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Research paper

# Combination therapy of Qi Huang Tong Mi soft capsule and probiotics enhances clinical outcomes in severe acute pancreatitis

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ABSTRACT

*Introduction:* Severe acute pancreatitis (SAP) involves systemic inflammation and intestinal barrier dysfunction. This study aimed to assess the efficacy of Qi Huang Tong Mi soft capsules combined with gut probiotics in the treatment of SAP.
*Methods:* A total of 120 SAP patients were randomised into four groups: the experimental group (Qi Huang Tong Mi + probiotics + standard care), Qi Huang group, probiotics group, and control group. Treatments lasted 14 days. Inflammatory markers, intestinal barrier indicators, and clinical outcomes were evaluated on days 7 and 14.
*Results:* The experimental group demonstrated the highest efficacy rate (96.67%), with significant reductions in C-reactive protein (CRP), IL-6, IL-8, TNF-α, procalcitonin (PCT), alone with improved gut barrier function. Faster symptom relief, shorter hospital stays, and fewer complications were observed ($P < 0.05$).
*Conclusions:* Qi Huang Tong Mi combined with probiotics effectively and safely reduces inflammation, restores intestinal barrier function, and improves clinical outcomes in SAP patients.

## Background

Severe acute pancreatitis (SAP) is a common and complex inflammatory disease characterised by multifactorial pathogenesis, including excessive pancreatic enzyme activation, reduced trypsin inhibition, and impaired microcirculation. These factors contribute to premature enzyme activation and localised inflammation (Beger and Rau, 2007). SAP is frequently associated with systemic inflammatory response syndrome (SIRS), which plays a central role in the development of multi-organ dysfunction syndrome (MODS). Gastrointestinal dysfunction is a hallmark of SAP and a key prognostic indicator, with contributing factors such as altered gastrointestinal hormones levels, microcirculation disturbances, and endotoxins (Garg and Singh, 2019).

Globally, the incidence of SAP is increasing, placing a considerable burden on healthcare systems due to its high mortality, prolonged hospitalisation, and limited recovery rates despite advancements in medical management (Mao, 2019; Petrov and Yadav, 2019). Probiotics have demonstrated potential in restoring intestinal dynamics, protecting the gut barrier, and maintaining intestinal homoeostasis (Qiu et al., 2024). Additionally, herbal therapies, such as rhubarb-can enhance intestinal peristalsis and reduce endotoxin-related infections.

In this context, this present study investigates the combined effects of Qi Huang Tong Mi Soft Capsule (QHTMSC), a standard Chinese patent medicine, and probiotics on inflammatory markers and intestinal barrier dysfunction in patients with SAP.

*Abbreviations:* SAP, Severe acute pancreatitis; SIRS, Systemic Inflammatory Response Syndrome; APACHE II, Acute Physiology and Chronic Health Evaluation II; GIDS, Gastrointestinal Dysfunction Score; CRP, C-reactive protein; PCT, Procalcitonin; HBP, Heparin-Binding Protein; DAO, Diamine oxidase; D-lac, D-lactic acid; HMGB1, High mobility group box 1 protein; QHTMSC, Qi Huang Tong Mi Soft Capsule; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte ratio; MODS, Multiple organ dysfunction syndrome; SIRS, Systemic inflammatory response syndrome

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## Methods

This study included 120 patients diagnosed with SAP and concurrent gastrointestinal dysfunction who were admitted to the Emergency Intensive Care Unit of the First Affiliated Hospital of Bengbu Medical University between 2022.10 and 2024.10. The study was approved by the hospital's Ethics Committee (Approval Number: 2024045), and written informed consent was obtained from all participants. Patients were randomly assigned into four groups (n = 30 per group) as follows: Experimental group: 17 males, 13 females; aged 24–75 years old, mean (50.07 ± 13.03) years old; Qi Huang group: 13 males, 17 females, aged 25–75 years old, mean (48.33 ± 14.66) years old, Probiotics group: 22 males, eight females, aged 25–75 years old, mean (49.63 ± 15.83) years old, Control group: 17 males, 13 females, aged 25–75 years, mean (50.70 ± 15.76) years. Randomisation was performed using a computer-generated random number sequence by an independent statistician who was not involved in any of other aspect of the study. Group allocation was concealed using sequentially numbered, opaque, sealed envelopes (SNOSE) to prevent selection bias. Due to the nature of the intervention (e.g., nasogastric administration of visible herbal preparations), blinding of patients and healthcare providers was not feasible. However, outcome assessors and data analysts remained blinded to group allocation throughout the study to ensure objectivity.

No sex-based stratification was applied during the randomisation process. Comparative analysis of baseline age and gender among the four groups revealed no statistically significant differences ($P > 0.05$), confirming the baseline comparability of the groups (Table 1).

### *Sample size calculation*

The sample size was calculated based on preliminary clinical data to ensure power to detect a clinically meaningful difference in treatment efficacy between groups. Assuming a treatment efficacy rate of 80% in the experimental group versus 50% in the control group, with a two-sided alpha level of 0.05 and a power of 80% ($\beta = 0.2$), the minimum required sample size was determined to be 27 patients per group. Considering potential dropouts and protocol deviations, 30 patients were enroled in each group, resulting in a total sample size of 120 participants.

### *Inclusion criteria*

(1) Patients meeting the diagnostic criteria for SAP and presenting with intestinal dysfunction; (2) age ≥ 18 years; (3) organ failure lasting more than 48 hours; (4) Acute Physiology and Chronic Health Evaluation II (APACHE II) score > 8, Gastrointestinal Dysfunction Score (GIDS) greater than or equal to 3; (5) hospitalisation time > 14 days with complete clinical history; (6) Provision of written informed consent.

### *Exclusion criteria*

Patients were excluded if they met any of the following conditions: (1) Allergic reaction to any of the medications in this study; (2) severe consciousness or communication disorders; (3) life expectancy ≤ 3 months; (4) who withdrew from the study during the course of treatment; (5) any of the following conditions: cardiovascular or cerebrovascular diseases, other systemic metabolic or infectious diseases, coagulation disorders, malignancies, end stage gastrointestinal motility disorders, mechanical intestinal obstruction, or a history of gastrointestinal surgery; (6) admitted to the hospital more than 72 hours after illness onset or who received treatment outside prior to admission; (7) pregnant or breastfeeding women.

