<u>PILOT STUDY</u>

Effects of lansoprazole and omeprazole Combined With Antimicrobial Agents on Gastric Juice pH and Inflammatory Factors in Elderly Patients With Hp Positive Gastric Ulcer

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ABSTRACT

Background • Helicobacter pylori (Hp) is one of the most prevalent pathogenic microorganisms in the world, which is related to gastric ulcer.

Objective • To observe the effect of lansoprazole and omeprazole combined with antibiotics on gastric juice pH and inflammatory factors in elderly patients with Hp positive gastric ulcer.

Design • This study was a prospective observation study. **Setting** • This study was performed in Department of Gastroenterology, First Affiliated Hospital of Soochow University.

Participants • One hundred and ten elder patients with Hp positive gastric ulcer admitted to our hospital from January 2019 to May 2020.

Intervention • The control group was treated with omeprazole combined with antibiotics, and the observation group was treated with lansoprazole combined with antibiotics.

Primary outcome measures • The level of gastric juice pH, interleukin-1 (IL-1), interleukin-8 (IL-8), tumor necrosis factor- α (TNF- α) and heat shock protein-70 (HSP-70).

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Gastric ulcer is a common clinical type of peptic ulcer. The clinical manifestations are chronic upper abdominal pain and acid regurgitation. Severe cases can have upper gastrointestinal bleeding, perforation and other complications. Helicobacter pylori (Hp) infection has been proved to be an important pathogenic factor of gastric ulcer. Therefore, the triple therapy of proton pump inhibitors combined with two **Methods** • The changes of gastric juice pH value, IL-1, IL-8, TNF- α and HSP-70 levels before and after treatment were detected in the two groups. The total effective rate, Hp eradication rate, mature type of regenerated mucosal tissue surrounding ulcer and adverse reaction rate were statistically analyzed.

Results • The total effective rate and Hp eradication rate in the observation group were higher than those in the control group, while the adverse reaction rate in the observation group was lower than that in the control group (P<.05). After treatment, the pH value of gastric juice and HSP-70 in the observation group were higher than those in the control group, while the IL-1, IL-8 and TNF- α were lower than those in the control group (P<.05). The mature type of regenerated mucosal tissue structure around ulcer in the observation group was better than that in the control group (P<.05).

Conclusion • The overall effect of lansoprazole combined with antibiotics in the treatment of Hp positive gastric ulcer in the elderly is better than that of omeprazole combined with antibiotics. (*Altern Ther Health Med.* 2023;29(2):213-217)

antibiotics is mainly used in clinical treatment to play the role of inhibiting acid and killing Hp.¹ The acidity of the stomach has a direct effect on the activity of Hp and the efficacy of antibiotics. Therefore, the selection of proton pump inhibitors is very important in the treatment of Hp positive gastric ulcer.²

Lansoprazole and omeprazole are commonly used in clinical proton pump inhibitors. Omeprazole is the first generation of proton pump inhibitors, and lansoprazole is the second generation of proton pump inhibitors. Both drugs can inhibit gastric acid secretion, and have application in the treatment of chronic gastritis, gastric ulcer and other diseases.³⁻⁴ However, there are few studies on the efficacy of the two drugs and the difference in their effects on inflammatory factors. This study observed the effects of lansoprazole and omeprazole combined with antibacterial drugs on gastric juice pH and inflammatory factors in elderly

patients with Hp-positive gastric ulcer, and provided reference for clinical treatment.

METHODS

Participants

This was a prospective observation study, which has been approved by the ethics committee of First Affiliated Hospital of Soochow University. This study was performed in Department of Gastroenterology, First Affiliated Hospital of Soochow University. One hundred and ten elderly patients with Hp positive gastric ulcer admitted from January 2019 to May 2020 were selected and divided into two groups according to treatment methods, 55 cases in each group.

Inclusion criteria: (1) It was in line with the standard of 'consensus on the diagnosis and treatment of peptic ulcer in the integrative medicine (Tianjin, 2011),⁵ and was diagnosed as active gastric ulcer by gastroscope and gastric mucosa biopsy. (2) Age \geq 60 years old, \leq 80 years old. (3) HP positive by C13 breath sampling. (4) History of drug use within 4 weeks. (5) Complete clinical data. Exclusion criteria: (1) Gastric ulcer biopsy found with atypical hyperplasia and canceration. (2) Patients with drug allergy. (3) Patients with pyloric obstruction, gastric perforation and other digestive system diseases. (4) Patients with important organ dysfunction. (5) Those with underlying diseases such as diabetes and hypertension. (6) Patients with mental diseases.

