Evaluation of Therapeutic Potential of Mesenchymal Stem Cells and Conditioned Medium in the Treatment of Cardiac Dysfunction Due to Obesity and Diabetes Mellitus Type II.

Daltro, P. S[1,4]; Barreto, B. C.[2]; Chenaud, P.[3]; Silva, P. G.[3]; Humberto, P.[3]; Neta, D.[3]; Carvalho, G. B.[4]; Nascimento, D.[4]; Alcantara, A. C.[4]; Vasconcelos, J. F.[4]; Freitas, L. A. R.[3,5]; Santos, R. R.[4]; Soares, M. B. P.[4,5]; Macambira, S. G.[1,4,5,6].

[1]Programa Multicêntrico de Pós-graduação em Bioquímica e Biologia Molecular, Universidade Federal da Bahia, Salvador, BA, Brazil.
[2]Faculdade de Biologia, Universidade Federal da Bahia, Salvador, BA, Brazil.
[3]Faculdade de Medicina, Universidade Federal da Bahia, Salvador, BA, Brazil.
[4]Centro de Biotecnologia e Terapia Celular, Hospital São Rafael, Salvador, BA, Brazil.
[5]Centro de Pesquisa Gonçalo Moniz, Fundação Oswaldo Cruz, Salvador, BA, Brazil.
[6]Departamento de Biofunção, Instituto de Ciências da Saúde, Universidade Federal da Bahia, Salvador, BA, Brazil.

Introduction: High fat diet (HFD) and poor lifestyle are related to obesity and type 2 diabetes and its cardiovascular abnormalities. Bone marrow mesenchymal cells (BMSC) arise as a therapeutic tool for degenerative conditions. Paracrine factors secreted by BMSC into the conditioned medium (CM) are used in tissue regeneration. **Objective:** To evaluate the effect of BMSC or CM on cardiac dysfunction in HFD mice. **Material and Methods:** Fifty C57BL/6 mice were divided into two groups: a standard (n=10) and a HF diet (n=40). After 36 weeks, HF mice were divided into three groups: BMSC treated (n=14), CM treated (n=14) and culture medium treated (n=12). Cardiac function was assessed by electrocardiography, echocardiography and treadmill test before HF diet and at 12, 24 and 36 weeks on HF diet. Body weight measurement and fasting glucose, were performed monthly. Biochemical analysis, ELISA and cardiac function were made quarterly, real time RT-PCR with cardiac tissue and vascular reactivity test were performed in 52 weeks. CM was characterized by protein array technique. **Results and Discussion:** At the end of induction period, HFD mice showed increased body weight, fasting plasma glucose, intolerance to glucose, cardiac arrhythmias and physical exercise incapacity. After returning to standard diet (52 weeks), and independent of treatment, body weight and glycemic levels were normalized to control group. Six animals in each treatment group with MSC and CM recovered the normal sinus rhythm and partially recover the physical ability after cellular therapy. Adiponectin levels were similar between the control group and treated ones. TNF expression was reduced in CM and the GATA-4 in BMSC. Vascular reactivity to phenylephrine and sodium nitroprusside was improved in BMSC

group. Adhesion molecules, cytokines, and growth factors were detected in CM. **Conclusions:** Cellular therapy induced arrhythmias reversion, inflammatory reduction and vascular response improvement by mechanisms that are under investigation.

Acknowledgements

Keywords: Conditioned medium. Diabetic Cardiomyopathy. Mesenchymal stem cells.

Financial Support: FAPESB, CNPq & FINEP