### *SAP diagnostic and evaluation criteria*

The diagnosis of SAP was established based on the consensus protocol formulated by the Branch of Gastrointestinal Diseases, China Association of Chinese Medicine, as previously described (Li et al., 2019). The diagnostic criteria for acute pancreatitis (AP) included the following:

(1) Persistent and severe upper abdomen pain radiating to the back, often accompanied by abdominal distension, nausea, and vomiting. (2) Serum lipase and/or amylase activity > 3 times above the upper limit of normal. (3) Imaging finding consistent with pancreatitis.

A diagnosis of AP was made when at least two of the above three criteria were met. Patients diagnosed with AP were further classified as having SAP if organ failure persisted more than 48 hours. The severity of the disease was primarily evaluated using the APACHE II scoring system (Suvarna et al., 2011), with higher scores indicating more disease severity.

### *Diagnostic criteria for gastrointestinal dysfunction*

The diagnostic criteria for GIDS in critically ill patients were applied, with GIDS categorised into five grades, ranging from 0 to 4 (Reintam Blaser et al., 2021).

*Score 0 (No dysfunction):*

Asymptomatic, or presenting with only one of the following symptoms, in the absents of oral intake: absent bowel sounds, vomiting, gastric retention > 200 ml, gastrointestinal paralysis, abdominal distension, mild diarrhoea, no-severe gastrointestinal bleeding (not require transfusion), or an intra-abdominal pressure > 20 mmHg.

*Score 1 (increased risk):*

Presence of any two of the symptoms listed above, without oral intake.

*Score 2 (gastrointestinal dysfunction):*

Presence of at least three of the symptoms listed under score 1, or any two of the following symptoms: severe diarrhoea; gastrointestinal bleeding requiring transfusion; or IAP > 20 mmHg.

*Score 3 (gastrointestinal failure):*

Presence of at least three of the following: use of prokinetic drugs; gastrointestinal paralysis; abdominal distension; severe diarrhoea; gastrointestinal bleeding requiring transfusion; or IPA > 20 mmHg.

*Score 4 (life-threatening dysfunction):*

Gastrointestinal bleeding leading to haemorrhagic shock, mesenteric ischaemia, or abdominal compartment syndrome.

Additionally, severe diarrhoea was defined according to the Bristol stool form scale as ≥5 bowel movements per day or ≥1000 ml of stool

**Table 1**
Baseline demographic and clinical characteristics of patients across the four treatment groups.

| Data | Control group (n = 30) | Qi Huang group (n = 30) | Probiotics group (n = 30) | Experimental group (n = 30) | $\chi^2$ | *P* |
|---|---|---|---|---|---|---|
| Gender (case) | | | | | 5.558 | 0.135 |
| Male | 17 | 13 | 22 | 17 | | |
| Female | 13 | 17 | 8 | 13 | | |
| Age ($\bar{x}$ ± s, years) | 50.70 ± 15.759 | 48.33 ± 14.660 | 49.63 ± 15.830 | 50.07 ± 13.030 | 0.136 | 0.938 |

QHTMSC, Qi Huang Tong Mi Soft Capsule.
Including age and gender distribution at admission across the four treatment groups (experimental, QHTMSC, probiotics, and control). No statistically significant differences were observed among the groups, indicating comparability ($P > 0.05$).

per day (Lewis and Heaton, 1997). Gastric residual volume (GRV) and Intra-abdominal pressure (IAP) were routinely measured in all patients using nasogastric tubes and indwelling bladder catheters, respectively.

### *Treatment protocols*

All patients across four groups received standard hospital care, which included:

(1) Fasting and gastrointestinal decompression using a nasogastric tube until bowel function recovered; (2) Fluid resuscitation with isotonic saline or Ringer's lactate at an initial rate of 250–500 ml/H, adjusted according to hemodynamic monitoring; (3) Electrolyte and acid-base balance correction, monitored every 6–12 hours; (4) Pain control with intravenous parecoxib sodium or fentanyl as needed (e.g., parecoxib 40 mg q12h); (5) Pancreatic secretion suppression with continuous intravenous infusion of octreotide at 25 μg/H for 5–7 days; (6) Antibiotic prophylaxis was not routinely used unless infection was suspected; (7) Oxygen therapy or mechanical ventilation as required for patients with hypoxaemia; (8) Nutritional support started early via nasojejunal feeding once intestinal sounds resumed; (9) Close monitoring of laboratory markers and imaging to assess disease progression.

Control Group: Received only basic treatment without Qi Huang Tong Mi soft capsules (QHTMSC, NMPN: Z20090050, Shineway, Qi Huang Tong Mi soft capsule is a standardised traditional Chinese medicine formulation included in the Pharmacopoeia of the People's Republic of China (2020 Edition). It consists of the following ingredients: *Astragali Radix* (*Astragalus membranaceus*), *Angelicae Sinensis Radix* (*Angelica sinensis*), *Polygoni Multiflori Radix* (*Polygonum multiflorum*), *Rhei Radix et Rhizoma Praeparata* (*Rheum palmatum*), *Cistanches Herba* (*Cistanche deserticola*), *Sesami Semen Nigrum* (*Sesamum indicum*), *Juglandis Semen* (*Juglans regia*), *Cassiae Semen* (*Cassia obtusifolia*), *Aurantii Fructus Immaturus* (*Citrus aurantium*), *Armeniacae Semen Amarum Praeparatum* (*Prunus armeniaca*), and *Persicae Semen* (*Prunus persica*).) or probiotics ( Chang Le Kang capsules, NMPN: S20020015, SINOVAC). Qi Huang Group: Basic treatment plus QHTMSC (1.5 g dissolved in 20 ml lukewarm water, administered via naso-enteric tube twice daily). Probiotic Group: Basic treatment plus Chang Le Kang capsules (1 260 mg dissolved in 20 ml lukewarm water, totalling 2 520 mg/d, equivalent to $6.0 \times 10^7$ CFU live bacteria). Experimental Group: Basic treatment with a combination of QHTMSC (1.5 g/dose, twice daily) and Chang Le Kang capsules (1 260 mg/dose, twice daily, totalling 2 520 mg/d). The treatment lasted for 14 days, with clinical and laboratory assessments conducted on days 7 and 14 (Fig. 1).

