Investigating the microRNAs as a key regulatory molecule in Diabetic Cardiomyopathy

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ABSTRACT

Diabetic Cardiomyopathy (DCM) is a state in which cardiomyopathy occurs in patients due to diabetes mellitus without valvular and coronary artery disease. The DCM prevalence is about 50% in patients diagnosed with diabetes at either clinical or preclinical stages. DCM is characterized by structural and metabolic myocardial changes established in patients with diabetes mellitus. These changes are triggered by insulin resistance and hyperinsulinemia that lead to the dysregulation of different signaling pathways. Despite the improvement in pharmacological interventions in DCM, still, new reliable strategies are required. MicroRNAs are small non-coding molecules that play a significant role in the regulation of genes at transcriptional and translational levels. We have found the clinical testing genes involved in DCM by gene target registry (GTR), and different miRNAs targeting these genes were identified by using bioinformatics tools NCBI, miRanda, TargetScan, miRBase, and TarBase. From the clinical data of DCM patients, we concluded that the number of genes is dysregulated which can be the putative target of miRNAs as they directly target these genes by binding with 8mer unit i.e STAT3 (regulated by miR-124-3p.1, miR125-5p), MAPK14 (targeted by miR128-3p, miR-124-3p.2, miR-124.3p.1), PRKAA1 (regulated by miR-137, miR-19-3p, miR-148-3p), FOXO1 (directly targeted by miR-135-3p, miR-96-5p), STK11 (regulated by miR17-5p/20-5p), and SOCS3 can be a direct target of miR-30-5p, miR-19-3p, miR-218-5p. Conclusively, we put forward the different miRNAs which are targeting the genes involved in DCM which may serve as a platform for the treatment of a miRNA-based therapeutic or diagnostic strategy for the treatment of diabetic cardiomyopathy.

INTRODUCTION

Diabetic cardiomyopathy (DCM) is defined as abnormality of heart structure and function in diabetic patient without any other cardiac risk factors. The prevalence of heart failure in clinical trials of diabetic patient is 25 % in chronic heart failure and 40 % in acute heart failure. In diabetic cardiomyopathy insulin resistance, hyperglycemia, and hyperinsulinemia leads to different structural and metabolic changes including, oxidative stress, inflammation, ER stress, free fatty acid metabolism, production of advanced glycation end products, mitochondrial dysfunction, apoptosis, necrosis, and cardiac cell injury. The systolic and diastolic dysfunction ultimately caused the heart failure. In DCM pathophysiological condition includes abnormalities in protein kinase C, AMP protein kinase, , O-linked N-acetylglucosamine, and microRNA. MicroRNAs are non-coding, small and highly conserved RNA molecules are evolving to control and regulate the gene expressions at post transcriptional level. miRNA are involved in different biological processes like proliferation, inflammation, developments, differentiation, adhesion, apoptosis and necrosis.

Number of miRNA are involved in the pathogenesis of DCM i.e, miR-34c, miR-199b, miR-210, and miR-34b are contributed in the pathogenesis of myocardium in diabetic patients.Some miR-223, miR-133, miR-141, miR-1, and miR-206 are upregulated in DCM, whereas miR-133a, miR-499, and miR-373 are downregulated.Therefore, it is important to investigate the role of miRNA in diabetic cardiomyopathy and gain insight at its diagnostic potential.

OBJECTIVE

To Investigate the role of micro RNAs in regulating the expression of different genes involved in diagnosis and prognosis of diabetic cardiomyopathy

MATERIALS & METHODS

Figure 1: Identification of gene targets and prediction of microRNAs

RESULTS

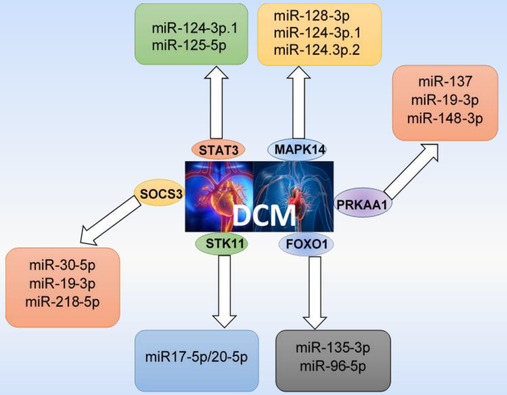

Figure 2 : Gene targets regulated by microRNAs

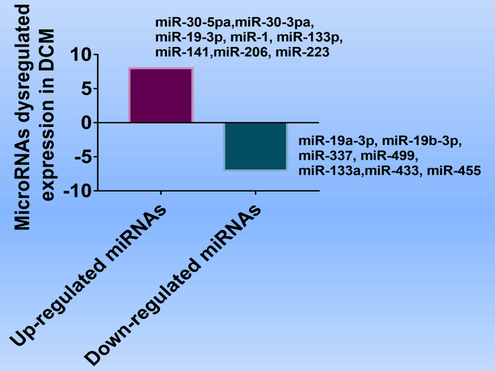

Figure 3: Upregulated and downregulated microRNAs expression in DCM

Discussion

Diabetic cardiomyopathy is an irreversible complication of diabetes and a risk factor for CVDs. Cardiac miRNAs are a major regulators, controlled gene expressions at both transcriptional and post-transcriptional levels in diabetic cardiomyopathy. The epigenetic changes in miRNAs disrupt their normal function and act as an actors in the etiology of DCM. From bioinformatics tools we predicted various miRNAs which are highly conserved and have 8nt binding sites. Theses miRNAs have the potential to directly regulate the expressions of DCM genes and showed the potential to understand the pathophysiological mechanism of the disease. Therefore, miRNAs can be used for therapeutic and diagnostic interventions in DCM.

SUMMARY

In diabetic cardiomyopathy number of miRNAs are dysregulated and contributed in pathogenesis of the disease. Our study suggested some potential miRNA as a target that are not previously reported. These circulating miRNA can be used as diagnostic and therapeutic targets for the treatment of the disease. Further advanced studies are required to use them for the prognosis of the disease.

CONCLUSION

Conclusively, as miRNAs are involved in the pathophysiological events of the disease. They can be used with some advancement as a novel therapeutic approach for the diagnosis of the disease.

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