Int J Clin Exp Med 2020;13(9):6835-6840
www.ijcem.com /ISSN:1940-5901/IJCEM0114375

Original Article

Effects of esomeprazole sodium combined with somatostatin on serum inflammatory indexes and intestinal barrier function in patients with severe acute pancreatitis

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Received May 15, 2020; Accepted June 23, 2020; Epub September 15, 2020; Published September 30, 2020

Abstract: Objective: To explore the effect of esomeprazole sodium combined with somatostatin (ESCS) regimen on serum inflammation indexes and intestinal barrier function in patients with severe acute pancreatitis (SAP). Methods: 160 patients with SAP were randomly divided into an observation group (OG) (N=80) and a control group (CG) (N=80). CG received symptomatic treatments such as suppression of pancreatic exocrine secretion, fasting, and enteral and external nutrition; The OG was treated with esomeprazole sodium and somatostatin. The efficacy, clinical indicators, inflammatory factors in serum and intestinal mucosal barrier before and after treatment were compared between the two groups. Results: The marked response and total response rate were higher in the OG than those in the CG (P<0.05). The observation also showed shorter intestinal function recovery time, shorter duration of abdominal pain and distension and hospitalization time than the CG (P<0.05). After treatment, the OG had lower IL-2, IL-6 and TNF-α and higher IL-4, IL-10 and TGF-β levels than the CG (P<0.05). The levels of urinary amylase, D-lactate, endomycin and diamine oxidase were reduced in both groups, and the reduction in the OG was more obvious than the CG (P<0.05). There was no significant difference in treatment safety between two groups (P>0.05). Conclusion: Esomeprazole sodium combined with somatostatin can regulate inflammatory factors and enhance the function of intestinal mucosal barrier in patients with SAP.

Keywords: Esomeprazole sodium, somatostatin, severe acute pancreatitis, serum inflammatory markers, intestinal mucosal barrier function

Introduction

Severe acute pancreatitis is an inflammation of the pancreas. It is painful, develops quickly, and it can, in some cases, be fatal. It destroys the normal structure of the intestinal mucosa, causes mucosal atrophy, increases the permeability of the intestinal mucosa, and then disrupts the intestinal mucosa barrier function, resulting in infections and inflammations in the body, which is the root cause of systemic inflammatory response syndrome [1, 2]. If not treated appropriately, it will further induce the failure of other organs, causing clinical death of patients, and the mortality rate of acute pancreatitis has remained at about 10% [3]. The symptoms of SAP mainly include fever, nausea, abdominal distension, and abdominal pain, and SAP could be caused by many factors, such as living environment, living habits, and genetics. Treatment for SAP aims to maintain bodily function and ease symptoms while the pancreas is repairing itself, including intravenous fluids, feeding tubes and surgery [4, 5]. Esomeprazolemost is the most powerful inhibitor of acid secretion identified so far, while somatostatin can inhibit the secretion of pancreatic juice via inhibiting the excitement of the vagus nerve [6]. It is a first-line treatment in the clinical treatment of acute pancreatitis. This study explored the effect of esomeprazole sodium combined with somatostatin regimen on serum inflammation indexes and intestinal mucosal barrier function-related indexes in SAP patients.

Material and methods

General information

160 patients with SAP who were treated in our hospital from April 2014 to April 2017 were randomly divided into observation group (OG) (n=80 cases) and control group (CG) (n=80 cases). Inclusion criteria: ① patients who met the Guidelines for the Diagnosis and Treatment of Acute Pancreatitis (2014) [7]; ② have a history of overeating; ③ are accompanied by symptoms of nausea, retching and abdominal pain. Exclusion criteria: ① patients admitted 2 or more days after onset of symptoms; ② women during pregnancy; ③ patients with history of pancreatitis or malignant tumor. This study has been approved by the Ethics Committee of the First People's Hospital of Lianyungang. All study participants provided written informed consent before participating in the study.

Treatment

The CG received symptomatic treatment such as fasting, fluid replacement, enteral and parenteral nutrition, anti-infection, and suppression of pancreatic secretion; patients in the OG were given intravenous injection of 3 mg somatostatin and 40 mg esomeprazole (q.d.) in addition to the treatment of the CG. After 1 week of treatment, intravenous injection of 6 mg somatostatin, q.d, intravenous injection of 40 mg esomeprazole, once every 12 hours, were given for two weeks as one course.