### *Biochemical and microbiological analysis*

Peripheral venous blood samples (5.0 ml) were collected from patients at three time points: admission (before treatment) and on 7th and 14th days of treatment. Samples were placed in anticoagulation tubes, and serum was separated by low-speed centrifugation. Serum levels of inflammatory response indicators (IL-8, IL-6, TNF-α, CRP, HBP, PCT) were measured by radioimmunoassay. Serum levels of ET (CSB-E07007h, CUSABIO), D-lac (S0204S, beyotime), DAO (CSB-E10137h, CUSABIO), HMGB-1 (CSB-E08223h , CUSABIO ) were assessed by ELISA.

Fresh stool samples (0.5 g) were collected from patients in all four groups at three time point: at admission (prior to treatment), and on 7th and 14th days of treatment. Samples were collected using disposable fecal collector and diluted to 10–9 times using the 10-fold dilution method. After dilution, 50 μl of the diluted solution was taken for incubation. Anaerobic bacteria (*Bifidobacterium, Lactobacillus*) were cultured in ( MRS Agar, HB0384-9, Hopebio) using Anaeropack systems ( Mitsubishi Gas Chemical, Japan ) in an anaerobic jar at 37'C for 48 hours, while aerobic bacteria (*Enterococcus, Enterobacteriaceae*) were cultured in ( BS agar HB0268–2, Hopebio ) and incubated at 37 under aerobic conditions for 24 hours.

Colony forming units (CFUs) were counted manually, and the results were expressed as the logarithm of CFU per gram of wet stool weigh (lgCFU/g). The formula used for CFU calculation was:

CFU/ml = (sample weight + amount of diluent)/sample weight × colony dilution factor × colony number. Each sample was analyzed in triplicate (n = 3 independent cultures per time point per patient) to ensure accuracy, and the mean value was used for analysis.

### *Observation indicators*

#### *Clinical efficacy*

The following clinical parameters were recorded before treatment, as well as on the 7th and 14th days after treatment: time to relief of abdominal pain, time of anal exhaustion, time of normalisation of intestinal peristalsis, and length of hospital stay. Additionally, clinical efficacy and incidence of complications, such as ascites, paralytic intestinal obstruction, pancreatic pseudocyst, and respiratory distress syndrome were compared among the four groups.

Treatment efficacy was evaluated using the follows criteria:

Markedly effective: Symptoms such as nausea, vomiting, fever, signs of peritoneal irritation, epigastric pain with abdominal distension disappeared after treatment, and laboratory test indexes returned to normal;

Effective: Symptoms such as nausea, vomiting, fever, peritoneal irritation signs, epigastric pain with abdominal distension were improved, and laboratory test indexes returned to normal;

Ineffective: No significantly improvement of the patient's condition compared to pre-treatment, or the condition worsened or resulted in death.

The total effective rate (%) = (number of cases with apparent effect + number of effective cases)/total number of cases × 100.

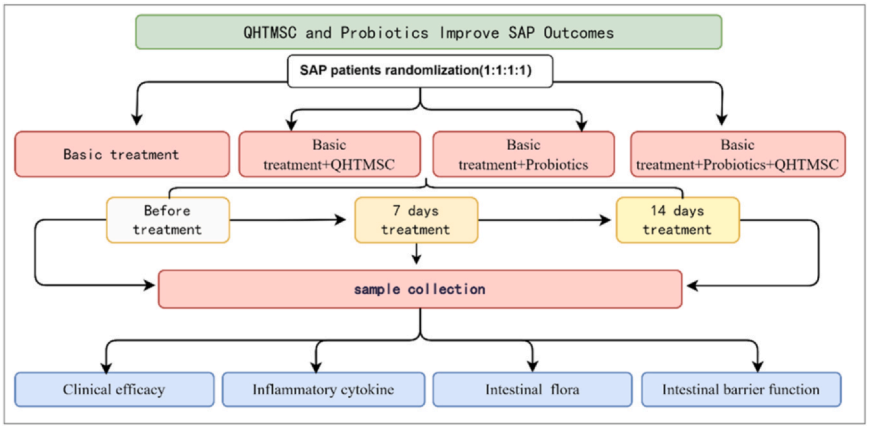


**Fig. 1.** Flowchart of the experiments design. Patients were randomised into four treatment groups and evaluated at baseline, day 7, and day 14. For continuous variables, between-group comparisons were performed using one-way ANOVA (if normally distributed) or Kruskal-Wallis test (for non-normal distributions). Categorical variables were analyzed using the Chi-square test. Statistical significance was set at $P < 0.05$. Note: All statistical analyses were performed using SPSS 27.0.

*Biochemical and microbiological indicators*

The intestinal barrier function (endotoxin, D-lac, DAO, HMGB1, GIDS, APACHE II score), intestinal flora count (*Lactobacillus, Bifidobacterium, Escherichia coli,* and *Staphylococcus*), and inflammatory indexes (CRP, IL-6, IL-8, TNF-α, NLR, PLR, PCT, and HBP) were assessed before and after treatment.

*Statistical processing*

Statistical analysis was performed using SPSS 27.0 software. Measurement data were expressed as (x ± s) and analyzed using *t*-test, assuming normal distribution.

Categorical data were expressed as percentages (%) and analyzed using $\chi 2$. A $P$ value of $< 0.05$ was considered statistically significant.

## Results

*Clinical efficacy*

The experimental group exhibited significantly shorter times to abdominal pain relief, anal exsufflation, normalisation of intestinal peristalsis, and overall hospitalisation compared to the other groups. The incidence of complications was 36.7% (control), 26.7% (Qi Huang), 23.3% (probiotic), and 13.3% (experimental), with statistically significant differences among the groups ($P < 0.05$).

The treatment efficacy rate in the experimental group was 97.67%, which was significantly higher than that observed in the Qi Huang (83.33%), the probiotic group (80.00%), and the control groups (76.67%) ($P < 0.05$). The experimental group also had the lowest rate of complication, highlighting the potential benefit of combination therapy (Table 2).

The overall effective rate was defined as the proportion of patients who demonstrated improvement in clinical symptoms and laboratory parameters after treatment (apparent + effective cases). In contrast, the complication rate referred to the incidence of adverse clinical events during hospitalisation, such as ascites, paralytic ileus, pseudocyst, or respiratory distress. While both outcomes are presented together in (Table 2), they represent distinct clinical endpoints (*$P <$ 0.05 compared with the control group).

*Intestinal barrier function*

Before treatment, there were no statistically significant differences among the four groups in APACHE II, GIDS scores, and intestinal barrier markers (endotoxin, D-lac, DAO, HMGB1) ($P > 0.05$). However, after 7 and 14 days of treatment, the experimental group exhibited significantly greater reductions in all these scores and biomarkers compared to other groups ($P < 0.05$) (Table 3).

