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Original Article

Effect of octreotide acetate combined with somatostatin on treating acute pancreatitis and expression of miRNA-200 family

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Abstract: Objective: Acute pancreatitis (AP) is a severe disease of acute onset, rapid progression, multiple complications and high mortality. In this study, patients with pancreatitis were respectively treated with octreotide acetate, somatostatin or the combination of both. The clinical efficacy and genesis of complications in the 3 groups were compared and analyzed. Expression of miR-200 family in serum of the patients was detected to provide theoretical basis for the treatment of pancreatitis. Data and methods: The case information of 153 patients with acute pancreatitis treated in our hospital during Jan. 2010 to Dec. 2014 was retrospectively analyzed. There were 52 cases in octreotide acetate treatment group, 48 cases in somatostatin treatment group and 53 cases in octreotide acetate combined with somatostatin treatment group. The patents were assessed according to the following indexes: the main symptoms and remission of signs; blood and urine amylase, and WBC changes before treatment and 3, 6, 9, and 12 days after treatment; recovery of laboratory parameters including WBC of AP, AST, blood glucose, and blood calcium, as well as complication rate and case fatality rate; days of symptoms and signs disappearing, days of blood amylase, urine amylase and blood WBC recovery; hepatic function recovery *etc.* Results: the efficacy of octreotide acetate combined with somatostatin on acute pancreatitis was good. Remission of symptoms and signs, as well as recovery of blood amylase, urine amylase and blood WBC recovery, was fast. In early or mid period of AP treatment, the combination of octreotide acetate and somatostatin could reduce complication rate or death rate. Recovery effect of WBC, AST, blood glucose and blood calcium was significant. As for patients with AP complicated with hepatic injury, the combination treatment had good effect of liver protection. The adverse reactions of octreotide acetate combined with somatostatin were few. And the efficacy of combination treatment was better than using octreotide acetate or somatostatin alone. Expression of miR-200 family members including miR-200a, miR-200b, miR-200c, miR-141 and miR-429 was up-regulated, showing a positive correlation with combination treatment. Conclusion: Octreotide acetate combined with somatostatin was a new effective approach of treating AP, and could effectively improve symptoms, with protective effect on multi-organ damage. Moreover, detection of miR-200 family expression in blood could dynamically monitor the effect of combination treatment on AP clinically, with more objectivity and rationality.

Keywords: Octreotide acetate, somatostatin, acute pancreatitis, miR-200 family

Introduction

Acute pancreatitis (AP) is a severe disease of acute onset, rapid progression, multiple complications and high mortality. It is mainly a chemical inflammation induced by trypsin digesting pancreas itself and the surrounding tissues. The occurrence possibility is high in normal functioning pancreas [1-3]. Acute pancreatitis is generally accepted as a kind of acute abdomen, with typical manifestations including abdominal pain and increasing amylase in blood and urine induced by pancreatitis lesions. It is divided into mild form (simple edema) and severe form (hemorrhagic necrosis) in clinical. Mild acute pancreatitis has self-confinement, so the prognosis is good, with mortality rate of about 5%. Severe acute pancreatitis (SAP) often spreads to adjacent tissues and cause organ damage, with multiple complications. Therefore, SAP is the difficulty and hot spot in surgical clinical treatment at present [4]. Study has demonstrated that system inflammatory response syndrome (SIRS)

could appear in SAP [5]. If it is not treated promptly, multiple organ dysfunction syndrome (MODS) can be caused, even multi-organ failure thus inducing death [6]. SAP occupies 22%-30% of AP, with multiple complications, critical condition, poor prognosis and high mortality rate [7]. Necrosis complicated with infection is a severe local complication of SAP. Systemic inflammatory response and gastrointestinal involvement are the principle factor of exacerbation. The severity of external pancreatic organ damage and its clinical importance is far beyond the pancreas disease itself in the early course of SAP [8]. Its pathogenesis is not completely elucidated at present, so the therapy needs to be further explored.

