ORIGINAL RESEARCH

# Clinical Efficacy of Diet Intervention Combined with Bismuth Potassium Citrate in *Helicobacter pylori*-Related Chronic Atrophic Gastritis

Xiu Yuan, BD; TianWen Yang, MD; Jie Yao, BD; Shan Ou, MD; Yun Xu, MD, Xin Zuo, MD


## ABSTRACT

**Objective** • To investigate the clinical impact of dietary intervention in combination with bismuth potassium citrate in the management of chronic atrophic gastritis (CAG) caused by *Helicobacter pylori*.

**Methods** • From April 2019 to October 2022, 160 patients with newly identified *Helicobacter pylori*-related CAG were treated at our facility. They were split into two groups at random: the bismuth potassium citrate medication group (n = 80) and the diet intervention + bismuth potassium citrate experimental groups (n = 80). The bismuth potassium citrate treatment group was given bismuth potassium citrate capsule treatment only, and the diet intervention + bismuth potassium citrate treatment group was given diet intervention based on bismuth potassium citrate capsule. The diet intervention score, symptom score, and pathological score of the two groups were observed at baseline and after treatment, and the relationship between dietary intervention and symptoms and pathology of *Helicobacter pylori*-related CAG was analyzed.

**Results** • During the baseline period, there was no discernible difference in the diet intervention score, symptom score, or pathology score between the two groups ($P > .05$); after the diet intervention combination treatment, the diet intervention score, diet intervention + bismuth potassium citrate experimental groups symptom score, and pathology score were considerably lower than those in the bismuth potassium citrate treated group ($P < .05$).

**Conclusions** • Dietary intervention combined with bismuth potassium citrate exhibited more effective treatment than bismuth potassium citrate-only treatment in *Helicobacter pylori*-related CAG, which hinted us proper diet has a positive impact on improving the therapeutic efficacy of bismuth potassium citrate. (*Altern Ther Health Med.* 2023;29(8):846-849).


**Xiu Yuan, BD; TianWen Yang, MD; Jie Yao, BD; Yun Xu, MD; Shan Ou, MD; Xin Zuo, MD;** Department of Gastroenterology, The Sixth People's Hospital of Chongqing, Chongqing, China.

*Corresponding author: Xin Zuo, MD*
*E-mail: 377364578@qq.com*

## BACKGROUND

As a result of an inflammatory process, chronic atrophic gastritis (CAG) is a degenerative stomach mucosal lesion.[1] However, CAG generally sustains an asymptomatic condition at the initial stage of the disease, which leads to being largely underdiagnosed.[2] Because of this, it is still unknown how often CAG affects people. A thorough evaluation of 107 papers by researchers revealed that the estimated CAG prevalence was 33% globally.[3] The overall incidence of CAG among adults in China was 49.4% in 2014, according to the report.[4] The incidence rate of CAG was also on the rise in recent years. The main cause of CAG is *Helicobacter pylori* infection and the other is autoimmune dysregulation. Though they are different types of diseases, they generally share overlapping characteristics. The pathological manifestations of CAG are glandular decrease or disappearance, atrophy and thinning of gastric mucosa, and moderate and severe intestinal metaplasia are found in severe cases. Additionally, CAG not only causes symptoms such as acid regurgitation, belching, and abdominal pain, but also trends to develop into gastric cancer with the progression of the disease. Its prevention and treatment are regarded as an important challenge by medical and academic communities.[5]

Bismuth agent is now the first-line treatment for *Helicobacter pylori* (*H. pylori*) eradication in patients with *H. pylori* associated gastrointestinal illness.[6-7] Researchers assessed the effectiveness and safety of bismuth potassium citrate capsules and other three bismuth medicines in a clinical trial (NCT04209933). The results demonstrated that all these bismuth agents could be used in *H. pylori* eradicating therapy.[8] Also, Wang L et.al. recruited 351 *H. pylori*-related CAG patients and gave them a bismuth-containing therapeutic agent, which showed a high efficacy in these patients.[9] Thus, bismuth agents could be the first-line drugs

for *H. pylori*-related CAG. Furthermore, the occurrence and development of CAG have a close relationship with improper diet. According to a previous study, the intake of fruits, vegetables, or dietary vitamin C have a positive effect, while the milk consumption increased the risk of CAG advancement in patients.[10] Additionally, it reported that a healthy diet may have strong antibacterial effects against *H. pylori*, suggesting that dietary changes may reduce the risk of CAG caused by *H. pylori*.[11] However, it is unclear how nutrition intervention affects CAG prognosis.

