Endocrinología, Diabetes y Nutrición

CO-001 - MITOCHONDRIAL OXIDATIVE STRESS IMPACT ON THE IMMUNE SYSTEM AS A BOOSTER OF CVD RISK IN T2D

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Resumen

Introduction and objectives: We aimed to evaluate if non-invasive blood tests based on the evaluation of immunometabolic biomarkers could be used for CVD risk assessment in T2D subjects.

Material and methods: We recruited a cohort of well controlled T2D patients of both sexes and monitored for early signs of CVD through the evaluation of carotid thickness (IMT) by ultrasound. The patients were classified as normal (N) or abnormal (A) based on IMT values bellow or over 0.8 mm respectively. Blood samples were collected and separated into plasma and PBMCs.

Results: The subjects with abnormal IMT showed higher levels of circulating oxidated DNA and lower mtDNA content in PBMCs than normal IMT subjects suggesting increased mitochondrial dysfunction in these subjects. Consistently, targeted gene expression analysis of PBMCs further showed that subjects with abnormal IMT had significantly lower expression levels of SOD2 a mitochondrial antioxidant than normal IMT subjects, indicative of poor mitochondrial antioxidant control. Nevertheless, systemic antioxidant capacity was not reduced in abnormal IMT subjects as indicated by the evaluation of total antioxidant capacity in plasma samples. These alterations were associated with a significantly increased ND4/ND1 mitochondrial-gene ratio in abnormal IMT subjects detectable in plasma samples, suggesting increased mtDNA instability in these subjects. Furthermore, gene expression correlation analysis of PBMCs samples showed that the adjusted linear regression of PDK4, fatty acid oxidation biomarker, with PRDX3, a mitochondrial oxidative stress biomarker, was significantly altered in abnormal IMT subjects, that displayed higher PRDX3 levels for an any given PDK4 value than normal IMT subjects, further indicating the presence of enhanced mitochondrial oxidative stress in abnormal IMT subjects. Importantly, the evaluation of inflammatory markers showed that the expression levels of the anti-inflammatory cytokine IL-4 were significantly lower in PBMCs of abnormal IMT subjects and the correlation analysis with PDK3 showed a similar pattern to that observed with PDK4, suggesting that enhanced mitochondrial oxidative stress may be related to the lower IL-4 levels observed in abnormal IMT subjects.

Conclusions: IMT is associated with increased signs of mitochondrial dysfunction, oxidative stress and mtDNA damage that may be related with an altered inflammatory profile that could be relevant in CVD development in T2D subjects despite of the preservation of a good control of glucose levels.