*Inflammatory factor indicators*

Baseline levels of CRP, IL-6, IL-8, TNF-α, NLR, PLR, PCT, and HBP were comparable across all groups. Following treatment, the experimental group exhibited the most significant reductions in these inflammatory makers ($P < 0.05$), whereas the Qi Huang and probiotic groups demonstrated moderate improvements compared to the control (Table 4).

*Intestinal flora*

Pre-treatment counters of intestinal flora (*Lactobacillus, Bifidobacterium, Escherichia coli, Staphylococcus*) were comparable among all groups. Following treatment, the experiment group showed a significant increase in *Bifidobacterium* and *Lactobacillus* levels along with a greater reduction in Escherichia coli and Staphylococcus levels compared to the other groups ($P < 0.05$) (Table 5).

**Table 2**
Clinical efficacy and complication rates across four treatment groups.

| Indices | Control group (n = 30) | Qi Huang group (n = 30) | *t* | *P* | Probiotics group (n = 30) | *t* | *P* | Experimental group (n = 30) | *t* | *P* |
|---|---|---|---|---|---|---|---|---|---|---|
| Pain relief time ($\bar{x}$ ± s, d) | 7.824 ± 0.397 | 6.392 ± 0.298 | 15.803 | < 0.001 | 6.230 ± 0.223 | 19.156 | < 0.001 | 4.705 ± 0.184 | 39.021 | < 0.001* |
| Anal exhaust time ($\bar{x}$ ± s, d) | 5.908 ± 1.305 | 4.811 ± 1.067 | 4.041 | < 0.001 | 4.679 ± 0.917 | 4.870 | < 0.001 | 1.992 ± 0.545 | 18.344 | < 0.001* |
| Intestinal peristaltic sound recovery time ($\bar{x}$ ± s, d) | 4.828 ± 1.083 | 3.633 ± 0.918 | 4.613 | < 0.001 | 3.495 ± 0.858 | 5.288 | < 0.001 | 1.892 ± 0.369 | 14.063 | < 0.001* |
| Overall response rate (%) | 36.700 | 26.700 | | | 23.300 | | | 13.300 *P | | |
| Markedly effective (case) | 8 | 11 | | | 10 | | | 15 | | |
| Effective (case) | 15 | 13 | | | 15 | | | 14 | | |
| Noneffective (case) | 7 | 6 | | | 5 | | | 1 | | |
| Complication (%) | 76.67% | 80% | | | 83.33% | | | 96.67% | | |
| Ascites | 3 | 3 | | | 3 | | | 2 | | |
| Paralytic intestinal obstruction | 3 | 2 | | | 1 | | | 1 | | |
| Septicemia | 1 | 1 | | | 2 | | | | | |
| Pancreatic pseudocyst | 2 | 1 | | | | | | 1 | | |
| Peripancreatic abscess | 1 | | | | 1 | | | | | |
| Acute respiratory distress syndrome | 1 | 1 | | | | | | | | |

