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Study of Endothelial Dysfunction in Children with Obesity and Rare Genetic Variants

Background: Endothelial dysfunction (ED) is an early feature atherosclerosis and is a well-established predictor of cardiovascular disease. This novel study investigates the relationship between ED in children with rare genetic obesity variants.
Objective: To determine the difference in ED in children with rare genetic variants to a control group.
Methods: In our endocrinology clinic, under IRB-approved protocol, we measured ED using EndoPat® in children with obesity (BMI ≥95%), ages 1-21 years who have obesity related gene variants (PCNT, BBS, SEMA3, MC4R, ALMS1, and SDCCAG8), compared to controls. EndoPAT® non-invasively measures Reactive Hyperemia Index (RHI, ref >1.67) by analyzing pulse wave amplitudes in response to transient ischemia. We used descriptive statistics and t-tests for comparisons between two groups.
Results: We assessed endothelial function in 24 (17 females, 7 males). Among them, 21 tested positive for variants, while 3 tested negative, with mean age 14 years, BMI 33.31 kg/m2, A1c 5.5% and insulin level 42 mIU/L. The most common variants were PCNT (n=5), BBS (n=4), ALMS1 (n= 4), SH2B1 (n= 3), and SDCCAG8 (n= 3). No difference was found between positive genetic variants and controls (p=0.8335, RHI 1.0367 ± 0.2639 (SD) vs 1.1200 ± 0.3509 respectively [CI -1.5850 to 1.4184]). PCNT group had higher RHI (p=0.02, mean RHI 1.34 ± 0.10 vs 1.12 ± 0.30, respectively). Conversely, RHI in BBS, ALMS1, SH2B1, and SDCCAG8 were not statistically different compared to their controls.
Conclusion:
In this small pilot study, there was no difference in endothelial function between the two groups with genetic variants and without. A limitation is the small control group. However, within the genetic variant group, a significant difference in RHI was observed for PCNT variant, which is contrary to our expectation. PCNT had higher RHI than those without the variant. Further research is needed to investigate ED in children with obesity variants.