WEIGHT REDUCTION DECREASES EXPRESSION OF GENES INVOLVED IN NFKAPPA-B PATHWAY IN PERIPHERAL BLOOD MONONUCLEAR CELLS IN SUBJECTS WITH THE METABOLIC SYNDROME

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Background and aims: The transcription factor NFÎB is implicated in inflammatory responses. Genes involved in the NFÎB pathway have been related to insulin resistance, obesity and the metabolic syndrome (MS). We evaluated how moderate weight reduction (WR) affected the expression of genes involved in the NFÎB pathway in peripheral blood mononuclear cells (PBMCs) and their association with insulin and glucose metabolism.

Methods: Data from 34 (32.6±3.1 kg/m²) subjects with abnormal glucose metabolism and the MS were analyzed. Subjects were randomized to a WR (n=28) or control group (n=18) for 33 weeks. Assessments were done at baseline and wk 33. An intravenous glucose tolerance test was performed. Quantitative real-time PCR was used for gene expression analysis (WR: n=24, control group: n=10). Results are expressed in arbitrary units related to an endogenous control gene (GAPDH).

Results: WR decreased mRNA levels of TNF receptors (TNFR) 1 and 2 (TNFR1: 1.27±0.35 vs. 1.20±0.29, TNFR2: 1.10±0.22 vs. 0.94±0.25, $p<0.05$). IL1 receptor I (IL1RI) and toll-like receptor 4 (TLR4) expression also decreased in the WR group (IL1RI: 1.19±0.49 vs. 1.12±0.38, TLR4: 1.18±0.31 vs. 1.02±0.22, $p<0.05$). After adjusting for changes in body weight, the decrease in TNFR1 and TLR4 expression were correlated with the increase in the insulin sensitivity index ($r=-0.57$ and $r=-0.43$, $p<0.05$).

Conclusions: Long-term moderate weight loss decreased gene expression of receptors involved in NFκB pathway in PBMCs. These changes were related to the improvement in insulin sensitivity, suggesting an immunomodulatory effect of insulin and glucose metabolism on genes related to inflammation and insulin resistance.