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BASIC RESEARCH

Experimental study of therapeutic efficacy of Baicalin in rats with severe acute pancreatitis

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Abstract

AIM: To observe the therapeutic efficacy of Baicalin in rats with severe acute pancreatitis (SAP) and explore its therapeutic mechanisms.

METHODS: The SAP rat models were randomly divided into the model control group, Baicalin treatment group, octreotide treatment group and sham operation group. All groups were randomly subdivided into 3 h, 6 h and 12 h groups with 15 rats in each group. The survival, ascites volume and pathological changes of pancreas in all rats were observed at different time points after operation. The plasma amylase content and serum TNF-α, IL-6, malonaldehyde (MDA) and PLA_2 contents were also determined.

RESULTS: The survival was not obviously different between the treated groups, and was significantly higher in treated groups at 12 h compared to the model control group ($P < 0.05$, 15 *vs* 10). The ascites/body weight ratio at 3 h and 6 h was significantly lower in Baicalin treatment group compared to the model control group and octreotide treatment group ($P < 0.05$, 1.00 *vs* 2.02 and 1.43 and $P < 0.001$, 2.29 (1.21) *vs* 2.70 (0.80) and 2.08 (2.21), respectively). The contents of amylase, TNF-α, IL-6, MDA and PLA_2 were significantly lower in the treated groups than in the model control group ($P < 0.05$, 4342 *vs* 5303, 5058 *vs* 6272 in amylase, $P < 0.01$, 21.90 *vs* 36.30, 23.80 *vs* 39.70, 36 *vs* 54.35 in MDA and 56.25 *vs* 76.10 in PlA_2, or $P < 0.001$, 65.10 and 47.60 *vs* 92.15 in TNF-α, 3.03 *vs* 5.44, 2.88 *vs* 6.82, 2.83 *vs* 5.36 in IL-6, respectively). The pathological scores of pancreas in the treated groups were significantly lower than that in the model control group ($P < 0.05$, 9.00 *vs* 10.05, 6.00 *vs* 9.00, 8.00 *vs* 10.05), but no marked difference was found between the treated groups.

CONCLUSION: The Baicalin injection has significant therapeutic effects on SAP rats, its effects are similar to those of octreotide. The Baicalin injection is also cheap and has a big application range, quite hopefully to be used in clinical treatment of SAP.

Key words: Severe acute pancreatitis; Baicalin; Octreotide; Rats; Serum amylase; TNF-α; IL-6; Malonaldehyde; PLA_2

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INTRODUCTION

As one of the life-threatening severe diseases, severe acute pancreatitis (SAP) has acute onset, rapid progression, multiple complications, and its mortality has reached 20%-30%. The pathogenesis of SAP is still unknown, and no breakthrough has ever been made in its treatment. Currently, mainly somatostatin and its analog octreotide are effective drugs for SAP treatment in the clinic.

Octreotide, also named sandostatin, as an analog of

natural somatostain plays an important role in improving the survival rate of SAP animals, inhibiting secretion of pancreatin and alleviating multiple organ injury[1-3]. However, the expensive price, short half-life and inconvenient administration of these drugs have restrained their clinical popularization, especially in remote poor areas. So, it is necessary to find some cheap and highly effective drugs.

In "Qing Yi Tang" which is a representative prescription of Chinese medicine for SAP treatment, the enormous clinical practices also suggest its sound therapeutic effects on SAP[4]. Scutellaria baicalensis georgi is a main material in "Qing Yi Tang" while Baicalin (monomer) is its main active constituent. The intravenous administration with very low price can overcome the shortcomings of oral administration of "Qing Yi Tang", including poor absorption and inconvenience. The *in vitro* experiments of Baicalin have proved[5-7]: it has anti-bacterial, anti-viral and anti-inflammatory activities. It can also inhibit platelet aggregation and eliminate oxygen-free radicals. In animal experiments, Baicalin with choleretic effectcan can relieve fever, inhibit the thrombin-induced transforming process from fibringen to fibrin, lower endotoxin generation, treat and prevent endotoxemia-induced disseminated intravascular coagulation. In addition, the initial metabolite of Baicalin in body is baicalein that can more effectively inhibit pancreatin. All these pharmacologic effects can antagonize many processes during SAP onset. Its several effects are similar to those of somatostatin and its analog such as octreotide, but it has a broader application range. It is theoretically feasible to use it for SAP treatment.