## MATERIALS AND METHODS

### General information

160 patients with CAG caused by *H. pylori* were randomly assigned between the diet intervention + bismuth potassium citrate therapy group (n = 80) and the bismuth potassium citrate treatment group (n = 80) from April 2019 to October 2022. The general data for the two groups were comparable and evenly distributed, as shown in Table 1 ($P > .05$).

This clinical study has been approved by the ethical committee of Jinshan District Tinglin Hospital. All human investigations were conducted in compliance with the ethical guidelines outlined in the appropriate version of the Declaration of Helsinki since they had been approved by the appropriate Tecnologico de Monterrey ethics committee. The Shanghai Jinshan Tinglin Hospital's ethical committee gave their clearance (approval number: NO.2018-kylw-05). All individuals taking part in the study gave their informed consent.

### Case selection criteria

**Inclusion criteria.** (1) Every patient met the CAG's diagnostic standards for chronic gastritis in China (Shanghai, 2017)[12]; (2) patients were newly identified with *Helicobacter pylori*; (3) patients were 18-65 years old; (4) patients had not participated in other clinical studies recently; (5) patients had not received other formal treatment before treatment; and (6) patients were informed of the study and they signed informed consent.

**Exclusion criteria.** (1) Patients who suffer from liver and renal issues, or malignant tumor; (2) patients with other types of gastritis; (3) women in lactation or pregnancy; (4) patients with neurological or mental diseases; (5) patients who have used acid suppressants, gastric mucosal protectants, and nonsteroidal anti-inflammatory drugs in the past three months; and (6) patients who are negative for *Helicobacter pylori* infection.

### Intervention methods

The bismuth potassium citrate treatment group was given 2 capsules of bismuth potassium citrate only (Lizhu Pharmaceutical Factory, China), 4 times/day for 3 months. The diet intervention (carbonated drinks, fast food, or spicy food uptake) + bismuth potassium citrate treatment group was given both diet intervention and bismuth potassium citrate. The self-made "Chronic atrophic gastritis diet guidance manual", includes eating time, eating quantity, eating methods, cooking materials, cooking methods, and other contents. Patients were required to standardize their diet according to this manual, and the intervention lasted for 3 months.

**Table 1.** Comparison of General Data Between the Two Groups (n, $\bar{x} \pm s$)

| Group | Observation group (n = 80) | Control group (n = 80) | $t/\chi^2$ | *P* value |
|---|---|---|---|---|
| Gender | | | 0.023 | >.05 |
| Male | 48 | 45 | | |
| Female | 32 | 35 | | |
| Education level | | | 0.875 | >.05 |
| Junior high school and below | 26 | 23 | | |
| High school | 35 | 37 | | |
| College or above | 19 | 20 | | |
| Family history of gastric cancer | | | 0.054 | >.05 |
| Yes | 69 | 70 | | |
| Nothing | 11 | 10 | | |
| History of anticoagulant use | | | 0.044 | >.05 |
| Yes | 14 | 13 | | |
| Nothing | 66 | 67 | | |
| Course of disease (years) | 1.36 ± 0.28 | 1.37 ± 0.45 | 0.168 | >.05 |
| Age (one year old) | 42.16 ± 5.24 | 42.45 ± 5.46 | 0.342 | >.05 |

### Observation index

**Dietary intervention score.** Self-made " Dietary intervention scale", composed of "drinking", "spicy diet", "eating speed", "carbonated drinks", "whether the meal was divided or not", and "whether the three meals were regular". The final score ranged from 0 to 8. The worse the dietary intervention was, the higher the score.[13-15] Experts investigated and evaluated the scale's validity and reliability, and found that the reliability coefficient was 0.914 and the validity coefficient was 0.902.

**Symptom score.** Self-compiled "Symptom scale of chronic atrophic gastritis". The scale was composed of "acid regurgitation", "belching", "abdominal pain", "abdominal distension", "anorexia", and "nausea and vomiting". The final score ranged from 0 to 18. The more severe the symptoms were, the score was higher.[16-18] The scale's validity and dependability were examined and evaluated by experts. The Cronbach'α reliability coefficient and validity coefficient were 0.946 and 0.935 respectively.

