

# Immune Response of Helicobacter pylori and disadvantages of antibiotic therapy

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## ABSTRACT

Helicobacter pylori (H. pylori) is a gram-negative bacterium which is closely related to many digestive diseases and only parasitic on gastric mucosa and its surface. In China, the infection rate of Hp is more than 60%, and only 20% of them are infected and seek medical treatment voluntarily. Therefore, Hp often lives in the stomach and other digestive organs of patients, becoming a direct cause of diseases such as chronic gastritis and duodenal ulcer[1]. As the treatment of Hp patients often contains a variety of antibiotics, the problem that resistant Hp is difficult to cure has become the focus of people's attention in recent years.

**Keywords:** *Helicobacter pylori is immune to escape antibiotics*

## 1. INTRODUCTION

Helicobacter pylori (H. pylori) is a gram-negative bacterium which is closely related to many digestive diseases and only parasitic on gastric mucosa and its surface. In China, the infection rate of Hp is more than 60%, and only 20% of them are infected and seek medical treatment voluntarily. Therefore, Hp often lives in the stomach and other digestive organs of patients, becoming a direct cause of diseases such as chronic gastritis and duodenal ulcer[1]. Whether patients show symptoms after infection and the severity of symptoms depend on a variety of factors, such as the subtype of bacteria and the strength of its virulence factors, so that different environments may affect the final outcome of patients infected with Hp, and most patients will have Hp for a lifetime without treatment[2].

As bacteria coexisting with the host for a long time, Hp can evade the surveillance and elimination of the human immune system in various forms. With the occurrence of infection, the immune response of the human body also starts one after another, but neither innate immunity nor adaptive immunity is sufficient to completely eliminate Hp. In addition, in the course of routine treatment, the repeated use of antibiotics has become one of the hidden dangers of fighting AGAINST Hp. [11]

## 2. INFECTION AND IMMUNE RESPONSE OF HP

### 2.1 Characterization of Hp infection

The confirmation of Hp infection is usually based on gastric mucosa samples of patients. If there are multiple types of white blood cells infiltrated in the patient's samples, such as neutrophils, eosinophils, macrophages, etc., it indicates that Hp is continuously infected. In addition, the levels of interleukin-1 and tumor necrosis factor  $\alpha$  that could be detected in the stomach of Hp patients were significantly higher than those of uninfected patients.

### 2.2 Adaptive immune response

T cell mediated immune response plays an important role in adaptive immune response. After Hp infection, dendritic cells in lymph nodes recognize and present antigen information to activate primitive T cells, which migrate to the site of Hp infection and play an immune role under the guidance of  $\alpha 4\beta 7$  integrin receptor.

Th1, Th2, Th17 and Treg are derived from the differentiation of primitive CD4+ helper T cells, among which Th1 and Th2 can produce different kinds of active cytokines and indirectly participate in the defense function against different types of infection by inducing the differentiation of B cells[3]. In addition, Treg has

been found to prevent severe immune disorders by inhibiting the production of T cell proliferation-related cytokines.

In the latest study, Hp was found to be able to increase Treg concentration and decrease Th17 concentration by changing the polarity of dendritic cells. Experimental results showed that Th17 response was significantly enhanced and Hp concentration decreased with Treg depletion. It was confirmed that the restriction function of Treg on T cells was a new mechanism evolved by Hp for colonization in human body [4].

### **3. MULTIPLE IMMUNE ESCAPES OF HP**

#### **3.1 Structural correlation escape of Hp**

Hp can change the structure of surface molecules such as LPS through self-modification to weaken the immunogenicity of PAMPs and thus escape recognition by PRRs. In addition, Hp also expresses Lewis antigens similar to human blood group antigens and lipid A, also known as endotoxin. Studies have shown that these endotoxins are 1,000 times weaker than normal gut bacteria such as *E. coli*. The low phosphorylation of Hp LPS was the main reason for the decrease of endotoxin immunogenicity [2].

#### **3.2 Regulation of Hp on innate immune cells**

Hp infection causes macrophages, lymphocytes, and neutrophils to gather at the site of infection, and Hp can interfere with the function of these innate immune cells in a variety of ways. For example, Hp can be directly induced by the Fas pathway, or by inducing macrophages to express arginase to promote apoptosis of macrophages, and limit the immune response of Th17.

### **4. COMMON METHODS FOR TREATING HP**

Triple therapy is often used as the primary treatment for Hp infection. The triple combination method is a combination of one PROTON pump inhibitor and two antibiotics for patients. The combination of proton pump inhibitor and antibiotics is selected based on the patient's previous treatment history. Patients took the drug orally twice a day for two weeks as a course of treatment. To test successful eradication of Hp, a <sup>13</sup>C-urea breath test is performed.

According to a traditional triple method eradication rate survey test, the eradication rate of Hp is closely related to gender, place of residence and other factors. From the perspective of gender, the eradication rate of Hp in male patients is 74.2%, while that in female patients is 61.0%. The risk of eradication failure in

female patients is 1.428 times higher than that in male patients. Women often use antibiotics to fight infection, which makes bacteria in their bodies resistant [5]. Resistance makes Hp difficult to kill when it is cleared by similar antibiotics.