Presently, to the best of our knowledge, there has not been any study report on Baicalin treatment of SAP internationally. In this experiment, we have established the SAP rat model, discussed the effects of Baicalin in treating SAP rats, compared its effects with those of octreotide and observed the therapeutic efficacy of Baicalin and explored its therapeutic mechanisms in order to provide the reliable basis for Baicalin treatment of SAP.

MATERIALS AND METHODS

Experimental animals and reagents

Clean grade healthy male Sprague-Dawley (SD) rats weighing 250-300 g were purchased from the Experimental Animal Center of Medical School, Zhejiang University, China. Sodium taurocholate and sodium pentobarbital were purchased from Sigma Company, USA. Octreotide was purchased from Swiss Pharmaceutical Company Novartis, and 5% Baicalin injection (China National Invention Patent Number ZL200310122673.6) was prepared by the first author with 305 mmol/L osmotic pressure. The TNF-α ELISA kit was purchased from Jingmei Bioengineering Corporation (China) and the calculation unit for content is pg/mL (ng/L). The IL-6 ELISA kit was purchased from Shanghai Shenxiong Biotech Company (China) and the calculation unit for content is pg/mL (ng/L). The serum malonaldehyde (MDA) kit was purchased from Nanjing Jiancheng Bioengineering Research Institute, China. The calculation units for content are respectively nmol/mL. The serum secretory phospholipase A_2 enzyme assay ELA kit (PLA_2) was purchased from R&D System Ins, USA and the calculation unit for content is U/mL.

Animal grouping

The improved Aho's method[8] was adopted to prepare SAP rat models *via* retrograde injection of 3.5% sodium taurocholate to the pancreatic duct through epidural catheter and duodenal papilla. The 135 SAP rat models were randomly divided into model control group, Baicalin treatment group and octreotide treatment group with 45 rats in each group; other 45 rats were selected as sham operation group, which only received laparotomy. All groups were then randomly subdivided into 3 h, 6 h and 12 h groups with 15 rats in each group.

Observation index

We examined the rat mortality at 3 h, 6 h and 12 h after operation and calculated the survival, observed the gross changes of pancreas and ascites volume. Ascites/body weight ratio was measured as follows: Dry gauze was used to wipe intra-abdominal hydrops; then, a scale was used to weigh the weights of gauze before and after its soaking; the difference between weights (g) was converted into ascites volume (mL); and ascites/body weight ratio was thus obtained. After mercy killing the rats anesthetized by sodium pentobarbital in batches, the samples of pancreas were collected, fixed according to the requirements, and the pathological changes of pancreas after hematoxylin-eosin (HE) staining were observed. The contents of plasma amylase and serum TNF-α, IL-6, MDA and PLA_2 were determined *via* blood sampling from heart. The full automatic biochemical analyzer was used to determine the plasma amylase level and the calculation unit for content is U/L. The serum TNF-α, IL-6 and PLA_2 levels were determined by ELISA method.

Pancreatic pathological score

A modified Schmidt's pathological score system was used (Table 1) and two pathologists in double-blind control condition performed the evaluation of severity of pancreatic tissue pathology. We modified the pathological score of pancreas, because the Schmidt's pathological score[9] was too difficult and complex to be used in our experiment.

