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Atropine plus omeprazole for acute gastritis: Efficacy and safety analysis

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Abstract: This article primarily discusses the efficacy and safety of atropine (ATR) plus omeprazole (OME) for the treatment of acute gastritis (AG). From May 2022 to May 2024, 95 AG patients were selected, including 50 cases treated with ATR+OME (observation group) and 45 cases with anisodamine (ADM) plus OME (control group). Comparative analyses of the following dimensions were then carried out: Clinical efficacy, safety (xerostomia, palpitations, and headaches), symptom remission time (stomach pain, abdominal distension and nausea and vomiting), serum inflammatory factors (tumor necrosis factor [TNF]-α, interleukin [IL]-6 and interferon [IFN]-β) and plasma gastrointestinal hormones (epidermal growth factor [EGF], gastrin [GAS] and somatostatin [SS]). After analysis, the observation group had a higher total effective rate, a lower overall incidence of adverse reactions and a shorter remission time of symptoms such as stomach pain, abdominal distension, and nausea and vomiting than the control group, all with statistical significance. Moreover, compared with the baseline (before medication) and the control group, TNF-α, IL-6, IFN-β and GAS were reduced statistically in the observation group after medication, while EGF and SS were markedly increased. Thus, ATR plus OME has significant efficacy in the treatment of AG while ensuring high clinical safety, which deserves clinical promotion.

Keywords: Atropine, omeprazole, acute gastritis, efficacy, safety.

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INTRODUCTION

Acute gastritis (AG), as a common digestive disease mainly manifested as gastrointestinal inflammation, is related to factors such as viruses, bacteria, or parasitic pathogens in terms of etiology (Ryoo, 2021). According to statistics, AG has a high incidence (approximately 10.0%) in the United States, resulting in nearly 180 million cases annually (Schmidt, Groom *et al*., 2022). Patients with the disease experience clinical symptoms such as stomach pain, abdominal distension, diarrhea, abdominal pain, nausea, vomiting, and fever, adversely affecting their daily normal life (Feyisa and Woldeamanuel, 2021, Graves, 2013). Adverse events such as hematochezia, dehydration, acidosis and even shock may occur as the condition progresses (Granado-Villar, Cunill-De Sautu *et al*., 2012). Clinically, drug therapy is commonly used for the treatment of AG, including oral and intravenous rehydration. Oral rehydration has an obvious curative effect and is associated with lower medical expenses and phlebitis risk, but this therapy is underused in clinical application for various reasons (doctor's preferences, family members' concerns about dehydration, etc.) (Bender, Ozuah *et al*., 2007, Chow, Leung *et al*., 2010, Ozuah, Avner *et al*., 2002). Therefore, this study plans to optimize AG treatment from the perspective of intravenous rehydration, hoping to contribute to the optimization of the treatment of this disease.

Atropine (ATR) and anisodamine (ADM) are both anticholinergics that can relax the gastrointestinal smooth muscle by blocking the binding of acetylcholine and its receptors, thus relieving stomach cramps (Krueger, Michel *et al*., 2013). ATR has nearly 8 to 10 times the bioavailability and only one-seventh the urinary excretion rate than ADM, demonstrating more pharmacokinetic advantages (Tian, Li *et al*., 2015). Omeprazole (OME), on the other hand, is a first-generation proton pump inhibitor that protects the gastric wall barrier by reducing gastric acid secretion and can also help relieve clinical symptoms and prevent gastric ulcers in obese patients undergoing bariatric surgery (Le Merdy, Tan *et al*., 2021). In an animal model of gastrointestinal diseases, OME was shown to mitigate cysteamine hydrochloride-induced anxiety-related behaviors, which may be one of the underlying mechanisms by which OME exerts therapeutic effects on the gastrointestinal tract (Chamniansawat, Kampuang *et al*., 2021, Sri Rethinavel, Selvaraj *et al*., 2022). It has also been reported that OME inhibits the de novo adipogenesis of gastric epithelial cells, with significant therapeutic potential for Helicobacter pylori (HP) infection-associated gastric diseases (Chen, Li *et al*., 2020).

This study mainly compares the efficacy and safety of ADM plus OME versus ATR plus OME in the treatment of AG, aiming at providing strong reference arguments for the clinical drug selection of AG.

