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A Review Article on Myocardial Infarction Biomarkers.

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ABSTRACT

Cardiovascular diseases are the primary cause of mortality all over the world among both women and men. These diseases are expected to account for the highest mortality rates in developing countries until 2020. Due to the clinical side effects, diagnosis and treatment are needed. The diagnosis of myocardial infarction is based on clinical symptoms, the results obtained from electrocardiogram and laboratory test results in terms of the biomarkers existing in blood. Since after the ischemia of heart tissues and their cells, the biomarkers specific to heart cells are released, these factors play a key role in diagnosing and preventing these patients. They can alter the therapeutic approach of these patients. Given the importance of the issue, a selection of articles published in PubMed database were investigated aiming to look into cardiac biomarkers in myocardial infarction.

Keywords: myocardial infarction, coronary artery disease, ischemia

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INTRODUCTION

Myocardial infarction is one of the key causes of mortality worldwide. However, in the United State (U.S.) and Europe about 15 millions of patients annually complain the chest pain or other symptoms of the disease and visit emergency wards. The term myocardial infarction is used once the evidences of myocardial necrosis are observed in clinical investigations [1]. According to the reports of the American Heart Association, the coronary artery diseases (CAD) mortality rate in the U.S. was over 400,000 cases in 2007. This is equal to one among every six death. Approximately, in the U.S. Due to cardiovascular disease one person dies every minute. Myocardial infarction can be the first manifestation of CADs. Early diagnosis and treatment of the patients can prevent the occurrence of severe injuries caused by myocardial ischemia. Coronary bypass surgery and percutaneous coronary intervention can be noted as proper treatments of the disease. Finally, the ischemia would lead to cardiac cells death, which, depending on the location and extension of the ischemia, would cause disorders in heart functioning. To diagnose the disease, we can make use of electrocardiographic findings, increased biomarkers due to myocardial necrosis, imaging and pathologic findings [2]. According to World Health Organization, myocardial infarction is based on unusual evidence of ECG as well as cardiac enzymes. By increasing the sensitivity and specificity of diagnostic tests in terms of myocardial biomarkers as well as increasing the precision of imaging techniques we could diagnose very low rates of the damage caused by myocardial necrosis. Biomarkers are the main determining factors in patients suspected to have myocardial infarction. Therefore, interpreting the results of a biomarker or a selection of biomarkers is essential [3]. If the diagnostic tests low precision, they could discharge patients who are in need of medical care. Moreover, if the tests have low specificity, they could lead to the hospitalization of a great deal of low-risk patients. This would exert pressure on the medical system. Over the past decade, cardiac biomarkers were the main topic of many biologic investigations. The serum level of heart-specific troponin in acute myocardial infarction (AMI) is increased within less than 3.5 hours after the onset of chest pain. Nevertheless, due to a delayed troponin release, a specific and sensitive biomarkers for early diagnosis of myocardial infarction in order to cut down on the mortality rate is needed. Besides sensitivity and specificity, clinical diagnostic tests need to have three other criteria: 1- Ease of access: sampling should be done easily. For instance, it should include accessible body fluids such as plasma, serum and urine. 2- Predictability: biomarkers should have a relatively good half-life in blood so that the possibility of detecting them in the sample can be predictable. Moreover, the level of biomarkers should be commensurate with the extent of tissue damage and recovery after the process. 3- High reliability: the measurement method should be fast, accurate, sensitive, affordable, and void of the need for special equipment so that it can be used by the public and be adequately credible [4]. Presently, the most of the biomarkers are made of protein or polypeptides. Newer biomarkers of molecular or genetic types are also being investigated to prove their efficiency. One of them is miRNA, which will be introduced later [5]. Whether the specificity of cardiac troponin is adequate for myocardial infarction or not has led to the introduction of other factors so as to increase the sensitivity of the diagnostic tests of myocardial infarction [6]. Therefore, in this review research, we intend to investigate the common and new biomarkers involved in the diagnosis of myocardial infarction.

