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C24 - PANCREATIC LESIONS AND METABOLIC AGGRAVATION ARE PREVENTED BY LOW DOSES OF SITAGLIPTIN IN A RAT MODEL OF TYPE 2 DIABETES

Mega, C[1,2], Vala, H[2,3], Oliveira, J[2,3], Fernandes, R[1], Mascarenhas-Melo, F[1], Parada, B[1], Pinto, R[4], Teixeira, F[1], Teixeira de Lemos, E[1-3], Reis, F[1]

1 Laboratory of Pharmacology & Experimental Therapeutics, IBILI, Medicine Faculty, Coimbra University, Coimbra; 2 ESAV. 3 Educational, Technologies and Health Study Center, Polytechnic Institute of Viseu, Viseu; 4 Unit of Pharmacology and Pharmacotoxicology, Faculty of Pharmacy, University of Lisbon, Lisbon. Portugal. anacristinamega@gmail.com

Introduction: Management of type 2 diabetes is aimed at reducing disease-related complications and improving long-term outcomes. Inhibition of dipeptidyl peptidase-4 (DPP-4) activity by sitagliptin has been shown to improve glycaemic control in patients with type 2 diabetes Mellitus (T2DM) by prolonging the actions of incretin hormones, but the real impact of low-dose sitagliptin treatment on cardiometabolic risk factors and pancreatic lesions is almost unknown. This study aimed to evaluate the effects of low doses of sitagliptin on cardiovascular risk factors and histological pancreas parameters in Zucker Diabetic Fatty rats (ZDF (fa/fa), an animal model of T2DM.

Materials and Methods: Twenty-week-old diabetic obese (fa/fa) ZDF male rats were treated with vehicle or sitagliptin (10 mg/kg BW/day) for 6 weeks (n=8 each). The following parameters were assessed: glycaemia, HbA1c, insulin, lipid profile; blood pressure. Pancreas specimens for histopathological examination were stained with haematoxylin-eosin and periodic-acid-Shiff and examined under light microscopy. Endocrine and exocrine pancreas were evaluated semiquantitatively for inflammatory infiltrate, fibrosis, vacuolisation and congestion, and scored from 0 (absent) to 3 (severe and extensive damage).

Results: Sitagliptin in diabetic obese ZDF rats exerted a positive effect on dysglycaemia and dyslipidaemia, and prevented increases in blood pressure. Endocrine and exocrine pancreas displayed a reduction/improvement in fibrosis severity, inflammatory infiltrate, intra-islet vacuolation, and congestion with respect to vehicle-treated diabetic rats.

Conclusion: Simultaneous and sustainable improvement in the glycaemic profile and in pancreatic histopathological lesions supports the favorable cardiovascular risk profile and may prove beneficial in reducing the long-term complications of T2DM.

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