At present, comprehensive therapy of SAP that mainly uses internal medicine drug has been generally recognized clinically. Somatostatin (SS) and its analogue octreotide are the commonly used drugs in clinical treatment of AP at present [9]. SS is a peptide hormone with 14 amino acids first isolated from the hypothalamus in 1973. It is a regulatory peptide that can inhibit multiple hormones releasing, with 5 different receptor subtypes widely distributed on cell membrane. SS can effectively inhibit exocrine secretion of pancreatin, reduce pancreatic duct pressure, reduce pancreatic juice entering pancreatic tissue from pancreatic duct, thus alleviating autodigestion of pancreas [10, 11]. Though the role of SS is broad, but the selectivity is not strong. Biological half-life is short in serum, therefore the reaction time is not long thus limiting its clinical application [12].

Due to the own limitations of SS in clinical use, employing proteinase inhibitor and drugs of inhibiting pancreatin secretion gradually become hotspots. Octreotide acetate is an octapeptide somatostatin analogue artificially synthesized by natural somatostatin, with advantages such as long half-life, convenient, multiple physiological activities etc. [13]. Octreotide acetate can effectively inhibit secretion of growth hormone, thyroid stimulating hormone, gastrointestinal and pancreatic endocrine hormones, as well as gastric acid, trypsin, glucagon and insulin [14]. In addition, octreotide acetate can protect pancreatic cells, inhibit platelet-activating factor releasing and reducing relevant complications [15].

Studies have reported that microRNA was widely involved in regulation of series of biological function including proliferation, differentiation, metabolism and apoptosis in body cells. As tumor inhibiting gene, miRNA-200 family has differential expression in blood of patients with cancer, autoimmune disease and coronary artery disease. The deletion expression can promote migration and metastasis of tumor cells [16]. There are 5 members in miR-200 family: miR-200a, miR-200b, miR-429, miR-200c and miR-141 [17, 18]. Since there is high specificity of miRNAs regulating genes, abnormal expression of miRNAs usually indicates regulatory network anomalies of related diseases. Therefore, miRNAs can be a new type of specific diagnostic marker. In most pancreatic carcinoma cell line, methylation reduction of miR-200a and miR-200b genes resulting in its abnormal expression is detected. Hence we speculate that miR-200 family can involve in genesis and development by target-regulating its target gene. In this study, the serum of patients with pancreatitis was set as object of study to explore the correlations between miR-200 family expression in serum of patients with AP and drug therapy.

For observing the clinical efficacy of octreotide acetate combined with somatostatin on treating AP, in this study, 153 cases of patients diagnosed with AP in our hospital were randomly divided into octreotide acetate group, somatostatin group and octreotide acetate combined with somatostatin group. The clinical data in the 3 groups were compared. miR-200 family expression in serum was detected to provide evidence for exploring new specific diagnostic marker in AP.

Materials and methods

Objects of study

There were 153 cases of patients with AP treated in our hospital during Jan. 2010 to Dec. 2014, including 98 cases of males and 55 cases of females, at the age of 18-82 years old with average of (44.2±9.5) years. They had symptoms including upper abdominal pain, fever, nausea and vomiting on admission, and were diagnosed with AP after imaging examination. There were 33 cases of overeating, 45 cases of biliary tract infection history, 27 cases of excessive fat intake and 48 cases of unknown origin. The patients had no contraindications of octreotide acetate and panax notoginseng saponins. Patients with chronic

cholecystitis, biliary and pancreatic calculus, pregnancy and lactation were excluded. Then they were randomly divided into 3 groups according to tail number of case, including 52 cases in octreotide acetate group, 48 cases in somatostatin group and 53 cases in combination group. There was no significant difference in age, gender, cause of disease, pathogenetic condition, symptoms of the disease *etc.* (P> 0.05) among the 3 groups, with comparability.