Intervention

The control group was treated with omeprazole entericcoated capsules (Kangpu Pharmaceutical Co., Ltd., specification: 20 mg, Chinese medicine standard word H43020287) combined with amoxicillin capsules (Tongyao Pharmaceutical Group Co., Ltd., specification: 0.25g, Chinese medicine standard word H22022851) and clarithromycin capsules (Shanghai Xudong Haipu Pharmaceutical Co., Ltd., specification: 0.25g, Chinese medicine standard word H20000449), oral omeprazole 20mg/ time, twice a day; amoxicillin 0.5g/time, 2 times/d; clarithromycin 0.25 g/time, twice daily.

The observation group was treated with Lansoprazole Enteric-coated Capsules (Suzhou Yushi Pharmaceutical Co., Ltd., specification: 30 mg, Chinese Medicine Zhunzi H20103716) combined with antibiotics, and oral Lansoprazole 30 mg/time, once/d. The varieties and usages of antibiotics were the same as those of the control group. Both groups were treated for 14 days.

Primary outcome measures

The changes of gastric juice pH value, interleukin-1 (IL-1), interleukin-8 (IL-8), tumor necrosis factor- α (TNF- α) and heat shock protein-70 (HSP-70) levels before and after treatment were detected in the two groups. The total effective rate, Hp eradication rate, mature type of regenerated mucosal tissue surrounding ulcer and adverse reaction rate were statistically analyzed.

5ml fasting peripheral venous blood was collected before treatment and 14 days after treatment, and centrifuged at

3000r/min for 10 min. The levels of IL-1, IL-8, TNF- α and HSP-70 in serum were detected by enzyme-linked immunosorbent assay (ELISA). The detection instrument was ELX800 enzyme-labeled instrument of American Betem Company, and the kit was purchased from Shanghai Jiyi Biotechnology Co., Ltd.

After 8 courses of treatment evaluation, (1) Cure: After treatment, the ulcer surface completely healed, endoscopic inflammation. (2) Effective: After treatment, the ulcer surface was reduced by \geq 75%, and the endoscopic inflammatory symptoms were significantly improved. (3) Effective: after treatment, 50% ulcer surface reduction <75%, endoscopic inflammatory symptoms improved. (4) Invalid: did not meet the above standards. Total effective rate=cure rate+significant efficiency+effective rate.⁵

Statistical analysis

SPSS19.0 was used to process the data. The measurement index was described as ($\overline{\chi} \pm s$). Independent sample *t* test was used for comparison between groups. Paired *t* test was used for comparison within groups. χ^2 test was used for comparison of rates. *P* < .05 was statistically significant.

RESULTS

Participants

There were 31 males and 24 females in the control group; 60–76 years old, with an average of (68.23 ± 4.12) years old. the course of disease was 6 months–12 years, with an average of (4.96 ± 1.86) years; the ulcer area ranged from 2 mm to 12 mm², with an average of (8.56 ± 2.06) mm². 29 males and 26 females in the control group; 60–78 years old, with an average of (67.96 ± 4.85) years old; the course of disease was 6 months–12 years, with an average of (5.02 ± 1.94) years; the ulcer area ranged from 2mm to 12mm², with an average of (8.58 ± 2.14) mm². The general data of the two groups were not statistically significant (*P*>.05).

Clinical efficacy and Hp eradication

Table 1 showed that the total effective rate and Hp eradication rate in the observation group were 94.55% and 89.09%, respectively, which were higher than those in the control group (81.82% and 74.55%). Further comparison between groups showed that the difference was significant (P < .05).

Gastric juice pH

Table 2 showed that there was no significant difference of the pH value between two groups before treatment (P > .05). After treatment, the pH value of gastric juice in the two groups gradually increased (P < .05). Further comparison between groups showed that the pH value of gastric juice in the observation group was higher than that in the control group (P < .05).