Preparation methods of animal models

Fasting but water restraint was imposed on all rat groups 12 h prior to the operation. The rats were anesthetized by intraperitoneal injection of 2% sodium pentobarbital (0.25 mL/100 g), then laid and fixed, and the routine shaving, disinfection and draping were performed. We first established the right external jugular vein transfusion passage to use the microinfusion pump for continuous transfusion (1 mL/h per 100 g) and then used 3.5% sodium taurocholate to prepare SAP model.

Model control group: After entering the abdomen *via* median epigastric incision, we confirmed the bile-pancreatic duct, hepatic hilus and common hepatic duct, disclosed the pancreas, identified the duodenal papilla inside the duodenum duct wall, and then used a No. 5 needle to drill a hole in the mesenteric avascular

Table 1 Improved Schmidt score of pathological changes of the pancreas

Edema		Acinar necrosis (necrotic cells/HPF)		Inflammation and perivascular infiltrate (intralobular or perivascular leukocytes/HPF)		Hemorrhage and fat necross (focus)	
Absent	0	Absent	0	0-1	0	Absent
Focal expansion of interlobular septae	1	1-4	1	2-10	1	1-2
Same as 1 + diffuse expansion of interlobar; Septae/diffuse expansion of interlobar septae	2	5-10	2	11-20	2	3-4
Same as 2 + expansion of interacinar septae	3	11-16	3	21-30	3	5-6
Same as 3 + expansion of intercellular spaces	4	> 16	4	> 30/microabscesses	4	> 7

area. After inserting a segmental eqidural catheter into the duodenum cavity *via* the hole, we inserted the bile-pancreatic duct toward the direction of the papilla in a retrograde way, used the microvascular clamp to nip the duct head temporarily and meanwhile used another microvascular clamp to temporarily occlude the common hepatic duct at the confluence of the hepatic duct. After connecting the anesthetic tube end with the transfusion converter, we transfused 3.5% sodium taurocholate (0.1 mL/100 g) by retrograde transfusion *via* the microinjection pump (made by Zhejiang University) at a speed of 0.2 mL/min, then stayed for 4-5 min after injection and removed the microvascular clamp and eqidural catheter. After checking for bile leakage, we sutured the hole in the lateral duodenal wall, used the disinfected cotton ball to absorb up the anesthetic in the abdominal cavity and closed the abdomen. During the laparotomy in the sham operation group, we performed pancreas and duodenum turning over, observed pathological changes of multiple organs and finally closed the abdomen.

Dosage and methods

In Baicalin treatment group, the animal experiments of 5% Baicalin injection were completed including the acute toxicity test and SAP rat treatment by small, middle and large dose. The large dose could achieve the best therapeutic effect (dose is 10 mg/h per 100 g) and the dosage referred to the result of the previous preliminary experiment. Ten minutes after successful modeling, Baicalin treatment group was first injected 5% Baicalin injection 10 mg/100 g *via* the external jugular vein passage, followed by continuous intravenous administration (10 mg/h per 100 g) by microinfusion pump; octreotide treatment group was first injected octreotide 0.2 μg/100 *g via* the external jugular vein passage, followed by continuous intravenous transfusion (10 mg/h per 100 g) by microinfusion pump at a transfusion speed of 0.2 μg/h per 100 g. All above dosages have been proved as effective dosages in the previous preliminary experiment. Both of the sham operation group and model control group were injected saline of equivalent volume at the corresponding time points after operation.

Statistical analysis

The values were presented as mean ± SD for nomal distribution variables or median and quartile range for highly skewed variables. The significance of differences among the four groups was tested using the Kruskal-Wallis test for highly skewed data and analysis of variance (ANOVA) for normal distribution data. Multiple comparisons were subjected to Bonfferoni correction test. The Chi-square test was used to evaluate equality of frequencies for discrete variables. Correlations were tested using the Spearman rank correlation coefficients. A P value less than or equal to 0.05 was considered statistically significant. All statistical analyses were conducted using SPSS version 11.5 for windows.