Classification, inclusion and exclusion criteria of AP

The diagnostic criteria of SAP in this study was in accordance with *Chinese Acute Pancreatitis Treatment Guidelines (Draft)* enacted by Study Group of Pancreatic Disease, Digestive Diseases Branch of the Chinese Medical Association in 2003. Patients were diagnosed with SAP when they had one of the following symptoms: pancreatic local complications (pancreatic necrosis, pseudocyst, pancreatic abscess); combining with organ dysfunction or organ failure; Ranson score ≥3, Acute Physiology and Chronic Health Indicator Evaluation (APACHE-II score) ≥8; D or E in CT Balthazar grading.

Inclusion criteria: acute onset of persistent upper abdominal pain (minority without abdominal pain), accompanied or not accompanied by fever, nausea and vomiting; increasing blood amylase more than three times the upper limit of normal (minority without increasing or slightly increasing); with or without changes in pancreatic morphology in imaging examination, excluding other acute abdomen.

Exclusion criteria: combined with tumor.

Grouping of patients with AP

The patients were divided into 3 groups according to clinical administration, including 52 cases in octreotide acetate group, with 29 cases of MAP and 23 cases of SAP; 48 cases in somatostatin group with 31 cases of MAP and 17 cases of SAP; and 53 cases in combination group, with 29 cases of MAP and 24 cases of SAP. The cause of disease included 61 cases of biliary, 33 cases of alcohol consumption or (and) overeating, 8 cases of hyperlipidemia and 31 cases of unknown origin. There was no significant difference in age, gender, cause of disease, disease severity *etc.* (P>0.05) among the 3 groups.

Therapeutic method

Relevant treatments according to the patients' condition were preceded in experimental group and control group, such as anti-infection, fasting, continuous gastrointestinal decompression, acid suppression, continuous gastrointestinal decompression, correction of electrolyte and acid-base balance, intravenous nutritional support, fluid replacement, potassium supplement *etc*. Octreotide acetate (purchased from Beijing Novartis Pharmaceutical Co., Ltd.) group: Intravenously infusing 0.6mg octreotide acetate for 24 h, when symptoms such as abdominal pain, bloating *etc.* improved, the dose reduced to 0.3 mg by 24 h continuous intravenous infusion or subcutaneous injection 3 times a day. Somatostatin (purchased from Techpool Biochemical Pharmaceutical Co., Ltd. Guangzhou) group: The drug was intravenously infused 100,000 units 3 times a day, when symptoms such as abdominal pain, bloating *etc.* improved, infusion reduced to twice a day. Octreotide acetate combined with somatostatin group: Treatment method was in reference with octreotide acetate group and somatostatin group. In the 3 groups, medication was stopped when the symptoms disappeared. During the period, the number and ratio of therapeutically effective cases, signs and recovery time of clinical symptoms in the 3 groups were recorded and analyzed.

Main outcome measures

The main outcome measures were listed as follows: remission of main symptoms (abdominal pain, bloating, nausea, vomiting, fever *etc.*); remission of experimental indexes (blood AMY, urine AMY, blood WBC, AST, blood glucose, blood calcium *etc.*); disappearing days of symptoms and signs, recovery days of blood AMY, urine AMY, blood WBC and diet; comparison of complication rate and mortality rate; recovery of hepatic function.

Detection of miR-200 family expression in serum using RT-PCR

Total RNA was extracted using miRNEasy RNA extraction kit in serum of each group (including small non-coding miRNA). The mass of RNA

Table 1. Remission of main symptoms

Symptoms	Octreotide acetate group (n=52)		Somatostatin group (n=48)		Combination group (n=53)	
	After/Before	Remission rate (%)	After/Before	Remission rate (%)	After/Before	Remission rate (%)
Abdominal pain	33/35	88.6	41/46	89.1	50/52	96.2
Abdominal distension	32/37	86.5	35/43	81.4	46/47	97.9
Tenderness	34/41	82.9	31/38	81.6	43/44	97.7
Guarding	10/17	58.8	10/14	71.4	18/19	94.7
Jaundice	13/17	76.5	11/15	73.3	18/18	100
Nausea	23/30	76.7	22/25	88.0	31/33	93.9
Emesis	20/31	64.5	23/28	82.1	28/29	96.6
Fever	10/16	62.5	13/21	61.9	17/19	89.4