METHODOLOGY

This review article aims to look into the cardiac biomarkers involved in myocardial infarction. These articles were obtained from PubMed database. The inclusion criteria were: English language, free access to the full texts, being indexed PubMed from 1.1.2012 to 30.1.2015. Moreover, these articles needed to conduct on human beings. All research types could be included such as review articles, clinical trials, meta-analyses, etc.). In order to search the articles, the term 'myocardial infarction biomarkers' was used. The articles, which included this term, entered to the study.

Text analysis

In a review article published by Salic et al. the latest findings of microRNA were investigated in order to complete the diagnostic criteria of myocardial infarction. According to these investigations, the microRNAs derived from myocardia including miRNA 1, 133, 499 and 208 could be useful as potential biomarkers for diagnosing Myocardial Infarction. These miRNAs are found in a great extent in the heart. However, in normal conditions, they exist in lesser degrees in blood circulation. Moreover, these biomarkers are stated to raise the diagnostic power despite being costly. To encourage the use of microRNAs, the development of new techniques that can make a fast diagnosis of the microRNAs of blood is essential [2].

In a study carried out by Eschalier et al., biomarkers of myocardial fibrosis were analyzed one month after Myocardial Infarction as a predictive factor of remodeling the left ventricle. In this research, 264 patients with their first Myocardial Infarction entered the study. Upon their discharge and also 12 months after Myocardial Infarction, they had an echocardiography. Within one month, the BNP (Brain Natriuretic Peptide) was increased in 218 patients. In this study, the proportion of type-III amino peptide procollagento Type-I telopeptide collagen was 1≥1. One month after Myocardial Infarction, BNP>100pg/ml was correlated with the remodeling of the left ventricle. In a 3-year follow up, patients with these traits were faced with the highest rates of tragic events, deaths and hospitalization [3].

In their review article, Li et al, reviewed the latest data about serum RNAs and plasma as new biomarkers in the diagnosis and prognosis of AMI. According to this research, blood microRNAs are emergency biomarkers in detecting AMI. They require a great many clinical investigations before using these biomarkers in the clinic. A completion of the fastest methods of high precision and specificity which are effective in diagnosing and measuring microRNAs can improve the effects of these biomarkers as diagnostic, medical and prognostic factor of AMI [4].

In another review research, Cheng et al. investigated all studies published since January, 2013 which were concerned with Myocardial Infarction and microRNA. They included 19 studies, 15 of which had reported on the sensitivity, specificity and AUC of biomarkers in diagnosing Myocardial Infarction. The results revealed that microRNAs especially miR499 and miR-133a might be appropriate to be used as Myocardial Infarction diagnostic biomarkers [5].

Kim G. Smolderen et al. investigated the correlation of depression symptoms (physical or cognitive) and the biomarkers of those afflicted with AMI. In this study, the level of blood biomarkers (such as hs-CRP, NT-proBNP, WBC and Plt) was investigated within one month of the life of 1265 patients suffering from AMI who had depression symptoms as well. According to the findings of this study, none of the investigated biomarkers were correlated with depression symptoms [6].

Evans et al. in their review study, looked into the serum level of P53-Responsive Micro-RNA as a diagnostic biomarker in patients who get afflicted with AMI after a heart failure. MicroRNAs of blood get linked to a collection of protein. This would prevent their being ruined by nucleases. The proteins joined to microRNAs would make the detection of the microRNAs specific to each tissue as possible. This characteristic would increase the sensitivity and specificity of microRNAs in diagnosing such diseases as myocardial infarction. In fact, microRNAs are factors which help us to diagnose AMI in patients afflicted with heart failure [7].

Hata S. looked into the need for and significance of the predictor biomarkers of AMI, in his review research. The biochemical biomarkers investigated in this research included serum creatine kinase (CK), myoglobin, CK-MB, troponin T or I, heart- type fatty acid-binding protein (H-FABP). H-FABP and COPEPTIN along with the troponin specific to heart can contribute to the diagnosis of myocardial infarction immediately after the occurrence of symptoms. Yet another biomarker, C-reactive protein can predict the occurrence of death after an acute chest syndrome. Myeloperoxidase can estimate the risk of affliction with a coronary artery disease in healthy individuals. It helps the medical system to take whatever therapeutic steps needed to save those in danger. Pregnancy-associated plasma protein A is a substance produced by unstable plaques. The serum level of this substance in patients complaining about a sore chest can predict the risk of myocardial infarction and a need for revascularization [8].

