

# The effect of somatostatin retained enema in the treatment of pancreatic ileus

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**Abstract. – OBJECTIVE:** To analyze the therapeutic effects of somatostatin retained enema in the treatment of pancreatic ileus in the clinic.

**PATIENTS AND METHODS:** 79 patients randomly divided into 41 cases in the observation group and 38 cases in the control group were analyzed. The control group applied basic treatment plan. The observational group applied the same treatment combined with somatostatin retained enema, conducted twice every day and at least 30 minutes every time. Every 7 days' treatment made a course. The clinical therapeutic effects were compared.

**RESULTS:** The levels of the hemo diastase and urinary amylase in both groups were decreased prominently after treatment. The levels of blood calcium were prominently increased ( $p<0.05$ ) with even more improvement in the observation group ( $p<0.05$ ). The relief times of the abdominal ache and distention, the recovery time of bowel sound and the first defecation time in the observation group were shorter ( $p<0.05$ ) than those in the control group. The levels of blood serum IL-6 and TNF- $\alpha$  in the two groups were prominently decreased ( $p<0.05$ ) after treatment, with even more obvious improvement in the observation group. The therapeutic effective rate of the observational group was prominently higher ( $p<0.05$ ) than that in the control group. The occurrence rate of the complications was lower.

**CONCLUSIONS:** The application of somatostatin retained enema in the treatment of pancreatic ileus is preferably safe and effective, and it deserves clinical promotion and application.

Key Words:

Somatostatin, Retained enema, Pancreatic ileus, IL-6, TNF- $\alpha$ .

## Introduction

Severe acute pancreatitis (SAP) takes a percentage of about 30% in acute pancreatitis, the conditions by which it is critically severe when it occurs. It has a percentage of up to 70-90% of the severe complication and important organ

failure and extremely high death rate<sup>1</sup>. The body of SAP patient releases a large number of cytokines and mediators of inflammation. It aggravates the acid-base unbalance and disorder of water and electrolyte, and induces paralytic ileus, also called pancreatic ileus<sup>2</sup>. The occurrence of ileus may further aggravate the condition of the patients. So, it is of important significance of the positive and effective intervention of pancreatic ileus in the early stage for the improvement of the therapeutic effect and survival prognosis<sup>3</sup>. Researches confirm that somatostatin plays an important role in the aspects of the relief of SAP disease progress and the promotion of the functional recovery of the organs<sup>4</sup>. Previous animal experiments indicate that somatostatin retained enema can prominently reduce the incidence of pancreatic ileus and relieve the complication after the obstruction. Based on the theories above, this work aimed at analyzing the clinical effect of somatostatin retained enema in the treatment of pancreatic ileus, in order to provide references to increase the safety and effectiveness of the SAP therapy.

## Patients and Methods

### Patients Data

79 cases of patients were firstly seeking treatment in our hospital during July 2013 to July 2015. This study was approved by the Ethics Committee of Beijing Tongren Hospital. Signed written informed consents were obtained from the patients and/or guardians. They were diagnosed with acute severe pancreatitis (SAP) complicated with pancreatic ileus. They were consecutively selected, following the criteria of "treatment guidance of severe pancreatitis" provided by the Division of Pancreatic Surgery, Branch of Surgery, Chinese Medical Associa-

tion. The diagnosis criteria of the paralytic ileus included: occurrence of abdominal distention, no anus exhaust and defecate, and disappearance of borborygmus 72 hours after the onset of the disease, as well as the abdominal CT and plain film display of acute ileus. The following conditions were excluded: 1. Disease record of ileus, mechanical ileus and vascular ileus; 2. Primary disease of biliary tract, like cholelithiasis and cholangiolithiasis; 3. Intestinal necrosis, severe complications which include sepsis, serious infection, cachexia and multiple organ failure, and anticipated lifetime less than 3 months; 4. Allergic to somatostatin, unable to bear retained enema for at least 30 minutes; 5. Primary underlying disease, like serious dysfunction of organs including heart, liver, lung, kidney, brain and so on; 6. Bad compliance, incomplete clinical data and so on.