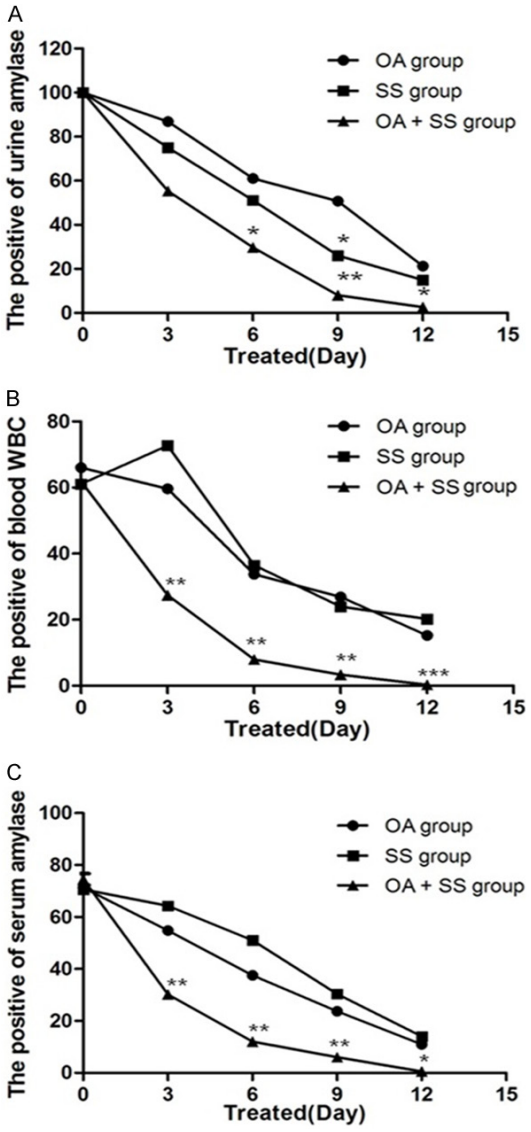

Figure 1. Recovery of blood amylase, urine amylase and WBC in each group. A. Recovery of urine amylase in each group. B. Recovery of blood amylase in each group. C. Recovery of WBC in each group. $^{*}P<0.05$, $^{**}P<0.01$, $^{***}P<0.001$.

was detected by Nano Drop-1000 (Thermo Scientific), and the purity of RNA was assessed using its ratio at 260 nm and 280 nm. As for miRNA detection, we acquired the sequence of miR-200a, miR-200b, miR-200c, miR-141 and miR-429 in miR-200 family. RT-PCR primer with loop-stem structure was designed for specific hybridization of miR-200a, miR-200b, miR-200c, miR-141 and miR-429. RNU6B was used as normalized internal reference gene.

Statistical treatment

Measurement data were represented as mean ± standard deviation ($\bar{x} \pm s$). *t* test was used for pairwise comparisons between measurement data in small samples (degree of freedom <60). *u* test was used for pairwise comparisons between measurement data in large samples (degree of freedom >60). ANOVA was used for comparison of measurement data among 3 groups. χ^2 test and Fisher's exact test were used for count data that were expressed as rate.

Results

Octreotide acetate combined with somatostatin could effectively alleviate clinical symptoms including abdominal pain, bloating, nausea, vomiting, fever etc. in patients with AP

The remission rate of symptoms including abdominal pain, bloating, nausea, vomiting, fever *etc.* was different in the 3 groups after treatment. The remission rate of all symptoms in combination group was the highest, all of which were between 93.9% and 100%, significantly higher than that in octreotide acetate group and somatostatin group ($P<0.05$). The remission rate of fever in combination treatment group (94.7%) was significantly higher

Table 2. Recovery of main experimental indexes before and after treatment of SAP ($\bar{x}\pm s$)