Table 2 Comparison of ascites/body weight ratio [M (Q_R)]

Groups	3 h	6 h	12 h
Sham operation	0.28 (0.23)	0.44 (0.15)	0.39 (0.22)
Model control	2.02 (0.89)	2.62 (0.97)	2.70 (0.80)
Baicalin treatment	1.00 (1.30)	1.16 (0.73)	2.29 (1.21)
Octreotide treatment	1.43 (0.62)	2.15 (0.88)	2.08 (2.21)

RESULTS

Survival rate

The mortality rates of the model control group were 0% (0/15), 13.33% (2/15) and 33.33% (5/15) at 3 h, 6 h and 12 h, respectively, while those of Baicalin treatment group and octreotide treatment group were 0% at different time points. The whole sham operation group survived at different time points. The survival rate of the model control group was 66.67% (10/15) at 12 h, while the survival rate of each of Baicalin treatment group and octreotide treatment group was 100% at 12 h, indicating a marked difference ($P < 0.05$).

Comparison of ascites/body weight ratio among all groups

The ascites/body weight ratio of the model control group and treatment group significantly exceeded the sham operation group at different time points ($P < 0.001$), while there was no significant difference between the octreotide treatment group and model control group at different time points. Ascites/body weight ratio of the Baicalin treatment group was significantly less than the model control group ($P < 0.01$) and octreotide treatment group at 3 h ($P < 0.05$). Ascites/body weight ratio of the Baicalin treatment group was significantly less than the model control group and octreotide treatment group at 6 h ($P < 0.001$). However, there was no significant difference among the Baicalin treatment group, model control group and octreotide treatment group at 12 h (Table 2).

Table 3 Comparison of different indexes of blood [*M* (Q_R)]

Indexes	Sham operation			Model control			Baicalin treatment			Octreotide treatment		
	3 h	6 h	12 h	3 h	6 h	12 h	3 h	6 h	12 h	3 h	6 h	12 h
Amylase (U/L)	1582 (284)	1769 (362)	1618 (302)	5303 (1373)	6276 (1029)	7538 (2934)	4342 (1496)	5130 (1591)	5571 (2307)	5419 (1670)	5058 (1314)	6531 (2280)
TNF-α (ng/L)	3.90 (3.20)	4.00 (1.70)	5.30 (3.00)	41.44 (37.72)	92.15 (23.12)	65.02 (26.81)	44.93 (45.84)	65.10 (27.51)	47.65 (25.52)	39.30 (30.60)	47.60 (16.50)	54.50 (41.40)
IL-6 (ng/L)	1.8460 (0.35)	1.74 (0.84)	2.04 (0.82)	5.44 (1.03)	6.82 (0.81)	5.36 (0.75)	3.03 (0.87)	2.88 (1.39)	2.83 (0.60)	2.65 (1.37)	3.08 (1.210)	2.46 (1.35)
MDA (nmol/mL)	9.90 (9.90)	16.50 (13.20)	16.50 (13.20)	36.30 (13.40)	39.70 (9.90)	54.35 (19.00)	21.90 (13.45)	23.80 (14.60)	36.00 (11.60)	29.60 (18.60)	33.00 (9.90)	40.30 (16.80)

Table 4 Comparison of serum PLA2 content (mean ± SD)

Groups	3 h	6 h	12 h
Sham operation	14.62 ± 3.02	17.49 ± 3.82	19.02 ± 5.07
Model control	76.10 ± 16.70	101.46 ± 14.67	105.33 ± 18.10
Baicalin treatment	56.25 ± 22.43	67.91 ± 20.61	66.86 ± 22.10
Octreotide treatment	74.37 ± 19.94	63.13 ± 26.31	53.63 ± 12.28

Comparison of plasma amylase content among all groups

The plasma amylase content in the model control group and two treatment groups significantly exceeded that in the sham operation group at different time points ($P < 0.001$). However, there was no significant difference between the Baicalin treatment group and octreotide treatment group at different time points. Although the plasma amylase content of the Baicalin treatment group was lower than that of the model control group at different time points, the difference did not reach statistical significance at 6 h and 12 h, but reached statistical significance at 3 h ($P < 0.05$). Although plasma amylase content was significantly less in the octreotide treatment group compared to the model control group at 6 h ($P < 0.05$), no significant difference was observed at 3 h and 12 h (Table 3).