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MATERIALS AND METHODS

General data

The participants were 95 AG patients who visited and treated in our hospital between May 2022 and May 2024. Among them, 50 cases in the observation group received ATR+OME and 45 cases in the control group received ADM+OME. The observation and control groups were clinically comparable with no statistical difference in general data (P>0.05).

Patient selection criteria

Inclusion criteria: All patients developed varying degrees of nausea, abdominal pain and other symptoms, met the diagnostic criteria for AG (Kang, Kim *et al*., 2023), agreed to cooperate with the study and had complete clinical data.

Exclusion criteria: Patients with other tumor diseases, chronic gastritis, allergic to study medication, severe cardiovascular, pulmonary, brain, or renal insufficiency, as well as those with psychological diseases and mental disorders, were excluded.

Medication methods

The control group was treated with ADM+OME. OME was administered intravenously by dissolving 40mg of OME in 0.9% sodium chloride injection, once a day, 40 mg each time. If the pain was not relieved after two hours of medication, 10mg of ADM hydrochloride injection was given via an intravenous bolus. The observation group was treated with ATR+OME. The 1.6mg ATR was administered as an intravenous bolus, followed by OME treatment consistent with the control group in 30 days. In case of no alleviation of clinical symptoms after two hours of treatment, a second intravenous bolus of ATR was given according to the doctor's advice (the C_{max} was 9.6ng/mL and the T_{max} went from 3 to 60 minutes).

Outcome measures

1. Clinical efficacy. Criteria for judging efficacy: Cure is defined as basically resolved clinical symptoms and signs after treatment, as well as the basic return of anal exhaust and defecation to normal; Effectiveness refers to the significant improvement in clinical symptoms and signs of patients after treatment, as well as a significant reduction in stomach discomfort; Ineffectiveness corresponds to no change or even aggravation of clinical symptoms and signs in the treated patients.
2. Safety. We observed and recorded the number of cases of side effects such as xerostomia (XS), palpitations, and headaches in two groups of patients after treatment, and calculated the overall incidence rate.
3. Time to symptom remission. The duration of stomach pain, abdominal distension, as well as nausea and vomiting was observed and recorded.
4. Serum inflammatory factors. Before and after treatment, 5mL of fasting venous blood was drawn to obtain serum via centrifugation. Tumor necrosis factor (TNF)-α, interleukin (IL)-6 and interferon (IFN)-β were detected by enzyme-linked immunosorbent assays (ELISAs).
5. Plasma gastrointestinal hormones. ELISAs were conducted to determine epidermal growth factor (EGF), gastrin (GAS) and somatostatin (SS) levels in plasma samples.

ETHICAL APPROVAL

The study is exempt from review by the Ethics Committee of Jian'ou Municipal Hospital based on the basis that this type of study and waived the need for informed consent. This study follows proper guidelines (Ref No. JMH/Pharm/EA/28) according to the principles of declaration. This study has received approval from the Jian'ou Municipal hospital's Ethics Committee and informed consent from all subjects.

STATISTICAL ANALYSIS

This study used the Mean ±SEM to describe continuous data; independent sample t-tests were used for inter-group comparisons and paired t-tests for intra-group comparisons before and after medication. Categorical data were expressed by the rate (percentage), and between-group comparisons were made by χ^2 tests. The collected experimental data were analyzed by SPSS 20.0. Statistical significance was declared if the P-value was less than 0.05.

RESULTS

Inter-group comparison of general data

The inter-group comparison revealed no statistical differences in age, sex, disease course, disease type, and family history (P>0.05) (table 1).

Inter-group comparison of clinical efficacy

The total effective rate was 94.00% in the observation group and 71.11% in the control group, indicating markedly higher efficacy in the observation group treated with ATR+OME (P<0.05) (table 2).

Inter-group comparison of safety

There were 2 cases of XS in the observation group, compared to 4 cases of palpitations, 3 cases of headaches, and 2 cases of XS in the control group, with a significant difference in the overall incidence of adverse reactions (P<0.05) (table 3).

Inter-group comparison of symptom remission time

Statistical analysis of the remission time of symptoms such as stomach pain, abdominal distension, and nausea and vomiting in the two groups showed that the control group had statistically longer remission time of the above symptoms than the observation group (P<0.05) (fig. 1).