Experimental indexes	Octreotide acetate group (n=19)		Somatostatin group (n=17)		Combination group (n=23)	
	Before	After	Before	After	Before	After
WBC ($\times10^9$/L)	16.7±3.8	8.7±2.1	17.1±3.2	9.5±1.9	16.9±3.6	6.2±2.3*
AST (U/L)	215±9	77±8	217±8	65±5	211±10	49±6*
Blood glucose (mml/L)	11.8±2.6	7.1±1.6	12.1±2.8	7.8±1.7	11.7±2.5	5.3±1.5*
Blood calcium (mmol/L)	1.96±0.64	2.12±0.36	1.89±0.69	2.03±0.48	1.93±0.71	2.26±0.29*

*Compared with octreotide acetate group and somatostatin group. *P<0.05.

Table 3. Comparison of incidence rate of complications and fatality rate in each group after treatment

Groups	With complications	Without complications	Total	Incidence rate of complications (%)
Octreotide acetate group	5	14	19	26.3
Somatostatin group	6	15	21	28.6
Combination group	6	17	23	26.1

than that in octreotide acetate group (62.5%) and somatostatin group (61.9%). The remission rate of signs including abdominal tenderness, tension of abdominal muscle and jaundice in combination group was between 94.7% and 100%, with significant difference compared to octreotide acetate group and somatostatin group (P<0.05) **Table 1**.

Recovery of blood amylase, urine amylase and blood WBC was fast after treatment of octreotide acetate combined with somatostatin in patients with AP

Positive rate change of blood amylase, urine amylase and blood WBC was observed before treatment and 3, 6, 9, 12 days after treatment in the 3 groups. The results indicated that there was no significant difference of all positive rates before treatment among the 3 groups (P>0.05). After treatment, recovery of blood amylase, urine amylase and WBC was faster in combination group, and more significantly 6 days after treatment, with significant difference compared with octreotide acetate group and somatostatin group (P<0.05) **Figure 1**.

Recovery of experimental indexes including WBC, AST, blood glucose, blood calcium etc. in combination group was better than that in octreotide acetate group and somatostatin group

There was no significant difference of experimental indexes including WBC, AST, blood glucose, blood calcium *etc.* before treatment in the 3 groups (P>0.05). After treatment, the above indexes in combination group significantly recovered, with significant difference compared with octreotide acetate group and somatostatin group (P<0.05). The results indicated that recovery of experimental indexes including WBC, AST, blood glucose, blood calcium *etc.* after treated by octreotide acetate combined with somatostatin was significantly better than that in octreotide acetate group and somatostatin group (P<0.05) **Table 2**.

Mortality rate could be significantly reduced after the treatment of octreotide acetate combined with somatostatin in patients with AP

The complications of AP mainly include acute respiratory distress syndrome (ARDS), septicemia, acute renal failure, electrolyte and acid-base balance disorders, acute heart failure, pancreatic encephalopathy, alimentary tract hemorrhage, pancreatic pseudocysts *etc*. There was no significant difference of symptom incidence rate in the 3 groups after hospitalization (P>0.05), indicating that octreotide acetate combined with somatostatin could not effectively reduce symptom incidence rate (**Table 3**). Therefore, we further analyzed the mortality rate in each group, and found that the mortality rate in combination group was significantly less than that in octreotide acetate group and somatostatin group (**Table 4**). This indicated that octreotide acetate combined with somatostatin mainly reduced mortality rate.

