Effect of octreotide combined with ulinastatin on the serum endotoxin and intestinal mucosal permeability in patients with severe pancreatitis.

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Abstract

Objective: This study aims to investigate the effect of octreotide combined with ulinastatin on the serum endotoxin and intestinal mucosal permeability in patients with severe pancreatitis.

Methods: A total of 88 patients with severe pancreatitis were randomly selected in our hospital from January 2015 to June 2016. They were then randomly assigned to either the observation group (n=44) or the control group (n=44) using the random number method. The patients in the control group were treated with octreotide, whereas those in the observation group were given octreotide combined with ulinastatin. The serum endotoxin and hypersensitive C Reactive Protein (hs-CRP) levels as well as intestinal mucosal permeability of the two groups were investigated before and after treatment.

Results: Before treatment, no significant difference was observed in the serum endotoxin, hs-CRP, plasma Diamine Oxidase (DAO), and Lactulose/Mannitol (L/M) levels of patients between the two groups (P>0.05). However, the endotoxin and hs-CRP levels of the patients in the two groups were significantly lower after treatment than those before treatment (P<0.05). After treatment, the plasma DAO levels of the patients in the two groups were significantly lower than those before treatment (P<0.05), and their L/M levels were significantly higher than those before treatment (P<0.05). However, the serum endotoxin, hs-CRP, plasma DAO, and L/M levels of the patients in the observation group were significantly lower than those in the control group (P<0.05).

Conclusion: Octreotide combined with ulinastatin can significantly decrease the serum endotoxin level of patients with severe pancreatitis. Furthermore, this treatment can help in the restoration of intestinal mucosal function barrier in patients.

Keywords: Severe pancreatitis, Octreotide; Ulinastatin, Endotoxin, Intestinal mucosal permeability.

Introduction

Severe pancreatitis is one of common severe digestive system diseases. This illness has a sudden onset, rapid development, and relatively high mortality rate. The main clinical manifestations include abdominal pain and distension, dysphoria, shock, and jaundice. It is dangerous, and it has a high complication occurrence rate. Moreover, severe pancreatitis is a tough clinical disease [1,2] that can lead to the generation of a substantial amount of intestinal endotoxins and intestinal dysfunction in patients. Reducing the intestinal endotoxin amount in the early stage of treatment is of great significance to prevent intestinal dysfunction [3]. Therefore, this study investigated the effect of octreotide combined with ulinastatin on the serum endotoxin and intestinal mucosal permeability in patients with severe pancreatitis to provide a reference for clinical treatment.

General Data and Methods

General data

Eighty-eight patients with severe pancreatitis were randomly selected in our hospital from January 2015 to June 2016. All patients were evaluated in accordance with the diagnostic criteria for severe pancreatitis, including clinical symptoms, laboratory indicators, and imaging examinations. Patients with drug allergy and immune or liver and kidney disease as well as those who were pregnant or lactating were excluded from the research. The study was approved by the Medical Ethics Committee of our hospital and the patients themselves. The patients signed an informed consent. The patients were then randomly assigned to either the observation or the control group using the random number method. Each group was composed of 44 cases. The observation group had 26 male cases and 18 female cases with ages of 31-54 years old

(average, 42.14 ± 9.78 years). The control group had 27 male cases and 17 female cases with ages of 31–55 years old (average, 43.18 ± 9.24 years). No significant difference was noted in terms of sex, age, and other general data between the two groups. Therefore, the two groups were comparable (P>0.05).

Treatment methods

After admission, the two patient groups underwent the same physical indicator detection, sedation, nutritional support, infection prevention therapy, complication treatment, and other basic treatments. The patients in the observation group were treated with octreotide combined with ulinastatin under the following conditions: subcutaneous injection of octreotide (Beijing Bai'ao Pharmaceutical Industry Co. Ltd., approval number H20061309; specification, 1 ml: 0.1 mg) at 0.1 mg, 4 times/day for 1 week, and intravenous infusion of ulinastatin (Guangdong Epson Pharmaceutical Limited by Share Ltd., approval number H19990134; specification, 50,000 units) at l00,000 units, dissolved in 500 ml of 5% glucose injection, for 2 h, bid, for 10 days. The patients in the control group were treated with octreotide. The treatment method was similar to that of the observation group.