Observation indicators

(1) Evaluation of treatment efficacy [8]: Marked response: The patient's clinical symptoms disappeared, the vital signs were stable with normal indicators; Response: The patient's clinical symptoms improved, the vital signs were nearly stable, and the indicator gradually recovered to the normal levels; No response: The clinical symptoms, vital signs and indicators of the patients did not change significantly or even worsened. Total response rate = (Marked response + response)/total number of cases. (2) Intestinal function recovery time, duration of abdominal pain, distension and hospitalization time. (3) 4 mL of fasting venous blood was extracted from the patients before and after treatment, respectively. After centrifugation, the serum was separated, and the expression levels of serum IL-2, IL-6, TNF-α, IL-4, IL-10 and TGF-β were detected by ELISA kit. (4) ELISA kits were used to detect ndicators of intestinal mucosal barrier function. D-lactic acid, urine amylase, diamine oxidase and endomycin.

Statistical analysis

Data was processed by SPSS16.0. Measurement data was compared by t test and one-way analysis of variance; χ^2 test was used for count data, and $P<0.05$ was considered statistically significant.

Results

Comparison of baseline data between the two groups

There was no significant difference between the two groups in terms of age, gender, disease course, severity of disease and detected inflammatory factors ($P>0.05$), suggesting that the data in the two groups are well balanced and comparable (**Table 1**).

Esomeprazole sodium combined with somatostatin can significantly improve the clinical efficacy of patients with SAP

The OG exhibited higher marked response and response rates than the CG ($P<0.05$), suggesting that esomeprazole sodium combined with somatostatin can significantly improve the clinical efficacy of patients with SAP (**Table 2**).

ESCS can accelerate the recovery

The OG showed shorter recovery time of intestines, duration of abdominal pain and distension as well as hospitalization time than the CG ($P<0.05$), suggesting ESCS can significantly promote the recovery of intestinal function and improve symptoms (**Figure 1**).

ESCS can significantly increase the level of serum proinflammatory factors

Before treatment, there was no significant difference in serum IL-2, IL-6 and TNF-α levels

Table 1. Comparison of baseline data ($\bar{x} \pm sd$)

Data	Control group	Observation group	t/χ^2	*P*
Age	63.34 ± 8.53	63.41 ± 7.97	0.054	0.957
Gender (Male/Female)	42/38	44/36	0.101	0.751
Course of disease (hours)	10.43 ± 4.75	11.32 ± 4.92	1.164	0.246
APACHE II score	13.97 ± 4.54	14.04 ± 5.01	0.093	0.926
Pro-inflammatory factor (pg/mL)				
IL-2	138.45 ± 43.23	135.65 ± 39.8	0.426	0.671
IL-6	156.32 ± 56.32	162.54 ± 57.21	0.693	0.489
TNF-α	103.45 ± 23.11	104.32 ± 21.32	0.247	0.805
Anti-inflammatory factor (pg/mL)				
IL-4	76.23 ± 19.34	75.54 ± 18.69	0.229	0.819
IL-10	34.56 ± 9.87	35.14 ± 9.65	0.376	0.708
TGF-β	28.65 ± 8.65	29.55 ± 9.11	0.641	0.523
Intestinal mucosa index				
D-lactic acid (mg/L)	19.32 ± 4.21	19.41 ± 4.54	0.130	0.897
Urine amylase (U/L)	13.32 ± 4.35	13.54 ± 4.65	0.309	0.758
Diamine oxidase (ng/L)	6.43 ± 2.04	6.51 ± 2.33	0.231	0.818
Endomycin (EU/mL)	7.54 ± 2.43	7.77 ± 2.87	0.547	0.585

Table 2. Comparison of treatment efficacy (n, %)

Curative effect	Control group (n=80)	Observation group (n=80)	χ^2	*P*
Marked response	20 (25)	48 (60)	25.064	0.000
Response	36 (45)	28 (35)	2.083	0.149
No response	24 (30)	4 (5)	21.645	0.000
Total response rate	56 (70)	76 (95)	21.645	0.000

between the two groups (*P*>0.05). These indicators were decreased in both groups, and they were lower in the OG than the CG (*P*< 0.05), suggesting that esomeprazole sodium combined with somatostatin can significantly reduce the level of serum proinflammatory factors (**Figure 2**).

ESCS can significantly increase the level of serum anti-inflammatory factors

There was no statistically significant difference in serum IL-4, IL-10 and TNF-β levels between the 2 groups (*P*>0.05). They were significantly increased after treatment, and the levels of IL-4, IL-10 and TNF-β in the OG were higher than those in the CG (*P*<0.05) (**Figure 3**).

ESCS can significantly improve the intestinal mucosal function of patients

After treatment, the levels of D-lactic acid, urinary amylase, diamine oxidase, and endomycin decreased in both groups, and they were lower in the OG than the CG (P<0.05) (**Table 3**).

