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Therapeutic experience of the application of anisodamine on acute lung injury

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ABSTRACT

Objective: To investigate the effect of anisodamine combining with conventional therapy on the degree of lung injury and inflammatory reaction of patients with acute pulmonary contusion.

Methods: A total of 48 patients with acute pulmonary contusion treated in our hospital emergency department from April 2011 to October 2015 were enrolled as the research object and were divided into experimental group and control group by using a method of random number table. Experimental group received anisodamine combining with conventional therapy and control group received conventional therapy. In the process of the treatment, the mechanical ventilation time, hospital stays in intensive care unit and the number of cases developed into acute respiratory distress syndrome and multiple organ dysfunction syndromes of patients in two groups were observed. Oxygenation indexes of patients were respectively calculated on Days 1, 2 and 3 after treatment. The contents of inflammatory mediators in serum were detected on Day 3 after treatment.

Results: The mechanical ventilation time and hospital stays in intensive care unit [(9.52 ± 1.41) *vs.* (14.57 ± 2.51) days] of patients in experimental group were significantly shorter than those in control group, and the number of cases developed into acute respiratory distress syndrome [1 (4.17%) *vs.* 9 (37.50%)] and multiple organ dysfunction syndrome [1 (4.17%) *vs.* 7 (29.17%)] was significantly less than those in control group. Oxygenation indexes (294.52 ± 41.26 *vs.* 257.63 ± 38.52; 357.74 ± 47.74 *vs.* 279.87 ± 31.46; 396.71 ± 55.12 *vs.* 279.87 ± 31.46) of patients were respectively calculated on Days 1, 2 and 3 after treatment, which were significantly higher than those in the control group. On Day 3 after treatment, the contents of serum C-reactive protein [(7.94 ± 1.05) *vs.* (14.49 ± 2.97) mg/L], tumor necrosis factor α [(264.69 ± 41.58) *vs.* (417.87 ± 64.51) ng/L], interleukin-6 (IL-6) [(147.72 ± 21.36) *vs.* (257.68 ± 41.54) ng/L], IL-8 [(93.68 ± 12.52) *vs.* (145.62 ± 22.65) ng/L], IL-10 [(205.64 ± 31.56) *vs.* (336.62 ± 51.38) ng/L] and myeloid cells-1 (73.32 ± 10.39 *vs.* 114.45 ± 18.51) of patients in experimental group were significantly lower than those in the control group.

Conclusions: The anisodamine combining with conventional therapy can relieve the degree of lung injury caused by acute pulmonary contusion, improve ventilatory function, lower the incidence of acute respiratory distress syndrome and multiple organ dysfunction syndrome and inhibit the activation of inflammatory reaction and the release of inflammatory mediators.

1. Introduction

Among the emergency trauma patients, more than one-third of patients have blunt chest injury, while pulmonary contusion is the most common complications after blunt chest injury[1,2]. Pulmonary contusion can increase the risk of the incidence of acute respiratory distress syndrome (ARDS) and meanwhile, severe patients need to be assisted breathing with ventilator, which can increase the incidence of ventilator-associated pneumonia. In the pathogenic process

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The study protocol was performed according to the Helsinki declaration and approved by hospital ethical committee (the name of the ethic committee which approved the investigations). Informed written consent was obtained from the objects enrolled.

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of multiple organ dysfunction caused by severe trauma, acute lung injury occurs the earliest and has the highest incidence, which runs through each pathologic stage of multiple organ dysfunction[3–5]. Hence, a reasonable and effective treatment schedule set for acute lung injury can stop further development of illness condition and lower the morbidity and mortality of multiple organ dysfunction syndrome (MODS).

The main pathological features of pulmonary contusion include the bleeding and edema of lung tissue in contusion area combining with a large number of inflammatory cells infiltrations. The activation of inflammatory reaction and the release of inflammatory mediators in local tissues are the critical pathological links for causing lung injury. Inhibiting the inflammatory reaction is an important objective to treat pulmonary contusion and prevent MODS[6–8]. Anisodamine, namely, 654-2, is a kind of alkaloid drug extracted and purified from Solanaceae botany, *Anisodus tanguticus* (Maxim.), which can relieve the bronchospasm, improve the function of pulmonary exchange and ventilation, alleviate microcirculatory disturbance, enhance the effect of microcirculatory blood supply, relieve the local inflammatory reaction of wound tissues and promote the absorption of inflammatory mediators[9–11]. In the following research, we used anisodamine combining with conventional scheme to treat acute lung injury.

