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Efficacy and Clinical Safety Study of Rabeprazole Combined with Amoxicillin Dual Therapy for Type 2 Diabetes Mellitus Patients with *Helicobacter pylori* Infection

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Abstract: *Objective:* To explore the clinical efficacy, safety, and impact on inflammatory factor levels of rabeprazole combined with amoxicillin dual therapy in the treatment of patients with type 2 diabetes mellitus (T2DM) and Helicobacter pylori (Hp) infection, providing a reference for clinical treatment. *Methods:* A total of 526 patients with T2DM and Hp infection who were treated in our hospital from January 2022 to December 2024 were selected as the study subjects. Among them, 33 patients withdrew due to allergies or other reasons, and 493 patients completed the treatment. They were divided into a control group (n = 246) and an observation group (n = 247) using a random number table method. The control group received quadruple therapy, while the observation group received high-dose dual therapy. The general information, clinical efficacy, serum interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), hypersensitive C-reactive protein (hs-CRP), Hp eradication rate, recurrence rate, and incidence of adverse reactions were compared between the two groups. *Results:* After treatment, the indicators of both groups improved compared to before treatment. The observation group showed significant advantages in various indicator improvements: In terms of clinical efficacy, the observation group (95.144%) was significantly better than the control group (83.74%) ($\chi2 = 16.982$, $P = 0.000 < 0.001$). Regarding inflammatory factor levels, IL-6, TNF-α, and hs-CRP levels decreased more significantly in the observation group compared to the control group ($P = 0.000 < 0.001$). In terms of Hp eradication rate and recurrence rate, the Hp eradication rate was higher in the observation group than in the control group ($\chi2 = 14.481$, $P = 0.000 < 0.001$), and the recurrence rate was lower ($\chi2 = 32.740$, $P = 0.000 < 0.001$). In terms of safety, the incidence of adverse reactions (4.04%) was lower in the observation group than in the control group (14.63%) ($\chi2 = 16.325$, $P = 0.000 < 0.01$). *Conclusion:* Rabeprazole combined with amoxicillin dual therapy is effective in the treatment of patients with T2DM and Hp infection. It can effectively reduce inflammatory factor levels, improve the Hp eradication rate, reduce recurrence, and has high safety. It is worthy of clinical promotion and application.

Keywords: Rabeprazole; Amoxicillin; Dual therapy; Quadruple therapy; Type 2 diabetes mellitus; Helicobacter pylori

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1. Introduction

Helicobacter pylori (Hp) is a common worldwide chronic infectious disease that is closely related to the pathogenesis of various gastrointestinal diseases such as gastritis, peptic ulcer, and gastric cancer [1]. Type 2 diabetes mellitus (T2DM) is a metabolic disease in which patients often experience long-term hyperglycemia, leading to decreased immune function

and damage to the gastrointestinal mucosal barrier, making them susceptible to Hp infection. Additionally, Hp infection may worsen diabetes through various mechanisms, such as affecting gastrointestinal hormone secretion and disrupting glucose metabolism, creating a vicious cycle. Therefore, early and efficient eradication of Hp is crucial for improving the prognosis of patients with T2DM and concomitant Hp infection. Currently, quadruple therapy is the primary treatment for Hp. Although it has a certain therapeutic effect, it faces challenges such as multiple medications, long treatment courses, poor patient compliance, high incidence of side effects, and the potential for drug resistance. Given the increasing problem of antibiotic resistance, finding an efficient, safe, and simple treatment method is a current research focus. Rabeprazole, a new type of proton pump inhibitor, can effectively block gastric acid secretion and provide favorable conditions for the bactericidal effect of antibiotics in the stomach. Amoxicillin is a broad-spectrum antibiotic that has a good inhibitory effect on Hp. The combination of these two drugs forms a dual therapy that is simple to administer and has good patient compliance [2]. This study compares the efficacy and safety of dual therapy with conventional quadruple therapy in the treatment of T2DM with concomitant Hp infection, aiming to provide new ideas for its clinical treatment.

