Clinical significance of plasma level of AT-III determination in sepsis patients

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ABSTRACT

Objective: Through measure changes of anticoagulant enzyme (AT-III) activity in plasma in sepsis patients, this paper discusses the clinical significance of AT-III activity changes in predicting sepsis occurrence and prognosis. Methods: The non-sepsis 30 cases, with sepsis 76 cases, including 25 cases of severe sepsis, use method of thrombin gelatum lacuna for determining activity of AT-III in plasma, platelet count and APACHE III score simultaneously. Results: Sepsis group, severe sepsis groups contrast with the non-sepsis group respectively, activity of AT-III reduced significantly ($P<0.01$), severe sepsis group lower than sepsis group ($P=0.055$). Conclusion: AT-III activity reduced early in sepsis patients, with patient's condition aggravat, its value further reduced, hints measurement of AT-III activity has certainly clinical significance in predicting sepsis occurrence and prognosis.

1. Introduction

Sepsis is the systemic inflammatory response syndrome caused by infection. As studies on its pathogenesis go deeper, it is believed that dysfunction of the coagulation/fibrinolysis system plays an important role in occurrence and development of sepsis.

Due to an invasion of microorganisms and their toxins after sepsis occurs, there is imbalance between the coagulation system and the fibrinolytic system in the early stage of coagulation[1]. After the coagulation system is activated, a large amount of thrombin and fibrinous protein is produced, and the anti-coagulation system is also activated. AT-III, a strong inhibitor of the clotting cascade system, passivates thrombin and inhibits a number of serum protease[2]. After infection and DIC, AT-III is consumed greatly. As a result, the increase of AT-III is regarded as one of the indicators reflecting prognostics of sepsis[3]. The activity of AT-III was determined in the treatment of 76 patients with sepsis hospitalized from January, 2008 to December, 2009, and the clinical significance of AT-III in prognostics of patients with sepsis was touched on.

2. Patient and methods

2.1. Patients

30 patients, admitted to the department of ICU over the same period and without DIC, were chosen into the control group; 51 patients were chosen into the sepsis group, 30 males and 21 females aged 16 to 86 (61.90±17.29); 25 patients were chosen into the severe sepsis group, 13 males and 12 females aged 16 to 76 (61.84±19.54).

(1) Disease distribution: The sepsis group contained 27 patients with pneumonia, 5 patients with chronic bronchitis with acute infection, 3 patients with skin infection, 7 patients with intestinal infection, 6 patients with biliary tract infection, 1 patient with purulent peritonitis, and 2 patients with urinary infection. The severe sepsis group contained 11 patients with pneumonia, 5 patients with biliary tract infection, 5 patients with intestinal infection, 1 patient with urinary infection and 3 patients with acute severe pancreatitis.

(2) The normal reference value was (90.3±26.4), as was attached to the AT-III determination kit produced by Shanghai Institute of Biological Products Co., Ltd. of Ministry of Health (batch number:...
between three groups.

(3): Groups of AT-III comparison: there were significant differences on the day when they were hospitalized, and tested collectively with PLT, AT-III.

(2) Plaque techniques with thrombin and gelatum were used to determine the activity of AT-III.

(3)All of the data were tested and analyzed for the between-group comparison with the SPSS 13.0 statistical software, \( \chi^2 \) test. \( P<0.05 \) indicated significant differences.

3. Results

Multiple group of APACHE II scores, AT-III, PLT (Table 1).

(1): Groups of APACHE II score comparison: There were significant differences between the control group and the sepsis group and between the control group and the severe sepsis group; there were not significant differences between the sepsis group and the severe sepsis group.

(2): Groups of AT-III comparison: There were significant differences between the control group and the sepsis group and between the control group and the severe sepsis group; there were not significant differences between the sepsis group and the severe sepsis group.

(3): Groups of AT-III comparison: there were significant differences between three groups.

Table 1.

<table>
<thead>
<tr>
<th>Group</th>
<th>APACHE II scores</th>
<th>AT-III</th>
<th>PLT</th>
</tr>
</thead>
<tbody>
<tr>
<td>The control group</td>
<td>21.31±7.43</td>
<td>101.37±23.56</td>
<td>230.42±40.99</td>
</tr>
<tr>
<td>The sepsis group</td>
<td>23.98±8.47*</td>
<td>84.45±21.38*</td>
<td>150.42±30.21*</td>
</tr>
<tr>
<td>The severe sepsis group</td>
<td>25.03±5.22*</td>
<td>74.12±20.12*#</td>
<td>95.32±71.20*#</td>
</tr>
</tbody>
</table>

*Means comprise with control group, \( P<0.05 \), there’s Statistical significance.