Table 1: Inter-group comparison of general information

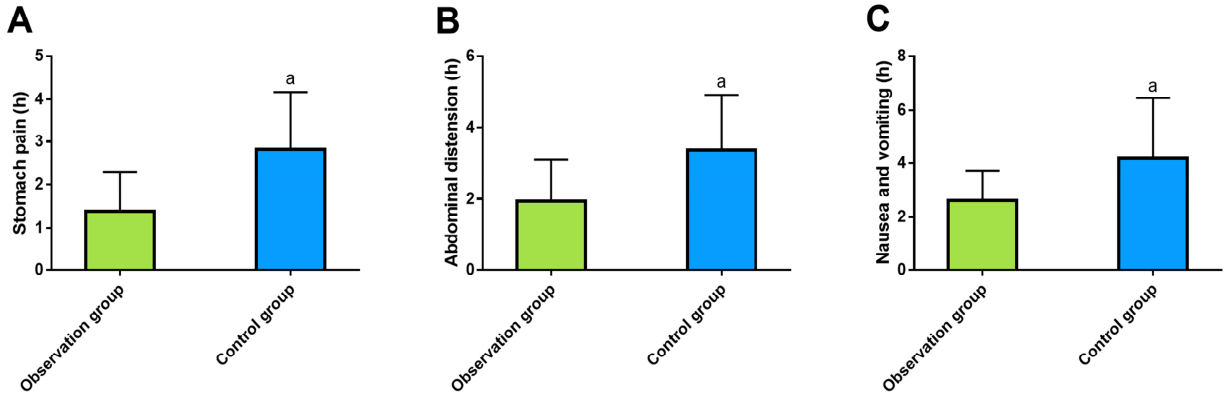
General information	Observation group (n=50)	Control group (n=45)	χ^2/t	P
Age (years old)	44.12±8.55	43.49±7.74	0.375	0.709
Sex			0.068	0.794
Male	28 (56.00)	24 (53.33)		
Female	22 (44.00)	21 (46.67)		
Disease course (days)	3.10±1.45	2.67±1.62	1.365	0.176
Disease type			0.322	0.851
Acute simple gastritis	15 (30.00)	14 (31.11)		
Acute erosive gastritis	25 (50.00)	24 (53.33)		
Acute suppurative gastritis	10 (20.00)	7 (15.56)		
Family medical history			1.085	0.298
With	8 (16.00)	4 (8.89)		
Without	42 (84.00)	41 (91.11)		

Table 2: Inter-group comparison of clinical efficacy

Curative effect	Observation group (n=50)	Control group (n=45)	χ^2	P
Cure	27 (54.00)	18 (40.00)		
Effectiveness	20 (40.00)	14 (31.11)		
Ineffectiveness	3 (6.00)	13 (28.89)		
Total effectiveness	47 (94.00)	32 (71.11)	8.859	0.003

Table 3: Inter-group comparison of safety

Safety	Observation group (n=50)	Control group (n=45)	χ^2	P
Xerostomia	2 (4.00)	2 (4.44)		
Palpitations	0 (0.00)	4 (8.89)		
Headaches	0 (0.00)	3 (6.67)		
Total	2 (4.00)	9 (20.00)	5.922	0.015



A. Stomach pain remission time of the two groups. B. Abdominal distension remission time of two groups. C. Nausea and vomiting remission time of two groups. Note: [a]P<0.01.

Fig. 1: Inter-group comparison of symptom remission time.