After being informed and consented, this study divided the patients into 41 cases of the observation group and 38 cases of the control group, using the method of random digits' table. There were 26 males and 15 females in the observation group, the age ranged from 24 to 68 years old, averaged at  $(47.6 \pm 9.2)$ ; the disease course of SAP averaged at  $(3.2 \pm 0.6)$  h, and the disease course of ileus averaged at  $(2.5 \pm 0.7)$  h; the hemo diastase averaged at  $(1562.4 \pm 342.7)$  U/L (the regular reference value by Somogyi was 40-180 U/L), the urinary amylase averaged at  $(1023.5 \pm 421.5)$  U/L (the regular reference value by Somogyi was 80-300U/L), the blood calculus averaged at  $(1.67 \pm 0.33)$  mmol/L (the regular reference value was 2.25-2.75 mmol/L). There were 23 males and 15 females in the observation group, the age ranged from 28 to 70 years old, averaged at  $(48.1 \pm 10.5)$ ; the disease course of SAP averaged at  $(3.3 \pm 0.5)$  h, and the disease course of ileus averaged at  $(2.6 \pm 0.8)$  h; the hemo diastase averaged at  $(1468.9 \pm 386.5)$  U/L, the urinary amylase averaged at  $(1213.6 \pm 456.7)$  U/L, the blood calculus averaged at  $(1.72 \pm 0.46)$  mmol/L.

The general data of the two groups were compared, and the differences had no statistical significance.

### **Therapeutic Method**

All the patients applied the basic treatment, including food and water deprivation, gastrointestinal decompression and expansion, magnesium sulfate spasmolytic, inhibition of the pancreatic endocrine and exocrine enzyme by somatostatin and octreotide, inhibition of gas-

tric acid secretion by PPI depressant, rectification of acid-base balance and disorder of the electrolyte and blood glucose, intimate supervision of the disease process, prevention and rectification of incidence of the organ function disorder in time, full dose application of the selected antibacterial in early stage, surgical pancreatic fenestrated drainage when necessary, supplement of nourishment such as amino acid, fat milk, microelements.

Based on the treatment above, the control group applied 500 ml warm normal saline retained enema twice every day; the observation applied 3 mg somatostatin retained enema twice every day and at least 30 minutes every time; every 7 days' treatment made a course.

### **Observation Index and Judgment Criteria**

The levels of hemo diastase, blood calculus and urinary amylase 7 days after treatment in the two groups were compared; the relief time of the abdominal ache and distention, the recovery time of bowel sound and the first defecation time were compared. The levels of blood serum interleukin-6 (IL-6) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) before and after treatment were compared. The therapeutic effective rate and the occurrence rate of the complications were compared. The ELISA kit provided by Jiancheng Biotechnology Co., Ltd., Nanjing, China was used for the tests of blood serum IL-6 and TNF- $\alpha$ , the microplate reader was provided by the Bio-Rad Co., Hercules, CA, USA. The standard concentration curve was built, and data after rectification were compared. The judging standard of the therapeutic effect was as follows: cure meant that both the clinical symptoms and physical signs disappeared, and each biochemical indicator recovered to the normal level; marked effectiveness meant that there was no complication, or there was slight complication which can turn to the normal level after expected treatment, or had no influence on the future life, and each biochemical indicator may recover to the normal level; effectiveness meant that both the clinical symptoms and physical signs of the SAP and ileus relieved prominently, and each biochemical indicator relieved prominently than before, while further treatments were still needed. Ineffectiveness meant that both the clinical symptoms and physical signs became progressively severe and no biochemical indicator indicated prominent relief, one or several kinds of complications occurred.