IL-1, IL-8, TNF-a, HSP-70 levels

Table 3 showed the IL-1, IL-8, TNF- α , HSP-70 levels of two groups before and after treatment. The two groups were

Table 1. Comparison of clinical efficacy and HP eradication between two groups [n (%)]

Group	Number of cases	Recovery	Remarkable effect	Effective	Invalid	Total effective rate	HP eradication rate
Control group	55	21 (37.18)	17 (30.91)	7 (12.73)	10 (18.18)	45 (81.82)	41 (74.55)
Observation group	55	28 (50.91)	18 (32.73)	6 (10.91)	3 (5.45)	52 (94.55)	49 (89.09)
χ^2						4.274	3.911
P value						.039	.048

Table 2. Comparison of pH value of gastric juice between two groups $(\bar{x} \pm s)$

	Number	PH value of gastric juice			
Group	of cases	Before treatment	After treatment		
Control group	55	4.23 ± 0.55	5.16 ± 0.56^{a}		
Observation group	55	4.21 ± 0.61	5.94 ± 0.68^{a}		
t		0.181	6.567		
P value		.857	.000		

 ^{a}P < .05 compared with before treatment

Table 3. IL-1, IL-8 and TNF in two groups- α Comparison of HSP-70 levels ($\bar{x} \pm s$)

		IL-1 (ng/L)		IL-8 (μg/L)		TNF-a (ng/L)		HSP-70 (µg/L)	
	Number	Before	After	Before	After	Before	After	Before	After
Group	of cases	treatment	treatment	treatment	treatment	treatment	treatment	treatment	treatment
Control group	55	51.23 ± 7.85	26.63 ± 6.21^{a}	45.23 ± 5.45	33.23 ± 4.15^{a}	54.23 ± 8.23	35.02 ± 5.36^{a}	251.02 ± 32.74	336.96 ± 35.12^{a}
Observation group	55	50.98 ± 8.22	18.24 ± 5.12^{a}	44.96 ± 5.85	22.86 ± 3.78^{a}	56.02 ± 8.17	29.11 ± 5.41^{a}	248.21 ± 33.26	412.02 ± 38.45^{a}
t		0.163	7.731	0.250	13.700	1.145	5.755	0.447	10.690
P value		.871	.000	.803	.000	.255	.000	.656	.000

 $^{a}P < .05$ compared with before treatment

Table 4. Comparison of mature types of tissue structure of regenerative mucosa around ulcer between the two groups [n(%)]

Group	Number of cases	Superior	Good grade	Differential order	
Control group	55	24 (43.64)	28 (50.91)	3 (5.45)	
Observation group	55	37 (67.27)	17 (30.91)	1 (1.82)	
χ ²		6.456			
P value		.040			

compared before treatment, and the difference was not significant (P > .05). After treatment, HSP-70 in the two groups gradually increased (P < .05), and IL-1, IL-8 and TNF- α gradually decreased (P < .05). Further comparison between the two groups showed that HSP-70 in the observation group was higher than that in the control group (P < .05), and IL-1, IL-8 and TNF- α were lower than those in the control group (P < .05).

Tissue structure and maturity types of regenerative mucosa around ulcers

Table 4 showed that the mature type of regenerated mucosal tissue structure around ulcer in the observation group was mainly excellent, accounting for 67.27%, and that in the control group was mainly good, accounting for 50.91%. The mature type of regenerated mucosal tissue

structure around ulcer in the observation group was better than that in the control group, and the difference was significant (P<.05).

Adverse reactions

Table 5 showed that the incidence of adverse reactions was compared between the observation group (5.45%) and the control group (7.27%), and the difference was not significant (P > .05).

DISCUSSION

Gastric ulcer is an ulcer that occurs between cardia and pylorus. Gastric mucosa is attacked by gastric acid and pepsin and causes tissue damage that exceeds the muscularis mucosa. Because of the long course of chronic gastritis, the elderly are high incidence of gastric ulcer.⁶ The mechanism of

Group	Number of cases	Gastrointestinal discomfort	Dizzy	Rash	Total
Control group	55	3 (5.45)	0 (0.00)	1 (1.82)	4 (7.27)
Observation group	55	3 (5.45)	1 (1.82)	0 (0.00)	3 (5.45)
χ^2					0.153
P value					.696

