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Clinical Analysis of Combining Probiotics with High-Dose Dual Therapy for *Helicobacter pylori* Eradication

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Abstract: *Objective:* To compare the eradication rates of Helicobacter pylori (HP) and the incidence of adverse reactions among three treatment methods. *Methods:* A total of 139 patients with Helicobacter pylori infection diagnosed at the outpatient clinic or during hospitalization in the Department of Gastroenterology of West Electric Group Hospital from January 2022 to April 2023 were enrolled. Patients were divided into three groups: dual therapy group (46 cases), triple therapy group (62 cases), and quadruple therapy group (31 cases). The dual therapy group received omeprazole and amoxicillin; the triple therapy group received omeprazole, amoxicillin, and probiotics; the quadruple therapy group received omeprazole, colloidal bismuth pectin capsules, amoxicillin, and furazolidone. All treatments lasted for two weeks. The eradication rates and incidence of adverse reactions were compared among the three groups. *Results:* The eradication rates for the dual, triple, and quadruple therapy groups were 84.8%, 85.5%, and 85%, respectively ($P > 0.05$). The primary adverse reactions included gastrointestinal symptoms such as bloating, abdominal pain, loss of appetite, and abdominal discomfort, with incidence rates of 1, 2, and 6 cases in the dual, triple, and quadruple therapy groups, respectively ($P = 0.574$). However, a significant difference was found between the dual and quadruple therapy groups ($P = 0.03$) and between the triple and quadruple therapy groups ($P = 0.026$). Neurological side effects, such as dizziness and headache, were rare, with incidences of 0, 1, and 1 cases in the dual, triple, and quadruple therapy groups, respectively ($P = 0.611$). *Conclusion:* The efficacy of dual, triple, and quadruple therapy for eradicating Helicobacter pylori showed no significant difference. However, the dual and triple therapy groups had lower adverse reaction rates, making them suitable alternatives to traditional quadruple therapy for reducing patient discomfort. The probiotic group also contributed to the restoration of normal gastrointestinal microbiota.

Keywords: *Helicobacter pylori*; Eradication rate; Adverse reactions

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1. Introduction

Helicobacter pylori (*H. pylori*, HP) has been identified as a causative agent for chronic gastritis, digestive system

ulcers, and gastric cancer. Recently, the 15th edition of carcinogens published by the U.S. Public Health Service confirmed HP as a carcinogen, with global natural bacterial infections exceeding 50% [1]. The sixth national consensus on the management of HP infection (non-eradication treatment) emphasized that all confirmed HP infections, regardless of symptoms or complications, should receive eradication therapy in the absence of contraindications [1,2].

Currently, the most common methods for eradicating HP include bismuth-based quadruple therapy and triple therapy. In recent years, high-dose amoxicillin combined with proton pump inhibitors has emerged as a new option for HP eradication, endorsed by the Toronto Consensus and the American Gastroenterological Association guidelines as a recommended regimen. Studies have demonstrated that high-dose dual therapy achieves eradication rates comparable to traditional bismuth-based quadruple and triple therapies [3].

However, the increasing resistance to HP and the prominent side effects of medications pose challenges. Probiotics, which are active microorganisms capable of colonizing the gastrointestinal and reproductive systems, play a crucial role in maintaining microbiota balance. They have been incorporated into HP eradication treatments, with multiple studies showing that probiotics can enhance eradication rates and mitigate adverse reactions [4].

Currently, there are no reports on combining probiotics with high-dose dual therapy for HP eradication. This study aims to evaluate the clinical effects of adding probiotics to high-dose dual therapy for HP eradication.

2. Materials and methods

2.1. Patient selection

A total of 139 Helicobacter pylori (HP)-positive patients who attended the Department of Gastroenterology outpatient clinic or were hospitalized at West Electric Group Hospital from January 2022 to April 2023 were enrolled in the study. Patients were randomly divided into three groups: dual therapy group (46 cases), triple therapy group (62 cases), and quadruple therapy group (31 cases).

(1) Dual therapy group: 46 cases, 18 males, 28 females, average age (46.61 ± 9.50) years.

