

ORIGINAL RESEARCH

The Efficacy of Morodan in Combination with Rabeprazole for the Treatment of Chronic Gastritis and its Impact on Gastric Mucosal Repair

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ABSTRACT

Objective • This study aimed to investigate the application and effectiveness of Morodan combined with rabeprazole in patients with chronic gastritis, focusing on its impact on gastric mucosa repair.

Methods • A cohort of 109 patients diagnosed with chronic gastritis, who received treatment at our hospital between January 2020 and January 2021, were included in this study. Among them, 56 patients were assigned to the control group and received treatment with rabeprazole alone, while 53 were assigned to the research group and received a combination therapy of Morodan and rabeprazole. A comparative analysis was conducted between the two groups, assessing clinical efficacy, gastric mucosa repair effects, serum-related factors, and the incidence of adverse reactions.

Results • The research group exhibited a higher total effective rate of treatment (94.64%) compared to the control group (79.25%) ($P < .05$). Following treatment, the

research group showed lower levels of pepsinogen II, serum transforming growth factor α , serum epidermal growth factor, tumor necrosis factor- α , interleukin 6, and C-reactive protein compared to the control group ($P < .05$). Additionally, the research group displayed higher levels of pepsinogen I compared to the control group ($P < .05$). There was no significant difference in the incidence of adverse reactions between the research group and the control group ($P > .05$).

Conclusions • The combination therapy of Morodan and rabeprazole demonstrates efficacy in the treatment of chronic gastritis. It promotes gastric mucosa repair, reduces inflammatory damage, and exhibits a higher safety profile with no significant increase in adverse reactions. This treatment approach holds a higher clinical application value. (*Altern Ther Health Med.* 2023;29(6):306-310).

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INTRODUCTION

Chronic gastritis is a common clinical condition affecting the gastrointestinal tract. It is characterized by chronic inflammation of the gastric mucosa, resulting from various causes. Patients with chronic gastritis often experience symptoms such as abdominal pain, discomfort, and acid reflux.¹ The onset of chronic gastritis is insidious, and the condition progresses slowly, frequently leading to recurrent

episodes that significantly impact patients' normal functioning and overall quality of life.²

In recent years, extensive research on the pathogenesis of chronic gastritis and the development of therapeutic drugs have yielded remarkable advancements. Proton pump inhibitors, a class of drugs, have shown notable efficacy in treating chronic gastritis. Rabeprazole, a second-generation proton pump inhibitor, is capable of inhibiting gastric acid secretion and providing gastric mucosal protection.^{3,4} However, the desired therapeutic effect cannot be achieved through the use of a single drug alone.⁴

In traditional Chinese medicine, chronic gastritis is categorized as "stomach pain" and "fullness." It is primarily attributed to factors such as emotional and mental disorders, unclean diet, and external infections.⁵ Moluodan (*Morodan*) is a compound prescription of Chinese herbal medicine developed by Professor Li EF. It consists of the following ingredients: baizhu (*Atractylodes Macrocephala*), fuling (*Poria*), jinei-jin (*Endothelium Corneum Gigeriae Galli*), jiujiuchangpu (*Anemone altaica Fisch*), zexie (*Alismatis*

Rhizoma), puhuang (*Pollen Typhae*), sanqi (*Notoginseng Radix*), chuanxiong (*Chuanxiong Rhizoma*), danggui (*Angelicae Sinensis Radix*), diyu (*Sanguisorbae Radix*), baihe (*Lilii Bulbus*), shihu (*Dendrobii Caulis*), maidong (*Ophiopogon japonicus* (Linn. f.) *Ker-Gawl*), xuanshen (*Scrophulariae Radix*), yanhusuo (*Corydalis Rhizoma*), wuyao (*Linderae Radix*), and baishao (*Paeoniae Radix Alba*).⁶ Moluodan was included in the MAPS II in 2019 and has been recommended as a treatment for gastric precancerous lesions.⁷

Conversely, Rabeprazole has demonstrated its effectiveness in treating chronic gastritis.^{8,9} However, limited studies have explored the effects of combining Moluodan and Rabeprazole. We hypothesized that the combination therapy of Morodan and Rabeprazole could potentially yield improved efficacy and provide a more reliable treatment option for patients with chronic gastritis. Therefore, the objective of this study was to observe and analyze the effect of combining Morodan with Rabeprazole in the treatment of chronic gastritis, with a specific focus on the gastric mucosa repair effect in patients. The ultimate goal was to provide valuable clinical reference and guidance for treating chronic gastritis in the future, offering more reliable therapeutic approaches.

