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ORIGINAL

Serum proteome in acute myocardial infarction

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KEYWORDS
Myocardial-infarction;
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Abstract
Introduction: Acute myocardial infarction (AMI) is one of the major causes of mortality and morbidity worldwide. Despite the efforts being made, there is a lack of early markers for the prevention, diagnosis and treatment of ischemic syndromes. Proteomic expression profiling technologies are a highly important tool for research into new serum biomarkers for the diagnosis and prognosis of acute coronary syndromes.
Methods: Serum samples were sub-fractionated with different methods for the depletion of high-abundance proteins. The low-abundance fraction was analyzed by two-dimensional electrophoresis (2-DE), followed by protein identification with mass-spectrometry (MALDI-TOF). The proteomic profiles of serum samples from AMI patients and controls were analyzed and compared.
Results: Through depletion of six high-abundance proteins in 2-DE analysis of serum samples, 569 spots were detected, of which 131 spots were only detected in the AMI group and 27 were only detected in controls. The comparative analysis between AMI-patients and controls revealed a group of differential protein spots involved in seven different biological functions. The main changes were found in proteins involved in the immune system and lipid metabolism.
Conclusions: In this study, by using a 2-DE differential approach, we developed a highly reproducible methodology for the analysis of coordinated changes in serum proteome patterns that occur within the first 6 hours after the onset of an AMI.

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PALABRAS CLAVE
Infarto de miocardio;
Suero;
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Resumen
Introducción: El infarto agudo de miocardio (IAM) es una de las mayores causas de mortalidad y morbilidad en el mundo. A pesar de todos los esfuerzos hay una falta de marcadores para la prevención, el diagnóstico y el tratamiento de la fase temprana de los síndromes isquémicos. Las técnicas proteómicas son una herramienta muy importante para la búsqueda de nuevos biomarcadores para el diagnóstico y el pronóstico de los síndromes coronarios agudos.
Métodos: Las muestras de suero se sub-fraccionaron mediante diferentes métodos para eliminar las proteínas mayoritarias. La fracción de proteínas de menor abundancia se analizó mediante electroforesis bidimensional (2-DE), seguida de la identificación de proteínas mediante espectrometría de masas (MALDI-TOF). Se analizó y comparó el patrón proteómico de los pacientes IAM y el grupo control.
Resultados: Mediante la eliminación de las seis proteínas mayoritarias en el análisis por 2-DE se detectaron un total de 569 spots, de los cuales 131 sólo se detectaron en el grupo infarto y 27 sólo en el grupo control. El análisis comparativo entre los pacientes IAM y los controles reveló un grupo de spots proteicos con un patrón de distribución diferencial entre ambos grupos. Estos spots diferenciales pertenecen a siete grupos diferentes en función de su papel biológico, de los cuales los cambios más importantes se ven en las proteínas involucradas en el sistema inmune y en el metabolismo lipídico.
Conclusiones: En el presente estudio, mediante el uso de técnicas de 2-DE hemos desarrollado una metodología altamente reproducible para el análisis de los cambios coordinados que se dan durante las seis primeras horas desde el inicio de un evento.

Introduction

Ischemic atherothrombotic syndromes induce structural and functional modifications that are reflected in serum levels of proteins and other biomarkers. However, biomarkers characterization is nowadays incomplete and their prognostic value is not clear. Increased concentrations of inflammatory biomarkers such as C reactive protein (CRP), serum amyloid A, myeloperoxidase and interleukin-6 (IL-6) are detectable in a substantial proportion of patients with acute coronary syndromes. Several biomarkers of myocardial ischemia are under investigation, ischemia-modified albumin (IMA) is among the most thoroughly studied of these markers.[1] There are also biomarkers for the detection of cardiac injury, from those ones the protein of choice is troponin.[2]

Some of those biomarkers lack of consensus because, up to now, it is not clear whether their measurement would be useful in the diagnosis and prognosis of ischemic atherothrombotic syndromes.

Despite the success of cardiac troponins as markers of myocardial injury there is still a need for the development of early markers for prevention, diagnosis and treatment of ischemic syndromes.

Proteomics is one of the most important strategies for the study of complex protein associations. By using proteomic techniques we can determine modifications in protein structure, expression levels, and post-translational modifications that may be associated to the presence of disease. Indeed, proteins are excellent targets for disease diagnostic and prognostic markers and to develop therapeutic strategies. Proteomic techniques are a good tool for the analysis of the protein content in a determined sample.[3]

Serum has the advantage of being one of the most accessible sources for biomarker discovery, but also has the disadvantage of its great complexity as it has a lot of different proteins in a very dynamic range of concentrations. Near 85% of serum proteome is represented by a reduced group of proteins that are known as the high abundant fraction and usually have no interest in proteomic analysis as they are very well characterized. Potential serum biomarkers are in very low abundance and so they are masked by high abundant proteins such as albumin and IgGs.

The aim of this study is to characterize the serum proteomic profile in healthy individuals and acute myocardial infarction patients by using two different subfractionation methods.

Materials and methods

Study population

The study population comprised 27 new-onset AMI patient (20 men and 7 women; mean age: 61 ± 2 years) who were admitted with chest pain and suspected of ACS at the Emergency Room of Santa Creu i Sant Pau Hospital.

At the emergency department, routine diagnostic procedures were applied to establish the onset of symptoms as accurately as possible (i.e. description of chest pain, pulmonary edema, severe dyspnea, and syncope). In addition to the general patient history, clinical examination, 12-lead ECG, and laboratory tests were also run to characterize AMI-patients. All AMI-patients showed (1) typical chest pain lasting more than 30 minutes; (2) ST segment elevation >0.2 mV in at least 2 contiguous leads; (3) admission to the hospital within the first 6 hours after chest pain onset; (4) normal serum CK and CKMB levels at admission; (5) negative troponin T at admission (excluding subacute myocardial infarction); (6) sinus rhythm. Exclusion criteria were a previous documented or suspected myocardial infarction and antithrombotic treatment because of the AMI onset before arriving to the emergency room and time of