(2) Triple therapy group: 62 cases, 34 males, 28 females, average age (47.63 ± 9.55) years.

(3) Quadruple therapy group: 31 cases, 21 males, 19 females, average age (51.58 ± 9.24) years.

There were no significant differences in general characteristics, including sex, age, family history of gastric cancer, or alcohol consumption, among the three groups.

Inclusion criteria: (1) Age 18–70 years, no sex restrictions; (2) HP-positive patients diagnosed by ^{13}C-urea breath test with DOB ≥ 6 or ^{14}C-urea breath test with DPM ≥ 150; (3) First-time eradication treatment; (4) No use of antibiotics, Jin Hua Weikang, Pudi Lan, Moluo Dan, berberine, Scutellaria-containing herbal medicines, or similar agents within four weeks before treatment; (5) No use of PPIs, H2 receptor antagonists, aluminum magnesium carbonate, bismuth agents, sucralfate, or misoprostol within two weeks before treatment; (6) Patients provided informed consent to participate in the study.

Exclusion criteria: (1) Severe dysfunction of the heart, lungs, liver, kidneys, malignant tumors, or other conditions that could affect study evaluation; (2) Pregnant or breastfeeding women; (3) Complications such as pyloric obstruction, perforation, or upper gastrointestinal bleeding; (4) Allergic history to the study drugs; (5) History of esophageal, gastric, or duodenal surgery; (6) Poor compliance.

Termination criteria: (1) Intolerable adverse reactions during treatment, as determined by the investigator; (2) Disease progression or deterioration, rendering the study protocol unsuitable for continuation.

2.2. Methods

2.2.1. Dual therapy group

Omeprazole enteric-coated tablets (manufacturer: AstraZeneca; approval number: H201811233; specification: 20 mg) 40 mg/dose, BID (30 minutes before breakfast and dinner); amoxicillin capsules (manufacturer: CSPC Zhongnuo Pharmaceutical Co., Ltd.; approval number: H13021770; specification: 0.5 g) 1.0 g/dose, TID (30 minutes after breakfast, lunch, and dinner). Treatment duration: 14 days.

2.2.2. Triple therapy group

Same as the dual therapy group, with the addition of *Clostridium butyricum* (manufacturer: Northeast Pharmaceutical Group Co., Ltd.; approval number: S10950019; specification: 0.25 g) 0.5 g/dose, TID (2 hours after breakfast, lunch, and dinner). Treatment duration: 14 days.

2.2.3. Quadruple therapy group

Furazolidone (manufacturer: Tianjin Lisheng Pharmaceutical Co., Ltd.; approval number: H12020160; specification: 0.1 g) 0.1 g/dose, BID (30 minutes after breakfast and dinner); colloidal bismuth tartrate capsules (manufacturer: Shanxi Xinbaoyuan Pharmaceutical Co., Ltd.; approval number: H20059772; specification: 55 mg) 220 mg/dose, BID (30 minutes before breakfast and dinner); amoxicillin capsules (same as above) 1.0 g/dose, BID (30 minutes after breakfast and dinner); omeprazole enteric-coated capsules (manufacturer: Shandong Luoxin Pharmaceutical Co., Ltd.; approval number: H20033444; specification: 20 mg) 40 mg/dose, BID (30 minutes before breakfast and dinner). Treatment duration: 14 days.

2.3. Observation indicators

(1) HP eradication rate: After discontinuing the medication for at least one month, ^{13}C-urea or ^{14}C-urea breath tests were performed. Negative results indicated successful eradication; positive results indicated eradication failure.

(2) Adverse reaction rate: The incidence of adverse reactions was recorded.

2.4. Statistical analysis

Statistical analysis was conducted using SPSS 26.0 software. Count data were expressed as [*n* (%)], and differences between groups were compared using the χ^2 test or Fisher's exact test. Normally distributed measurement data were expressed as mean ± standard deviation (SD), and differences between groups were compared using the *t*-test. A P value < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of general information

The age of enrolled patients ranged from 21 to 68 years, with an average age of 48.17 ± 9.59 years. There were 68 male and 71 female patients. No statistically significant differences were observed among the groups in terms of age, sex, family history of gastric cancer, or history of alcohol consumption (P > 0.05). See **Table 1**.

