Role Of miRNAs In AMI Of Young Adults

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Abstract

Acute myocardial infarction (AMI) is the leading cause of death worldwide. In Malaysia, people are getting AMI at younger age. The role of miRNA in pathogenesis of AMI in young population has not been studied. miRNA profiling will be done using small RNA sequencing and significantly dysregulated miRNAs will be validated using quantitative real-time PCR (qRT-PCR). The mRNA analysis will be done by fluorescent-based real time PCR (RT-PCR). The significance of miRNA and mRNA expression will be analyzed using appropriate statistical analysis. The discovery of miRNA involved in this study maybe used as novel biomarker for early detection of cardiac injury, prognosis and therapeutic intervention.

Keywords: acute myocardial infarction, microRNA, quantitative real-time PCR

Introduction

Acute myocardial infarction (AMI) is the leading cause of death worldwide. In Malaysia, people are getting AMI at younger age compared to well-developed countries (Zuhdi et al, 2013; Lu et al., 2014). The role of microRNA (miRNA) in pathogenesis of AMI is not well elucidated and its involvement in young population has not been studied. There were studies done in human but majority of the studies have been done in animal models and observation in cell cultures (Aurora et al., 2012; Porello et al., 2013). miRNAs possibly affect the atherogenesis, a precursor for AMI by affecting the genes that regulate endothelial stability as well as the genes involved in atherosclerotic plaque destabilization, fibrogenesis and heart remodeling post infarction. However, their complex regulatory mechanisms have not yet been completely understood. Understanding the pathogenesis of AMI in this young population is important in providing accurate diagnosis and prompt management of the disease.

Methods

This study consists of 20 Young AMI patients, 20 Mature AMI patients and 20 Healthy Controls. Blood sample is taken and divided into 2 aliquots for the miRNA profiling analysis and mRNA analysis. The miRNA profiling will be done using small RNA sequencing. The significantly dysregulated miRNAs will be validated using quantitative real time PCR (qRT-PCR). The mRNA analysis will be done using fluorescent-based real time PCR (RT-PCR). The significance of miRNA and mRNA expressions will be assessed using appropriate statistical analysis.

Results

The miRNAs that are differently expressed (either upregulated or downregulated) between these 3 groups will be analyzed using One-way ANOVA. Post-hoc analysis will be done if $p < 0.05$, to determine the significant dysregulated miRNAs between each group. The dysregulated miRNAs that involved in specific pathway of AMI event in Young AMI group will be categorized accordingly. This descriptive analysis will be based on database, mirdb.org. The mRNA expressions of the dysregulated miRNAs between Young AMI & Mature AMI will be analyzed using Unpaired student t-test.

Conclusions

AMI remains the leading cause of morbidity & mortality worldwide. Therefore, obtaining novel insights into the role of miRNAs in the pathophysiology of AMI, might contribute for a better management of AMI especially for the Young patients. The findings of this study may be used for risk stratification, prognostication & assessing complication post AMI as well as for monitoring treatment response.

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ABSTRACT

Acute myocardial infarction (AMI) is the leading cause of death worldwide. In Malaysia, people are getting AMI at younger age compared to well-developed countries. The role of microRNA (miRNA) in pathogenesis of AMI is not well elucidated and its involvement in young population has not been studied. miRNAs possibly affect the atherogenesis, a precursor for AMI by affecting the genes that regulate endothelial stability, atherosclerotic plaque destabilization, fibrogenesis and heart remodelling post infarction. Understanding the pathogenesis of AMI in this young population is important in providing accurate diagnosis and prompt management of the disease. The aim of our study is to investigate how miRNAs contribute to the pathogenesis of AMI by profiling specific miRNAs that are dysregulated following an AMI in young group and to determine whether these miRNAs lead to the dysregulation of their target mRNA. Blood sample will be taken from the control, young and mature AMI groups and divided into 2 aliquots for the miRNA profiling analysis and mRNA analysis. The gene expressions will be analysed using the Bio-Rad CFX96 software. The significance of miRNA and mRNA expressions will be assessed using appropriate statistical analysis. The discovery of miRNAs involved in the AMI pathogenesis in this study could lead to potential usage as novel biomarkers for detection of early cardiac injury, prognosis and therapeutic intervention.