

PROGRESS IN THE INVESTIGATION OF TRADITIONAL MEDICINE'S THERAPEUTIC EFFECTS ON HELICOBACTER PYLORI INFECTION

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Abstract: Helicobacter pylori infection is the main cause of gastric cancer, peptic ulcer, chronic gastritis, gastric mucosa-associated lymphoid tissue lymphoma and other diseases, and is related to some extra-gastrointestinal diseases such as iron deficiency anemia. Eradication therapy is the only effective way to cure Helicobacter pylori-related diseases, but the increase in drug resistance makes it increasingly difficult to eradicate Helicobacter pylori with chemical drugs and antibiotics. Finding active ingredients that inhibit and kill Helicobacter pylori from traditional medicine is an effective way to develop new Helicobacter pylori treatment drugs. This article reviews the current status of the application of traditional Chinese medicine, Tibetan medicine, Mongolian medicine, Yao medicine, Zhuang medicine and other traditional Chinese medicine methods in the treatment of Helicobacter pylori infection.

Keywords: Traditional medicine; Helicobacter pylori; Alternative therapy

1 TRADITIONAL CHINESE MEDICINE TREATMENT

Barry Marshall and Robin Warren of Australia first isolated Helicobacter pylori (Hp) in 1982 and found it to be the main pathogenic factor causing gastritis and peptic ulcer. For this great discovery, the two jointly won the Nobel Prize in Medicine in 2005 [1]. Later research findings confirmed that H. pylori infection is not only related to gastritis and peptic ulcer, but also the main cause of gastric cancer and gastric mucosa-associated lymphoid tissue lymphoma (MALT) [2]. It may also be related to unknown diseases. It is related to the occurrence of extra-gastrointestinal diseases such as iron deficiency anemia and immune thrombocytopenic purpura [3]. Therefore, how to successfully eradicate Helicobacter pylori has always attracted the attention of medical workers at home and abroad. However, with the growth of drug-resistant strains in recent years, eradication treatment of H. pylori has become increasingly difficult. Unconventional therapy (Unconventional therapy) for Hp eradication treatment, that is, alternative therapy (Alternative therapy) or phytotherapy (Medicinal therapy), has gradually attracted widespread attention at home and abroad [4-6]. Medical workers in many countries are trying and evaluating the direct application of plants to treat pyloric screw [4, 7, 8]. my country's traditional medicine is extensive and profound, with a development history of thousands of years. In order to discover new therapeutic drugs for Hp, it is also necessary to delve deeply into the treasure trove of traditional medicine and explore possible alternative treatment options. This article provides a relatively comprehensive summary of the current clinical application status of traditional Chinese medicine, Tibetan medicine, Mongolian medicine, Yao medicine, Zhuang medicine and serotherapy in the treatment of Hp infection.

Traditional Chinese medicine has appeared since primitive society and was basically formed during the Spring and Autumn Period and the Warring States Period. It has a history of thousands of years. Its main theoretical basis is the theory of Yin and Yang and the Five Elements [9]. Wang Xuwu et al. conducted an in vitro bacteriostatic test on 200 Chinese herbal medicines that may be anti-Hp, and found 38 Chinese medicines with varying degrees of Hp inhibitory effects. Among them, the four drugs with strong inhibitory effects are Huangfang, Coptis, rhubarb, Phellodendron, other traditional Chinese medicines with inhibitory effects include cassia twig, ground bark, rose flower, smilax, galangal, black plum, mountain orange, Magnolia officinalis, etc. [10]. Wang Hengqi et al. studied the in vitro anti-Hp activity of 10 kinds of Chinese herbal medicines and found that Angelica dahurica and gallnut have strong effects. Mulberry bark, Malan, madder, and gentian also have certain anti-Hp effects [11]. Xu Yi et al. conducted an in vitro study on the anti-Hp activity of 136 single Chinese herbal medicines and 11 Chinese medicine prescriptions [12] and found that Coptis chinensis has a strong inhibitory effect on Hp, and those with moderate inhibitory effects include Huangfang, rhubarb, Salvia miltiorrhiza, Wu Rongmeng, Xuanhu, Daqingye, Licorice, Diyu. Huangbai is one of the Chinese herbal medicines that is more sensitive to Hp in the research of Wang Xuwu and others, but it is only a low-sensitivity drug in the research of Xu Yi and others [10, 12]. This inconsistency in research conclusions is likely to be related to the different extraction methods of active ingredients of traditional Chinese medicine used in the trials. The former uses alcohol extracts prepared by biochemical methods, while the latter uses traditional Chinese herbal medicine boiling and concentration methods in research [10, 12]. Zhang Jinyan et al. used decoctions of Coptis chinensis and Huangfang to study the in vitro antibacterial activity of four bacteria, and also found that Coptis chinensis and Huangfang had strong inhibitory activity against Helicobacter pylori [13]. The active ingredient of coptis is mainly berberine, and an analysis of the clinical treatment of Hp infection using berberine combined with Western medicine triple antibiotic eradication

program found that berberine can indeed significantly improve the eradication rate of Hp and reduce the incidence of adverse reactions [14].