Comparison of serum TNF-α content among all groups

Serum TNF-α content significantly exceeded in the model control group and treatment groups compared to the sham operation group at different time points ($P < 0.001$). There was no significant difference in serum TNF-α content among the model control group, Baicalin treatment group and octreotide treatment group at 3 h and 12 h. However, at 6 h, both Baicalin treatment group and octreotide treatment group had significantly less serum TNF-α content compared to the model control group ($P < 0.001$); and the octreotide treatment group had significantly less serum TNF-α content than the Baicalin treatment group ($P < 0.01$) (Table 3).

Comparison of serum IL-6 content among all groups

The serum IL-6 content at 3 h and 6 h was significantly higher in the model control group and treated groups than in the sham operation group ($P < 0.001$). Baicalin treatment group and octreotide treatment group had no significant difference in serum IL-6 content at all time points. The Baicalin treatment group and octreotide treatment group had significantly lower serum IL-6 content than the model control group at all time points ($P < 0.001$). However, the model control group had significantly higher serum IL-6 content than the sham operation group at 12 h ($P < 0.001$), and so had the Baicalin treatment group ($P < 0.01$), but no significant difference was found between the octreotide treatment group and the sham operation group (Table 3).

Comparison of serum MDA content among all groups

Serum MDA content significantly exceeded in the model group, Baicalin treatment group and octreotide treatment group compared to the sham operation group at different time points ($P < 0.05$). Serum MDA content was significantly less in the Baicalin treatment group than the model group ($P < 0.01$). Similarly, serum MDA content was significantly less in the octreotide treatment group than the model group at 6 h and 12 h ($P < 0.05$). However, serum MDA content was significantly less in the Baicalin treatment group compared to the octreotide treatment group at 12 h ($P < 0.05$) (Table 3).

Comparison of serum PLA_2 content among all groups

Serum PLA_2 content significantly exceeded in the model group and treatment groups compared to the sham operation group at different time points ($P < 0.001$). At 3 h, the Baicalin treatment group had significantly less serum PLA_2 content than the model group ($P < 0.01$), while there was no marked difference between the octreotide treatment group and the model group, and the Baicalin treatment group had significantly less serum PLA_2 content than the octreotide treatment group ($P < 0.01$). At 6 h and 12 h, the Baicalin treatment group and octreotide treatment group had significantly less serum PLA_2 content than the model group ($P < 0.001$). At 6 h, there was no marked difference between the Baicalin treatment group and the octreotide treatment group, whereas at 12 h, the octreotide treatment group had significantly less serum PLA_2 content than the Baicalin treatment group ($P < 0.001$) (Table 4).

Macroscopic and microscopic pathological changes of the pancreas

Sham operation group: Macroscopically, there were only some amber ascitic fluid within the abdominal cavity, and no pathological changes visible to naked eyes in other