### **5. STUDY ON VACCINE ASSOCIATED ANTIGEN OF HELICOBACTER PYLORI**

#### **5.1 Advantages of Helicobacter pylori vaccine**

In view of the high cost of routine treatment of *Helicobacter pylori* and the reduction of eradication rate, more effective measures are needed to deal with it. The research and development of related vaccines are responding to this need.

With the further study of Hp, many related antigens have been found, such as lipopolysaccharide (LPS), urease (Ure) and flagellin-led surface proteins.

At present, the research on Hp vaccine in China is at the leading level in the world, and the relevant research has carried out the phase III clinical trial in children aged 6-15 years. After the evaluation of the screened fusion protein vaccine, the general efficacy of the vaccine after one year of vaccination is 71.8% [6]. The results showed that the vaccine was both safe and effective and had immunogenicity.

#### **5.2 Categories of Helicobacter pylori associated antigens**

##### **5.2.1 Thallus surface antigen**

As a potential target for evaluating the risk of gastric cancer, the immunogenicity of flagellate filament polymeric protein FliD has attracted extensive attention. It was found that dual-antigen epitope vaccine constructed by FlaA could induce strong humoral immune response in human body and also mediate Th1 cell immunity.

##### **5.2.2 Bacterial extracorporeal membrane layer**

The outer membrane of bacteria is composed of phospholipid bilayer, lipoprotein (LPP) and lipopolysaccharide (LPS). Lpp20 expressed by *Lactococcus* as a vector has the ability to activate CD4+T cells and Th1 cells, indicating that it has certain immunogenicity and can be used in vaccine development.

##### **Holdings UreB**

UreB is a relatively conserved subunit of urease activity in Hp, resulting in a therapeutic strategy based on disruption of urease activity, and antigen fragments containing urease activity centers can themselves be good vaccine material.

### 5.3 Study on adhesive Hp1188 protein

A large number of clinical studies have found that Hp can adhere to gastric mucosa with the help of bacterial surface adhesive proteins, which is an important factor for long-term colonization of Hp in the stomach. This discovery opens up a new direction for Hp related vaccine research.

Adhesin Hp1188 protein is an important part of Hp adhesive protein, which is expressed on Hp surface in large quantities. It has adhesion ability and strong immunogenicity, which fits the relevant conditions of vaccine construction. In some studies, purified Hp1188 protein coated enzyme plate was used to detect clinical samples by ELISA method, and it was found that the coincidence rate of Hp1188 protein was 95.7%, the specificity was 94.3%, and the detection sensitivity was 93.8% [7]. Showed its effectiveness as Hp antigen.

## 6. HP EFFECT OF TREATMENT ON INTESTINAL FLORA

In the physiological state, the bacteria in the human intestinal tract are in a stable state of mutual checks and balances. If this stable state is changed, the infection of some opportunistic pathogens may be induced. Probiotics commonly found in the intestinal tract, such as Lactobacillus and bifidobacterium, can protect the liver, improve lactose digestion and prevent cardiovascular diseases. [8] And enterococcus, staphylococcus are opportunistic pathogens, severe infection can cause life-threatening meningitis, sepsis and so on. [9] According to relevant studies, after traditional Hp eradication treatment, the number of Lactobacillus and bifidobacteria in the patient decreased significantly compared with before treatment, while the number of enterococcus and staphylococcus increased significantly, suggesting that the patient had signs of intestinal flora disorder. [10] How to avoid the imbalance of flora caused by Hp treatment is an inevitable problem in future HP-related therapies

## 7. CURRENT SITUATION OF ANTIBIOTIC ABUSE AND PROSPECT OF HP TREATMENT

Microbial corresponding resistance to antibiotics is the inevitable result of the natural evolution, and human abuse of antibiotics greatly magnified by the process, accelerated the birth of the so-called "super bacteria", as the most populous country, and antibiotics consumption of our country, [11] judicious use of antibiotics is very necessary and related drugs, prevent the abuse of antibiotics.

The help of antibiotics for the treatment of Hp is reflected in the relatively mature triple antibiotic treatment method at present, while its disadvantages are

mainly reflected in the emergence of drug-resistant strains caused by the abuse of antibiotics in recent years, and the eradication rate of Hp has decreased significantly. [12]

With the introduction of amoxicillin, furazolidone, tetracycline and other antibiotics into the eradication treatment of Hp, the generation rate of drug-resistant strains is increasing day by day, but the emergence of drug-resistant bacteria not only causes the waste of medical resources, but also increases the burden of patients. [13]

Today, there is an urgent need for a highly viable non-antibiotic approach to the treatment of Hp [14]. In the future, with the rapid progress of the research on intestinal flora, there may be a new therapy that utilizes the inhibitory effect of intestinal flora to regulate the resident flora of patients with Chinese patent medicine and other drugs.

## 8. CONCLUSION

It is not easy to eradicate Hp in a modern society where antibiotics are overused. Under the guidance of the traditional triple method, we also need to study the infection mechanism of *Helicobacter pylori*, or pay attention to the regulatory role of other microorganisms in the intestinal environment on the human body. By doing so, different treatment methods and methods can be found. On this basis, we should also have confidence in the development of HP-related vaccines. I believe that in the near future, resistant Hp will no longer be a mountain to conquer.

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