Table 4. Mortality rate of SAP in each group

Groups	Death	Survival	Total	Mortality rate (%)
Octreotide acetate group	3	16	19	15.8
Somatostatin group	5	16	21	23.8
Combination group	1	22	23	4.3

Table 5. Comparison of treatment in each group ($\bar{x}\pm s$)

Indexes	Octreotide acetate group (n=52)	Somatostatin group (n=48)	Combination group (n=53)
Days of symptoms disappearing	5.0±1.6	5.3±1.8	3.1±1.3
Days of signs disappearing	5.8±1.7	6.5±1.8	3.7±1.4
Days of blood amylase recovery	5.9±2.5	6.0±2.2	4.1±1.9
Days of urine amylase recovery	8.0±3.6	8.4±3.2	4.5±2.1
Days of WBC recovery	6.4±2.5	6.2±2.3	4.2±1.5
Days of diet recovery	7.9±3.9	7.5±3.6	4.9±2.2

Comparison of main indexes in each group after treatment

After single treatment or combination treatment, the recovery time of main indexes in combination group was significantly less than that in octreotide acetate group and somatostatin group ($P<0.05$). This indicated that using octreotide acetate combined with somatostatin on patients with AP could reduce disappearing days of symptoms and signs, recovery days of blood amylase, urine amylase, blood WBC and diet (**Table 5**).

Octreotide acetate combined with somatostatin could effectively promote hepatic function recovery in treating AP

There were 78 cases (50.98%) of patients accompanied by different extent of hepatic function damage in the 153 cases of patients with AP. After treatment with octreotide acetate, somatostatin and octreotide acetate combined with somatostatin, the recovery of hepatic function indexes including AST, ALT, ALP, TBIL, DBIL and ALB in combination group was significantly better than that in octreotide acetate group and somatostatin group ($P<0.05$). The remission rate of AST, ALT and ALP was respectively 65%, 61.9% and 60.9% in octreotide acetate group; and 66.7%, 62.5% and 65% in somatostatin group, with no significant difference (**Table 6**). The remission rate of AST, ALT and ALP in combination group was respectively 95.2%, 95.7% and 95.8%, with significant difference compared with the other 2 groups ($P<0.05$). The remission rate of TBIL in combination group was 100%, significantly higher than that in the other 2 groups (69.2% and 66.7%, $P<0.05$).

Expression of miR-200 family members significantly increased after treated with octreotide acetate combined with somatostatin

MiR-200 family members include miR-200a, miR-200b, miR-200c, miR-141 and miR-429, which are divided into 2 subfamilies according to the difference of nucleotide sequence of the seed region. They were miR141 and miR-200a; miR-200b, miR-200c and miR-429. In this study, we detected the expression of miR-200 family members in serum of patients with AP to analyze the correlations. 15 pairs of samples were collected in each group to detect relative levels of miR-200 expression in serum suing RT-PCR. The result indicated that the expression of miR-200a, miR-200b, miR-200c, miR-141 and miR-429 significantly decreased in octreotide acetate group and somatostatin group, with significant difference ($P<0.05$, **Figure 2**). In combination group, expression of miR-200a, miR-200b, miR-200c, miR-141 and miR-429 significantly increased, with significant difference ($P<0.05$, **Figure 2**). This had correlations with combination treatment effectively alleviating main clinical symptoms and recover indexes including urine amylase, blood amylase and WBC, as well as recovering tumor-inhibiting role played by miR-200 family.

Discussion

Acute pancreatitis is one of the most common critical diseases in clinic, and divided into mild form (simple edema) and severe form (hemorrhagic necrosis) [19]. Patients with mild form mainly manifest pancreatic edema, most with self-confinement and good prognosis. But mild form in about 15%-20% of patients can exacerbate to severe pancreatitis, accompanied by organ failure or local complications. Once AP generates, its clinical manifestations are dan-

Table 6. Comparison of hepatic function recovery in each group

Hepatic function	Octreotide acetate group (n=52)		Somatostatin group (n=48)		Combination group (n=53)	
	After/ Before	Remission rate (%)	After/ Before	Remission rate (%)	After/ Before	Remission rate (%)
AST	13/20	65.0	14/21	66.7	20/21	95.2
ALT	13/21	61.9	15/24	62.5	22/23	95.7
ALP	14/23	60.9	13/20	65.0	23/24	95.8
TBIL	9/13	69.2	10/15	66.7	16/16	100
DBIL	10/16	62.5	11/15	73.3	17/18	94.4
ALB	9/16	56.3	9/17	52.9	16/17	94.1

gerous, with high fatality rate of 40% [20]. The genesis of AP has correlations with many factors and diseases. Causative agent causes a sudden increase in pancreatic exocrine secretion, thus increasing pancreatic duct pressure and causing acinus rupture. This will activate trypsin and cause extravasation of pancreatin that contains a lot of activity, thus releasing various inflammatory mediators and cytokines. Then hypovolemia and dysfunction of multiple organs such as heart, lung, kidney *etc.* and cause series of clinical symptoms [21, 22].

