The mechanisms underlying the cardiac effects of modified citrus pectin in obese rats with myocardial ischemia: Role of galectin-3

Sara Jiménez-González [1], Beatriz Delgado-Valero [1], Ana Romero-Miranda [1], Fabian Islas [2], María Luaces [3], Bunty Ramchandani [4], María Cuesta-Corral [1], Alejandro Montoro-Garrido [1], María Luisa Nieto [5], Ernesto Martínez-Martínez [6], Victoria Cachofeiro [7]

Abstract

Background: Modified citrus pectin (MCP) is used as a nutritional supplement that inhibits galectin-3 activity, a central player in the cardiac damage associated with different pathological situations. In fact, we have previously observed that MCP improved cardiac function in obese infarcted rats that was associated with a reduction in cardiac fibrosis. Therefore, the aim of the present study was to further explore whether this effect could involve the modulation of gene expression of ECM components and their mediators as well as whether it could affect another two mechanisms involved in cardiac damage: mitochondrial dynamics and autophagic flux.

Methods: Male Wistar rats were fed an atherogenic diet with a high content of saturated fat (35%). MI was induced by the ligation of left anterior descendant (LAD) coronary artery 6 weeks after and MCP (100mg/kg/day) or vehicle were administered for 4 weeks more. A group of rats fed a standard diet (5.3% fat) and subjected to a sham operation was used as controls.

Results: Obese infarcted animals presented an increase in cross-linked collagen that was not affected by the administration of galectin-3 inhibitor. However, MCP reduced the increase in gene expression observed in obese infarcted rats of ECM components and mediators (collagen I, fibronectin, transforming growth factor-β and connective tissue growth factor), of components of endoplasmic reticulum stress (binding immunoglobulin protein, CCAAT-enhancer-binding homologous protein and activating transcription factor 4), of oxidative stress mediator (NADPH oxidase-4) and normalized those of the interleukin 33/ST2 system. MCP is also able to increase the levels of the mitochondrial protein Dynamin-1-like and those of both proteins involved in autophagic flux (p62 and LC3) that were reduced by the myocardial ischemia in the context of obesity.

Conclusions: The data show that the beneficial effect of the nutritional supplement MCP on the cardiac consequences associated with myocardial ischemia in the context of obesity could rely on its capacity to inhibit galectin-3 and to consequently modulate different downstream mechanisms, including inflammation, ER stress, oxidative stress, autophagy and mitochondrial function, which can facilitate fibrosis and cardiac remodeling in this pathological context.

Keywords: Autophagic flux; Estrés oxidativo; Fibrosis; Flujo autofágico; Galectin-3; Galectina-3; Infarto de miocardio; Inflamación; Inflammation;

Mitochondria; Mitocondrias; Myocardial infarction; Obesidad; Obesity;

Oxidative stress.