#Means comprise with sepsis group, \( P=0.05 \), there’s Statistical significance.

4. Discussion

AT-III, a kind of single-stranded glycoprotein, is produced in parenchymal liver cells. As the strongest physiological inhibitor in the anti-coagulation system, it participates in anti-coagulation with Protein C and Protein S. When the anti-coagulation system is disordered, AT-III turns against coagulation after combining with heparin. As heparin increases its activity, AT-III neutralizes a number of enzymes produced in the coagulation cascade reaction, such as blood coagulation factor Xa and blood coagulation factor XIa, or thrombin is turned to thrombin-antithrombin (TAT)*4. Once formed, TAT is immediately cleared out by the reticuloendothelial system. Accordingly, AT-III is also cleared out, or its activity decreases.

The studies of a multicenter showed that the incidence of decrease in activity of AT-III for patients with sepsis was 81.7%[5], a figure showing how common coagulation dysfunction was among patients with sepsis. After sepsis occurs, the extrinsic pathway of blood coagulation is activated due to the impact of cellular components like endotoxin or lipopolysaccharide, and the tissue factors expressed by mononuclear cells and endothelial cells; meanwhile, hypercoagulability occurs after the weakening of important physiological anti-coagulants like AT-III, the Protein C system and tissue factor pathway inhibitors. With respect to fibrinolysis, due to an increase in the number of plasminogen activator inhibitor-1, much less plasminogen is converted to plasmin, therefore fibrinolytic activity inhibited[6]. After the number of AT-III in plasma decreases, the vigorous intravascular fibrinolytic system is activated, so blood coagulation accelerates, and secondary ischemia in tissue occurs, making patients’ conditions worsened. According to foreign reports, the activity of AT-III might decrease even in the early stage after infection. And after the coagulation function was tested in the laboratory, the patients with systemic inflammatory response syndrome were found with lower activity of AT-III than those of healthy people[3]. The results of this experiment indicated that, when the activity of AT-III decreased after sepsis occurred, the activity of AT-III in the plasma of the patients in the sepsis group was obviously lower than that in the control group (\( P<0.05 \)), showing that the coagulation system was disordered in the early stage after infection. With a number of blood coagulation factors and platelets consumed, the anti-thrombin started to work and be consumed. As sepsis developed, the number of platelets went down progressively, making the extrinsic coagulation pathway activated, and the activity of the intrinsic anti-coagulation system enhanced. After the severe sepsis occurred, the activity of AT-III in the plasma of the patients decreased to a level that was lower than that of the patients in the sepsis group (\( P>0.05 \), no difference). With reference to the detection, the activity of AT-III went down progressively as the conditions were worsened, a sign of unfavorable prognosis.

By analyzing the activity of AT-III, the number of platelets and the APACHE II scores in this experiment, the activity of AT-III and the number of platelets negatively correlated with the APACHE II scores, and the activity of AT-III positively correlated with the number of platelets, indicating the changes of AT-III could be applied to the assessment of severity of illness, namely, a diagnostic indicator of the development of sepsis. With reference to the studies
carried out by Maria et al [7], the activity of AT-III of patients with sepsis on Day 1 was related to the severity of illness at that time. Many animal experiments carried out in foreign countries showed that the construction of AT cut off the activation of the coagulation system, decreasing the incidence of organ failure and mortality [8]. In the Phase III of an international multicenter clinical trial named KyberSept, it was found that patients with severe infection might benefit from the AT treatment in the early stage. However, when combined with heparin, it was of no effect [9].

To sum up, patients with sepsis suffer from distinct imbalance between the coagulation system and the anti-coagulation system even in the early stage. It is manifested by lower activity of AT-III, consumption of platelets, an important role played in the pathogenesis of MODS, and a close relationship between activity of AT-III and severity of illness. It is worthy to apply to practice a combination of determination of activity of AT-III in plasma of patients with sepsis and the APACHE II Scoring System.

Reference


