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Adipose Tissue, Appetite, & Obesity

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Expression of Vitamin D Receptor Pathway Genes Across Tissues of Individuals with Obesity

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Introduction: Vitamin D deficiency is a substantial comorbidity in 50% of pediatric patients and is linked with poorer health outcomes in children. Vitamin D levels are inversely related to BMI. Therefore, the prevalence of children with low vitamin D levels is increasing as the prevalence of pediatric obesity increases. Pediatric patients with obesity and vitamin D deficiency also have a uniquely increased risk of metabolic syndrome, as compared to their lean peers. However, measured levels of vitamin D correlate with other physiological markers of vitamin D effects in lean individuals but not obese individuals. Since vitamin D levels measured as 25-hydroxyvitmain D (serum 25(OH)D) reflect a storage form of vitamin D, their levels may not be a true reflection of vitamin D action in the body in an obese population. The aim of this study was to provide foundational knowledge to understand if expression of vitamin D receptor (VDR)-target genes in different metabolic pathways correlate with each other in diverse tissues, and thus may be used as a reference standard for vitamin D action in the body.

Methods: We performed a secondary analysis of samples obtained from 89 obese adolescents aged 12 to 18 years old that were consented under a past IRB-approved protocol. The samples were collected at the time of bariatric surgery between 2004 and 2019. Subject data included age, gender, race/ethnicity, and BMI. Samples collected included blood, intestinal, and subcutaneous adipose tissue. The tissues were analyzed via Real Time-PCR to obtain quantitative levels of VDR-target gene expression, which included TLR4, THBD, and VDR in subcutaneous adipose tissue; and TRPV6, S100G, and VDR in intestinal tissue. Gene expression levels were normalized to the average of two housekeeping genes, GAPDH and RPLPO. Blood samples were analyzed for vitamin D levels.

Results: VDR-target gene expression of THBD, VDR, and TLR4 in subcutaneous adipose tissue was significantly correlated ($p < 0.05$). In intestinal tissue, we also saw significant correlation between TRPV6, S100G, and VDR ($p < 0.05$). THBD, TLR4, TRPV6, S100G, and VDR gene expression levels from the respective tissues did not correlate with circulating serum 25(OH)D levels ($p > 0.05$).

Conclusion: These important preliminary findings show VDR-target genes have correlated expression patterns within different tissues – one which stores vitamin D (adipose) and one which doesn't (intestinal). Interestingly, the VDR-target gene expression levels correlated with each other despite the genes being involved in different metabolic pathways in diverse tissues. These findings also show that VDR-target gene expression does not correlate with circulating serum 25(OH)D levels. This discrepancy supports that 25(OH)D levels do not indicate levels of vitamin D action and may not be an appropriate indicator of vitamin D deficiency in the obese population. Thus, VDR-target gene expression levels may provide a better reference standard for vitamin D action in the body. This study may provide the first step in determining a new and more accurate biomarker for vitamin D deficiency and treatment in obesity.

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