2. Materials and methods

2.1. Case data

A total of 48 patients with acute pulmonary contusion treated in our hospital emergency department from April 2011 to October 2015 were enrolled as the research objects. The approval was obtained from the hospital ethical committee and informed consent was obtained from the objects enrolled. All the patients had positive history of chest trauma and were confirmed with pulmonary contusion by the CT examination of chest after admission, and patients with the trauma of other organs or active bleeding and a history of chronic respiratory disease were excluded. A total of 48 patients enrolled included 33 male cases and 15 female cases and their age were 15–68 years with a mean age of (37.6 ± 5.2) years. The causes of injury included traffic accident (33 cases), crush injury (7 cases) and fall injury (8 cases).

2.2. Grouping methods

The 48 patients enrolled were divided into experimental group and control group with a method of random number table and each group included 24 cases. After admission, the patients of experimental group and control group were actively disposed and treated at the original injury locations to keep unobstructed respiratory tract, and ventilator should be offered for the severe patients to assist breathing. Also the antibiotics were used to prevent pulmonary infection. Hormone and appropriate volume of human serum albumin or blood component transfusion were used as needed. The patients of experimental group received anisodamine treatment based on the above treatment and the method was listed as follow: 1.0 mg/kg anisodamine injection was used for intravenous injection for continuous 3 days (3 times/day).

2.3. Evaluation methods of clinical indexes

In the process of treatment, the mechanical ventilation time, hospital stays in intensive care unit (ICU) and the number of cases developed into ARDS and MODS of patients in two groups were observed. Oxygenation indexes of patients were respectively calculated on Days 1, 2 and 3 after injecting anisodamine. About 5–10 mL peripheral-blood specimens of patients in two groups were collected. After getting serum centrifuged, ELISA was used to detect the contents of serum C-reactive protein (CRP), tumor necrosis factor α (TNF-α), α interleukin-6 (IL-6), IL-10 and myeloid cells-1 (sTREM-1) on Day 3 after treatment.

2.4. Statistics process methods

The data were inputted by using SPSS 22.0 software and measurement data underwent homogeneity test for variance, which fitted normal distribution were expressed as mean ± SD. The measurement data of normal distribution between two groups were analyzed by using *t*-test. Enumeration data were expressed by using frequency number and were analyzed by *Chi*-square test. Differences were considered statistically significant when $P < 0.05$.

3. Results

3.1. General clinical data

The gender, age, respiratory frequency, oxygenation index, APACHE II score and the contents of serum creatinine, urea nitrogen, alanine aminotransferase and aspartate aminotransferase had no significant difference (Table 1).

Table 1
The general data of patients in the two groups.

General data	Experimental group (n = 24)	Control group (n = 24)
Gender (male/female)	17/7	16/8
Age (years)	38.5 ± 5.9	37.1 ± 4.4
BMI (kg/m^2)	22.19 ± 3.14	22.68 ± 2.95
Respiratory frequency (times/min)	26.52 ± 3.12	26.18 ± 3.32
Oxygenation index	239.52 ± 42.29	242.45 ± 39.45
APACHE II score	17.69 ± 2.96	17.14 ± 2.64
BUN (mmol/L)	8.51 ± 0.92	9.14 ± 1.26
Scr (μmol/L)	94.33 ± 14.25	96.18 ± 12.77
ALT (IU/L)	32.85 ± 5.69	34.12 ± 4.86
AST (IU/L)	29.38 ± 4.72	30.52 ± 4.24

3.2. General conditions of treatment

The mechanical ventilation time and hospital stays in ICU of patients in experimental group were significantly shorter than those in control group, and the number of cases developed into ARDS and MODS cases was significantly less than those in control group (Table 2). Oxygenation indexes (294.52 ± 41.26 *vs.* 257.63 ± 38.52; 357.74 ± 47.74 *vs.* 279.87 ± 31.46; 396.71 ± 55.12 *vs.* 279.87 ± 31.46) of patients were respectively calculated on Days 1, 2 and 3 after treatment, which were significantly higher than those in the control group (Table 2).