Safety assessment of patients in two groups

There was no statistically significant difference between the two groups in the occurrence of adverse reactions such as nausea, dizziness, abdominal pain and bloating (*P*>0.05) (**Table 4**).

Discussion

Patients with severe pancreatitis will experience complications in many tissues and organs and changes in inflammation indicators during onset [9, 10]. Inflammatory factors include two types of pro-inflammatory factors and anti-inflammatory factors, which antagonize and inhibit each other. When healthy, anti-inflammatory factors play a major role, the pro-inflammatory factors are low in serum [11]. Studies have found that during the onset of severe pancreatitis, the concentration of proinflammatory factors will increase rapidly, accompanied by symptoms of high fever and limb weakness [12]. In addition to the changes in inflammatory factors, it will also cause damage to the intestinal mucosa, disrupt normal absorption of the intestine and the balance of

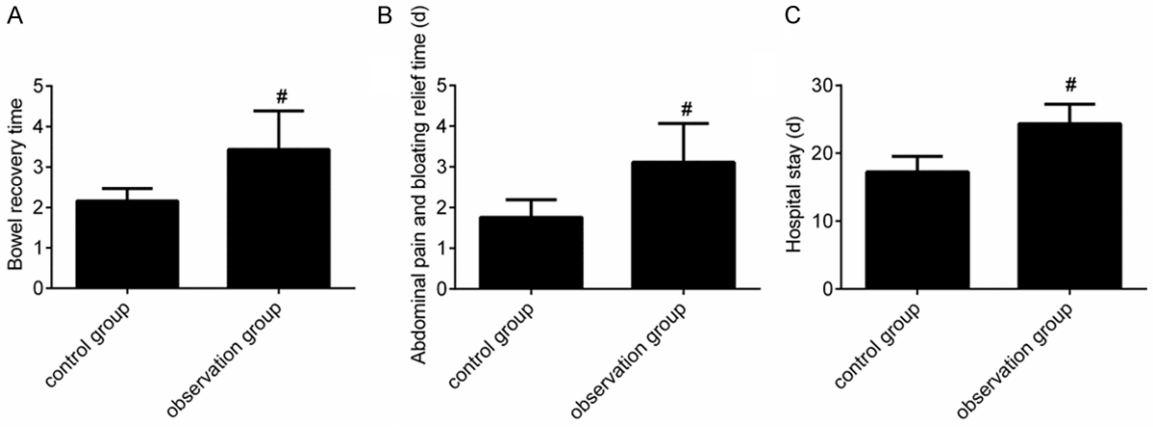

Figure 1. Comparison of clinical indicators. Note: Compared with the control group, $^{*}P<0.05$.

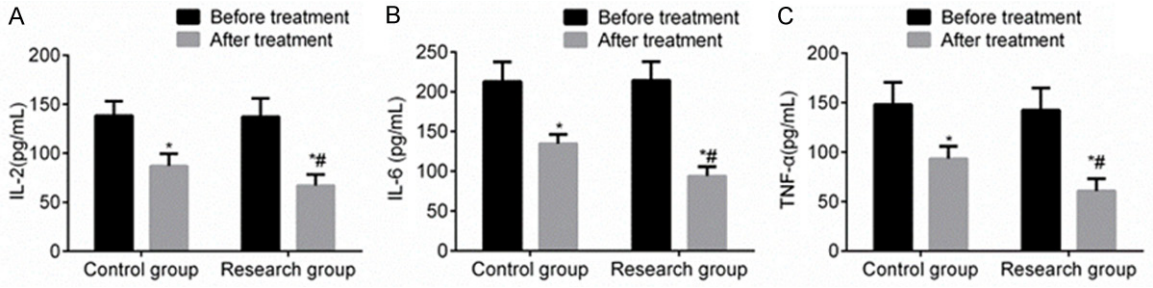

Figure 2. Comparison of pro-inflammatory factor levels before and after treatment. Note: Compared with before treatment, $^{*}P<0.05$; compared with the control group, $^{\#}P<0.05$.

