

EFFECT OF THE SODIUM-GLUCOSE CO-TRANSPORTER-2 (SGLT2) INHIBITORS ON PLATELET ACTIVATION AND LIPID PEROXIDATION: RESULTS OF A PILOT STUDY.

P. Simeone¹, R. Liani¹, M. Alfonsetti¹, B. Cancelli¹, M. Frezza¹, G. Raggiunti¹, S. Zeeba², F. Cipollone¹, G. Renda², F. Santilli¹.

(1Department of Medicine and Aging Sciences, Center for Advanced Studies and Technology, University of Chieti; ²Department of Neuroscience, Imaging and Clinical Sciences, G D'Annunzio University of Chieti-Pescara; ³University Cardiology Division, Heart Department, Policlinico SS Annunziata) Chieti,.

Background and aim: Sodium-glucose co-transporter-2 inhibitors (SGLT2is), or gliflozins, represent the most recent class of antihyperglycemic agents and have been shown to confer significant cardioprotective effects in patients with and without type 2 diabetes (T2D).

Thromboxane (TX)-dependent platelet activation and lipid peroxidation—reflected in vivo by urinary excretion of 11-dehydro-TXB₂ and 8-iso-prostaglandin (PG)F_{2α}—play a critical role in the development of atherothrombosis in type 2 diabetes mellitus (T2DM). Since oxidative stress and platelet activation play a key role in the development of atherothrombotic complications, we hypothesized that gliflozins may exert modulatory effects on these pathways.

Methods: We conducted a pilot prospective observational study in diabetic patients naïve to gliflozins, in whom these drugs are prescribed according to clinical indications, be-

fore-after interventional study in 20 patients with T2D receiving background therapy with metformin. Oxidative stress and platelet activation, were evaluated at baseline and after 15 days of treatment.

Results: In patients treated with gliflozins, we observed significant reductions markers of platelet activation and oxidative stress: 11-dehydro-TXB₂ ($p = 0.032$) (figure, panel A), 8-iso-prostaglandin (PG)F_{2α} ($p = 0.026$) (figure, panel B). Delta 8-iso-prostaglandin (PG)F_{2α} was directly correlated with delta 11-dehydro-TXB₂ ($\rho = 0.7639$, $p < 0.001$) (figure, panel C).

Conclusions: These findings suggest that gliflozins possess antiplatelet and antioxidants properties, potentially mediated through 11-dehydro-TXB₂ and 8-iso-prostaglandin (PG)F_{2α} downregulation. This mechanism may contribute to the cardiovascular benefits observed with SGLT2i therapy in patients with and T2D.

Email: paola.simeone@unich.it

