



ORIGINAL

Reduced thrombin activatable fibrinolysis inhibitor and enhanced proinflammatory cytokines in acute coronary syndrome

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Received 11 August 2016; accepted 11 October 2016

KEYWORDS

Acute coronary syndrome;
Thrombin activatable fibrinolysis inhibitor;
Proinflammatory cytokine;
Acute phase protein;
Coronary disease

Abstract

Objective: A study was made of the changes in the serum levels of thrombin activatable fibrinolysis inhibitor (TAFI), proinflammatory cytokines and acute phase proteins in the acute stage of acute coronary syndrome (ACS), in order to explore the possibility of using TAFI as a biomarker for ACS risk assessment.

Methods: A total of 211 patients with ACS were enrolled, and healthy subjects were used as controls. Blood samples were taken within 24h after admission. Serum TAFI levels were determined by immunoturbidimetry. Serum levels of interleukin-1 β (IL-1 β), interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF- α) were determined by enzyme linked immunosorbent assay (ELISA). Procalcitonin (PCT) and C-reactive protein (CRP) levels were measured by gold-immunochromatographic assay.

Results: Serum TAFI levels in ACS patients were significantly decreased versus the controls. The IL-1 β , IL-6, TNF- α , PCT and CRP levels were markedly higher in the ACS patients than in the controls. Correlation analysis revealed a strong negative correlation between TAFI concentration and the IL-1 β , IL-6, TNF- α , PCT and CRP levels in ACS patients and in controls. Multivariate logistic regression analysis suggested decreased serum TAFI to be an independent risk factor for

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ACS (OR 9.459; 95% CI 2.306–38.793; $P=0.002$). The area under the receiver operating characteristic (ROC) curve for TAFI was 0.872 (95% CI 0.787–0.909; $P<0.001$). The optimum TAFI cutoff point for the prediction of ACS was 24 $\mu\text{g/ml}$, with a sensitivity of 75.83% and a specificity of 72.57%.

Conclusion: These findings suggest that TAFI can be useful as a potential biomarker for ACS risk assessment.

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PALABRAS CLAVE

Síndrome coronario agudo;
Inhibidor de la fibrinólisis activado por trombina;
Citocina proinflamatoria;
Proteína de la fase aguda;
Cardiopatía coronaria

Reducción del inhibidor de la fibrinólisis activado por trombina y aumento de las citocinas proinflamatorias en pacientes con síndrome coronario agudo

Resumen

Objetivo: Esta investigación se ha diseñado para analizar el cambio en las concentraciones séricas del inhibidor de la fibrinólisis activado por trombina (TAFI), las citocinas proinflamatorias y las proteínas de la fase aguda en pacientes con síndrome coronario agudo (SCA) con el fin de explorar la posibilidad de utilizar TAFI como biomarcador para evaluar el riesgo de SCA.

Métodos: Se incluyó un total de 211 pacientes diagnosticados de SCA y se seleccionó a voluntarios sanos como controles. Se extrajeron muestras de sangre de 24 h después de la admisión. La concentración sérica de TAFI se determinó mediante inmunoturbidimetría. Las concentraciones séricas de interleucina (IL)-1 β , IL-6 y factor alfa de necrosis tumoral se determinaron mediante ensayo de inmunoabsorción enzimática. Las concentraciones de procalcitonina y de proteína C reactiva se evaluaron mediante ensayo inmunocromatográfico.

Resultados: La concentración sérica de TAFI en los pacientes con SCA fue significativamente menor que en el grupo control. Las concentraciones de IL-1 β , IL-6, factor alfa de necrosis tumoral, procalcitonina y proteína C reactiva fueron notablemente mayores en los pacientes con SCA que en el grupo control. Un análisis de correlación mostró que existía una sólida correlación negativa entre la concentración de TAFI y las concentraciones de IL-1 β , IL-6, factor alfa de necrosis tumoral, procalcitonina y proteína C reactiva, tanto en los pacientes con SCA como en los del grupo control. El análisis de regresión logística multivariante evidenció que la disminución de la concentración sérica de TAFI constituía un factor de riesgo independiente de SCA (OR 9,459; IC 95% 2,306-38,793; $p=0,002$). El área bajo la curva de eficacia diagnóstica (curva ROC) del TAFI fue de 0,872 (IC 95% 0,787-0,909; $p=0,001$). El punto de corte óptimo del TAFI para la predicción del SCA fue de 24 $\mu\text{g/ml}$, con una sensibilidad del 75,83% y una especificidad del 72,57%.

Conclusión: Estos hallazgos evidencian que el TAFI constituye un posible biomarcador del riesgo de SCA.

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Introduction

Coronary heart diseases are a leading cause of morbidity and mortality in the world. Acute coronary syndrome (ACS) is a term representing the main clinical manifestation of atherosclerotic progression in the coronary plaque.¹ In the pathological process of ACS, thrombosis plays a critical role. Disruption of an atherosclerotic plaque exposes flowing blood to subendothelial collagen, tissue factor, and other procoagulant substances that trigger the activation of platelets and the formation of fibrin within the local vessel lumen. Endothelial damage, inflammation and coagulation are closely related to the patho-physiology of acute coronary syndrome and might be inter-related.²

Thrombin activatable fibrinolysis inhibitor (TAFI) is a zymogen that links coagulation and fibrinolysis.³ When

activated, it potently inhibits fibrinolysis through the removal of the carboxy-terminal lysine and arginine residues from partially degraded fibrin polymers. In addition, TAFI has a suppressive effect on conversion of inactive plasminogen to plasmin.⁴ Since impaired fibrinolysis is a well established risk factor for cardiovascular events, detecting TAFI concentration in ACS patients may be helpful to the risk assessment of this life threatening disease. However, the results of current investigation are paradoxical. Some studies showed a trend for increased TAFI level in coronary artery disease, while others found decreased level of TAFI in these patients.⁵⁻⁷

Inflammation plays an important role in the onset and development of atherosclerosis which is the underlying cause of ACS.⁸ Coagulation and inflammation are closely inter-related processes. Pro-inflammatory cytokines

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