In addition, Yang Xingtang found that other single drug ingredients, such as licorice, also have good anti-Hp activity, and their effects are equivalent to clarithromycin [15]. The main inhibitory and killing effects come from the glycyrrhizic acid and licorice flavonoids in licorice, both of which show equal inhibitory and killing effects on Hp in vitro [15]. Gu Shengqing and others used the prescription Gancao Xiexin Decoction containing licorice combined with quadruple therapy of Western medicine (rabeprazole, colloidal pectin spade, amoxicillin, clarithromycin) to treat *Helicobacter pylori*-related gastric ulcer, and found that the combined treatment of Chinese and Western medicine can eradicate it. The rate (90.32%) is significantly better than Western medicine treatment alone (64.52%) [16, 17]. Studies in recent years have found that Tianjihuang extract and extracts, patchouli alcohol, mastic gum, *Heridium fermentum* fermentation broth, and bitter melon aqueous extract all have varying degrees of inhibitory effects on Hp in vitro. However, the actual eradication efficacy remains to be determined. A large number of clinical practices are used to further verify [18, 19].

Gastritis, peptic ulcer and other diseases caused by Hp infection are classified as "stomach pain" and "fullness" in traditional Chinese medicine. Traditional Chinese medicine prescriptions are mostly treated with drugs that reduce qi, stop vomiting, warm the middle and dispel cold. Traditional Chinese medicine prescriptions and patent medicines such as semi-Xia Xiexin Decoction, Qingyou Jianzhong Decoction, Sanhuang Xiexin Decoction, Sihuang Tiaowei Decoction, Jinghua Weikang Capsules, Morodan, etc. all have such effects [20-22]. Xu Yi et al. conducted anti-Hp tests on 11 commonly used traditional Chinese medicine prescriptions and found that Zuojin Pills had a strong inhibitory effect, while Xianglian Pills and Qingyou Yangwei Pills had a moderate inhibitory effect. There are many similar TCM syndrome differentiation prescriptions for the treatment of gastritis and gastric ulcer caused by Hp infection. When combined with antibiotics to treat Hp infection, they can increase the eradication rate of Hp infection with conventional antibiotics to varying degrees and reduce adverse reactions.

2 TIBETAN MEDICINE TREATMENT

The systematic theory of Tibetan medicine was formed approximately in the fifth century BC. Tibetan medicine is a traditional medicine with a long history in my country and has a relatively complete theoretical system. Different from traditional Chinese medicine, Tibetan medicine theory believes that "Long, Triba, and Bacon" are the three major elements that make up the human body, which is called the "three causes" theory. This is the theoretical core and foundation of Tibetan medicine [23]. According to Tibetan medicine theory, both gastritis and ulcer are "Bacon's disease". Clinical studies have confirmed that simple Tibetan medicine treatment is highly effective in improving symptoms and promoting recovery. Patients' subjective symptoms can be quickly relieved, and the eradication rate of *H. pylori* infection is also relatively ideal. For example, Huaerjiang uses a combination of Renqing Mangjue Pills, Eryiwei Hanshuishi Pills, Xia Sadesi Pills, and Erwuwei Datang Powder to treat *H. pylori*, with an eradication rate of 87.5% [24]. Suojinlan treats patients with pyloric screw-related peptic ulcer using Western medicine combined with Tibetan medicine (Renqing Changjue Pills, Zhituo Jiebai Pills, Twenty-one-flavored Hanshuishi Pills, Thirteen-flavored Muxiang Pills, and Fifteen-flavored Black Pills). and simple western medicine triple therapy (omeprazole, amoxicillin, tinidazole) for 2 weeks of treatment. It was found that the eradication rate of Hp in the treatment group with Western medicine alone was 82.1%, while the eradication rate of Hp in the treatment group with Tibetan medicine combined with Western medicine and antibiotics reached 93% [25]. It shows that the combined application of Tibetan medicine can significantly improve the eradication rate of Hp infection with Western medicine [25]. If Tibetan medicine theory can be properly combined with the patient's condition for syndrome differentiation analysis, and Tibetan medicine and Western medicine can be combined for treatment, the result will be twice the result with half the effort.