Table 1. Comparison of general information among groups

Group	Age (years)	Gender (male) [*n* (%)]	Family history of gastric cancer [*n* (%)]	History of alcohol consumption [*n* (%)]
Total	48.17 ± 9.59	68 (48.9)	3 (2.1)	26 (18.7)
Dual therapy	46.61 ± 9.50	18 (26.5)	0 (0.0)	7 (26.9)
Triple therapy	47.63 ± 9.55	34 (50)	1 (33.3)	11 (42.3)
Quadruple therapy	51.58 ± 9.24	16 (23.5)	2 (66.7)	8 (30.8)
Statistical value	$F = 2.74$	$\chi^2 = 2.72$	$\chi^2 = 3.03$	$\chi^2 = 1.43$
P value	0.068	0.26	0.16	0.50

3.2. Comparison of HP eradication rates among groups

The eradication rates of HP were 84.8% (39/46) in the dual therapy group, 85.5% (53/62) in the triple therapy group, and 83.9% (23/31) in the quadruple therapy group. There were no statistically significant differences among the three groups ($P > 0.05$). Pairwise comparisons between groups also showed no significant differences ($P > 0.05$). See **Table 2**.

Table 2. Comparison of HP eradication rates among groups

Group	Total cases (*n*)	Effective cases (*n*)	Ineffective cases (*n*)	χ^2 value	*P* value
Dual therapy	46	39	7		
Triple therapy	62	53	9	0.138	> 0.05
Quadruple therapy	40	34	6		

3.3. Comparison of adverse reactions after HP eradication therapy among groups

The main adverse reactions in the three groups were gastrointestinal symptoms (e.g., abdominal pain, bloating, and abdominal discomfort) and neurological symptoms.

(1) Gastrointestinal symptoms: The incidence was 1 case in the dual therapy group, 2 cases in the triple therapy group, and 6 cases in the quadruple therapy group. Although there was no overall significant difference among the three groups ($P > 0.05$), pairwise comparisons revealed significant differences between the dual and quadruple therapy groups ($P = 0.03$) and the triple and quadruple therapy groups ($P = 0.026$). No significant difference was found between the dual and triple therapy groups ($P > 0.05$).

(2) Neurological symptoms: The incidence of neurological side effects (e.g., dizziness, headache) was low, with 0 cases in the dual therapy group, 1 case in the triple therapy group, and 1 case in the quadruple therapy group ($P = 0.611$).

Table 3. Comparison of adverse reactions among groups

Adverse reaction	Dual therapy (*n*)	Triple therapy (*n*)	Quadruple therapy (*n*)	*P* value
Gastrointestinal symptoms	1*	2#	6	0.574
Cardiovascular symptoms	0	0	0	
Neurological symptoms	0	1	1	0.611
Allergy reactions	0	0	0	
Other adverse effects	0	0	0	

Note: * indicates a significant difference between the dual and quadruple therapy groups ($P < 0.05$); # indicates a significant difference between the triple and quadruple therapy groups ($P < 0.05$).

4. Discussion

Probiotics are a class of active microorganisms beneficial to human health when ingested. They colonize specific parts of the body, altering the microbial community to benefit the host. Common probiotics include yeast, *Bacillus licheniformis*, *Clostridium butyricum*, and *Lactobacillus* species. In this study, the probiotic used was *Bacillus licheniformis* (sold as "Intestin-bac"). This Gram-positive, non-pathogenic, spore-forming organism antagonizes pathogenic bacteria like *Staphylococcus* and yeast-like fungi while promoting the growth of beneficial bacteria such as *Bifidobacterium* and *Lactobacillus*. *Bacillus licheniformis* has demonstrated the ability to inhibit *H. pylori*, and its secretion of antibiotics has been known for at least 40 years. These antibiotics, which include peptides, lipopeptides, and aminoglycosides, sometimes have unique primitive chemical structures. *Bacillus licheniformis* secretes an antimicrobial substance with properties similar to isocoumarin antibiotics, which exhibit anti-inflammatory effects and anti-stress ulcer properties [5].