Inter-group comparison of serum inflammatory factors

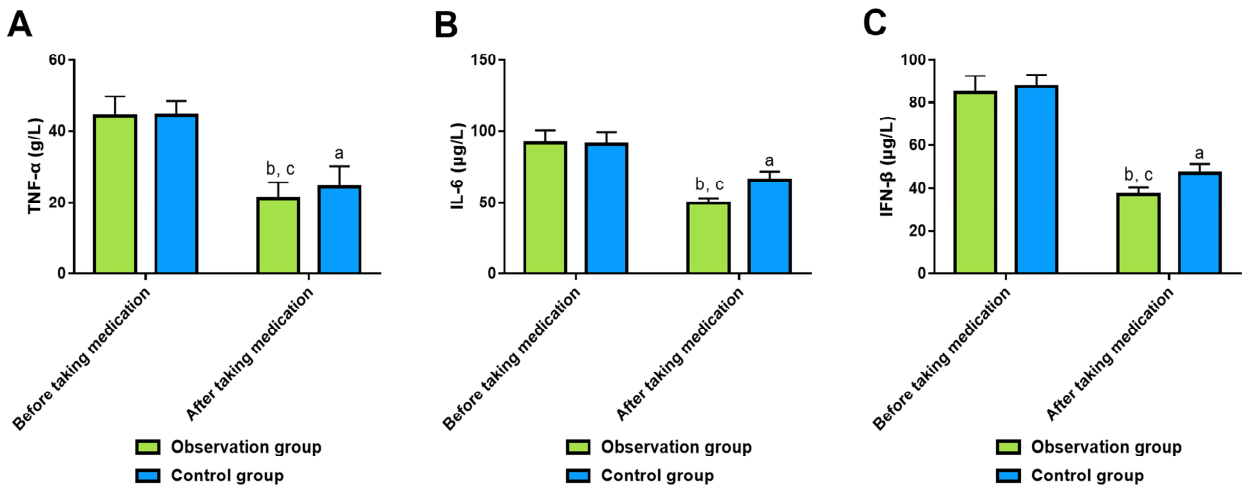
The two groups differed little in serum inflammatory factors such as TNF-α, IL-6 and IFN-β before medication (P>0.05); all these indexes were statistically inhibited after taking the medicine (P<0.05), with even lower levels in the observation group compared to the control group (P<0.05). fig. 2.

Inter-group comparison of plasma gastrointestinal hormones

EGF, GAS and SS presented similar levels in the two groups before medication (P>0.05); EGF and SS increased statistically after taking the medicine and were higher in the observation group versus the control group (P<0.05); while GAS was markedly inhibited, with even lower levels in the observation group (P<0.05). fig. 3

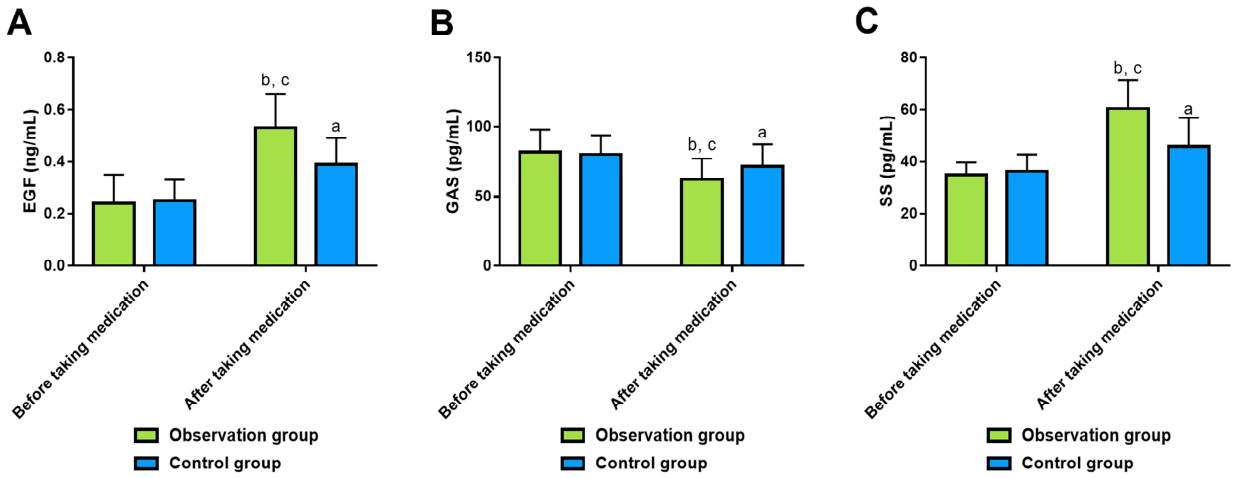
DISCUSSION

As an upper digestive tract disease, AG can be divided into several pathological types, such as acute simple, erosive and suppurative gastritis, among which acute



A. TNF-α levels before and after medication. B. IL-6 levels before and after medication. C. IFN-β levels before and after medication. Note: [a]P<0.05 and [b]P<0.01 vs. before medication; [c]P<0.05 vs. Control.

Fig. 2: Inter-group comparison of serum inflammatory factors.



A. EGF levels before and after medication. B. GAS levels before and after medication. C. SS levels before and after medication. Note: [a]P<0.05 and [b]P<0.01 *vs.* before medication; [c]P<0.05 *vs.* Control.