METHODS

Study Design and Participants

A prospective cohort study design was employed to assess the effectiveness of Rabeprazole monotherapy versus the combination therapy of Morodan and Rabeprazole in patients with chronic gastritis. The patients were selected based on their diagnosis of chronic gastritis and their treatment at our hospital between January 2020 and January 2021. Among the participants, 56 patients were assigned to the control group, receiving Rabeprazole monotherapy, while 53 patients were assigned to the research group, receiving combination therapy. The ethics committee approved the study design (Approval No. WNWTC-2019-104), and all study participants provided informed consent.

Inclusion and Exclusion Criteria

Inclusion criteria were as follows: (1) Patients who meet the diagnostic criteria for chronic gastritis and have been diagnosed by gastroscopy; (2) have negative results for *Helicobacter pylori*; (3) patients who have received treatment in our hospital after diagnosis and have complete medical records. Exclusion Criteria was as follows: (1) Patients with significant organ dysfunction, such as heart, liver, or kidney disorders; (2) patients with combined peptic ulcers; (3) patients with combined malignant tumors; (4) patients with severe heterogeneous hyperplasia of the gastric mucosa or pathological diagnosis of suspected malignant lesions; (5) patients with combined autoimmune system or endocrine system lesions; (6) female patients during pregnancy or lactation; (7) patients who are allergic to the drugs used in this study.

Treatment Regimens and Medication Administration

The control group was administered Rabeprazole alone, specifically Rabeprazole sodium enteric dissolved capsules (manufactured by Lizhu Pharmaceutical Factory of Lizhu Group, State Drug Administration H20052317, dosage: 10 mg), orally at a dose of 20 mg per administration, twice daily (20 mg/time, 2 times/d). In the research group, Morodan (Huashan brand) (manufactured by Handan Pharmaceutical Co., Ltd, GMP Z13021324, dosage: 9 g per 55 capsules) was added to the control group's treatment regimen. Patients in the research group were instructed to take 8 pills of Morodan orally per day. Both groups received their respective medications continuously for a duration of 2 months.

Efficacy Assessment

The efficacy assessment was conducted based on the "Diagnostic, Dialectical and Therapeutic Criteria of Integrative Chinese and Western Medicine for Chronic Gastritis (Trial Scheme)" formulated by the Professional Committee of Digestive System Diseases of the Chinese Association of Integrative Chinese and Western Medicine Research Society.^{10,11} The following criteria were used to evaluate the treatment outcomes: (1) Effective results: Clinical symptoms were observed to disappear or significantly improve, with the gastric mucosa returning to a normal state as observed during gastroscopy. Additionally, there was a notable reduction in inflammatory infiltrate; (2) Ineffective results: No improvement in clinical symptoms was observed, and gastroscopy revealed no significant changes or even a worsening of the gastric mucosa and inflammatory infiltrate. The total effective rate was calculated as the sum of the apparent and effective rates.

Outcome Measures

Clinical Efficacy. The clinical efficacy and gastric mucosal repair effect were assessed before and after treatment by measuring the levels of Pepsinogen I (PGI), Pepsinogen II (PGII), and the PGI/PGII ratio using a fully automated TRFIA assay. Furthermore, the levels of serum transforming growth factor α (TGF- α) and serum epidermal growth factor (EGF) were measured using an enzyme-linked immunosorbent assay to evaluate their impact on the gastric mucosal repair.

Inflammatory Reactions. Inflammatory reactions, including the levels of Tumor necrosis factor α (TNF- α), interleukin-6 (IL-6), and C-reactive protein (CRP), were assessed using ELISA before and after treatment to determine their changes.

Adverse Reactions. Lastly, the occurrence of adverse reactions, such as headache, diarrhea, skin rash, and nausea, was evaluated.