**Table 3**
Effect of QHTMSC combined with probiotics on serum indexes of intestinal mucosal barrier.

| Indices | Control group (n = 30) | Qi Huang group (n = 30) | *t* | *P* | Probiotics group (n = 30) | *t* | *P* | Experimental group (n = 30) | *t* | *P* |
|---|---|---|---|---|---|---|---|---|---|---|
| D-lactic acid ($\bar{x} \pm s$, mg/L) | | | | | | | | | | |
| Before treatment | 24.208 ± 1.491 | 24.382 ± 1.0998 | −0.514 | 0.609 | 24.383 ± 1.090 | −0.518 | 0.606 | 25.065 ± 3.398 | −1.265 | 0.211 |
| After 1 wk of treatment | 23.571 ± 1.041 | 19.699 ± 1.988 | 9.452 | < 0.001 | 16.984 ± 1.765 | 17.607 | < 0.001 | 16.071 ± 1.411 | 23.424 | < 0.001* |
| *t* | 1.918 | 11.293 | | | 19.535 | | | 13.388 | | |
| *P* | 0.060 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| After 2 wk of treatment | 23.325 ± 2.144 | 13.713 ± 1.220 | 21.348 | < 0.001 | 15.838 ± 2.095 | 13.682 | < 0.001 | 9.537 ± 1.631 | 28.039 | < 0.001* |
| *t* | 1.852 | 35.603 | | | 19.818 | | | 22.566 | | |
| *P* | 0.069 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| DAO ($\bar{x} \pm s$, ul/L) | | | | | | | | | | |
| Before treatment | 54.973 ± 5.376 | 54.616 ± 4.793 | 0.135 | 0.893 | 55.042 ± 4.413 | −0.196 | 0.845 | 54.520 ± 4.807 | 0.191 | 0.849 |
| After 1 wk of treatment | 53.498 ± 4.501 | 29.882 ± 3.309 | 23.156 | < 0.001 | 31.929 ± 2.457 | 23.040 | < 0.001 | 17.561 ± 2.931 | 36.649 | < 0.001* |
| *t* | 1.012 | 23.261 | | | 25.063 | | | 35.979 | | |
| *P* | 0.316 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| After 2 wk of treatment | 55.340 ± 3.173 | 15.607 ± 1.581 | 61.381 | < 0.001 | 17.409 ± 1.953 | 55.754 | < 0.001 | 9.694 ± 1.384 | 72.212 | < 0.001* |
| *t* | −0.480 | 42.333 | | | 42.709 | | | 49.108 | | |
| *P* | 0.633 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| Endotoxin ($\bar{x} \pm s$, ul/L) | | | | | | | | | | |
| Before treatment | 11.337 ± 0.551 | 11.388 ± 0.621 | −0.339 | 0.736 | 11.404 ± 0.572 | −0.462 | 0.646 | 11.330 ± 0.557 | 0.047 | 0.963 |
| After 1 wk of treatment | 11.407 ± 0.820 | 8.408 ± 0.527 | 16.839 | < 0.001 | 8.978 ± 0.926 | 10.756 | < 0.001 | 6.378 ± 0.628 | 26.661 | < 0.001* |
| *t* | −0.386 | 20.034 | | | 12.214 | | | 32.322 | | |
| *P* | 0.701 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| After 2 wk of treatment | 11.217 ± 0.987 | 4.904 ± 0.269 | 33.805 | < 0.001 | 4.382 ± 0.303 | 36.269 | < 0.001 | 2.314 ± 0.297 | 47.311 | < 0.001* |
| *t* | 0.580 | 52.471 | | | 59.441 | | | 78.231 | | |
| *P* | 0.565 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| GIDS ($\bar{x} \pm s$, point) | | | | | | | | | | |
| Before treatment | 3.07 ± 0.254 | 3.13 ± 0.346 | −0.851 | 0.398 | 3.23 ± 0.430 | −1.828 | 0.074 | 3.20 ± 0.407 | −1.523 | 0.134 |
| After 1 wk of treatment | 2.33 ± 1.155 | 1.67 ± 1.124 | 2.266 | 0.027 | 1.83 ± 1.085 | 1.728 | 0.089 | 1.13 ± 0.819 | 4.642 | < 0.001* |
| *t* | 3.397 | 6.829 | | | 6.568 | | | 12.374 | | |
| *P* | 0.001 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| After 2 wk of treatment | 1.57 ± 0.728 | 1.07 ± 0.640 | 2.826 | 0.006 | 0.93 ± 0.691 | 3.455 | 0.001 | 0.13 ± 0.346 | 9.742 | < 0.001* |
| *t* | 10.658 | 15.567 | | | 15.469 | | | 31.460 | | |
| *P* | < 0.001 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| APACHE II score ($\bar{x} \pm s$, point) | | | | | | | | | | |
| Before treatment | 19.470 ± 4.392 | 21.000 ± 4.871 | −1.281 | 0.205 | 18.100 ± 4.715 | 1.162 | 0.250 | 19.730 ± 5.058 | −0.218 | 0.828 |
| After 1 wk of treatment | 18.870 ± 1.978 | 13.270 ± 2.258 | 10.218 | < 0.001 | 11.430 ± 2.239 | 13.628 | < 0.001 | 8.800 ± 2.631 | 16.749 | < 0.001* |
| *t* | 0.682 | 7.890 | | | 6.996 | | | 10.503 | | |
| *P* | 0.499 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| After 2 wk of treatment | 18.270 ± 3.140 | 8.270 ± 1.982 | 14.753 | < 0.001 | 7.300 ± 1.236 | 17.802 | < 0.001 | 5.530 ± 1.717 | 19.490 | < 0.001* |
| *t* | 1.217 | 13.263 | | | 12.136 | | | 14.562 | | |
| *P* | 0.229 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| HMGB1 ($\bar{x} \pm s$, ng/L) | | | | | | | | | | |
| Before treatment | 12.362 ± 3.833 | 12.548 ± 4.773 | −0.167 | 0.868 | 11.958 ± 4.650 | 0.368 | 0.715 | 11.202 ± 1.965 | 1.475 | 0.146 |
| After 1 wk of treatment | 12.571 ± 2.829 | 6.133 ± 3.077 | 8.436 | < 0.001 | 6.368 ± 3.190 | 7.698 | < 0.001 | 3.525 ± 1.562 | 15.331 | < 0.001* |
| *t* | −0.241 | 6.188 | | | 5.429 | | | 16.750 | | |
| *P* | 0.811 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| After 2 wk of treatment | 11.961 ± 2.257 | 3.937 ± 1.475 | 16.298 | < 0.001 | 4.181 ± 1.539 | 15.597 | < 0.001 | 1.084 ± 0.434 | 25.915 | < 0.001* |
| *t* | 0.493 | 9.442 | | | 8.697 | | | 27.534 | | |
| *P* | 0.624 | < 0.001 | | | < 0.001 | | | < 0.001 | | |

APACHE II, Acute Physiology and Chronic Health Evaluation II; DAO, diamine oxidase; GIDS, Gastrointestinal Dysfunction Score; QHTMSC, Qi Huang Tong Mi Soft Capsule.
Presented the serum indexes of intestinal mucosal barrier of the study population after 7 and 14 days treatment, including endotoxin, D-lac, DAO, HMGB1, APACHE II and GIDS scores, covering four treatment groups (experimental, QHTMSC, probiotics, and control). The treatment efficiency of the experimental group was significantly higher than the other three groups, and the difference was statistically significant (*$P < 0.05$ compared with the control group).