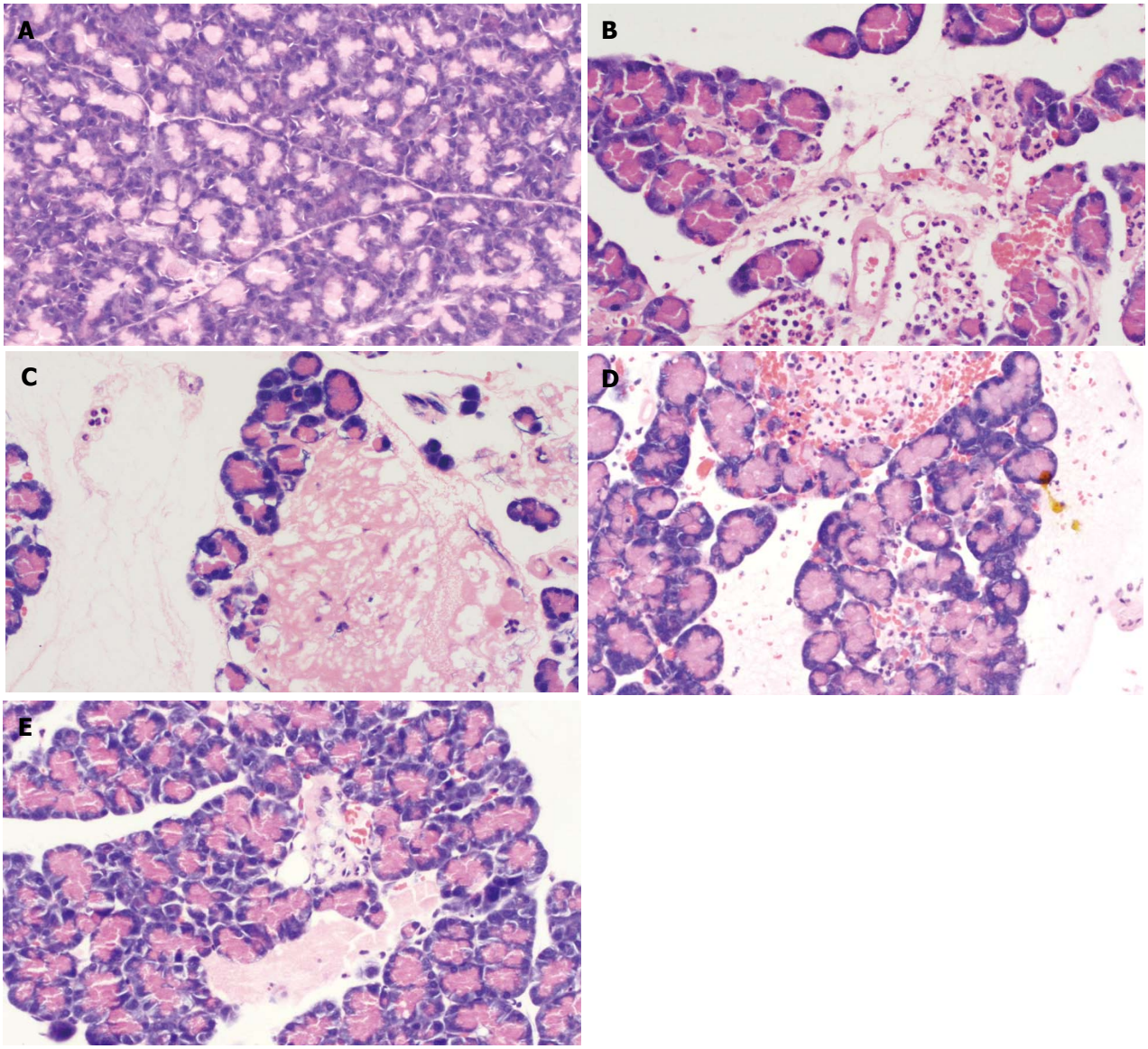

Figure 1 **A**: Sham operation group at 12 h (normal pancreas); **B**: Model control group at 12 h (Interacinar edema accompanied with piecemeal necrosis of acinus, a great deal of neutrophil infilatration among acini); **C**: Model control group at 12 h (Massive acinus necrosis); **D**: Baicalin treatment group at 12 h (interlobular and interacinar edema, focal necrosis of acinus, relatively much neutrophil infiltration among acini); **E**: Octreotide treatment group at 12 h (Interlobular edema accompanied with focal necrosis of acinus).

organs. The overall structure of the pancreas remained intact. There were no hemorrhagic changes in the pancreas, which was yellowish without volume reduction, and no significant abnormality in the pancreas, peripancreatic and epiploon at all time points. Microscopically, most remained normal with intact gland structure, mild interstitial edema occurred in very few cases, neutrophil infiltration was occasional, and no acinar cell and fat necrosis and hemorrhage were observed (Figure 1A).