Table 5. Comparison of adverse reactions between the two groups[n(%)]

gastric ulcer is complicated. Previous studies suggest that gastric ulcer is closely related to gastric acid secretion and Hp infection.⁷ Therefore, acid inhibition and anti-Hp infection are the key to the treatment of gastric ulcer. The conventional triple therapy uses proton pump inhibitor to inhibit acid, which inhibits the secretion of gastric acid by acting on H+-K+-ATPase in gastric wall cells and reducing the transport of H+ to the stomach. It not only reduces the attack of gastric acid on gastric mucosa, but also changes the strong acid environment suitable for Hp survival, inhibits Hp activity, and is more conducive to the efficacy of antibiotics.⁸

At present, there are many types of proton pump inhibitors used in clinical practice. Omeprazole, as the first generation of proton pump inhibitors, has a long history of clinical application and is widely used in the treatment of peptic ulcer, gastroesophageal reflux disease, acute gastric mucosal lesions, stress ulcer and other diseases.⁹ Lansoprazole is a second generation proton pump inhibitor for gastric ulcer, duodenal ulcer, reflux esophagitis and Zhuoai syndrome.¹⁰ The effects of lansoprazole and omeprazole in the treatment of active gastric ulcer were compared. It was found that the clinical effect of lansoprazole in the treatment of active gastric ulcer was significantly better than that of omeprazole, which may be related to the significant increase of serum SOD and NO levels and the decrease of serum MDA and ET-1 levels.¹¹

This study found that the total effective rate and Hp eradication rate of patients treated with lansoprazole were higher than those treated with omeprazole; the pH value of gastric juice after treatment was higher than that of omeprazole. There was no significant difference in the adverse reaction rate between the two groups. This result suggests that compared with omeprazole, lansoprazole has better acid inhibition effect and is more conducive to Hp eradication, thus playing a better curative effect without increasing the risk of adverse reactions. This is consistent with the existing clinical findings.¹² This is due to the similar mechanism of lansoprazole and omeprazole, can be converted into active metabolites in gastric acid environment, can specifically inhibit gastric parietal cells H+-K+-ATPase, blocking the last step of gastric acid secretion. The lipophilicity and bioavailability of lansoprazole were stronger than those of omeprazole, which could enter gastric wall cells more quickly and transform into sulfonic acid and ethinyl derivatives to exert therapeutic effect.13-14

Inflammatory response is an important pathological change of gastric ulcer. IL-1 and IL-8 are classic pro-

inflammatory factors, which can cause inflammatory injury of tissues.¹⁵⁻¹⁶ TNF-a is a pro-inflammatory factor, which can not only cause direct tissue damage, but also promote the release of pro-inflammatory factors and produce indirect inflammatory effect.¹⁷ HSP-70 is a heat shock protein that protects cells from ischemia and hypoxia.18 This study found that HSP-70 in patients treated with lansoprazole was higher than that in patients treated with omeprazole, and IL-1, IL-8 and TNF-a were lower than those in patients treated with omeprazole. This result suggested that lansoprazole combined with antibiotics had better anti-inflammatory effect in the treatment of Hp-positive gastric ulcer in the elderly. Endoscopic examination showed that the mature type of regenerative mucosal tissue structure around ulcer in patients treated with lansoprazole was better than that in patients treated with omeprazole. This is related to the better inhibitory effect of lansoprazole on gastric acid secretion. Lansoprazole can better inhibit gastric acid secretion and reduce its attack on gastric mucosa. At the same time, it helps to kill Hp, reduce Hp colonization in gastric mucosa, of gastric mucosa caused by it, and more conducive to the repair of damaged mucosa.19-20

The triple therapy of proton pump inhibitors combined with two antibiotics is a classic treatment for Hp-positive gastric ulcer, but there is no uniform provision for the selection of proton pump inhibitors. This study compared the effects of omeprazole and lansoprazole proton pump inhibitors, and found that lansoprazole had more advantages in inhibiting acid and killing Hp. This study also found that lansoprazole was more conducive to reducing inflammatory response and promoting mucosal regeneration around ulcer through laboratory serological and endoscopic examination. The results of our study can provide valuable guidance for clinical practice. However, there were some limitations as well. This study was performed in only one hospital, and the sample size was limited. Further prospective study with large cohort is required.

In summary, the overall effect of lansoprazole combined with antibiotics in the treatment of Hp-positive gastric ulcer in the elderly is better than that of omeprazole combined with antibiotics, which can effectively eradicate Hp, reduce inflammation and promote mucosal regeneration around ulcer.

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