Observation index

The serum endotoxin, hypersensitive C reactive protein (hs-CRP), plasma Diamine Oxidase (DAO), and Lactulose/ Mannitol (L/M) levels of the patients in the two groups were observed before and after treatment. A total of 4 ml of fasting venous blood was collected in the morning and centrifuged at 3000 r/min for 10 min. The supernatant was subsequently collected, and the endotoxin and hs-CRP levels were measured. The plasma DAO concentration was detected by enzymatic spectrophotometry. The urine L/M level of patients was determined using high-performance liquid chromatography [4].

Statistical analysis

The data were processed using SPSS22.0 software. The measurement data were expressed as $\bar{x} \pm S$ and compared using the t-test. The count data were represented in % and compared using χ^2. P<0.05 values indicated that the difference was statistically significant [2].

Results

Endotoxin and hs-CRP levels of the patients in the two groups before and after treatment

Before treatment, no significant difference was observed in the patients' endotoxin and hs-CRP levels between the two groups (P>0.05). However, the endotoxin and hs-CRP levels of the patients in the two groups were significantly lower after treatment than those before treatment (P<0.05). Moreover, the endotoxin and hs-CRP levels of the patients in the observation group were also significantly lower than those of the control group (P<0.05), as shown in Table 1.

Table 1. Endotoxin and hs-CRP of the patients in the two groups before and after treatment.

Group	Before treatment		After treatment	
	Endotoxin (EU)	hs-CRP (mmol/L)	Endotoxin (EU)	hs-CRP (mmol/L)
Observation group (44)	0.46 ± 0.03	88.15 ± 17.46	0.16 ± 0.04*	21.27 ± 6.25*
Control group (44)	0.45 ± 0.04	88.18 ± 17.44	0.06 ± 0.01*	9.06 ± 5.17*
t	1.326	0.008	16.088	30.904
P	0.188	0.994	0.000	0.000

*Significantly different compared with before treatment, P<0.05.

Plasma DAO concentration and L/M of the patients in the two groups before and after treatment

No significant difference was noted in the plasma DAO concentration and L/M between the two groups before treatment (P>0.05). However, after treatment, the plasma DAO concentrations of the patients in the two groups were significantly lower than those before treatment (P<0.05), and their L/M levels were significantly higher than those before treatment (P<0.05). Concurrently, the plasma DAO concentration and L/M of the patients in the observation group were significantly lower than those of the control group (P<0.05), as displayed in Table 2.

Table 2. Plasma DAO concentration and L/M of the patients in the two groups before and after treatment.

Group	Before treatment		After treatment	
	DAO (U/ml)	L/M	DAO (U/ml)	L/M
Observation group (44)	1.69 ± 0.32	0.030 ± 0.003	1.02 ± 0.14*	0.063 ± 0.005*

Control group (44)	1.65 ± 0.29	0.029 ± 0.003	1.34 ± 0.39*	0.088 ± 0.006*
t	0.614	1.563	5.122	21.232
P	0.541	0.122	0.000	0.000

*Significantly different compared with before treatment, P<0.05.

Levels of inflammatory factors

Before treatment, no significant difference was detected in the inflammatory factor levels of patients between the observation group and the control group (P>0.05). As shown in Table 3, the levels of each inflammatory factor (TNF-α, 989 ± 148 pg/ml; IL-1β, 415 ± 97 pg/ml; IL-6, 402 ± 105 pg/ml; IL-8, 373 ± 95 pg/ml) of patients in the observation group were lower than those in the control group (P<0.05).

Table 3. Inflammatory factor levels of patients with severe acute pancreatitis between the two groups ($\bar{x} \pm S$).