**Table 4**
Effect of QHTMSC combined with probiotics on inflammatory indexes in SAP patients.

| Indices | Control group (n = 30) | Qi Huang group (n = 30) | *t* | *P* | Probiotics group (n = 30) | *t* | *P* | Experimental group (n = 30) | *t* | *P* |
|---|---|---|---|---|---|---|---|---|---|---|
| CRP ($\bar{x} \pm s$, mg/L) | | | | | | | | | | |
| Before treatment | 152.643 ± 21.132 | 141.550 ± 33.159 | 1.545 | 0.128 | 152.807 ± 22.209 | −0.029 | 0.977 | 154.565 ± 25.160 | −0.320 | 0.750 |
| After 1 wk of treatment | 151.077 ± 27.502 | 68.003 ± 12.624 | 15.036 | < 0.001 | 66.815 ± 11.114 | 15.559 | < 0.001 | 47.842 ± 7.035 | 19.919 | < 0.001* |
| *t* | 0.247 | 11.354 | | | 18.966 | | | 22.375 | | |
| *P* | 0.806 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| After 2 wk of treatment | 147.786 ± 31.634 | 27.291 ± 5.144 | 20.593 | < 0.001 | 27.999 ± 4.675 | 20.518 | < 0.001 | 21.623 ± 5.158 | 21.560 | < 0.001* |
| *t* | 0.699 | 18.650 | | | 30.120 | | | 28.351 | | |
| *P* | 0.488 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| IL−6 ($\bar{x} \pm s$, ng/L) | | | | | | | | | | |
| Before treatment | 66.888 ± 4.932 | 68.193 ± 4.965 | −1.021 | 0.312 | 67.759 ± 4.333 | −0.726 | 0.470 | 69.149 ± 5.020 | −1.759 | 0.084 |
| After 1 wk of treatment | 64.645 ± 5.805 | 44.041 ± 3.041 | 17.221 | < 0.001 | 46.486 ± 2.858 | 15.371 | < 0.001 | 37.168 ± 4.434 | 20.603 | < 0.001* |
| *t* | 1.613 | 22.721 | | | 22.449 | | | 26.153 | | |
| *P* | 0.112 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| After 2 wk of treatment | 66.179 ± 5.539 | 23.507 ± 3.765 | 34.896 | < 0.001 | 25.348 ± 3.140 | 35.122 | < 0.001 | 18.030 ± 4.275 | 37.690 | < 0.001* |
| *t* | 0.524 | 39.278 | | | 43.412 | | | 42.463 | | |
| *P* | 0.602 | < 0.001 | | | < 0.001 | | | 0.159 | | |
| IL−8 ($\bar{x} \pm s$, ng/L) | | | | | | | | | | |
| Before treatment | 96.073 ± 38.126 | 97.924 ± 31.895 | −0.204 | 0.839 | 95.517 ± 30.012 | 0.063 | 0.950 | 96.086 ± 31.102 | −0.001 | 0.999 |
| After 1 wk of treatment | 97.888 ± 27.076 | 74.769 ± 13.445 | 4.189 | < 0.001 | 77.078 ± 14.876 | 3.690 | < 0.001 | 58.714 ± 11.558 | 7.288 | < 0.001* |
| *t* | −0.213 | 3.664 | | | 3.015 | | | 6.169 | | |
| *P* | 0.832 | < 0.001 | | | 0.004 | | | < 0.001 | | |
| After 2 wk of treatment | 98.646 ± 30.762 | 47.418 ± 7.889 | 8.835 | < 0.001 | 42.501 ± 9.053 | 9.590 | < 0.001 | 29.838 ± 11.694 | 11.452 | < 0.001* |
| *t* | −0.288 | 8.420 | | | 9.263 | | | 10.920 | | |
| *P* | 0.775 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| TNF-α ($\bar{x} \pm s$, pg/L) | | | | | | | | | | |
| Before treatment | 67.383 ± 14.140 | 66.105 ± 14.090 | 0.351 | 0.727 | 67.770 ± 14.270 | −0.105 | 0.916 | 66.476 ± 12.537 | 0.263 | 0.793 |
| After 1 wk of treatment | 66.718 ± 13.823 | 29.755 ± 9.737 | 11.973 | < 0.001 | 29.133 ± 7.752 | 12.989 | < 0.001 | 15.767 ± 5.312 | 18.844 | < 0.001* |
| *t* | 0.184 | 11.624 | | | 13.031 | | | 20.398 | | |
| *P* | 0.854 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| After 2 wk of treatment | 67.959 ± 15.618 | 15.292 ± 3.897 | 17.921 | < 0.001 | 17.043 ± 4.903 | 17.036 | < 0.001 | 4.829 ± 2.023 | 21.956 | < 0.001* |
| *t* | −0.150 | 19.037 | | | 18.414 | | | 26.589 | | |
| *P* | 0.881 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| NLR ($\bar{x} \pm s$, ng/L) | | | | | | | | | | |
| Before treatment | 13.025 ± 2.660 | 13.559 ± 1.072 | −1.020 | 0.312 | 12.997 ± 0.939 | 0.054 | 0.957 | 12.797 ± 0.939 | 0.444 | 0.659 |
| After 1 wk of treatment | 12.575 ± 1.966 | 6.503 ± 2.295 | 11.005 | < 0.001 | 6.950 ± 1.555 | 12.289 | < 0.001 | 5.151 ± 1.718 | 15.572 | < 0.001* |
| *t* | 0.746 | 15.259 | | | 18.234 | | | 21.387 | | |
| *P* | 0.459 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| After 2 wk of treatment | 12.246 ± 2.795 | 4.149 ± 1.286 | 14.417 | < 0.001 | 3.922 ± 1.272 | 14.848 | < 0.001 | 1.602 ± 0.555 | 20.461 | < 0.001* |
| *t* | 1.107 | 30.789 | | | 31.447 | | | 56.211 | | |
| *P* | 0.273 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| PLR ($\bar{x} \pm s$, ng/L) | | | | | | | | | | |
| Before treatment | 359.042 ± 116.752 | 353.839 ± 86.639 | 0.196 | 0.845 | 353.782 ± 71.373 | 0.211 | 0.834 | 358.954 ± 98.345 | 0.003 | 0.998 |
| After 1 wk of treatment | 354.502 ± 75.725 | 265.600 ± 80.319 | 4.376 | < 0.001 | 269.970 ± 66.600 | 4.591 | < 0.001 | 228.970 ± 66.237 | 6.834 | < 0.001* |
| *t* | 0.179 | 4.053 | | | 4.072 | | | 6.004 | | |
| *P* | 0.859 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| After 2 wk of treatment | 359.559 ± 54.300 | 219.140 ± 90.110 | 7.310 | < 0.001 | 184.007 ± 61.100 | 11.763 | < 0.001 | 128.173 ± 27.343 | 20.846 | < 0.001* |
| *t* | −0.022 | 5.902 | | | 9.897 | | | 12.383 | | |
| *P* | 0.983 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| PCT ($\bar{x} \pm s$, mg/L) | | | | | | | | | | |
| Before treatment | 12.124 ± 1.304 | 11.975 ± 1.140 | 0.471 | 0.639 | 11.880 ± 1.084 | 0.787 | 0.434 | 12.662 ± 1.801 | −1.325 | 0.190 |
| After 1 wk of treatment | 11.583 ± 1.234 | 7.690 ± 0.933 | 13.785 | < 0.001 | 7.675 ± 1.313 | 11.880 | < 0.001 | 5.450 ± 1.341 | 18.431 | < 0.001* |
| *t* | 1.649 | 15.937 | | | 13.528 | | | 17.588 | | |
| *P* | 0.104 | < 0.001 | | | < 0.001 | | | < 0.001 | | |

(*continued on next page*)

**Table 4** (*continued*)

| Indices | Control group (n = 30) | Qi Huang group (n = 30) | *t* | *P* | Probiotics group (n = 30) | *t* | *P* | Experimental group (n = 30) | *t* | *P* |
|---|---|---|---|---|---|---|---|---|---|---|
| After 2 wk of treatment | 11.407 ± 2.100 | 3.400 ± 0.697 | 19.820 | < 0.001 | 3.249 ± 0.661 | 20.296 | < 0.001 | 0.467 ± 0.287 | 28.260 | < 0.001* |
| *t* | 1.589 | 35.161 | | | 37.240 | | | 36.601 | | |
| *P* | 0.118 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| HBP ($\bar{x}$ ± s, mg/L) | | | | | | | | | | |
| Before treatment | 135.657 ± 32.538 | 133.041 ± 29.220 | 0.328 | 0.744 | 136.856 ± 24.838 | −0.160 | 0.873 | 133.899 ± 37.197 | 0.195 | 0.846 |
| After 1 wk of treatment | 132.027 ± 22.763 | 91.478 ± 8.273 | 9.170 | < 0.001 | 91.646 ± 8.729 | 9.072 | < 0.001 | 64.340 ± 13.555 | 13.994 | < 0.001* |
| *t* | 0.501 | 7.496 | | | 9.406 | | | 9.623 | | |
| *P* | 0.619 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| After 2 wk of treatment | 133.351 ± 31.456 | 52.716 ± 10.438 | 13.326 | < 0.001 | 59.721 ± 9.566 | 12.266 | < 0.001 | 14.034 ± 5.636 | 20.451 | < 0.001* |
| *t* | 0.279 | 14.179 | | | 15.873 | | | 17.451 | | |
| *P* | 0.781 | < 0.001 | | | < 0.001 | | | < 0.001 | | |

