Systematic Review and Meta-Analysis of Moluodan in Treatting Chronic Atrophic Gastritis

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Abstract: **Objective:** To evaluate the clinical efficacy of Moluodan in treating chronic atrophic gastritis by systematic review. **Methods:** Eight databases were retrieved, and the retrieval time is limited to August 2022. The published clinical trials of Moluodan in treating chronic atrophic gastritis were analyzed by Revman and TSA. **Results:** 2 studies and 592 cases were included. Compared with control group, Moluodan alone significantly improved the effective rate of disease detection [RR=1.73, 95% CI=(1.48,2.02), P<0.0001]. The trial sequential analysis showed that these results were conclusive. The funnel plot showed asymmetry of scattered points on both sides, suggesting that there may be publication bias. **Conclusion:** Moluodan can improve the efficiency of disease examination for patients with chronic atrophic gastritis, play a important role in slowing down the progress of chronic atrophic gastritis, and may have the value of further research.

1. Introduction

Gastric cancer is internationally recognized as a malignant tumor that with a high mortality [1]. In China, its incidence rate and mortality rate rank second in malignant tumors [2-3], showing an upward trend. At present, the mode of "atrophic gastritis- intestinal metaplasia- dysplasia- gastric cancer" is widely recognized by the medical community [4]. Precancerous lesion of gastric cancer refers to a pathological state of intestinal metaplasia and/or dysplasia, which is often accompanied by chronic atrophic gastritis [5]. Western medicine treats chronic atrophic gastritis mainly from the eradication of Helicobacter pylori and symptomatic treatment [6], but there is still a lack of effective reverse treatment [7], while Chinese medicine may have advantages in treating this disease. [8-9]. Studies showed that Moluodan, a Chinese medicine, can relieve the patient's discomfort with chronic atrophic gastritis, improve the degree of atrophy and dysplasia of gastric mucosal glands, reverse low-grade intraepithelial neoplasia [10], and ensure safety [11]. Because of its advantages in the treatment of gastric precancerous lesions, Moluodan was included in the clinical application guidelines of Chinese patent medicine for chronic gastritis (2020) [12], and was included in the latest European guidelines for the comprehensive management of gastric precancerous lesions in March 2019 [13]. This study will compare the clinical efficacy of Moluodan and conventional western medicine (folic acid/vitamin) in the treatment of chronic atrophic gastritis through systematic review

2. Methods

2.1. Literature search

CNKI, CBM, VIP, Wanfang, Web of Science, Embase, PubMed, and the Cochrane Library databases were searched. The retrieval time is limited to August 2022, and the subject words include Moluodan and chronic atrophic gastritis. Free words are expanded with the help of the database, and subject words and free words are combined for retrieval.

2.2. Inclusion and exclusion criteria

Inclusive criteria: (1) Data type: randomized controlled trial; (2) Subjects: It is consistent with the basic diagnosis of chronic atrophic gastritis; (3) Treatment plan: The experimental group took Moluodan, and the control group took conventional medicine. (4) Outcome measures: The main efficacy endpoint was the effective rate of disease detection, which referred to the treatment efficiency judged by disease examination.

Exclusion criteria: (1) Review, animal experiment, case report and other studies; (2) Research with incomplete data; (3) Research with duplicate data.

2.3. Literature screening, data statistics and bias risk

First, the literature was selected layer by layer, and finally the included literature was determined. Second, the documents will be classified and sorted, and the author, age, sample size, intervention measures, treatment course and other basic characteristics will be extracted and entered into the data statistics table. Third, Revman5.3 is used to judge the bias risk according to the required items. All operations are completed by the two authors, and any differences are resolved through discussion.

2.4. Statistical analysis

Meta-analysis was carried out by Revman5.3. Relative risk (RR) and 95% confidence interval (95%CI) were used to evaluate secondary variables. And the heterogeneity analysis was based on I^2 test. If $I^2 < 50\%$, the heterogeneity was small, so the fixed effect model (FEM) was used for analysis. Otherwise, we we chose to use the random effect model (REM). Trial sequential analysis was carried out by TSA0.9.5.10 beta. If the accumulated Z value exceeded the RIS or TSA inspection line, the result was trustworthy. The funnel chart was used to evaluate the publication bias, and scatter distribution is used to judge publication bias.