3 MONGOLIAN MEDICINE TREATMENT

Mongolian medicine was formed in the late tenth century AD. Its main theoretical basis is the "Three Roots Theory", which believes that the human body is composed of three roots, seven elements, and three impurities [26]. When the three roots and seven elements are out of balance, diseases will occur, and the process of treating diseases is the process of restoring the balance between them. Modern Mongolian medicine attributes *H. pylori* infection to the Badagan parasite that lives in the stomach. Wang Wuyue et al. used Mongolian medicines such as Chagan Urel, Alatan Arula, and Xihe Riebisi-6-flavored pills to clinically treat patients with *H. pylori* infective gastritis. The total clinical effective rate (94.0%) was significantly higher than The control group (82.0%) received triple therapy with Western medicine (omeprazole, amoxicillin, and erythromycin) [27]. Hu Wenhua et al. used the method of syndrome differentiation and treatment of Mongolian medicine to classify Hp infectious gastritis into Heyi type, Shila type, Badagan type, and Baoru type. They applied Ruda-6 Wei Powder, Zhuang Xi-6 Wei Powder, and Alatan Arula -5 flavor powder, Zhamusa -4 flavor soup, Haododun Arula -10 flavor pills, Zhuangxi -21 flavor powder, Hadungaridi 13 flavor pills, Yourel -13 flavor Mongolian medicine prescriptions such as pills were used for treatment, while the control group was treated with standard quadruple therapy of ytoprazole, potassium amoxicillin, amoxicillin, and clarithromycin [28]. The results

showed that the total effective rate of the Mongolian medicine group (91.78%) was significantly better than the control group (82.19%) using quadruple therapy with Western medicine [28]. Suyilatu used the Mongolian medicine Bater-7 pills alone to treat gastric Hp infection, and the control group used triple therapy with Western medicine (potassium tetrafluorophosphate, clarithromycin, and metronidazole). After completing 2 weeks of treatment, the total number of patients in the Mongolian medicine group was The effective rate (95.5%) was significantly better than that of the Western medicine group (86.4%), and the clinical symptoms of patients were significantly improved [29]. In short, Mongolian medicines are all developed from natural herbal medicines. They are easy to take, have few side effects, and have significant clinical therapeutic effects, which are worthy of attention. Extensive clinical promotion should be carried out based on further in-depth study of the mechanism of action.

4 YAO MEDICINE TREATMENT

Yaoyi uses the break-even theory as the basis for syndrome differentiation and treatment, and pays attention to the "three-yuan harmony" [30]. There are various treatment methods. In addition to herbal medicine, there are also acupuncture, anesthesia, egg moxibustion, cupping, etc. Liu Xiaomei et al. used a shaking medical jar made of twelve kinds of herbs combined with Western medicine quadruple eradication therapy to treat patients with spleen and stomach damp-heat type Hp-related pneumonia, while the control group only used Western medicine standard quadruple eradication therapy (rabeprazole, colloidal pectin spade, amoxicillin, clarithromycin) [31]. The results showed that the treatment group combined with shaking medical jar therapy achieved better results, with the treatment effective rate (96.77%) and eradication rate (93.54%) significantly better than the control group (82.75%, 89.65%). The recurrence of Hp infection was followed up for 6 months, and it was found that the recurrence rate of Hp infection treated with Yao medicine jar (9.67%) was lower than that of standard quadruple therapy (19.23%), achieving a more satisfactory effect [31]. It shows that Yao medicine medicine cup therapy is a treatment method worthy of promotion. However, there are currently no relevant reports on the therapeutic impact of Yao herbal medicine and other treatments on H. pylori eradication.

