

## Therapeutic effects of rhubarb on gastrointestinal failure

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### Abstract

**AIM:** To investigate the effects of rhubarb on gastrointestinal failure and the underlying pharmaceutical mechanism.

**METHODS:** Ninety-seven patients in intensive care unit were divided into a treatment group (76 critically ill patients complicated with gastrointestinal failure) and a control group (21 recovered patients). The effects of rhubarb on stress ulcer and toxic paralytic ileus in the patients were observed. The rectal and gastric intramural pH values, cardiac index, oxygen delivery, and oxygen consumption were measured.

**RESULTS:** Treatment with rhubarb achieved a significant curative effect in 30 of the 36 cases of stress ulcer complicated with gastrointestinal hemorrhage. Ha-2-receptor blocking agent had a poor effect on them ( $P < 0.05$ ). Among the 49 cases of toxic paralytic ileus treated with rhubarb, peristalsis was recovered in 41, and gastrointestinal nutrition could be tolerated in 24, while other medicine had no effect on them. According to gastric and rectal intramural pH, rhubarb could improve gut mucosa perfusion. Among the 23 cases of multiple organ dysfunction syndrome who received treatment with rhubarb, 9 survived.

**CONCLUSION:** This study suggests that rhubarb has a good curative effect on gastrointestinal failure.

**Key words:** Rhubarb; Multiple organ failure; Gastrointestinal disease

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### INTRODUCTION

Gastrointestinal failure is common in critical illness and potentially influences its pathophysiological process. Bacterial translocation and endotoxemia related to gut barrier damage result in activation of the white blood cell system which can release large amounts of cytokines, and cause systemic inflammatory response syndrome (SIRS) and ultimately, multiple organ dysfunction syndrome (MODS). Prevention of gastrointestinal failure is the key to preventing the occurrence of fatal complications in critical illness. Since 1991, we have been using a combination of western medicine with traditional Chinese medicine to treat gastrointestinal failure and have achieved good curative effects. The aim of the present study was to investigate the therapeutic effects of rhubarb on gastrointestinal failure and the underlying mechanism.

### MATERIALS AND METHODS

#### Subjects

Ninety-seven patients in intensive care unit (ICU) were enrolled. Twenty-one recovered patients were included as controls while the others complicated with gastrointestinal failure were contained in a rhubarb treated group. The diagnoses of gastrointestinal failure and MODS were in accordance with the guidelines set in 1992<sup>[1,2]</sup>.

#### Devices and materials

Devices and materials included multifunction monitor (Siemens 961, Germany); Swan-Ganze catheter (ARROW CO., United States); ABL-300 blood-gas analyzer (Radiometer CO., Denmark); gas exchange membrane (Fudan University, China); raw rhubarb powder (granted by Rhubarb Lab, Shanghai Xiang Shan Traditional Medical Hospital).

#### Treatment

Rhubarb was given to patients at a dose of 12 g, 1/6 h, after 12, 24, 48 h. The effects on gastrointestinal bleeding and toxic paralytic ileus were monitored and recorded.

#### Measurement of intramural pH

Gastric and rectal intramural pH values (pHi) were studied in 43 patients, including the control group (21 cases) and the rhubarb treated group (22 cases, who suffered from stress ulcer). Before treatment, the pHi measurement was performed in all the patients, then rhubarb at a dose of 12 g was given to the patients in the treatment group and the same dose was repeated 6 h later, while the patients in the control group only took the same volume of 0.9%

**Table 1** Effects of rhubarb on stress ulcer accompanied with gastric hemorrhage

Group	n	Hemostasis	Rebleeding
H <sub>2</sub> -RBA	8	2	2
H <sub>2</sub> -RBA plus Cold water and NE	12	5	5
Rhubarb	36	30 <sup>ac</sup>	6

<sup>a</sup>*P* < 0.005 vs H<sub>2</sub>-receptor blocking agent group (RBA); <sup>b</sup>*P* < 0.05 vs H<sub>2</sub>-RBA plus cold water and nonadrenaline (NE) group.

**Table 2** Effects of rhubarb on toxic paralytic ileus

Group	n	Peristalsis	Diet tolerance
H <sub>2</sub> -RBA	27	0	0
Rhubarb	49	41 <sup>e</sup>	24 <sup>e</sup>

<sup>e</sup>*P* < 0.005 vs H<sub>2</sub>-RBA. RBA: Receptor blocking agent group.