**Table I.** The comparisons on the levels of hemo diastase, blood calculus, and urinary amylase after treatment.

Group	Hemo diastase (U/L)	Blood calculus (mmol/L)	Urinary amylase (U/L)
Observation group	345.6±67.8	2.13±0.06	462.7±76.6
Control group	556.8±92.4	1.96±0.07	689.5±123.4
<i>t</i>	4.303	4.723	4.625
<i>p</i>	0.035	0.031	0.033

**Table II.** The comparisons on the relief times of the abdominal ache and distention, recovery time of bowel sound and the fist defecation time (d).

Group	The relief time of the abdominal ache and distention	The recovery time of bowel sound	The first defecation time
Observation group	4.7±0.6	6.3±1.7	6.8±2.0
Control group	5.5±0.8	7.0±1.8	7.5±2.2
<i>t</i>	5.135	5.246	5.467
<i>p</i>	0.027	0.025	0.021

**Statistical Analysis**

Software SPSS20.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Measurement data were presented by means ± standard deviation. Independent sample *t*-test was used for comparisons between groups; paired *t*-test was used for comparisons within the group. Enumeration data were presented by cases or (%); (rectified)  $\chi^2$  was used for comparisons between groups. Rank sum test was used for the ranked data. *p*<0.05 suggested statistical differences.

**Results**

**The Comparisons on the Levels of Hemo diastase, Blood Calculus, and Urinary Amylase after Treatment**

The levels the hemo diastase and urinary amylase from both groups decreased prominently after treatment. The level of blood calculus in-

creased prominently, with even more prominent improvement in the observation group. The differences were statistically significant (*p*<0.05) (Table I).

**The Comparisons on the Relief Times of the Abdominal Ache and Distention, Recovery Time of Bowel Sound and the fist Defecation Time**

The relief times of the abdominal ache and distention, as well as the recovery time of bowel sound and the first defecation time in the observation group were obviously shorter than that in the control group (*p*<0.05) (Table II).

**The Comparisons on the Levels of Blood Serum IL-6 and TNF- $\alpha$  Before and After Treatment**

The levels of blood serum IL-6 and TNF- $\alpha$  in the two groups were prominently decreased after treatment, with even more great improvement in the observation group (*p*<0.05) (Table III).

**Table III.** The comparisons on the levels of blood serum IL-6 and TNF- $\alpha$  before and after treatment (pg/ml).

Group	IL-6		TNF- $\alpha$	
	Before treatment	After treatment	Before treatment	After treatment
Observation group	78.6±10.8	39.8±7.9	34.2±6.7	15.6±5.7
Control group	76.4±9.7	58.2±8.6	33.6±6.5	20.3±5.9
<i>t</i>	0.125	5.623	0.236	5.529
<i>p</i>	0.867	0.018	0.648	0.020

**Table IV.** The comparisons on the rates of therapeutic effectiveness and the incidence of complications [cases (%)].

Group	Case	Cure	Marked effectiveness	Effectiveness	Ineffectiveness	rate	Effective Pyemia	Dystrophia failure	organ Death	Multiple complication	Rate of complication
Observation group	41	6 (14.6)	16 (39.0)	12 (29.3)	7 (17.1)	34 (82.9)	3 (7.3)	3 (7.3)	2 (4.9)	1 (2.4)	9 (22.0)
Control group	38	2 (5.3)	15 (39.5)	7 (18.4)	14 (36.8)	24 (63.2)	6 (15.8)	5 (13.2)	4 (10.5)	2 (5.3)	17 (44.7)
$\chi^2$		5.721	3.949	0.689	0.237	0.272	0.005	4.637			
<i>p</i>		0.126	0.047	0.407	0.627	0.602	0.946	0.031			

### The Comparisons on the Rates of Therapeutic Effectiveness and the Occurrence of Complications

The therapeutic effective rate of the observation group was prominently higher ( $p < 0.05$ ) than that in the control group, while the rate of the complications was lower (Table IV).