Statistical Methods

Statistical analysis of the data was performed using SPSS 23.0 statistical software. The results for the categorical data are presented as rates and were compared using the chi-

square test between groups. The measurement data are presented as mean ± standard deviation ($\bar{x} \pm s$), and the *t* test was used to compare the data between groups. The paired *t* test was utilized to compare the data before and after treatment. Statistical significance was defined as a *P* value less than .05 ($P < .05$).

RESULTS

Clinical and Demographic Characteristics

The comparison of age and gender between the two groups revealed no statistically significant differences ($P > .05$, Table 1), indicating that the two groups were comparable in terms of these demographic characteristics.

Clinical Efficacy

The research group demonstrated a significantly higher total effective rate of treatment compared to the control group ($P < .05$), see Table 2.

Effect of Gastric Mucosa Repair

Before treatment, there were no significant differences in the levels of PGI, PGII, TGF- α , and EGF between the two groups ($P > .05$). However, after treatment, there were notable changes. The levels of PGI increased in both groups, with the research group showing a higher increase compared to the control group ($P < .05$, Figure 1A). On the other hand, the levels of PGII, TGF- α , and EGF decreased in both groups, with the research group showing a more significant decrease compared to the control group ($P < .05$), refer to Figures 1B, 1C, and 1D.

Inflammatory Response

Before treatment, there were no significant differences in the levels of TNF- α , IL-6, and CRP levels between the two groups ($P > .05$). However, following treatment, both groups exhibited a reduction in inflammatory response markers. Interestingly, the research group demonstrated even lower levels of TNF- α , IL-6, and CRP compared to the control group ($P < .05$); see Figure 2A- 2C.

Adverse Reactions

The incidence of adverse reactions between the research and control groups showed no significant difference ($P > .05$); see Table 3.

DISCUSSION

Chronic gastritis is a common and prevalent gastrointestinal disease. Its development is closely

Table 1. Clinical information of the two groups of patients

	n	Gender (M/F)	Age (year)	Course of disease (year)
Research Group	56	30/26	45.81 ± 6.94	4.34 ± 1.31
Control Group	53	29/24	45.84 ± 6.97	4.36 ± 1.34
χ^2 (or <i>t</i>)	-	0.014	0.023	0.079
<i>P</i> value	-	.905	.982	.937

Abbreviations: M, Male; F, Female; χ^2 , chi-square test or *t* test. The *P* values indicate the statistical significance of the differences observed.

Table 2. Clinical Outcomes of The Two Groups

	n	Marked Response	Response	Non-Response	ORR
Research Group	56	28 (50.00)	22 (38.29)	3 (5.36)	53 (94.64)
Control Group	53	23(43.40)	19 (35.85)	11 (20.75)	42 (79.25)
χ^2	-	-	-	-	5.767
<i>P</i> value	-	-	-	-	.016

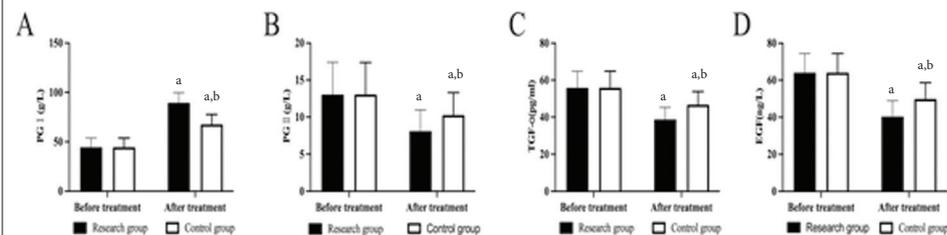
Abbreviations: ORR, Overall Response Rate.

Table 3. Adverse Reactions in The Two Groups

	n	Headaches	Diarrhea	Rash	Nauseating	Total
Research Group	56	2 (3.57)	1 (1.79)	1 (1.79)	1 (1.79)	5 (8.93)
Control Group	53	1 (1.89)	1 (1.89)	1 (1.89)	0 (0.00)	3 (5.66)
χ^2	-	-	-	-	-	0.428
<i>P</i> value	-	-	-	-	-	.513

Note: Values in parentheses represent percentages.