CRP, C-reactive protein; HBP, Heparin-Binding Protein; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte ratio; QHTMSC, Qi Huang Tong Mi Soft Capsule; SAP, severe acute pancreatitis. Presented the inflammatory indexes of the study population after 7- and 14-days treatment, including CRP, IL-6, IL-8, TNF-α, NLR, PLR, PCT and HBP across the four treatment groups (experimental, QHTMSC, probiotics, and control). The treatment efficiency of the experimental group was significantly higher than the other three groups, and the difference was statistically significant (*$P < 0.05$ compared with the control group).

## Discussion

Most acute pancreatitis (AP) cases are mild and response well to standard interventions, including fluid resuscitation, pain management, anti-inflammation treatments, and early enteral nutrition (Leppäniemi et al., 2019; Chinese Pancreatic Surgery Association, 2021). However, approximately 20–30% of patients progress to severe acute pancreatitis (SAP), which is associated with a mortality rate of approximately 15% (Van Santvoort et al., 2011).

A pivotal factor in the progression of SAP is gastrointestinal (GI) barrier dysfunction, which facilitates bacterial translocation, system inflammation, and the development of multiple organ dysfunction syndrome (MODS) (Liu et al., 2008). Studies have shown that SAP-related GI dysfunction is characterised by increased intra-abdominal pressure, microbial imbalance, and impaired intestinal mucosal integrity (Thandassery et al., 2013; Tan et al., 2015). These factors collectively exacerbate inflammation and contribute to poor clinical outcomes. Although conventional Western medicine interventions, such as octreotide, can suppress pancreatic secretion and alleviate symptoms, their effects on lone-term intestinal function are limited and maybe associated with adverse side effects (Li et al., 2017). As a results, there is growing interest in therapeutic strategies that directly target the intestinal barrier to reduce SAP-related complications.

From the perspective of traditional Chinese medicine (TCM), SAP is attributed to internal imbalances such as ‘heat,’ ‘stagnation of qi,’ and ‘blood stasis’ (Yang et al., 2021). Rhubarb-based herbal formulations, including Qi Hunag Tong Mi soft capsules (QHTMSC), have demonstrated anti-inflammatory, antibacterial, and gastrointestinal motility–enhancing properties (Wan et al., 2014). QHTMSC combines rhubarb with other TCM herbs such as *Astragalus membranaceus, Angelica sinensis,* and *peach kernel*, which are believed to synergistically improve gastrointestinal motility, restore intestinal microbial balance, and preserve intestinal mucosal integrity (Hu et al., 2018).

In parallel, probiotics have also been widely recognised for their role in maintaining gut homoeostasis. The intestinal microbiota plays as central role in metabolic, immune, and barrier functions (Caldeira et al., 2020). In particular, *Lactobacillus* and *Bifidobacterium* species can modulate host immunity responses, produce short-chain fatty acids (SCFAs), enhance strengthen tight junction integrity, and reduce endotoxemia and systemic inflammation (Li et al., 2020). Clinical trials have demonstrated that probiotics can reduce disease severity and accelerate recovery in patients with pancreatitis (Gao et al., 2023).

Our finding suggests that the combining QHTMSC and probiotics significantly enhances clinical outcomes in patients with SAP. Compared with the other groups, the experimental group exhibited the most substantial reduction in inflammatory markers (e.g., CRP, IL-6, IL-8, TNF-α, PCT), intestinal permeability indices (e.g., DAO, D-lactate, endotoxin), and severity scores (e.g., GIDS and APACHE II), alongside faster symptom resolution and shorter hospitalisation. Additionally, favourable alterations in the gut microbiota were observed in the experimental group, characterised by increased levels of *Lactobacillus* and *Bifidobacterium*, and decreased counts of *Escherichia coli* and *Staphylococcus*. These changes suggest a synergistic effect of QHTMSC and probiotics in restoring microbial balance and enhancing mucosal barrier function, thereby potentially preventing bacterial translocation, and attenuating systemic inflammatory responses.

Our findings support the hypothesis that a dual-modality approach-targeting both inflammation and intestinal barrier integrity-may be more effective than single-agent therapy in management of SAP. In contrast to previous studies that investigated probiotics or herbal medicine alone (Hu et al., 2018; Gao et al., 2023), our study provides novel evidence for the combined use of these interventions within a randomised controlled trial design. This integrative strategy may serve as a safe, accessible, and cost-effective adjunct to conventional supportive care, particularly in resource-limited clinical settings.

However, this study has several limitations. First, the following-up period was limited 14-days, which may not capture lone-term outcomes such as recurrence, chronic pancreatitis, or gut microbiota re-