**Table 3** Effects of rhubarb on gastric intramural pH (pHi) (mean ± SD)

Group	n	pHi
Pre-treatment	27	7.018 ± 0.117
Control	21	7.335 ± 0.180
Post-treatment	24	7.305 ± 0.095 <sup>f</sup>

<sup>f</sup>*P* < 0.001 vs pre-treatment.

**Table 4** Effects of rhubarb on rectal pHi (mean ± SD)

Group	n	pHi
Pre-treatment	27	7.071 ± 0.1860
Post-treatment	19	7.268 ± 0.0785 <sup>f</sup>

<sup>f</sup>*P* < 0.001 vs pre-treatment.

**Table 5** Hemodynamic parameters and gastrointestinal pHi (*n* = 8, mean ± SD)

Parameter	Before rhubarb treatment
CI (L·min <sup>-1</sup> /m <sup>2</sup> )	5.06 ± 0.73
DO <sub>2</sub> (ML·min <sup>-1</sup> )	977.75 ± 157.35
VO <sub>2</sub> (ML·min <sup>-1</sup> )	375.86 ± 161.34
Gastric pHi	7.02 ± 0.11
Rectal pHi	7.04 ± 0.14

**Table 6** Effects of the rhubarb on multiple organ dysfunction syndrome

Involved organs	n	Rhubarb treatment		Non-rhubarb treatment	
		Sum	Surviving	Sum	Surviving
2	8	5	4	3	2
3	11	7	3	4	2
4	16	11	2	5	0

sodium chloride instead of rhubarb. The pHi was again measured 12 h after intake of medicine. The method of pHi measurement was in accordance with that established by Le Bo.

### Evaluation of effects of rhubarb

The effects on stress ulcer were determined on the basis of occult blood examination (OBE) of gastric contents 48 h after treatment, OBE result changing from ++++ to “++” or from +++ to + represented effectiveness. Negative OBE was regarded as relatively good effects. Effects on toxic paralytic ileus referred to the recovery of gut peristalsis and diet tolerance. Bowel sound was weak or less than 3 times per minute was defined as treatment failure, more than 4 times/min of bowel sound represented effectiveness, and active peristalsis and tolerance of more than 2090 KJ/d of essential diet stood for good response to rhubarb.

### Statistical analysis

All values are expressed as mean ± SD. The unpaired Student's *t*-tests were used to compare the quantitative data, and chi-square tests were used to compare the qualitative data. *P*-values less than 0.05 were considered significant.

## RESULTS

Thirty-six patients with stress ulcer and gastric bleeding were treated with rhubarb, which was effective in 30 patients and had better effects in 18 patients. Two out of 8 patients received H<sub>2</sub>-receptor blocking agent which proved to be effective. However, they all rebled later. Among 12 patients treated with H<sub>2</sub>-receptor blocking agent plus cold water containing nonadrenaline, gastric bleeding ameliorated in 5 cases, but rebleeding occurred in all later (Table 1).

Forty-eight patients suffering from toxic paralytic ileus received rhubarb treatment and gut peristalsis recovered in 41 cases. Twenty-four cases could tolerate 2090 KJ/d of essential diet, while 12 patients inflicted with same disorder were treated with H<sub>2</sub>-receptor blocking agent, and none of them recovered from toxic paralytic ileus (Table 2).

Twenty-seven samples of the stomach and rectum for measurement of pHi were obtained in 22 patients before rhubarb treatment, including 5 samples collected from 5 patients who were harassed by gastric rebleeding and 24 and 19 samples were collected after treatment. The results showed that rhubarb had a good curative effect on stress ulcer (Tables 3 and 4).

Hemodynamic monitoring was performed in 8 patients. The hemodynamic parameters revealed that all the patients were in hyperdynamic condition and the cardiac index, oxygen delivery and oxygen consumption were far beyond the normal ranges, meanwhile gastric and rectal intramural pH values were obviously lower (Table 5). These findings mean that hypoperfusion existed in the gut mucosa.

In this study, out of 35 patients suffering from MODS, 23 received rhubarb treatment. Among whom 5, 7 and 11 cases had 2, 3 and more than 4 organs involved, respectively. Four, three and two patients survived for each, respectively (Table 6).

