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Professor Doutor Pedro Rodrigues

ijup@reit.up.pt

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21605 | SGLT2 Inhibitors: Novel Approach to Modulate Appetite Hormones and Cardiomyocyte Function

Beatriz Correia^{1,2}; Alexandre Rodrigues^{1,3}; Inês Alves^{1,3}; Sandra Moraña-Fernández^{4,5}; Cláudia Mendes¹; Juliana Morais^{1,6,7}; Alexandre Goncalves^{1,3}, Inês Falcão-Pires^{1,3}

Department of Surgery and Physiology, Faculty of Medicine of the University of Porto, Porto, Portugal¹; Faculdade de Ciências Médicas|NOVA Medical School, Universidade NOVA de Lisboa, Lisboa, Portugal²; UNIC@RISE, Department of Surgery and Physiology, Faculty of Medicine University of the Porto³; Cellular and Molecular Cardiology Research Unit, Santiago Institute of Health Research and Integrated Management Xerence (XXIS/SERGAS), Santiago de Compostela, Spain⁴; Singular Research Center in Molecular Medicine and Chronic Diseases (CiMUS), University of Santiago de Compostela, Spain⁵; CINTESIS, Center for Health Technology and Services Research, Porto, Portugal⁶; Department of Functional Sciences, School of Health, Polytechnic Institute of Porto, Porto, Portugal⁷

Background & Aim: Emerging as a class of oral antidiabetic drugs, sodium-glucose cotransporter 2 inhibitors (SGLT2i), used in patients with type 2 diabetes, offer promising results in weight loss, decreasing cardiometabolic biomarkers, thus improving overall cardiac function. The aim of this study is to assess whether SGLT2i can impact food and water consumption, hormone regulating appetite mechanisms, and morphologic parameters. **Methods:** Thirty-nine male ZSF1 rats were divided into two lean (Ln) and two obese (Ob) groups, fed with normal diet (ND) or treated with SGLT2i in food (30 mg/Kg/day). Body weight (BW), food, water, adiponectin and leptin were measured during nine weeks of treatment. Histochemistry analysis was performed with hematoxylin and eosin to determine the cross-section area in visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), and cardiomyocytes. **Results:** SGLT2i treatment promoted an increased food and water intake in lean rats (Ln_ SGLT2i). However, the BW in this group was markedly reduced compared with non-treated lean (Ln_ND). Furthermore, the treatment promoted higher water intake despite no differences in BW in obese rats (Ob_ SGLT2i) compared to control (Ob_ND). Exploring the hormone-regulating appetite mechanisms, SGLT2i treatment showed significant increased in adiponectin levels in both Ln and Ob, however leptin levels only validated the hyperleptinemia in Ob. The ratio adiponectin/leptin was markedly significant increase in Ln_ SGLT2i rats. At the endpoint, the treatment decreased perigonadal fat weight (PFW) in both groups. Aligned with these, cross-section areas of VAT, SAT and cardiomyocytes were markedly increased in Ob, and the treatment decreased these areas in Ob_ SGLT2i. **Conclusions:** SGLT2i treatment increased food and water intake as also the adiponectin/leptin

ratio in Ln. Additionally, the treatment promoted PFW loss and increased the adiponectin levels in both groups and decreased the cross-section area of VAT, SAT, cardiomyocytes in Ob.

Keywords: SGLT2i, Hormone Regulating Appetite, Adiponectin/Leptin Ratio, Cardiac Function.

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