Endocrinología, Diabetes y Nutrición

P-002 - RELEVANCE OF THE MICROBIOTA IN THE PHYSIOLOGICAL/MOLECULAR EFFECTS OF ENHANCED INTRACELLULAR HYDROGEN SULFIDE PRODUCTION

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Resumen

Introduction and objectives: Hydrogen sulfide (H_2S) is a gasotransmitter with the ability to freely diffuse through cell plasmatic membranes to induce intracellular signaling responses. Production of H_2S in cells can be generated by enzymatic and non-enzymatic mechanisms. However, some gut bacteria also can produce H_2S. The aim of this work is to understand the role of gut microbiota in the mechanisms altered by enhanced production of H_2S.

Material and methods: We used 4-month old C57/Bl6 wild type mice treated or not with antibiotics (microbiota free; MF) to deplete the microbiota during 6 months. In addition, both groups (MF and control) were treated or not with compound-? to enhance intracellular H_2S production. Body weight and food intake of mice were monitored weekly. Health status was measured by neurocognitive test and physical test. Furthermore, we also evaluated the effect of compound-? on glucose homeostasis. Enzymatic H_2S production was measure in liver by lead acetate method. On the other hand, we evaluated the survival, viability and effects in mitochondrial dynamics of primary hepatocytes treated with the serum of the mice after 6 months of treatment.

Results: Compound-? has the ability to reduce body weight and white adipose tissue mass independently of the presence or absence of microbiota. At a neurocognitive level, compound-? enhances odor discrimination and increases the conditioned response in mice. In functional capacity test, compound-? increases the resistance in mice and enhances wire hang performance in mice with microbiota. Insulin sensitivity was improved by compound-? regardless of the presence or absence of microbiota. Curiously, mice treated with antibiotics exhibited enhanced glucose and insulin tolerance, with no visible effects of compound-?. In addition, liver H_2S enzymatic production was increased in mice treated with antibiotics. Finally, primary hepatocytes treated with serum of mice supplemented with compound-? increased cell death. Moreover, basal oxygen consumption rate (OCR) and extracellular acidification rate (ECAR) were reduced by serum of control mice treated with compound-?. Serum of MF groups also reduced OCR and ECAR in primary hepatocytes.

Conclusions: Our results show that potentiation of sulfur metabolism has therapeutic potential, improving the neurocognition, physical health and insulin sensitivity. Furthermore, the microbiota was not required for the beneficial effects of compound-? in several neurocognitive and physical test. Finally, compound-?-induced

modulation of serum composition altering mitochondrial metabolism of primary hepatocytes.