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Penta-therapy for severe acute hyperlipidemic pancreatitis: A retrospective chart review over a 10-year period☆

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ABSTRACT

Introduction: The purpose of our study is to evaluate the efficacy of penta-therapy for HL-SAP in a retrospective study.
Methods: Retrospective study between January 2007 and December 2016 in a hospital intensive care unit. HL-SAP patients were assigned to conventional treatment alone (the control group) or conventional treatment with the experimental protocol (the penta-therapy group) consists of blood purification, antihyperlipidemic agents, low-molecular weight heparin, insulin, covering the whole abdomen with Pixiao (a traditional Chinese medicine). Serum triglyceride, serum calcium, APACHE II score, SOFA score, Ranson score, and other serum biomarkers were evaluated. The hospital length of stay, local complications, systematic complications, rate of recurrence, overall mortality, and operation rate were considered clinical outcomes.
Results: 63 HL-SAP patients received conventional treatment alone (the control group) and 25 patients underwent penta- therapy combined with conventional treatment (the penta-therapy group). Serum amylase, serum triglyceride, white blood cell count, C-reactive protein, and blood sugar were significantly reduced, while serum calcium was significantly increased with penta-therapy. The changes in serum amylase, serum calcium were significantly different between the penta-therapy and control group on 7th day after the initiation of treatment. The reduction in serum triglyceride in the penta-therapy group on the second day and 7th day were greater than the control group. Patients in the penta-therapy group had a significantly shorter length of hospital stay.
Conclusion: This study suggests that the addition of penta-therapy to conventional treatment for HL-SAP may be superior to conventional treatment alone for improvement of serum biomarkers and clinical outcomes.

1. Introduction

Severe acute pancreatitis (SAP) is a life-threatening condition which may cause systematic inflammatory response syndrome (SIRS), sepsis, and even multiple organ dysfunction syndromes(MODS). Cholelithiasis, alcohol abuse, and hyperlipidemia are the main causes of acute pancreatitis. The morbidity of SAP secondary to hyperlipidemia (HL-SAP) has apparently increased in recent years. SAP occurred in 12–38% of hyperlipidemic patients [1,2].

The main treatment for HL-SAP is to decrease serum triglyceride level and prevent systemic inflammatory response [3]. Although serum triglyceride could be decreased by plasmapheresis [4], there has been no formal therapeutic strategy to treat HL-SAP at present, and no previous study has investigated the association between serum calcium and effectiveness of treatment in HL-SAP.·The main body of literature is made with case reports of single treatment measure [1-4,6,7]. Since the development of penta-therapy, which consists of blood purification, antihyperlipidemic agents, insulin, heparin and topical application of Pixiao (a traditional Chinese medicine) over the whole abdomen [5], it is used widely in China. To the best of our knowledge, the evidence for using penta-therapy for HL-SAP is limited to anecdotal descriptions. Therefore, we evaluated the efficacy of penta-therapy combined with conventional treatment versus conventional treatment alone for HL-SAP in a retrospective chart review.

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2. Patients and methods

2.1. Patient selection

This is a retrospective study conducted between January 2007 and December 2016. HL-SAP patients admitted to our intensive care unit (ICU) who underwent experimental penta-therapy treatment in addition to conventional treatment and HL-SAP patients who underwent conventional treatment alone were reviewed. The inclusion criteria were patients ages 18 to 85 years who presented within 72 h of the onset of pain; the AP diagnosis was made according to the Atlanta classification. HL-SAP patients were identified if patients' triglyceride levels were >1000 mg/dL (11.3 mmol/L), >500 mg/dL (5.65 mmol/L) with lipidic plasma and no other obvious cause of pancreatitis was found. Exclusion criteria were as follows: flare-up of chronic pancreatitis; patients with a history of allergies to heparin or insulin; patients who presented with disseminated intravascular coagulation or severe active bleeding; patients who presented with respiratory failure, severe systemic circulatory failure, coma, or other life-threatening symptoms that were difficult to reverse and who were predicted to die within 24 h (with full-fluid resuscitation and norepinephrine usage at a dose of 25 mg/min, with a systolic blood pressure < 90 mm Hg and serum pH values < 7.0); patients who were delayed getting treatment because of some reason; patients who presented with APACHE II score < 3. Yun Xie and Mei Kang did our chart review, the investigators who reviewed the charts were blinded to the purpose of this study. These investigators were all trained. Laboratory data were obtained from the blood screening test at hospitalization. Patient's electronic medical records and paper charts were reviewed by one independent physician for information on demographics, physiologic variable, and disease severity. The protocol of the present study complied with the protocol and principles of the Declaration of Helsinki and was approved by the ethic committee of our hospital. Written informed consent was obtained from all patients or their legal guardians.