## DISCUSSION

Gut failure is common in critical illness, which is characterized by toxic paralytic ileus and stress ulcer usually accompanied with gastric bleeding. According to traditional opinion, pathophysiological basis of the latter is damage of the barrier which is resistant to retroflow of H<sup>+</sup>. However, recent studies have proved that stress ulcer not only occurs in the stomach, but in the whole digestive tract from the mouth to rectum. Mucosal blood hypoperfusion is its main pathophysiological mechanism. Stress can result in low basic and maximal secretion of gastric acid and hike of intragastric pH<sup>[3]</sup>. Change of gastric microecological environment promotes bacterial reproduction, bacterial translocation and endotoxin absorption. Through 5 years of study, we found that the traditional Chinese medicine rhubarb has a good curative effect on gut failure and can protect the gastrointestinal mucosa, and meanwhile has a unique capacity to ameliorate stress ulcer and to relieve toxic paralytic ileus. In this study, 30 out of 36 patients with gastric stress ulcer accompanied with hemorrhage had hemostasis. Among 49 cases of toxic paralytic ileus, peristalsis was recovered in 41 cases, and enteric nutrition could be tolerated in 24 cases, while other medicines had a poor effect on them.

Gut is a sensitive organ to MODS. It is the first organ to be easily damaged under some pathophysiological circumstances. The present study revealed that although the patients were in hyperdynamics, the gastric and rectal intramural pH values were much lower (gastric pHi, 7.018 ± 0.186 vs 7.335 ± 0.180 in control, *P* < 0.001), indicating that the blood flow supplied to the gut was compromised and the gut was in hypoperfusion and oxygen defect. Blood redistribution from the gut to the vital organs initiated by the neuro-endocrine system was implicated in the pathogenesis of gut failure<sup>[4]</sup>. The current research also proved that rhubarb could

markedly improve gastrointestinal ischemia and increase oxygen delivery (gastric and rectal pHi were  $7.305 \pm 0.095$  and  $7.268 \pm 0.079$  respectively). The pharmaceutical effects of rhubarb are conducive to gut recovery from toxic paralytic ileus and protection of gut barrier. This provides an important method to prohibit critically ill patients from fatal complications.

In general, gut communicates with the exterior, and a large amount of bacteria and endotoxin exists in the intestine crassum, whereas the stomach and intestine tenue are relatively sterile. However, some pathophysiological factors, such as surgical stress and use of H<sub>2</sub>-receptor blocking agent, can damage the gastrointestinal microecological environment, thus causing bacterial colonization and reproduction in the stomach and intestine tenue, meanwhile bacterial translocation and endotoxin absorption occur, inducing monocyte phagocytic system activation, especially hepatic Kupffer's cells, which release a large amount of inflammatory factors, resulting in SIRS. Border<sup>[5]</sup> regarded bacterial translocation and endotoxin absorption as the key factors which result in constant activation of white blood cell system. So the gut is not passively sacrificed, on the contrary, it actively participates in the pathophysiological process of SIRS and MODS. Clinical information showed that the patients inflicted with MODS involving two organs were treated simply, while patients had more than three organs involved were critically ill and difficult to treat. Rhubarb was used to relieve toxic paralytic ileus. Several advantages of rhubarb are as follows: (1) The patients recovering from toxic paralytic ileus can obtain benefits from decreased intraabdominal pressure, which can potentially affect cardiac-pulmonary function; (2) Recovery of gut peristalsis can promote excretion of endotoxin contained in the gut and is conducive to stability of gut microecologic environment; (3) Recovery of enteric nutrition can improve nutritional conditions, upgrade host defense and protect the gut barriers<sup>[6]</sup>; and (4) Rhubarb can prohibit some bacteria from reproduction<sup>[7]</sup> and maintain balance of gut flora. We observed that once the gut recovered from toxic paralytic ileus in critically ill patients, their pulmonary and cardiac function could be improved immediately. We once treated 16 patients who suffered from MODS involving

more than four organs, among whom 11 cases were treated with rhubarb, two of them survived, which had broken through the deadline that the mortality rate of the patients suffering from MODS involving more than four organs was 100%. The mechanism may be that rhubarb can prevent bacterial translocation and endotoxin absorption, and resolve the pathophysiological basis which results in continuous activation of white blood cell system and SIRS. Animal experiments displayed that rhubarb could prevent bacterial translocation and endotoxin absorption and scavenge oxygen free radicals in hemorrhagic shock models<sup>[8,9]</sup>.

Rhubarb is a kind of traditional Chinese herb, and gut is its main target organ. Its pharmaceutical mechanism is to promote gut peristalsis, protect the gastrointestinal mucosa, improve gut blood perfusion, promote recovery of cellular digestion, secretion and absorption of the gastrointestinal mucosa, and increase tolerance to enteric nutrition.

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