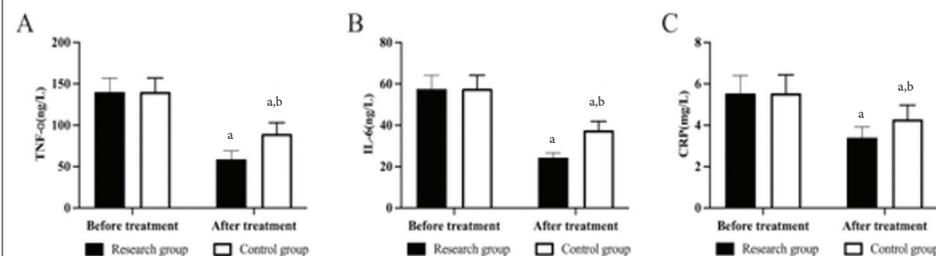
Figure 1. Changes in gastric mucosa-related indicators before and after treatment. (A) Changes in PGI; (B) Changes in PGII; (C) Changes in TGF- α ; (D) Changes in EGF.



^a $P < .05$

^b $P < .05$

Figure 2. Changes in indicators related to the inflammatory response before and after treatment. (A) Changes in TNF- α ; (B) Changes in IL-6; (C) Changes in CRP.



^a $P < .05$

^b $P < .05$

associated with factors such as *Helicobacter pylori* infection, autoimmunity, dietary structure, and genetics. It is characterized by atrophy of gastric mucosal glands and epithelial cells, accompanied by chronic inflammation and intestinal metaplasia.¹² Chronic gastritis, particularly chronic atrophic gastritis, is classified as a precancerous condition by the World Health Organization (WHO) and is closely linked to gastric cancer of the intestinal type.¹³ Therefore, proactive prevention and treatment of chronic gastritis are crucial.

In Western medicine, proton pump inhibitors are the primary clinical treatment for chronic gastritis, with Rabeprazole being a representative drug in this class. Rabeprazole is a partially reversible inhibitor of H⁺/K⁺-ATPase that binds to the target of H⁺/K⁺-ATPase, rendering it inactive and hindering the transfer of H⁺ from mucosal cells to the lumen. It effectively suppresses gastric acid secretion.^{14,15} Additionally, Rabeprazole is moderately priced and offers higher societal benefits compared to drugs such as esomeprazole. Consequently, most patients can adhere to the treatment regimen and complete their course of medication.

Rabeprazole demonstrates beneficial synergistic effects when combined with other drugs and has a high safety profile. However, its individual efficacy may not meet expectations, leading to the adoption of combination drug regimens in clinical practice. In recent years, there has been a growing preference for integrating Chinese and Western medicine in treating certain diseases. Traditional Chinese Medicine (TCM) attributes the development of chronic gastritis to various factors, including external pathogenic factors, emotional and psychological imbalances, dietary factors, and weakness of the spleen and stomach. These factors contribute to the obstruction of gastric ligaments, resulting in disturbances of stomach-qi, disharmony, the descent of the stomach, and subsequent pain.^{16,17}

Morodan is a compound preparation composed of 18 Chinese herbs, including lily of the valley, Xuan ginseng, maitong, and angelica. These herbs are known to strengthen the spleen, reduce distension, harmonize the stomach, alleviate rebelliousness, relieve pain, clear the ligaments, and promote liver and bile circulation. These properties align with the underlying pathogenesis of chronic atrophic gastritis.¹⁸ The inclusion of Morodan in the treatment regimen can lead to shorter overall treatment duration and improved treatment outcomes. The results of this study demonstrated that the combination of Morodan and Rabeprazole had significant advantages over Rabeprazole alone in the treatment of chronic gastritis, as evidenced by higher overall treatment efficacy in the research group.