2.2. Definitions

A diagnosis of HL-SAP was made per Atlanta criteria and the guidelines for the management of acute pancreatitis issued by the World Congress of Gastroenterology [8,9]. SIRS and MODS were diagnosed using the criteria of the American College of Chest Physicians (ACCP) and the Society of Critical Care Medicine (SCCM), respectively [10].

2.3. Outcome

The primary outcome was the change of triglyceride, the sceond outcome were the change of blood calcium (Ca^{2+}) and other laboratory parameters, the incidence of MODS, Shock, Pepticulcer/enterobrosis, DIC, AKI, ARF, ARDS, RPF, CF, Pancreatic pseudocyst / abscess, Transferred to operation, Length of hospital stay (days), Mortality, Recurrent.

2.4. Treatment

All patients received standard conventional treatment, including aggressive fluid resuscitation, oxygen supplementation, gastrointestinal decompression, insulin and/or heparin treatment, oral antihyperlipidemic therapy, dietary interventions, nutritional support, prophylactic antibiotics, and drainage of peripancreatic abscesses [8-12]. In addition to the standard conventional treatment, patients in the penta-therapy group underwent blood purification (elimination of triglyceride and hemofiltration) and topical application of Pixiao (a traditional Chinese medicine) over the whole abdomen. The penta-therapy was initiated in the first day of ICU admission. Body temperature, respiratory rate, blood pressure, heart rate, central venous pressure, PaO_2 and FiO_2 were monitored and recorded every 6 h. Biochemical parameters including white blood cell count (WBC), blood amylase (AMY), C-reactive protein (CRP), blood glucose (GLU), blood calcium (Ca^{2+}) were tested and recorded on the first and 7th day. Serum triglyceride (TG) was tested and recorded on the first, second and 7th day. Acute Physiology and Chronic Health Evaluation II (APACHE II) scores, SOFA scores, Ranson scores and CT severity index were calculated to evaluate the severity of the disease on the first day. Blood and effluent samples were taken before the initiation of treatment (day 1). All measurements were performed per protocols provided by the manufacturers.

2.5. Statistical analysis

Continuous variables are represented with mean and standard deviation. The differences in continuous variables between the serum TG of control and penta-therapy groups were estimated by the repeated measurement ANOVA. The *t*-test was used to evaluate the internal group differences for normal distribution continuous variables. The Wilcoxon matched-pairs test was used to evaluate the internal group differences for abnormal distribution continuous variables. For discrete variables, the chi-square and Fisher's exact-tests were used to evaluate the differences between groups. All statistical analyses were performed using the statistical package SPSS (version 20.0; SPSS Inc.). *P* values < 0.05 were considered statistically significant.

3. Results

3.1. Patient characteristics

Study enrollment began in January 2007 and was terminated in December 2016. During the 10-year study period, a total of 2113 patients were admitted with an AP diagnosis. Out of 2113 patients, 157 fulfilled the diagnostic criteria of HL-SAP. Of the 157, 35 participants were excluded due to the onset of pain >72 h prior to admission, 22 due to transfer from other hospitals, 8 due to delay in initiation of penta-therapy, and 4 due to other reasons not specified. Thus, a total of 88 patients were reviewed, with 63 patients identified in the control group and 25 patients to the penta-therapy group (Fig. 1).

The mean (SD) age was 37.0 ± 11.94 years and 36.33 ± 7.727 years for patients in the penta-therapy and the control group, respectively (Table 1). APACHE II scores were 10.56 ± 5.561 for the treatment group and 8.97 ± 3.307 for the control group. Ranson scores were 3.60 ± 1.936 for the treatment group and 4.33 ± 1.685 for the control group. SOFA scores were 1.80 ± 0.957 for the treatment group and 1.92 ± 0.829 for the control group. The CT severity index was not significantly different between the two groups. There were no significant differences in baseline characteristics between the two groups before treatment (Table 1).

3.2. Change in serum triglyceride

The serum triglyceride (TG) level was significantly reduced after 1 day of penta-therapy. The mean serum triglyceride (TG) level was reduced to 5.681 ± 4.083 mmol/L on the second day and 3.967 ± 2.52 mmol/L on the 7th day in the penta-therapy group. However, the mean serum TG level was reduced to 8.259 ± 4.508 mmol/L on Day 2, 5.849 ± 2.95 mmol/L on Day 7 in the control group. The changes in TG levels were significantly different between groups on Day2 5.681 ± 4.083 mmol/L versus 8.259 ± 4.508 mmol/L ($P = 0.012$) and Day7 3.967 ± 2.52 mmol/L versus 5.849 ± 2.95 mmol/L ($P = 0.002$) (Table 2).

3.3. Change in other laboratory parameters

Mean Ca^{2+} in the penta-therapy group increased from 1.7856 ± 0.4803 to2.18 ± 0.159 ($P = 0.003$), which in the control group increased from 1.9073 ± 0.3972 to 1.97 ± 0.1502 (P = 0.003). Mean serum AMY, WBC, CRP and GLU gradually decreased during

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