Fig. 3: Inter-group comparison of plasma gastrointestinal hormones.

erosive gastritis and acute simple gastritis are the most common, with the characteristics of rapid onset and varying severity of clinical symptoms (Kayaçetin and Güreşçi, 2014, Marques *et al*., 2024). The disease is complex, and effective treatment can help improve prognosis and quality of life (Duque-Buitrago, Tornero-Martínez *et al*., 2023, Tan and Wong, 2011). This study mainly analyzes two treatment methods for this disease, and a detailed report is hereby provided.

Despite the certain gastric protective activity of OME, its protective effect is limited to the intestinal canal, so it is often used in combination with other drugs to treat AG (Sánchez-Trigueros, Méndez-Cruz *et al*., 2021). A rat experiment shows that the preventive effect of OME on AG is related to its protection of gastric mucosal integrity, mainly by maintaining a high gastric pH and reducing total gastric acid (Topaloglu, Muftuoglu *et al*., 2004). ATR, an alkaloid extracted from belladonna, can not only be used as a common rescue drug to relieve spasms in clinical practice, but also play an effective role in relieving stomach cramps and pain in the treatment of AG (Danaie, Masoudi *et al*., 2023). In this study, the total effective rate of the observation group treated by ATR+OME was 94.00%, compared to 71.11% of the control group receiving ADM+OME, indicating that ATR+OME can achieve higher curative effects than ADM+OME. Safety comparison showed that only 2 cases of XS occurred in the observation group, while 4 cases of palpitations, 3 cases of headaches and 2 cases of XS occurred in the control group (Müller-Krampe, Oberbaum *et al*., 2007). The comparison revealed an obviously lower overall incidence of adverse events in the observation group, suggesting that ATR+OME has significant safety

for AG patients, which to some extent, can help reduce the risk of adverse events such as palpitations, headaches, and XS. Other data also revealed statistically shorter remission time of stomach pain, abdominal distension, and nausea and vomiting in the observation group compared with the control group, indicating that ATR+OME can statistically promote the recovery of clinical symptoms in AG patients. In the meta-analysis by Lin X *et al*. (Lin, Chen *et al*., 2021), the combination of ATR and OME in the treatment of AG shows a higher total effective rate, with fewer adverse reactions and an effective relieving effect on AG-related clinical symptoms such as abdominal pain, diarrhea, nausea and vomiting, consistent with our findings. Furthermore, we tested serum inflammatory indexes and found that TNF-α, IL-6, and IFN-β in the observation group were statistically inhibited after medication, statistically lower compared to the control group, suggesting that ATR+OME can statistically inhibit serum hyperinflammation in AG patients. Pro-inflammatory cytokines such as TNF-α, IL-6 and IFN-β all mediate gastrointestinal immunomodulation and physiological processes, among which TNF-α polymorphisms are closely associated with an increased risk of gastric cancer in the Chinese population, IL-6 is strongly related to HP infection-related gastric diseases and IFN-β can participate in the independent regulation of gastric metaplasia (Bauditz, Ortner *et al*., 1999, El-Zaatari, Bishu *et al*., 2020, Leja, Wex *et al*., 2012, Xie, Chen *et al*., 2012). As reported by Fuentes JM *et al*. (Fuentes, Fulton *et al*., 2008), ATR helped mitigate lipopolysaccharide-related inflammation in mice, statistically reduce TNF-α levels and improve the survival rate of mice to some extent, which is similar to our research results. In the report of Arciniega-Martínez IM *et al*. (Arciniega-Martínez, Pacheco-Yépez *et al*., 2022), ATR statistically suppressed aberrant inflammatory responses in the intestinal homeostasis of mice, mainly by effectively down-regulating IFN-γ/CD4 T or IL-6/CD4 T cell counts, which supports our research results. The detection of plasma gastrointestinal hormone determined statistically increased EGF and SS in the observation group, higher compared to the control group, as well as markedly inhibited GAS that was lower versus the control group, suggesting that ATR+OME can statistically ameliorate the abnormal performance of plasma gastrointestinal hormones in AG patients.

CONCLUSION

In conclusion, the combination of ATR and OME has demonstrated efficacy in the treatment of AG, yielding statistically significant improvements in overall effectiveness when compared to the treatment regimen of ADM plus OME. Additionally, this therapeutic approach is effective in diminishing the incidence of adverse reactions, including palpitations, headaches and XS, thereby facilitating the recovery of clinical symptoms. It also plays a crucial role in inhibiting serum inflammation and enhancing plasma levels of gastrointestinal hormones, underscoring its high value in clinical applications.

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