Clinical studies have demonstrated a close association between serum pepsinogen subgroups and the development of various gastric diseases.¹⁹ Pepsinogen is an inactive precursor of gastric protease and comprises two main subgroups, PGI and PGII. PGI is primarily secreted by glandular principal cells and cervical mucus cells in the gastric fundus. Its level increases significantly in response to

excessive gastric acid secretion. PGII, on the other hand, is mainly secreted by the fundic glands and gastric cardia glands, and it is closely linked to mucosal lesions in the gastric fundus.^{20,21}

TGF- α is an epidermal growth factor that plays a role in promoting the migration and proliferation of epithelial cells. It is involved in the response to the heterogeneous proliferation of gastric mucosa. On the other hand, EGF promotes the migration and proliferation of gastric mucosal cells and contributes to the repair of gastric mucosal damage.²²

The results of this study demonstrated that after treatment, the research group exhibited higher levels of PGI and lower levels of PGII, TGF- α , and EGF compared to the control group. These findings indicate that the combination of Morodan and Rabeprazole can effectively promote gastric mucosal repair in patients with chronic gastritis. The observed effects may be attributed to the individual properties of the herbs in Morodan, such as lily, maitong, and dendrobium, which possess nourishing properties for stomach yin. Additionally, *atractylodes*, *poria*, and *chicken naijin* contribute to spleen strengthening and dampness promotion.²³

Moreover, modern pharmacological studies have revealed that *Panax ginseng* and *Chuanxiong* can enhance blood supply to the gastric mucosa and reduce inflammatory responses within the mucosa. Yin Chen, Pu Huang, and Bai Shao can improve the internal gastric environment, while *Chicken Nei Jin* enhances gastrointestinal motility and prevents bile reflux, thereby improving the digestive capacity of the stomach and intestines. When combined with the potent acid-suppressive effect of Rabeprazole, this combination can effectively ameliorate gastric mucosal damage and promote mucosal repair.²⁴ Furthermore, the findings from these experiments suggest that in the future, PGI, PGII, TGF- α , and EGF have the potential to serve as indicators for assessing the development and prognosis of chronic gastritis. This valuable information can provide clinical insights and guide timely interventions for patients.

The inflammatory response plays a crucial role in the pathogenesis of chronic gastritis. TNF- α , IL-6, and CRP are common inflammatory factors in the human body and act as important mediators in the inflammatory process. Their levels are positively correlated with inflammatory activity.²⁵ The findings of this study demonstrated that, after treatment, the levels of TNF- α , IL-6, and CRP were lower in the study group compared to the control group. It suggests that the combination of Morodan and Rabeprazole can effectively reduce the inflammatory response in patients with chronic gastritis. The observed reduction may be attributed to the anti-inflammatory effects of *Chuanxiong*, *Yanhuosuo*, and *Panax notoginseng* present in Morodan.

Morodan, as a pure Chinese medicine preparation, has been shown to have a high safety profile for clinical use. The study results indicated no significant difference in the incidence of adverse reactions between the study group and the control group, confirming the favorable safety profile of Morodan.

Study Limitations and Recommendations for Future Research

However, this study has several limitations that should be addressed for future research. Firstly, the small sample size in this study may introduce a potential statistical calculation bias. Further studies with larger sample sizes are recommended to obtain more robust results. Additionally, future research should focus on conducting more comprehensive investigations and analyses regarding the therapeutic application of Morodan combined with Rabeprazole in chronic gastritis. It would also be beneficial to explore the underlying mechanisms associated with changes in inflammatory factors during the treatment of chronic gastritis. These efforts will contribute to providing more reliable and informative clinical references.

CONCLUSION

In conclusion, the combination of Morodan and Rabeprazole has demonstrated efficacy in the treatment of chronic gastritis. This treatment approach effectively promotes gastric mucosal repair and reduces inflammatory damage while maintaining a high safety profile and clinical applicability. The findings of this study highlight the potential benefits of this combined therapy in managing chronic gastritis. Further research with larger sample sizes and in-depth investigations into the underlying mechanisms are warranted to provide more robust evidence and strengthen the clinical references for this treatment approach. The positive outcomes observed in this study support using Morodan combined with Rabeprazole as a valuable therapeutic option for patients with chronic gastritis.

CONFLICTS OF INTEREST

The authors declared no conflicts of interest.

AUTHORS' CONTRIBUTIONS

All authors contributed equally to this work.

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