IDA, as one of the forms of complications of HP infection [3].

s noted by S. Yu. Tereshchenko, I. A. Olkhovsky (2014), in accordance with the conciliation documentEuropean (ESPGHAN) and North American (NASPGHAN) associations of pediatric gastroenterologists, currently the indications for testing for HP infection with subsequent eradication are: 1) endoscopically confirmed gastric or duodenal ulcer; 2) iron deficiency anemia refractory to conventional treatment; and 3) having a close relative with gastric cancer. But the authors are of the opinion that the European and North American recommendations are intended for populations with a low prevalence of HP infection, which requires the development of local Russian diagnostic protocols [12]. This opinion is supported by other authors, pointing out the need for an integrated approach to the treatment of inflammatory diseases of the digestive tract, taking into account the mechanisms of pathology [13] and possible complications [14]. Consequently, the most obvious mechanism for the occurrence of IDA against the background of HP infection should be considered competition for dietary iron, and it is advisable to take this into account in the treatment of children.

4. Conclusion

Thus, many pathogenesis mechanisms are interconnected with the development of iron deficiency anemia against the background of HP infection; therefore, in the treatment of children with chronic gastroduodenal pathology, the prescription of anti-HP bacterial therapy alternating with ferrotherapy is justified.

References:

1.Allanazarov A.Kh. Tazhribada gene-modificationlangan mahsulotlarning immuno tizimi kўrsatkichlariga tasirini qiyosiy baholash usuli // Uslubiy tavsiyanom. - Bukhoro, 2021. - 23 b.

2. Zharmukhamedova T.Yu., Semushina S.G., Pakhomova I.A., Pimenov M.S., Murashov A.N. International rules for working with laboratory animals during preclinical testing // Toxicological Bulletin. - Moscow, 2011. - No. 4 (109). - P.2-9.
3. Konoplyannikov A.G. Cellular bases of human radiation effects // In the book: “Radiation Medicine. Volume 1. Theoretical Foundations of Radiation Medicine. Under total ed. L.A. Ilyin. - Moscow: Ed. AT, 2004. - S.189-277.
4. Mikheev A.N. Small doses of radiobiology. My little radiological faith. - Kyiv, Photosocial Center, 2016. - 371 p.
5. Nikolaeva A.A. Comparative analysis of the radioprotective properties of bee venom in relation to the blood system of rats // Bulletin of the Nizhny Novgorod University named after N.I. Lobachevsky. - 2011. - No. 6 (1). - P.149-153.
6. Nuraliev N.A., Bektimirov A.M-T., Alimova M.T., Suvonov K.Zh. Rules and methods of work with laboratory animals in experimental microbiological and immunological studies // Methodological guide. - Tashkent, 2016. - 34 p.
7. Polevshchikov A.V. Unsolved problems of modern immunology. Molecular and cellular bases of immunoregulation, immunodiagnostics and immunocorrection (experimental models) // Medical Immunology. - 2009. - Volume 11, No. 4-5. - P.330-331.
8. Terentiev A.A., Poryadin G.V., Salmasi Zh.M., Alexandrova I.A., Tagirova A.K., Moldogazieva N.T., Kazimirsky A.N. Increased apoptosis of CD95+-lymphocytes under the influence of a synthetic peptide from human alpha-fetoprotein (AFP14-20) // Modern science-intensive technologies. - 2005. - No. 10. - P. 66-68;Barabanova A., Baranov A., Bushmanov A., Guskova A. Radiation Effects in Man Selected clinical lectures. Eds.: K. Kotenko, A. Bushmanov. – M.: ОАО «Издательство «Медицина», 2008. - 158 с.
9.Ron E., Jacob P. Late health effects of ionizing radiation: bridging the experimental and epidemiologic divide // Radiat. Res. - 2010. - V. 174, №6. - P.789-792.
10.Kreuzer M., Auvinen A., Cardis E. Low dose ionizing radiation and cardiovascular diseases – Strategies for molecular epidemiological studies in Europe // Mutat. Res. - 2015. - V. 764. - P. 90-100.