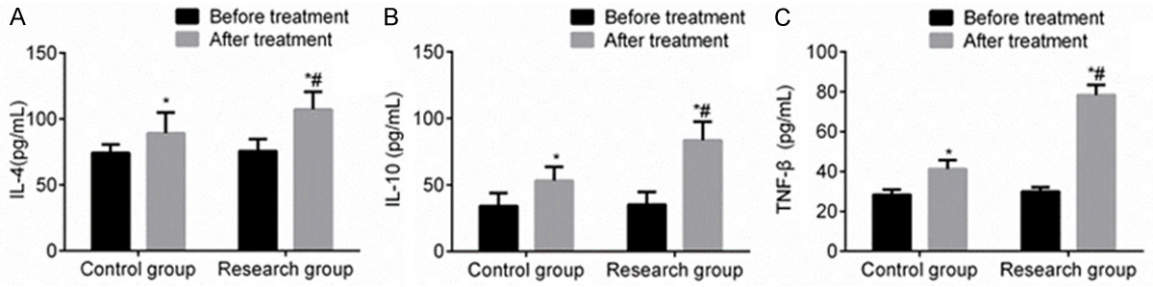

Figure 3. Comparison of anti-inflammatory factor levels before and after treatment. Note: Compared with before treatment, $^{*}P<0.05$; compared with the control group, $^{\#}P<0.05$.

the flora, thereby inducing inflammation of the gastrointestinal tract and endangering the lives of patients [13]. Currently, there is no optimal treatment option for severe pancreatitis, and it is treated mainly through nutrition and medicine. Esomeprazole not only inhibits gastric acid secretion, but also reduces chemotaxis of neutrophils in patients with severe pancreatitis, so that the antioxidant capacity in the intestinal mucosa is significantly improved. Some studies showed that esomeprazole also has anti-oxidation, anti-infection and vasodilatory effects. Somatostatin could increase immunity and inhibit pancreatic juice secretion. Somatostatin can also inhibit the nerve impulses of the vagus nerve, reduce blood flow, and reduce local inflammation [14, 15].

IL-2, IL-6, and TNF-α are typical representatives of pro-inflammatory factors, and show obvious changes before and after treatment

Table 3. Comparison of intestinal mucosal barrier function ($\bar{x} \pm sd$)

Group	D-lactic acid (mg/L)	Urine amylase (U/L)	Diamine oxidase (ng/L)	Endomycin (EU/mL)
Control group	13.22 ± 3.54	8.65 ± 2.03	5.32 ± 1.54	6.32 ± 1.23
Observation group	10.03 ± 2.23	5.65 ± 1.75	2.44 ± 0.87	4.09 ± 0.54
t	8.321	9.654	15.476	11.076
P	0.035	0.026	0.008	0.018

Table 4. The occurrence of adverse reactions (n, %)

Group	Number of cases	Nausea	Dizziness	Abdominal pain	Distension
Control group	80	2 (2.5)	2 (2.5)	2 (2.5)	2 (2.5)
Observation group	80	1 (1.25)	2 (2.5)	1 (1.25)	2 (2.5)
χ^2		0.000	0.000	0.000	0.000
P		1.000	1.000	1.000	1.000

Note: The correction formula of *Chi*-square test was used in all the tests.

of severe pancreatitis. It has been found that IL-2 is capable of killing virus and bacteria, but high concentration of IL-2 will produce cytotoxicity, causing patients to experience vomiting, fever and other uncomfortable feelings, and may also cause electrolyte disorders and abnormal function of multiple organs [16]. IL-6 can stimulate the proliferation and differentiation of immune cells, but in patients with severe pancreatitis, the IL-6 level will be rapidly increased, causing adverse reactions such as fever [17]. Also low levels of TNF-α could kill cancer cells, and high level will cause necrosis of human organs [18]. IL-4, IL-10 and TGF-β play a major role in anti-inflammation. IL-4 can inhibit the secretion of pro-inflammatory factors such as TNF-α and IFN-γ by mononuclear macrophages under the activity of NF-KB, and it plays a role in inhibiting the inflammatory response in both cellular immunity and humoral immunity [19]. IL-10 can inhibit the production of Th1 cells and hinder the release of pro-inflammatory factors such as IL-2 and TNF. Some studies have found that IL-10 can inhibit the immune response that antagonizes bacterial infections [20]. TGF-β inhibits the proliferation of lymphocytes, increases the maturation time of T cells and exhibits anti-inflammatory effects [21]. The results of this study also fully confirmed that IL-2, IL-6 and TNF-α were lowered after treatment, while IL-4, IL-10 and TGF-β were increased. It also found that the effect of esomeprazole combined with somatostatin is superior to nutritional support therapy in terms of efficacy, clinical manifestations, and changes in inflammatory factors.

This study also found that after treatment, the levels of D-lactic acid, urinary amylase, diamine oxidase, and endomycin decreased, and the intestinal mucosal function of the OG was significantly improved compared with the CG, indicating that the combination medication could more effectively repair the intestinal mucosa function. Several patients with adverse reactions after treatment quickly recovered, which confirmed its safety.

In summary, esomeprazole sodium combined with somatostatin can regulate inflammatory factors in patients with SAP, enhance the function of intestinal mucosal barrier, and has high clinical application value.

Disclosure of conflict of interest

None.

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