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An anti-inflammatory nutritional intervention selectively improves insulin sensitivity in overweight and obese adolescents wherein baseline metabotype predicts response

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Anti-inflammatory nutritional approaches may attenuate obesity-induced inflammation and insulin resistance[(1)]. However, results from randomised controlled trials are not entirely consistent[(2,3)], warranting increased focus on determinants of inter-subject variability particularly within young cohorts at high-risk. Baseline metabotype may partially discriminate responders from non-responders.

Metabolic effects of an anti-inflammatory nutritional supplement containing LC n-3 PUFA, vitamin C, vitamin E, and polyphenols, were determined in overweight and obese adolescents ($n = 58$; mean (SD) age 15.9(1.6) y; BMI 32.1(6.5) kg/m^2) by an 8-wk randomised, crossover, placebo-controlled intervention. Subjects who demonstrated >10% improvement in HOMA-IR were categorised as responders.

Anti-inflammatory nutritional supplementation selectively reduced HOMA-IR in40% of subjects (responders; supplement –32.05 (18.02)% v placebo 13.13(54.09)%, $p = 0.004$).In comparison with non-responders, responding subjects demonstrated an adverse pre-treatment metabotype characterised by increased HOMA-IR, total cholesterol and LDL cholesterol despite similar BMI ($p = 0.001$, $p = 0.029$, $p = 0.024$, $p = 0.236$, respectively). Stepwise multiple regression analysis confirmed baseline HOMA-IR, LDL:HDL ratio and CD163, as well as delta adiponectin and delta CD163as significant independent predictors of HOMA-IR response to anti-inflammatory supplementation ($R^2 = 0.673$, $p < 0.001$). On-going analysis is defining the molecular basis of the differential response.

These results demonstrate heterogeneity with respect to the insulin sensitising effects of anti-inflammatory nutritional supplementation. Despite similar BMI to non-responders, the insulin resistant and dyslipidaemic metabotype of responders enhanced the impact of anti-inflammatory nutritional approaches. This illustrates potential efficacy optimisation within the context of personalised nutrition. This trial was registered at clinicaltrials.gov as NCT01665742.

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