3. Results

3.1. Search results

460 literatures were retrieved, 240 duplicates were screened out, 202 literatures were screened out after reading the title and abstract, 16 literatures were excluded by consulting the full text, and 2 literatures were finally included [14-15].

3.2. Basic data

Two clinical studies and 592 patients were included (Table 1).

Table 1: Basic Data Sheet

ID	sample size		Pathology	experimental arm	control arm	course of treatment/ months
	experimental	control				
Tang XD 2015	200	196	Mild to moderate dysplasia	Moluodan 9g tid Placebo 5mg tid	Folate 5mg tid Placebo 9g tid	6
Du AM 2015	130	66	/	Moluodan 8pills tid	Folate 10mg tid Vitamin E 10mg tid	6

3.3. Bias risk assessment

In the two studies included, the risk of allocation concealment and implementation of blinding in Du AM 2015 was not clear, and the deviation in other areas was low risk. The deviation of Tang XD 2015 in all areas is low risk.

3.4. Meta analysis results

Due to the small heterogeneity, FEM was set for analysis. And the results showed that compared with the conventional drugs, the effective rate of disease detection in the Moluodan increased by about 73% [RR=1.73, 95% CI=(1.48,2.02), P<0.0001] (Figure 1).
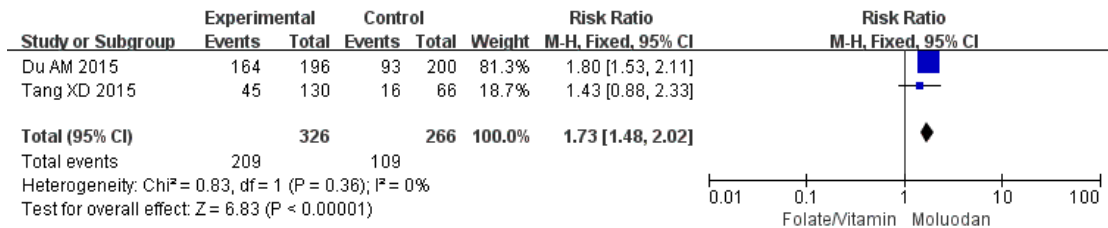

Figure 1: Meta analysis of Moluodan in the treatment of CAG

3.5. Trial sequential analysis results

RR and fixed effect models were used to set the bilateral class I error probability α=0.05 and class II error probability β=0.20. RIS is defined as the expected amount of information, and the positive rate is calculated by the inclusion study. The result showed that the cumulative Z-value curve crossed the RIS threshold (RIS=147) in the first study, suggesting the result is conclusive.

3.6. Publication bias

The funnel plot shows asymmetry of scattered points on both sides, Which mean the result might have a publication bias.

4. Discussion

CAG is a chronic inflammation of gastric mucosa caused by a variety of causes, and it is often associated with atypical hyperplasia and has a potential risk of canceration [16-17]. At present, early treatment of CAG is the effective measure to prevent gastric cancer [18]. Pathological examination is the gold standard for the diagnosis of CAG, so the efficiency of disease examination is the main efficacy endpoint of this study. Moluoden is a Chinese medicine, which is composed of Baihe, Maidong, Shihu, Xuanshen, Sanqi, Danggui, Puhuang, Chuanxiong, Fuling, Baizhu, Jineijin, Diyu,

Zexie, Jiujie Changpu, Yinchen, Baishao, Yanhusuo, Wuyao. It has the functions of invigorating the spleen and removing dampness, and activating blood circulation, which is consistent with the TCM pathogenesis of CAG [19]. Meta analysis results showed that, compared with folic acid or vitamin, the effective rate of disease detection in the Moluodan group was significantly improved. The trial sequential analysis showed that the current results were conclusive, suggesting that Moluodan could effectively slow down the pathological progress of CAG.

5. Conclusion

Moluodan can improve the efficiency of disease examination for patients with chronic atrophic gastritis, play a important role in slowing down the progress of chronic atrophic gastritis, and may have the value of further research.

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