2. Materials and methods

2.1. General Information

This study is a prospective investigation that enrolled 526 patients with T2DM combined with *Helicobacter pylori* infection who were treated in our hospital from January 2022 to December 2024. Among them, 33 withdrew due to allergies or other reasons, leaving 493 patients who completed the treatment. They were randomly divided into a control group (n = 246) and an observation group (n = 247) using a random number table method.

Inclusion criteria: (1) Meet the diagnostic criteria for type 2 diabetes established by the World Health Organization (WHO); (2) Confirmed diagnosis of Hp infection through urea breath test, rapid urease test of gastric mucosa biopsy, or pathological examination; (3) Age between 18–75 years old; (4) Voluntary participation in this study with signed informed consent.

Exclusion criteria: (1) Used antibiotics, proton pump inhibitors, bismuth agents, or other drugs that affect Hp detection or treatment in the past month; (2) Have severe cardiac, liver, kidney, or other important organ dysfunction; (3) Presence of severe gastrointestinal diseases such as gastrointestinal bleeding, perforation, or obstruction; (4) Allergic to the medications used in this study; (5) Pregnant or breastfeeding women; (6) Have mental illness, unable to cooperate with treatment and follow-up.

2.2. Methods

The control group received quadruple therapy, specifically rabeprazole enteric-coated tablets (10 mg/time, 2 times/day) + bismuth potassium citrate (220 mg/time, 2 times/day) + amoxicillin (1 g/time, 2 times/day) + clarithromycin (0.5 g, 2 times/day). Rabeprazole and bismuth potassium citrate were taken 30 minutes before meals, while amoxicillin and clarithromycin were taken after meals. The treatment course was 14 days.

The observation group was treated with high-dose dual therapy, specifically rabeprazole (10 mg/time, 4 times/day) + amoxicillin (0.75 g/time, 4 times/day), both taken 30 minutes before meals. The treatment course was also 14 days. During the treatment, both groups maintained their original diabetes treatment regimens and received dietary guidance to avoid spicy and stimulating foods, smoking, and alcohol consumption.

2.3. Observation indicators

(1) General information: Record the gender, average age, and disease duration of the two groups.

(2) Treatment effect: Four weeks after the treatment, the urea breath test was used to detect Hp infection, and the treatment effect was evaluated based on the improvement of clinical symptoms. Markedly effective: Complete resolution of clinical symptoms and negative urea breath test; Effective: Significant relief of clinical symptoms

and negative urea breath test; Ineffective: No improvement or worsening of clinical symptoms and positive urea breath test.

(3) Inflammatory factor levels: Collect 5ml of fasting venous blood from patients in both groups before and after treatment. Use enzyme-linked immunosorbent assay (ELISA) to detect serum interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and high-sensitivity C-reactive protein (hs-CRP) levels.

(4) Hp eradication rate and recurrence rate: Detect Hp eradication four weeks after treatment. The criterion for Hp eradication is a negative urea breath test. Six months after treatment, re-test for Hp infection and calculate the recurrence rate.

(5) Incidence of adverse reactions: Monitor adverse reactions such as nausea, vomiting, abdominal distension, loss of appetite, bitter taste in the mouth, belching, and peripheral neuropathy during treatment in both groups.

2.4. Statistical methods

Analyze the data using SPSS 27.0 statistical software. Normally distributed measurement data are expressed as mean ± standard deviation (SD), and paired *t*-tests are used for intra-group comparisons. Count data are expressed as [*n*(%)], and chi-square tests are used for inter-group comparisons. A P-value < 0.05 is considered statistically significant.

3. Results

3.1. Comparison of general information between the two groups

There were no statistically significant differences in age, gender, or disease duration between the two groups ($P > 0.05$). See **Table 1** for details.

Table 1. Comparison of general information between the two groups

Group	Number of cases (*n*)	Age (mean ± SD, years)	Gender (Male/Female)	Disease duration (years)
Control group	246	47.21 ± 4.38	126/120	5.18 ± 1.31
Observation group	247	47.25 ± 4.39	128/119	5.11 ± 1.29
χ^2/t value		0.101	0.018	0.598
p-value		0.919	0.894	0.550

3.2. Comparison of treatment effects between the two groups

Compared with the control group, the total clinical effective rate of the observation group (95.144%) was better than that of the control group (83.74%) ($\chi^2 = 16.982$, $P = 0.000 < 0.001$). See **Table 2**.