Group	Cases		TNF-α (pg/ml)	IL-1β (pg/ml)	IL-6 (pg/ml)	IL-8 (pg/ml)
Observation group	44	Before treatment	1349 ± 184	634 ± 127	591 ± 117	563 ± 114
		After treatment	989 ± 148[ab]	415 ± 97[ab]	402 ± 105[ab]	373 ± 95[ab]
Control group	44	Before treatment	1338 ± 180	650 ± 129	597 ± 121	560 ± 112
		After treatment	1203 ± 152[a]	572 ± 108[a]	536 ± 107[a]	483 ± 102[a]

[a]Significantly different compared with before treatment, P<0.05. [b]Significantly different compared with the control group, P<0.05.

Discussion

Severe pancreatitis is a serious acute abdominal disease that causes patients to experience organ disorders, necrosis, abscess, pseudocyst, and other complications. Acute pancreatitis can lead to the generation of a considerable amount of intestinal endotoxins and intestinal dysfunction in patients [5]. Plasma D-lactate is one of the bacterial metabolism and pyrolysis products of the human intestinal tract. Lactulose and mannitol cannot be metabolized. These markers can reflect the intestinal mucosal permeability and damage degree caused by severe pancreatitis [6]. The treatment of acute pancreatitis still presents several challenges. First, either nonsurgical or surgical treatment should be selected appropriately [7]. In terms of the surgical approach, the problems on how to reasonably supplement the blood volume, reduce the surgical time, master the surgical time, implement the operation, and rationally select the operation need to be further explored [8]. However, acute edematous pancreatitis and boundary haemorrhagic necrotizing pancreatitis are not completely independent [9]. Therefore, the development process should be closely observed during the nonsurgical treatment of acute edematous pancreatitis.

Octreotide is a synthetic octapeptide cyclic compound that shares similar effects with natural endogenous somatostatin. However, the effect of octreotide is stronger and more lasting. Its half-life period is 30 times longer than that of natural somatostatin. Octreotide can be used to treat severe pancreatitis because it is involved in a variety of physiological activities. For example, octreotide can inhibit the pathological hypersecretions of growth, thyroid-stimulating, gastrointestinal, and pancreatic endocrine hormones. It can also impede the secretions of gastric acid, trypsin, glucagon, and insulin as well as the pathological secretions of gastrointestinal and pancreatic endocrine hormones. Ulinastatin protease inhibitor can hinder trypsin, α-chymotrypsin serine protease, granulocyte elastase, hyaluronidase, sulfhydryl enzyme, and plasmin secretions. Moreover, it can stabilize lysosomal membrane; inhibit lysosomal enzyme, myocardial inhibitory factor, and inflammatory mediator release; and scavenge oxygen free radicals. Furthermore, ulinastatin can suppress trypsin activity and reduce endotoxin absorption [10]. This study investigated the effects of octreotide combined with ulinastatin on the serum endotoxin and intestinal mucosal permeability in patients with severe pancreatitis. The results showed that no significant difference was observed in the endotoxin, hs-CRP, plasma DAO concentration, and L/M levels of patients between the two groups (P>0.05) before treatment. However, the endotoxin and hs-CRP levels were significantly lower after treatment than those before treatment (P<0.05). Additionally, the plasma DAO concentrations of the patients in the two groups were significantly lower than that before treatment (P<0.05), and their L/M was significantly higher after treatment than that before treatment (P<0.05). Moreover, the endotoxin, hs-CRP, plasma DAO concentration, and L/M levels of the patients in the observation group were significantly lower than those in the control group (P<0.05). The results showed that octreotide combined with ulinastatin in the treatment of severe pancreatitis can reduce the adverse effects of endotoxin and promote the recovery of intestinal barrier dysfunction of severe acute pancreatitis [11].

Conclusion

In summary, octreotide combined with ulinastatin in the treatment of severe pancreatitis can minimize adverse

endotoxin effects. This therapeutic approach can also stimulate intestinal barrier dysfunction recovery in patients with severe acute pancreatitis.

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