**Table 5**
Effects of QHTMSC combined with probiotics on intestinal flora of SAP patients.

| Indices | Control group (n = 30) | Qi Huang group (n = 30) | *t* | *P* | Probiotics group (n = 30) | *t* | *P* | Experimental group (n = 30) | *t* | *P* |
|---|---|---|---|---|---|---|---|---|---|---|
| *E. coli* ($\bar{x} \pm s$, %) | | | | | | | | | | |
| Before treatment | 9.584 ± 0.346 | 9.566 ± 0.618 | 0.137 | 0.892 | 9.631 ± 0.701 | −0.331 | 0.742 | 9.680 ± 0.638 | −0.725 | 0.472 |
| After 1 wk of treatment | 9.389 ± 0.583 | 8.620 ± 0.692 | 4.651 | < 0.001 | 8.518 ± 0.744 | 5.044 | < 0.001 | 7.324 ± 0.411 | 15.832 | < 0.001* |
| *t* | 1.579 | 5.586 | | | 5.961 | | | 17.004 | | |
| *P* | 0.121 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| After 2 wk of treatment | 9.338 ± 0.646 | 7.317 ± 0.034 | 17.113 | < 0.001 | 7.348 ± 0.052 | 16.814 | < 0.001 | 6.936 ± 0.040 | 20.328 | < 0.001* |
| *t* | 1.839 | 19.920 | | | 17.774 | | | 23.520 | | |
| *P* | 0.071 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| *Staphylococcus* ($\bar{x} \pm s$, %) | | | | | | | | | | |
| Before treatment | 6.700 ± 0.188 | 6.595 ± 0.235 | 1.910 | 0.061 | 6.642 ± 0.229 | 1.067 | 0.290 | 6.624 ± 0.237 | 1.382 | 0.173 |
| After 1 wk of treatment | 6.641 ± 0.285 | 6.264 ± 0.320 | 4.822 | < 0.001 | 6.096 ± 0.215 | 8.372 | < 0.001 | 5.858 ± 0.049 | 14.855 | < 0.001* |
| *t* | 0.942 | 4.563 | | | 9.538 | | | 17.332 | | |
| *P* | 0.351 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| After 2 wk of treatment | 6.535 ± 0.429 | 5.963 ± 0.346 | 5.687 | < 0.001 | 5.842 ± 0.330 | 7.012 | < 0.001 | 5.193 ± 0.360 | 13.121 | < 0.001* |
| *t* | 1.934 | 8.283 | | | 10.923 | | | 18.169 | | |
| *P* | 0.580 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| *Bifidobacterium* ($\bar{x} \pm s$, %) | | | | | | | | | | |
| Before treatment | 3.276 ± 0.437 | 3.320 ± 0.403 | −0.408 | 0.684 | 3.251 ± 0.384 | 0.239 | 0.812 | 3.236 ± 0.301 | 0.410 | 0.684 |
| After 1 wk of treatment | 3.347 ± 0.664 | 4.343 ± 0.230 | −7.762 | < 0.001 | 4.148 ± 0.283 | −6.077 | < 0.001 | 5.503 ± 0.425 | −14.972 | < 0.001* |
| *t* | −0.489 | −12.068 | | | −10.301 | | | −23.845 | | |
| *P* | 0.627 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| After 2 wk of treatment | 3.265 ± 0.593 | 5.222 ± 0.241 | −16.745 | < 0.001 | 5.441 ± 0.347 | −17.344 | < 0.001 | 6.167 ± 0.430 | −21.748 | < 0.001* |
| *t* | 0.084 | −22.175 | | | −23.170 | | | −30.742 | | |
| *P* | 0.933 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| *Lactobacillus* ($\bar{x} \pm s$, %) | | | | | | | | | | |
| Before treatment | 3.490 ± 0.176 | 3.492 ± 0.466 | −0.026 | 0.980 | 3.449 ± 0.509 | 0.417 | 0.678 | 3.406 ± 0.429 | 0.988 | 0.327 |
| After 1 wk of treatment | 3.557 ± 0.319 | 4.306 ± 0.268 | −9.858 | < 0.001 | 5.113 ± 0.764 | −10.299 | < 0.001 | 5.883 ± 0.551 | −20.027 | < 0.001* |
| *t* | −1.003 | −8.295 | | | −9.931 | | | −19.429 | | |
| *P* | 0.321 | < 0.001 | | | < 0.001 | | | < 0.001 | | |
| After 2 wk of treatment | 3.540 ± 0.326 | 6.131 ± 0.168 | −38.729 | < 0.001 | 6.403 ± 0.154 | −43.566 | < 0.001 | 7.456 ± 0.147 | −60.075 | < 0.001* |
| *t* | −0.735 | −29.185 | | | −30.449 | | | −48.897 | | |
| *P* | 0.465 | < 0.001 | | | < 0.001 | | | < 0.001 | | |

QHTMSC, Qi Huang Tong Mi Soft Capsule; SAP, severe acute pancreatitis.
Presented the intestinal flora of the study population after 7 and 14 days treatment, including *Lactobacillus, Bifidobacterium, Escherichia coli* and *Staphylococcus* across the four treatment groups (experimental, QHTMSC, probiotics, and control). The counts of *Bifidobacterium* and *Lactobacillus* in the experimental group were significantly higher than those in the other three groups, while the counts of Staphylococcus and Escherichia coli in the experimental group were significantly lower than those in the other three groups (*$P < 0.05$ compared with the control group).

stabilisation. Second, only culturable bacteria were analyzed, without using high-throughput sequencing techniques that could provide deeper insights into microbial diversity and functional pathways. Third, the underlying molecular mechanisms through which QHTMSC and probiotics exert their protective effects remain unclear. Future studies involving multi-omics analysis and in vitro or clinical mechanistic validation (e.g., tight junction protein expression, cytokine pathway analysis) are warranted to further elucidate the pathways involved.

In conclusion, our study provides clinical evidence that the combination of Qi Huang Tong Mi soft capsules and probiotics can safely and effectively promote inflammatory resolution, restore intestinal barrier integrity, and improve clinical outcomes in patients with SAP. This combined therapeutic approach represents a promising adjunctive strategy for enhancing prognosis in severe pancreatitis and warrants further investigation in larger, multi-centre clinical trials.

## Ethical approval

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and was approved by the Ethics Committee of the First Affiliated Hospital of Bengbu Medical University (Approval Number: 2024045). Written informed consent was obtained from all participants prior to their inclusion in the study. The participants were assured of confidentiality, and their data were used solely for research purposes.

## Consent for publication

All authors have reviewed and approved the final version of this manuscript for publication.

## CRediT authorship contribution statement

**Feng Cheng:** Conceptualization, Data curation, Investigation, Writing – original draft. **Huicong Ma:** Writing – review & editing, Writing – original draft, Validation, Methodology, Investigation, Formal analysis, Data curation. **Zhaohui Du:** Writing – original draft, Resources, Formal analysis, Data curation. **Zhao Hongchang:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Conceptualization. **Zhaolei Qiu:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Funding acquisition, Conceptualization. **Zhaoyang Du:** Writing – original draft, Validation, Investigation, Formal analysis.

## Data and model availability statement

Any additional data generated or analyzed during this study are available from the corresponding author upon reasonable request.

## Declaration of Competing Interest

The authors declare that there are no conflicts of interest regarding the publication of this study. All authors have read and approved the final manuscript, and no financial or personal relationships influenced the research or its outcomes.

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