AGEs, FGF-23 and Cardiovascular remodeling in Chronic Kidney Disease on Dialysis (CKD-G5D): The Protective Role of sRAGE.

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Introduction. High levels of advanced glycated products (AGEs) and fibroblast growth factor-23 (FGF-23) are recognized as important cardiovascular risk factors. In chronic kidney disease (CKD), FGF-23 increases as a compensatory mechanism to keep normal phosphate and AGEs accumulate due both to the increased formation and reduced elimination. Being by-products of hyperglycemia, the formation of AGEs is further increased in patients with diabetes mellitus (DM). Recently, AGEs have been shown to induce cardiac remodeling in a mouse model of renal failure by promoting FGF-23 expression. Our aim was to explore whether Chronic Kidney Disease on dialysis (CKD-G5D) with DM suffer of an increased cardiac remodeling due to the to increased AGEs formation and the further amplification of the FGF-23 response.

Methods. We quantified plasma levels of glycated albumin (GA), sRAGE, the decoy receptor for AGEs, c-terminal FGF-23 (cFGF23), brain natriuretic peptide (BNP) and the inflammatory mediators C-reactive protein, tumor necrosis factor alpha and pentraxin-3 in 24 CKD-G5D patients with DM and 52 without DM.

Results. The levels of sRAGE, cFGF-23, BNP and the pro-inflammatory markers evaluated were over the ranges of normality in both DM and non-DM groups. GA and sRAGE were increased in DM CKD-G5D compared to non-DM CKD-G5D patients but cFGF-23 did not differ between the two groups. Similarly, the concentrations of the pro-inflammatory molecules and BNP were almost the same in the two groups.

Conclusions. The up-regulation of sRAGE could be a counteract-system against glycated products. sRAGE, by blocking glycated products, could reduce the activation of various damaging cellular mechanisms, including an increased stimulation of cFGF-23and inflammatory mediators. Indeed, since AGEs accumulation is a risk factor for development and progression of heart failure, the lack of difference also in BNP levels between the two groups reinforces the hypothesis of a protective role of sRAGE in DM CKD-G5D patients.