Model control group: Macroscopically, pathological changes of the pancreas tail were a little more obvious than those of the pancreas head; 5 min after model induction, the pancreas manifested edema, hemorrhage and necrosis. The overall severity of the pathological changes at 3 h, 6 h and 12 h increased with time after modeling. In the 3 h group, small amount of ascitic fluid mostly slightly bloody visible to naked eyes, obvious hyperemia and edema of the pancreas, partly jellly-like edema, hemorrhage and necrosis were observed. Most ascitic fluid after 6 h and 12 h was bloody with the larger average amount than that at 3 h. The amount and characters of ascitic fluid increased and deepened with time after modeling; the degree and range of the pancreas edema, hemorrhage and necrosis became more obvious than those at 3 h; many saponified spots on peripancreatic great epiploon and peritoneum, jelly-like change, contour vanishing, quite obvious hemorrhage and necrosis changes of the pancreatic tissue were also observed. Microscopically, in the 3 h group, obvious pancreas interstitial hyperemia and edema, small amount of inflammatory cell infiltration, sporadic focal necrosis and interstitial hemorrhage occurred among which some were hemorrhagic or lytic necrosis; in the 6 h group, pancreas interstitial edema and hemorrhage, visible focal or lamellar necrosis, comparatively large area of inflammatory cell infiltration around were observed; and in the 12 h group, obvious pancreas interstitial edema, interstitial

Table 5 Comparison of pathological lesion score for pancreas (M (Q_R))

Groups	3 h	6 h	12 h
Sham operation	0.00 (1.00)	0.00 (1.00)	0.00 (1.00)
Model control	8.00 (2.00)	9.00 (3.00)	10.50 (1.50)
Baicalin treatment	7.00 (1.50)	7.00 (3.00)	9.00 (4.00)
Octreotide treatment	7.00 (2.00)	6.00 (2.00)	8.00 (2.00)

hemorrhage, large area of necrosis, lobule contour damage with a large amount of inflammatory cell infiltration were observed (Figures 1B and C).

Treatment group: Macroscopically, in the 3 h group, the pancreatic tissue with hyperemia and edema changes, milder hemorrhage and necrosis than those of model control group were observed; in the 6 h and 12 h groups, compared with the model control group, relatively limited pancreas hemorrhage and necrosis, lighter ascitic fluid color, obviously less ascitic fluid, decreased distribution and area of saponified spot, milder pancreas hemorrhage and necrosis, and relatively integrated overall pancreas structure were observed. The pathological changes of pancreatic tissue of the octreotide treatment group resembled those of the Baicalin treatment group. Microscopically, the pathological changes of most cases in the treatment group were milder than those of the model control group at the corresponding time points, such as decreased degree of interstitial edema, reduced inflammatory cell infiltration, more clear cell structure than that of the model control group, reduced pancreas interstitial erythrocyte exudation, small amount of focal hemorrhage and necrosis with little lamellar hemorrhage and necrosis, and reduced hemorrhage and necrosis range. The pathological changes of pancreatic tissue of the octreotide treatment group resembled those of the Baicalin treatment group (Figures 1D and E).

Comparison of pancreas pathological score among all groups

Pancreas pathological scores of the model control group, Baicalin treatment group and octreotide treatment group significantly exceeded those of the sham operation group at different time points ($P < 0.001$). Pancreas pathological score of the Baicalin treatment group was significantly less than that of the model control group at 12 h ($P < 0.01$). Moreover, pancreas pathological score of the octreotide treatment group was significantly less compared to the model control group at 6 h and 12 h ($P < 0.01$). However, there was no significant difference between the Baicalin treatment group and the octreotide treatment group at different time points (Table 5).