Somatostatin (SS) and its analogue octreotide acetate can inhibit secretion of gastrin, gastric acid and pepsin. It has the following effects: analgesic effect, reducing pancreatic exocrine secretion and pancreatic duct pressure; removal of necrotic toxicants and protecting pancreatic cells; significantly reducing blood flow of internal organs without causing significant changes in systemic arterial blood pressure [23, 24]. The result in this study indicated that octreotide acetate combined with somatostatin could effectively alleviate clinical symptoms. The remission rate of abdominal pain and bloating in combination group was significantly higher than that in octreotide acetate group and somatostatin group. In combination group, the symptoms and signs of most patients alleviated within 3-4 days. Blood amylase, urine amylase and WBC returned to normal 6 days after treatment. The course of treatment was significantly shortened, with significantly higher total effective rate than octreotide acetate group and somatostatin group. The result of the study also indicated that when treating patients with SAP using octreotide acetate combined with somatostatin, the recovery of WBC, AST, blood glucose and blood calcium was significantly better than single use of octreotide acetate or somatostatin. In addition, the complication rate was also reduced.

In the study of Omata et al., the incidence rate of AP complicated with hepatic damage was 40.1%-56.6%, while the rate reached 88.9% in SAP complicated with hepatic damage [25]. In this study, 50.89% of patients complicated different extent of hepatic function damage, which was in accordance with the reported literatures. The mechanism of AP complicated with hepatic damage is complicated. The main cause is the injury effect of cytokine and oxygen free radical (OFR) on hepatic cells. AP can induce hepatic microcirculatory disturbance. Pancreatitis associated ascetic fluids (PAAF) will generate in acute necrotizing pancreatitis [26, 27]. The result in this study showed that recovery of hepatic function in combination group was significantly better than that in octreotide acetate group and somatostatin group. Somatostatin and octreotide acetate not only could alleviate hepatic damage caused by oxygen free radicals and lipid peroxidation at the cellular level, but also achieve hepatoprotective effect by promoting synthesis function of hepatic cells, improving cholestasis, inhibiting apoptosis of liver cells [28].

Moreover, various studies showed that miRNAs play important roles in biological functions such as apoptosis, differentiation, proliferation, migration, *etc*. [29]. Therefore, functional disorder of miRNA might cause multiple diseases such as cancer, hepatic disease, immune dysfunction and metabolic disorders in human [30, 31]. The results in this study showed that expression of miR-200 family members decreased in octreotide acetate group and somatostatin group, and significantly increased in combination group, indicating that the downregulation of miR-200 family played an important role in genesis of AP.

In summary, the result in this study demonstrated that octreotide acetate combined with somatostatin could improve clinical symptoms and signs in patients with AP. Blood amylase, urine amylase and WBC recovered to normal 6 days after treatment. The course of treatment