**Pathological score.** The pathological score of gastroscopy tissue was assessed in accordance with the consensus view on chronic gastritis in China (Shanghai, 2017) and the modified Sydney scoring system.[19] 0 to 18 was the final score. The more severe the subjects' pathological signs are, the higher the score.[12] Note that the authors do not declare data reproducibility in this study.

### Statistical methods

SPSS 20.00 was used to process all the data. If the measurement data is regularly distributed, the comparison between groups is stated as mean standard deviation ($\bar{x} \pm s$) by independent sample test; the counting data is expressed as n (%) by chi-square test, and the inspection level is set at = 0.05. Diet intervention and symptoms and pathology were analysed using a multivariate unconditional logistic regression model. A multi-factor unconditional logistic regression model was created for the evaluation of symptom

scores using the symptom score of patients with *H. pylori*-linked CAG as the dependent variable and the diet intervention score as the independent variable. The multivariate unconditional logistic regression model was developed for the evaluation of pathological score, using the pathological score of patients with *H. pylori*-linked CAG as the dependent variable and the diet intervention score as the independent variable.

## RESULTS

### Comparison of dietary intervention score, symptom score, and pathological score among two categories.

After diet intervention plus bismuth potassium citrate treatment, the diet intervention score, symptom score, and pathological score of this group were all significantly lesser compared to the bismuth potassium citrate intervention group, and the difference was found to be statistically relevant ($P > .05$). During the baseline period, there was no considerable difference in the two groups' diet intervention scores, symptom scores, and pathological scores (Table 2).

**Table 2.** Comparison of Dietary Intervention Score, Symptom Score, and Pathological Score Between the Two Groups at Baseline and After Diet Intervention Treatment (Points, $\bar{x} \pm s$)

| | Baseline period | | After treatment | |
|---|---|---|---|---|
| | Diet intervention + bismuth potassium citrate treatment group | Bismuth potassium citrate treatment group | Diet intervention + bismuth potassium citrate treatment group | Bismuth potassium citrate treatment group |
| Dietary intervention score | 6.15 ± 0.37 | 6.32 ± 0.95[a] | 2.61 ± 0.46 | 6.94 ± 0.99[b] |
| Symptom score | 13.59 ± 2.30 | 13.36 ± 2.75[a] | 7.89 ± 1.32 | 10.83 ± 2.04[b] |
| Pathological score | 10.74 ± 1.35 | 10.92 ± 1.14[a] | 6.25 ± 1.91 | 8.88 ± 1.76[b] |

[a] $t = 1.491, 0.573, 0.911$, $P > .05$
[b] $t = 35.477, 10.822, 9.057$, $P < .05$

Note: compared with diet intervention + bismuth potassium citrate treatment group.

**Table 3.** Multivariate Unconditional Logistic Regression Model of Diet Intervention and Symptoms of *H. pylori* Related CAG

| Factor | β | SE (β) | Wald $\chi^2$ | *OR* | 95% CI | | *P* value |
|---|---|---|---|---|---|---|---|
| | | | | | upper limit | lower limit | |
| Dietary intervention score | 0.319 | 0.917 | 16.525 | 3.413 | 4.427 | 2.364 | .000 |
| Constant term | 7.378 | 0.330 | 2.249 | 1.973 | 1.219 | 6.328 | 7.041 |

**Table 4.** Multivariate Unconditional Logistic Regression Model of Diet Intervention and Pathology of *H. pylori* Related CAG

| Factor | β | SE (β) | Wald $\chi^2$ | *OR* | 95% CI | | *P* value |
|---|---|---|---|---|---|---|---|
| | | | | | upper limit | lower limit | |
| Dietary intervention score | 0.202 | 0.247 | 9.446 | 5.519 | 4.986 | 2.606 | .000 |
| Constant term | 4.956 | 0.256 | 7.235 | 2.164 | 5.818 | 1.865 | 4.139 |

### Multivariate unconditional logistic regression model analysis of dietary intervention and symptoms of *H. pylori*-related CAG

By using regression approach, the independent variables were both included (α = 0.05) and eliminated (α = 0.10). Dietary intervention was discovered to be an independent preventive factor for symptoms of *H. pylori*-related CAG after confounding variables were taken into account (Table 3).