### Discussion

The main causes of the pancreatic ileus are as follows: 1.Exosmosis of the pancreatic fluid, leading to peripancreatic inflammatory reactions, which directly stimulate the coeliac plexus and bring enter paralysis<sup>6</sup>; 2.Inflammatory edema, bleeding, anabiosis and ulceration of the intestinal mucosa<sup>7</sup>. 3.Hyperpolarization of the nerves of the myenteric plexus and inhibition of the enterokina-se led by the endogenous morphine-like substances released by the body, which including met-enkephalin, leu-enkephalin and so on<sup>8</sup>; 4.Enteroparalysis led by the direct erosion of intestinal canal by the inflammatory fluid<sup>9</sup>. The paralytic ileus in the early stage may be playing an important role in the process of pancreatitis. Some scholars believe that<sup>10</sup> the paralytic ileus in the early stage is the originating factor leading to disorders of the systemic inflammatory response of SAP. Therefore, earlier improvement of the intestinal function disorder of the patients can release the pain, effectively shorten the disease course and improve the prognosis.

The somatostatin is a common clinical polypeptide hormone, which mainly distributes in the neurohypophysis, gastric mucosa, pancreas islet, central nervous system and the nerves of the gastrointestinal tract. The somatostatin has multiple biological functions, like inhibition of gastrointestinal peristalsis, inhibition of gastric acid secretion, inhibition of the releasing of the growth hormone and thyroid hormone, inhibition of the releasing of the hypothalamus-pituitary-growth hormone somatotropic hormone, inhibition of the releasing of the gastrin and the pepsin<sup>11</sup>. The somatostatin can also effectively reduce the bleeding of the internal organs and decrease the pressure of portal vein; it also has a certain function on the decrease of the blood perfusion pressure of the body collateral circulation, which effectively reduces the bleeding volume of the liver<sup>12</sup>. The somatostatin can reduce the digestive juice secretion of the patients and relieve the expansion and the ischemic disease of the intestinal canal induced by the aggregation of digestive juice, thus

stimulates the enteric blood circulation and decreases the permeability of the intestinal mucosa. This reduces the absorption of the toxin and the invasion of the bacteria, and helps to relieve the systemic inflammatory reaction<sup>13</sup>. Therefore, the somatostatin is of important clinical value in the treatment of the pancreatic ileus.

This study treated the pancreatic ileus with somatostatin retained enema, and the results suggested as follows: the levels of the hemo diastase and urinary amylase in observation group after treatment were prominently lower than that in the control group; the level of blood calcium were prominently higher; the relief times of the abdominal ache and distention, recovery time of bowel sound and the first defecation time were all shorter; the levels of blood serum IL-6 and TNF- $\alpha$  were prominently lower; the therapeutic effective rate was prominently higher, and the prevalence rate of the complications was lower. All the differences were statistically significant ( $p < 0.05$ ). The somatostatin retained enema can also be absorbed into blood quickly, it not only aggregates in the local intestinal tract in high concentration, and works directly on the damaged intestinal mucosa cells, which stimulates the functional peristalsis and reduces the inflammatory reaction<sup>14</sup>; but also has high biological availability, and brings no increase of the plasma concentration with the combined application of venous inflow, which means preferable safety of the application<sup>15</sup>.

IL-6 and TNF- $\alpha$  are proinflammatory factors produced by the mononuclear macrophage of the body. The blood serum expression level of which is positively related to the seriousness of acute pancreatitis, and intimately related to the prognosis<sup>16</sup>. At the same time, IL-6 and TNF- $\alpha$  in high concentration can straightly damage the cells of the blood vessel endothelium, which promotes the formation of microthrombus, inhibits the repairing of the endothelial cells and aggravates the body damage<sup>17</sup>. The treatment of pancreatic ileus with somatostatin retained enema is probably correlative with the decrease of expression levels of IL-6 and TNF- $\alpha$  in the blood serum, which is consistent with the result observed in animal model research<sup>18</sup>.

## Conclusions

The application of the treatment of pancreatic ileus with somatostatin retained enema is preferably safe and effective, and it deserves clinical promotion and application.

## Conflict of interest

The authors declare no conflicts of interest.

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