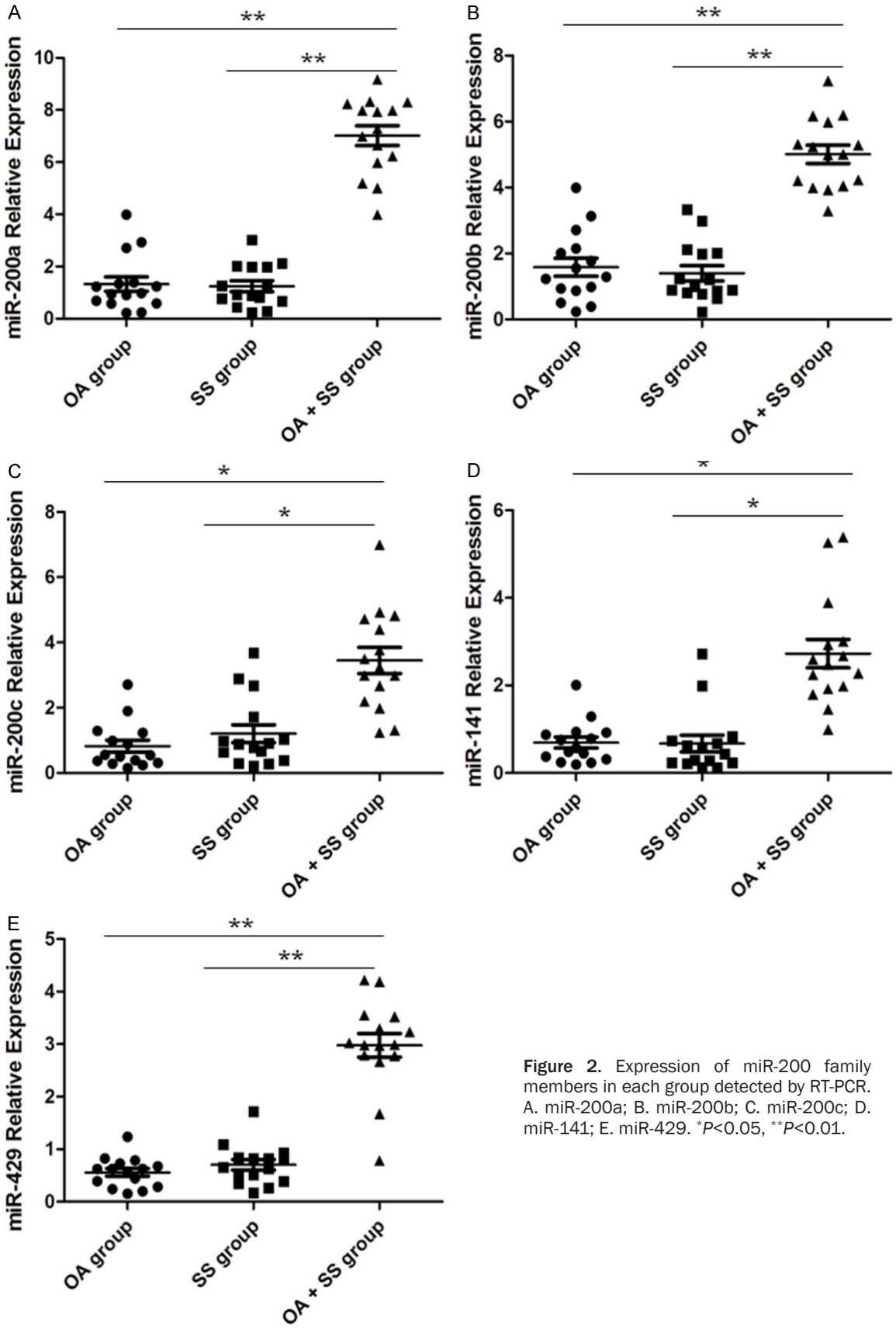

Figure 2. Expression of miR-200 family members in each group detected by RT-PCR. A. miR-200a; B. miR-200b; C. miR-200c; D. miR-141; E. miR-429. $^{*}P<0.05$, $^{**}P<0.01$.

was significantly shortened. Recovery of WBC, AST blood glucose and blood calcium in combination group was significantly better than that in octreotide acetate group and somatostatin group. The incidence rate of complications in patients with SAP could be reduced. Moreover, expression of miR-200 family in serum of combination group was significantly higher than that in single treatment group. The tumor-inhibiting function recovered. The results demonstrated that the effectiveness and safety are very reliable when using octreotide acetate combined with somatostatin as a drug for treating AP, showing good application prospects.

Disclosure of conflict of interest

None.

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