Recent research highlights the critical role of probiotics in eradicating *H. pylori* while reducing drug-related side effects. Zhang [6] demonstrated that combining *Bifidobacterium* triple viable capsules with traditional quadruple therapy significantly improved *H. pylori* eradication rates and reduced adverse reactions. Similarly, Feng *et al.* [7] found that adding probiotics to conventional quadruple therapy for *H. pylori*-associated gastritis reduced inflammation and improved eradication rates.

There are several advantages of high-dose dual therapy:

(1) Enhanced acid suppression to improve efficacy: Amoxicillin's antibacterial activity against *H. pylori* is pH-dependent. When gastric acid is adequately suppressed, maintaining a gastric pH level of 6 or above for most of the day, amoxicillin achieves optimal antibacterial effects. Increased dosage and frequency of acid suppressants enhance their effectiveness, thereby improving amoxicillin's efficacy. Since the effectiveness of proton pump inhibitors (PPIs) is influenced by genetic variations in drug metabolism, increasing the dosage and frequency minimizes these genetic effects and ensures sufficient acid suppression.

(2) Increased amoxicillin dosage and frequency to enhance efficacy: Amoxicillin's antibacterial effect against *H. pylori* is time-dependent, meaning its effectiveness improves with prolonged exposure to bacteria. Increasing the dosage frequency prolongs contact time with the gastric mucosa and maintains effective drug concentrations in the bloodstream, thereby enhancing its bactericidal effect and improving treatment success rates.

However, conventional quadruple therapy involving furazolidone is associated with serious side effects, such as irreversible neuritis and severe skin reactions. Furthermore, due to factors like patient compliance, antibiotic resistance, and drug side effects, eradication rates have declined from the original 80–95% to the current 60–85%. Therefore, finding new treatment strategies has become an urgent need.

5. Conclusion

In conclusion, the results of this study indicate that the *H. pylori* eradication rates were similar across all three groups. Thus, the authors suggest that the probiotic regimen could serve as a viable alternative to traditional quadruple therapy. The relationship between *H. pylori* infection, its eradication, and the disruption and restoration of intestinal microbiota balance is critical. Adding probiotics during *H. pylori* eradication therapy helps restore

normal gastrointestinal microbiota and reduces gastrointestinal side effects. However, the sample size in this study was relatively small. Further research with larger sample sizes is needed to confirm these findings.

Disclosure statement

The authors declare no conflict of interest.

References

[1] Helicobacter pylori is Listed as a Definite Carcinogen, n.d., 2022. Science 24 Hours, 2022(4): 35.

[2] Chinese Medical Association Gastroenterology Branch Helicobacter pylori Study Group, 2022, The Sixth National Consensus Report on the Management of Helicobacter pylori Infection (Non-Eradication Therapy Section). Chinese Journal of Digestion, 42(5): 289–303.

[3] Chen W, Shen Y, Zhang Y, 2022, Meta-Analysis of a Randomized Controlled Trial of High-Dose Dual Therapy for Helicobacter pylori. Modern Medicine, 50(2): 192–200.

[4] Zhao H, Zhong W, Liang J, et al., 2015, Observation on the Efficacy of Probiotics-Assisted Triple Therapy in Eradicating Helicobacter pylori. Guangxi Medical Journal, 37(1): 105–106.

[5] Pinchuk IV, Bressollier P, Verneuil B, et al., 2001, In Vitro Anti-Helicobacter pylori Activity of the Probiotic Strain Bacillus subtilis 3 is Due to Secretion of Antibiotics. Antimicrob Agents Chemother, 45(11): 3156–3161. https://doi.org/10.1128/AAC.45.11.3156-3161.2001

[6] Zhang N, 2021, Efficacy and Safety Analysis of Bifidobacterium Lactobacillus Triple Viable Bacteria Combined with Quadruple Therapy in the Treatment of Helicobacter pylori Infection. Clinical Research, 29(9): 56–57.

[7] Feng Y, Chen Z, Yang X, 2021, The Effect of Probiotic Adjuvant Therapy on Inflammatory Factors in Patients with Helicobacter pylori-related Chronic Gastritis. Contemporary Medicine, 27(11): 125–127.