5 APHRODISIAC TREATMENTS

Zhuang medicine began in the pre-Qin period, and its theoretical basis is the natural view of heaven and man of "balancing qi and blood" and "synchronization of the three qi". The main treatment for peptic ulcer, gastritis and other diseases caused by Hp infection is overall treatment. According to reports by Qin Jiemei et al., the Zhuang Yao Yuyang Powder was used for experimental treatment of peptic ulcer patients with Hp infection. The results showed that the eradication rate of Hp infection reached 95.0%, which was better than the use of Western medicine triple eradication therapy (omeprazole, Metronidazole, clarithromycin) control group (82.1%) [32]. However, the number of cases in the study was small, with only 40 cases in each group. This is also the only current study that uses strong drugs to clinically kill Hp. Therefore, more clinical research verification is needed. In addition, in order to find cheap and efficient anti-Hp strong drugs, Zhang Yu et al. selected 50 commonly used strong drugs that may have anti-Hp effects from more than 2,000 kinds of strong drugs, and conducted in vitro screening studies on the anti-Hp effects [33]. It was found that 5 kinds of herbs have strong antibacterial effect on Hp, and they are in order: Huangteng > Kudingcha = Areca Nut > Golden Fruit Olive > Little Flying Grass, followed by Diofeng and Yizhijian. In addition, there are 8 kinds of herbs that have a mild inhibitory effect on HP, including Jiubing Ying, Gangbangui, Wuzhifeng, Jinzhan Yinpan, papaya, Jiujie tea, Shixiantao and Daliwang [33]. Although the antibacterial effect in vitro does not mean that it is effective in vivo, and the effect in vivo and in vitro is not necessarily disproportionate, it can provide good clues and basis for future research.

6 DONG MEDICINE TREATMENT

Dong medicine is a traditional medical treatment method based on herbal medicine and based on the theory of six natures and six flavors. It classifies diseases into 12 categories and 560 conditions. Wu Weihua and others from Hainan used a rat model infected with Helicobacter pylori to study the in vitro treatment effect of Dong medicine Xue Ma Bu (Guangdong Purple Pearl) on Hp. They found that Xue Ma Bu had no effect on gastric acid secretion, but had a dose-dependent significant effect on H pylori. The inhibitory effect is even better than that of clarithromycin, but there is still a lack of clinical research and research on the mechanism of action [34]. Zhang Xihe et al. used simple oral administration of compound Dong medicinal powders (Casicasia, Shui Haitang, Di Guniu, Mountain Ginger, Paddy Seven, baking soda) and decoctions (Roadside Yellow, White Leaf Herring Gall, Wei Qing Cao, Lonicera Lonicerae, Tianjin). (Qingdihong, Yuyejinhua) in the treatment of duodenal ulcers caused by Hp infection. The eradication rate of Hp after 2 weeks of treatment reached 91.5%, which was significantly better than the control group treated with triple therapy of cimetidine, metronidazole and amoxicillin. (76.2%), and the recurrence rate (8.4%) was also significantly lower than the control group (25.7%) [35]. Although the Western medicine triple therapy used is not a standard triple regimen, it is still a promising Dong medicine prescription and deserves further study on its pharmacological mechanism at the molecular level.

7 OUTLOOK

Although the current Western medicine standard triple and quadruple eradication therapies are still the classic and mainstream therapies for the treatment of *H. pylori*, the emergence of increasing drug-resistant strains and the toxic and side effects of drugs are two major problems that trouble people. It is undoubtedly the most ideal to discover safe, economical, effective and non-toxic drugs to eradicate *H. pylori*. It is undeniable that traditional medicines may contain many unknown active ingredients that can effectively inhibit and kill HP. Especially in areas with backward economies and inconvenient transportation, traditional medicine still plays a huge role. Some people abroad have tried to use plant extracts to treat Hp infection and achieved certain results. Many cases of effective clinical treatment have also proven that in-depth exploration of therapeutic drugs for Hp infection-related diseases in traditional medicine is a shortcut to the development of new effective anti-Hp drugs. Because drug-resistant Hp strains are increasingly common in developing countries, the reinfection rate after eradication is much higher than in Western developed countries. All these require us to work hard to find more effective treatments with fewer side effects. Traditional medicine uses various herbal single and compound preparations to treat various diseases caused by Hp, and it has been confirmed that they contain ingredients with the activity of inhibiting and/or killing Hp. However, due to various reasons, the quantity and quality of clinical reports cannot be compared with Western medicine. On the one hand, this may be because medical workers who perform traditional ethnic therapies generally need to further strengthen their scientific research capabilities, and their clinical summary capabilities also need to be improved. On the other hand, many places where traditional treatments are performed have backward economic conditions, let alone scientific research environments. Therefore, there may still be a long way to go to carry out general and in-depth excavation, research and analysis of traditional medicine methods for treating various HP-related diseases, but it is undoubtedly a very meaningful work. The study of effective bacteriostatic and bactericidal ingredients in single drugs and prescriptions, and even the mechanism of action at the molecular level, is the focus of relevant research work in the future. We believe that through extensive and in-depth research on traditional medicine, safer and more effective anti-Hp drugs will emerge in the future.

COMPETING INTERESTS

The authors have no relevant financial or non-financial interests to disclose.

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