Table 2. Comparison of clinical efficacy between two groups

Group	Markedly effective	Effective	Ineffective	Total clinical effectiveness rate
Control Group ($n = 246$)	84 (34.15%)	122 (49.59%)	40 (16.26%)	206 (83.74%)
Observation Group ($n = 247$)	150 (60.73%)	85 (34.41%)	12 (4.86%)	235 (95.14%)
χ^2 value				16.982
p-value				< 0.001

3.3. Comparison of inflammatory factor levels between the two groups

After treatment, the levels of IL-6, TNF-α, and hs-CRP decreased in both groups, but the decrease was more significant in the observation group ($P = 0.000 < 0.001$). See **Table 3**.

Table 3. Comparison of inflammatory factor levels between two groups

Group	IL-6 (pg/mL)		TNF-α (pg/mL)		hs-CRP (mg/L)	
	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
Control group ($n = 246$)	8.63 ± 3.25	4.59 ± 1.82	9.46 ± 2.43	7.35 ± 1.34	12.48 ± 2.37	8.21 ± 1.87
Observation group ($n = 247$)	8.64 ± 3.26	3.90 ± 1.15	9.48 ± 2.49	6.21 ± 1.01	12.51 ± 2.40	6.35 ± 1.48
t-value	0.03	5.034	0.090	10.669	0.140	12.248
p-value	0.973	< 0.001	0.928	< 0.001	0.	

3.4. Comparison of Hp eradication rate and recurrence rate between the two groups

After treatment, the Hp eradication rate in the observation group was significantly higher than that in the control group (95.95 > 86.18), and the 1-year recurrence rate was lower than that in the control group (4.05% < 21.14%). See **Table 4**.

Table 4. Comparison of Hp eradication rate and recurrence rate between the two groups

Group	Hp eradication rate	1-year recurrence rate
Control group ($n = 246$)	212 (86.18%)	52 (21.14%)
Observation group ($n = 247$)	237 (95.95%)	10 (4.05%)
χ^2 value	14.481	32.740
p-value	0.000	0.000

3.5. Comparison of adverse reaction rates between the two groups

Compared with the control group, the total incidence of adverse reactions in the observation group (4.04%) was lower than that in the control group (14.63%) ($\chi^2 = 16.325$, $P = 0.000 < 0.01$). See **Table 5**.

Table 5. Comparison of adverse reactions between the two groups

Group	Nausea & vomiting	Abdominal distension	Decreased appetite	Bitter taste	Belching	Peripheral neuritis	Total adverse reaction rate
Control group ($n = 246$)	8 (3.25%)	3 (1.22%)	5 (2.03%)	6 (2.44%)	8 (3.25%)	6 (2.44%)	36 (14.63%)
Observation group ($n = 247$)	1 (0.01%)	0	1 (1.01%)	1 (1.01%)	1 (1.01%)	0	10 (4.04%)
χ^2 value							16.325
p-value							0.000

4. Discussion

T2DM is a metabolic disease caused by genetic and environmental factors [3]. Oxidative stress and inflammatory reactions caused by long-term hyperglycemia can damage multiple systems in the body, leading to the occurrence of infections.

Helicobacter pylori is a microaerobic Gram-negative bacterium that invades the gastric mucus layer through its unique helical structure and flagellar movement, forms infections on the surface of gastric mucosal epithelium, induces inflammatory reactions, and causes diseases such as gastritis, peptic ulcer, and even gastric cancer [4]. Epidemiological investigations have found that compared with the general population, diabetics have a significantly higher rate of Hp infection due to their weakened immune function and gastrointestinal motility disorders [5]. Furthermore, the chronic inflammation caused by Hp infection leads to the production of many inflammatory factors in the body, disrupting the body's insulin signaling pathway, exacerbating insulin resistance, and thereby affecting blood glucose control levels. Therefore, eliminating Hp infection is the key to the treatment of type 2 diabetes.