DISCUSSION

Severe acute pancreatitis (SAP) induces inflammatory reactions of pancreatic tissue itself or even systemic reactions, which is by a large portion related to excessive generation and cascade reactions of inflammatory mediators, mainly including endotoxin, oxygen-free radical, PLA_2, bradykinin, complement, acute-phase protein, vasoactive amine, arachidonic acid metabolite, cytokine (lymphokine) and PAF[10-14]. This study mainly investigates the therapeutic effects of Baicalin and octreotide by observing plasma amylase content and serum TNF-α and IL-6 content.

Table 6 Comparison of therapeutic efficacy of octreotide and Baicalin

Therapeutic efficacy	Curative	
	Baicalin	Octreotide
Improve survival rate	++	++
Decrease ascites volume	++	+
Decrease amylase	+	+
Decrease TNF-α	+	++
Decrease IL-6	++	+
Decrease MDA	+	++
Decrease PLA_2	++	+
Protect pancreatic tissue	++	++

++: Represents significant effect; +: Represents normal effect; -: No effect.

TNF-α participates in onset and progression of early-phase inflammations of acute pancreatitis (AP), and is also related to AP severity[15,16]. Excessive generation of TNF-α, or imbalance between it and other cytokines will stimulate cascade reactions, induce generation of IL-1, IL-6, IL-8, *etc*, later generate inflammatory mediators, and aggravate cell damage. Current studies found serum TNF-α had two aspects in regulating apoptosis, namely inducing apoptosis and promoting inflammation healing when its concentration was low, while leading to necrosis of pancreatic acinar cell when its concentration was high[17].

IL-6, mainly generated by monocyte after induction of IL-1, TNF, *etc*, has intensive inflammation-causing activity[18-21]. IL-6 can both directly increase the permeability of vascular endothelial cell, and has synergistic effect with TNF-α, *etc* to constitute a network of inflammatory mediators[20]. IL-6 level in serum can reflect AP severity[18,23,24]. It is generally recognized that the PLA_2 content or activity rises when SAP occurs[25]. The abnormal release and activation of PLA_2 can change lecithin into hemolytic lecithin, cause lysis and breakdown of pancreatic cell membrane, and lead to autodigestion of the pancreas[26-28]. The excessive free radicals generated in body during SAP may cause the accumulation of MDA, a lipid oxidative product. MDA content in serum can indicate the level of free radical overproduction[29,30].

In addition, a great quantity of endotoxin can induce TNF-α, stimulate or promote cytokine release including IL-1β[31], IL-6, TNF, and further mediate activation of leucocyte and platelet in multiple organs, such as pancreas, kidney and lung, and release lysosome, oxygen-free radical and lipid inflammatory substance. The excessive cytokines and inflammatory factors can cause waterfall-like cascade reactions, induce iNOS expression all over the body, generate a great deal of NO, damage blood vessel endothelium, and cause tissue necrosis[32-36].

Octreotide, a medicine currently adopted in the clinic for SAP treatment, mainly achieves its therapeutic effects

by inhibiting secretion of pancreatin and other digestive enzymes, and loosening the oddi sphincter. The most important is that octreotide can block the excessive expression of inflammatory mediators and cytokines, reduce iNOS mRNA expression and NO synthesis, and then alleviate injury of multiple organs, such as pancreas and lung[37,38]. This experiment found that compared with the model control group, both the Baicalin and octreotide treatment groups could effectively reduce the generation of ascites, plasma amylase content, and serum TNF-α, IL-6, MDA and PLA_2 content, alleviate pathological changes of pancreatic tissue, and lower mortality of SAP rats.

Compared with the octreotide group, Baicalin can more significantly inhibit the generation of ascites and excessive release of IL-6 and PLA_2 (Table 6). In addition, Baicalin also has features, such as a broad range of pharmacological actions, low side effect, and low price[37,39]. Therefore, using Baicalin to treat SAP will be an effective and cost-effective therapy for SAP.

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