In a study carried out by Hueb et al., 150 patients afflicted with CAD with an indication of CABG were examined. 50 of them had CABG along with CPB (CardioPulmonary Bypass). 50 had only CABG while 50 other patients undertook PIC and STENT. For all the patients, the markers of cardiac necrosis were measured and analyzed both before and after any medical step. The findings revealed an increase in cardiac necrosis biomarkers in the absence of real Myocardial Infarction after a mechanical intervention. An improper use of these biomarkers can lead to a misleading diagnosis and treatment in the patients [9].

In their study, Nursalim et al. investigated the power of new cardiac biomarkers in diagnosing Myocardial Infarction. Investigations showed that, used on their own or in combination with other biomarkers; these new biomarkers can reject AMI faster and precisely. Besides saving time and cost in either rejecting or confirming Myocardial Infarction, they would help to manage patients more efficiently and reduce the consequences of AMI-induced mortality. According to this study, new cardiac biomarkers are powerful in determining patients' risk and prognosis. This would contribute to knowing the prospective medical steps to be taken [10].

In an investigation conducted by Hsu A et al. to investigate serum microRNAs as strong biomarkers of AMI, the hypothesis was that ST-segment elevated myocardial infarction (STEMI) is correlated with microRNAs. They also hypothesized that blood microRNAs could be used as the diagnostic markers of STEMI. According to the findings of this research, there was a significant increase in miR-483-3p while a significant reduction was observed in mid-126-3p, miR-260-5p and miR-191-5p. These findings show that miRNAs serum level can be used as diagnostic biomarkers of STEMI [11].

In a study conducted by Talasaz et al., the effects of NAC (N-Acetylcystein) on the serum level of TGF-β and TNF-α as profibrotic and inflammatory biomarkers in patients afflicted with Myocardial Infarction were investigated in a ST-segment elevation. In this study, 88 patients whose Myocardial Infarction was already proved entered the research randomly. One group was treated using NAC in a 600-mg oral dose. Another group used a placebo for 3 days. 24 and 72 hours after the treatment, they received 10 cc of venous blood specimen collection so as to measure the level of TGF-β and TNF-α. As the results revealed, only patients who had received a placebo showed a significant rise in their TGF-β level. The others showed no significant difference. Moreover, a significant correlation was found between cardiac functioning and TGF-β level in these patients. NAC was found to be capable of improving TGF-β serum level within 72 hours [12].

CONCLUSION

CADs are considered to be a key problem in the medical system. Economic and medical impacts of CAD on the communities have great importance. Clinical definition Alterations, criteria and diagnostic biomarkers of the disease have led to a great need for investigating the issue. A considerable point is that some histological evidences of myocardial damage appear under non-ischemic myocardial infarction circumstances. These conditions include: pulmonary embolism, renal failure arrhythmias, percutaneous or surgical coronary procedures, heart failure, and embolic myocarditis. Therefore, diagnostic tests can differentiate these conditions [1]. In fact, cardiac necrosis biomarkers, in the absence of real Myocardial Infarction can be increased after a mechanical intervention. An inappropriate use of biomarkers in patients can lead to a misleading diagnosis and treatment [9]. Salic et al. indicated that microRNAs 1, 133, 499, and 208 can be used as powerful biomarkers in myocardial infarction diagnosis [2]. In STEMI, the serum level of miR-150-3 and miR-483-3 are increased while miR-260-5p and miR-191-5p are decreased [11]. According to the above-mentioned issues, using of microRNAs in diagnosing myocardial infarction is probable in the future. In another study, TNF-α and TGF-β were introduced as profibrotic and inflammatory biomarkers in STEMI [12]. Similarly, Nursalim et al, in their research proved that the new heart biomarkers, either on their own or in combination with other biomarkers could diagnose AMI with high precision and sensitivity. Therefore, this would not only add to the reliability of diagnostic tests, but also reduces the medical costs and hospitalization duration [10-12]. According to our investigation, microRNA has been highlighted as a new factor in immediately diagnosis of Myocardial Infarction and it would be an accessible test in suspected patients who suffer from Myocardial Infarction.

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