Quadruple therapy is currently the most commonly used treatment method. Rabeprazole, a novel proton pump inhibitor, can specifically target the H^+/K^+-ATP enzyme in gastric parietal cells, inhibiting gastric acid secretion and increasing the pH level in the stomach. This provides a favorable environment for antibiotics to exert their bactericidal effects. In an acidic environment, bismuth potassium citrate can generate bismuth salt-protein complexes that cover the surface of the gastric mucosa, offering protective effects, and it also exhibits antibacterial activity against Hp [6]. Amoxicillin and clarithromycin achieve the elimination of *Helicobacter pylori* by disrupting cell wall synthesis and inhibiting protein synthesis, respectively. However, in recent years, due to the extensive use of antibiotics, the resistance of *Helicobacter pylori* to clarithromycin, metronidazole, and other drugs has been increasing year by year, which has become a significant factor contributing to the failure of quadruple therapy to eradicate Hp infection. Additionally, the variety of quadruple therapy drugs and the frequent dosing lead to low patient compliance, and the combination of multiple drugs can cause side effects such as nausea, vomiting, abdominal distension, and decreased appetite, thereby adversely affecting the efficacy and quality of life of patients [7].

In high-dose dual therapy, the active metabolite of rabeprazole has more binding sites and stronger affinity for the H^+/K^+-ATP enzyme, enabling faster and more sustained inhibition of gastric acid secretion. This maintains a higher pH level in the stomach for a prolonged period, significantly enhancing the antibacterial activity of amoxicillin [8]. Amoxicillin belongs to the class of β-lactam antibiotics, and its antibacterial activity is enhanced in a near-neutral environment, exerting a bactericidal effect by inhibiting bacterial cell wall synthesis. The high-dose and high-frequency application of amoxicillin can increase its duration of action in the stomach and elevate its concentration in the body, thereby enhancing the clearance of Hp. The use of high-dose dual therapy in Hp infection is gradually increasing. Numerous studies have demonstrated that this approach yields high cure rates with few side effects, both in initial treatment and rescue therapy.

Previous research has confirmed the advantages of high-dose dual therapy in improving the effectiveness of Hp infection treatment. The results of this study indicate that the efficacy of the observation group was significantly better than that of the control group. This is primarily due to the continuous and potent inhibition of gastric acid secretion by high-dose rabeprazole, which provides a favorable gastric microenvironment for amoxicillin to exert its bactericidal effects, enhancing its ability to kill Hp and subsequently improving the clinical manifestations of patients. Complete eradication of Hp can significantly reduce inflammatory responses in the body and improve the inflammatory status of patients [9]. High-dose dual therapy can more thoroughly eradicate Hp, alleviate inflammatory reactions induced by pathogenic bacteria and virulence factors, and further inhibit the secretion of inflammatory cytokines. This is consistent with the research conclusions presented in this article. Additionally, the Hp eradication rate in the observation group was significantly higher than that in the control group, and the recurrence rate was also significantly lower. This is because high-dose dual therapy effectively addresses the challenge of resistance development encountered in conventional quadruple therapy, optimizing the dose of proton pump inhibitors and the frequency of amoxicillin administration. Complete eradication of Hp effectively reduces the risk of bacterial remnants and secondary infections, thereby decreasing the recurrence rate. Numerous previous studies have confirmed the safety of dual therapy [10]. This is attributed to the relatively fewer types of drugs used in high-dose dual therapy, which reduces the risk of drug interactions and adverse reactions. Simultaneously, the simplicity of the high-dose dual therapy regimen enhances patient compliance, further decreasing the probability of adverse reactions caused by missed or incorrect drug administration.

5. Conclusion

In summary, the combination of rabeprazole and amoxicillin as a dual therapy for the treatment of T2DM patients with concurrent Hp infection demonstrates significant efficacy. It effectively reduces inflammatory cytokine levels, improves the Hp eradication rate, reduces recurrence, and exhibits high safety. This approach is worthy of clinical promotion and application.

Disclosure statement

The author declares no conflict of interest.

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