### Multivariate unconditional logistic regression model analysis of dietary intervention and pathology of *H. pylori*-related CAG

By using the regression approach, the independent variables were both included (α = 0.05) and eliminated (α = 0.10). Dietary intervention was demonstrated to be an independent preventive factor of *H. pylori*-related CAG after confounding factors were taken into account. (Table 4).

## DISCUSSION

Epidemiological studies showed that CAG has regional characteristics, which are related to the local environment, diet, and lifestyle.[20] As a progressive precancerous lesion, it had been reported that improper diet might affect the CAG initiation and progression. The objective existence of eating habits has risen from experience to statistical data verification, which provides the basis and guidance for the research direction of CAG.

The patients who intake carbonated drinks, fast food, or spicy food were found with gastric mucosa injury and were pathologically aggravated. However, side dishes of vegetables and fruits might benefit the gastric mucosa in CAG patients. The relationship between diet intervention and the prognosis of CAG deserved exploration.[21]

In this study, we recruited 160 patients diagnosed with *H. pylori*-related CAG and gave them regular bismuth potassium citrate treatment or diet intervention combined with bismuth potassium citrate treatment, respectively. The single-factor analysis found that diet intervention combined with bismuth potassium citrate reversed symptoms and pathological condition of *H. pylori*-related CAG. This implied that diet intervention was associated with the pathology and symptoms of CAG, and that patients who received effective food intervention had improved clinical outcomes compared to those who had ineffective CAG. Individuals with CAG who receive adequate dietary advice had milder symptoms and pathology than those with CAG who receive poor dietary advice. In order to further examine the connection between food intervention and the pathology and symptoms of CAG, a multivariate unconditional logistic regression model was employed. It was concluded that dietary intervention was an independent protective factor for symptoms and pathology of CAG. Symptom severity in patients receiving diet therapy was 3.413 times lower than that in patients with poor diet intervention, and the severity of pathology in patients with good diet intervention was 5.519 times lower than that in patients with poor diet intervention. This is in line with what researchers Fan et al. reported in their study.[22] Dietary modification, therefore, has a close relationship with the pathology and symptoms of CAG caused by *H. pylori*. This may be connected to the rise in epidermal growth factor seen in patients' stomachs[23] because a reasonable diet will make the digestive glands

secrete more epidermal growth factor, and in turn, more digestive juice from the gastric mucosa.

Inflammation of the stomach mucosa and intestinal glands taking the role of the normal gastric glands, pseudo pylorus gland, fibrous tissue, or fibro muscular gland is the pathological process of CAG. Fang *et al.* proposed that the pathological changes of CAG have a critical point.[24] Active treatment and intervention for patients with CAG before the critical point can still delay or reverse the progression of CAG.[25] Therefore, alleviating, delaying, or reversing gastric gland atrophy, epithelial metaplasia, and atypical hyperplasia has become a consensus in the treatment of CAG. After many considerations, this study finally selected a bismuth potassium citrate capsule which has been frequently employed as a control in the first-line treatment of CAG linked to *H. pylori*. The results showed that compared to bismuth potassium citrate alone, additional diet intervention on this basis can alleviate, delay, or reverse the condition of CAG. The reason may be that good diet intervention combined with bismuth potassium citrate has a synergistic effect on *H. pylori*-related CAG. Thus, giving patients a reasonable diet can establish a benign cycle of gastric digestion, and aid in the management of long-term atrophic gastritis in a complementary manner.[26]

## CONCLUSION

In conclusion, diet intervention is an independent protective factor of symptoms and pathology of *H. pylori*-related CAG. This result also suggests us that improving diet habits might have a positive impact on the prognosis of CAG. The optimization of diet intervention for CAG will become the main direction of our further research.

### DATA AVAILABILITY

The data used to support this study are available from the corresponding author upon request.

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### AUTHOR DISCLOSURE STATEMENT

The authors declare that they have no conflicts of interest.

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Contributions of the author: Cuiping Wang and Min Xu came up with the study's concept and design. Xiuhong Yang handled data analysis and interpretation. Cuiping Wang, Xiuhong Yang, Pengsheng Tan, and Min Wang wrote the manuscript; Cuiping Wang and Min Xu have reviewed the manuscript critically for significant intellectual substance. The final manuscript was read and approved by all writers.

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