Endocrinol Diabetes Nutr. 2023;70(Suplemento 4):18

Endocrinología, Diabetes y Nutrición

CO-018 - INTRACELLULAR PRODUCTION OF HYDROGEN SULFIDE REPRESENTS A KEY ROLE IN LIPID METABOLISM IN INSULIN TARGET TISSUES

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Resumen

Introduction and objectives: Hydrogen sulfide (H_2S) is a gasotransmitter, that plays a relevant function in the regulation of glucose and lipid metabolism, with a potential role on diabetogenesis. H_2S could modulate the activity of different types of proteins, such as membrane ion channels, enzymes and transcription factors. Several studies indicate that obese and diabetic individuals have lower blood levels concentrations of H_2S than non-obese/non-diabetic patients, suggesting that this molecule plays a significant role in the survival and functionality of metabolic tissues. This study aimed to evaluate the functional and mechanistic effects of the modulation of intracellular H_2S production on insulin sensitivity.

Materials and methods: We determined the effects of the overexpression by lentivirus infection, and the reduction of the expression by small interfering RNA (siRNA) of the main genes involved in H_2S synthesis, cystathionine-β-synthase (CBS), and cystathionine gamma-lyase (CTH) on 3T3L1 mature adipocytes and mouse primary hepatocytes. Our experiments were focused on evaluating the mitochondrial coupling (in vivo monitoring of oxygen consumption/extracellular acidification of the media), insulin-stimulated glucose uptake, lipolysis, metabolic activity (MTT test, lipid content using Oil Red O staining) and determination of H_2S production.

Results: CTH and CBS is required for the accumulation and maintenance of lipid content in adipocytes and hepatocytes. CTH interference reduces the expression of genes involved in liponeogenesis in hepatocytes and adipocytes. Remarkably, reduction of CBS expression is not associated with alterations in mitochondrial metabolism, while CTH interference is associated with reduced maximal oxygen consumption in hepatocytes.

Conclusions: These results indicate a relevant role of CBS and CTH in lipid metabolism in insulin target tissues. Moreover, alteration of CTH expression resulted in reduced mitochondrial functional dynamics in hepatocytes.