

## The association between dietary macronutrient intake and fibrogen growth factor 21 in a sample of White UK adults with elevated cardiometabolic risk markers

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Increased levels of Fibrogen growth factor 21 (FGF21) is an emerging risk marker for cardiometabolic (CM) disease<sup>(1)</sup>. Little detail is known about the impact of the human diet on FGF21 levels. The aim of this investigation was to assess potential associations between mean daily dietary macronutrient intake and FGF21 levels in a sample of 10 healthy normal-weight and overweight Caucasian adults aged 32–60 (80 % male) at increased CM risk<sup>(2)</sup>. This pilot study received ethical approval from Liverpool John Moores University Research Ethics Committee (16/ELS/029) and was registered with ClinicalTrials.gov (Ref. NCT03257085).

Participants were randomly allocated to one of two groups and asked to either consume <50 g/d of dietary CHO (low-carb (LC)) or to follow the UK dietary guidelines and obtain >50 % energy from CHO for a duration of 8 weeks. Blood plasma samples were collected at baseline (BL), interim point (IP) and endpoint (EP) after a 12-hour overnight fast, immediately processed and frozen at –80°C. Thawed plasma samples were analysed via Quantikine<sup>®</sup> enzyme-linked immunosorbent assay (ELISA) (R&D Systems) for FGF21 levels. Two-way mixed ANOVA and Pearson’s partial correlation adjusted for estimated weekly moderate and vigorous activity was undertaken using IBM SPSS 24<sup>®</sup>.

There were no effects for diet between groups or over time (data not shown). Significant correlations between macronutrient intakes and FGF21 levels were found for both groups at IP, but not at BL or EP. Moderate and significant positive correlations were found in the overall group for intake (g/d) for glucose ( $r_{\text{partial}} = .699$ ,  $p = .04$ ) and fructose ( $r_{\text{partial}} = .686$ ,  $p = .04$ ) and strong and significant positive correlations for non-milk extrinsic sugars ( $r_{\text{partial}} = .742$ ,  $p = .02$ ). Strong and significant positive correlations were also found in the LC group for glucose intake (g/d) ( $r_{\text{partial}} = .980$ ,  $p = .02$ ) and fructose ( $r_{\text{partial}} = .967$ ,  $p = .03$ ) and for protein ( $r_{\text{partial}} = .998$ ,  $p = .002$ ) after adjusting for physical activity. Mean carbohydrate intake (g/d) was 160.0 (s.d. 124.5) overall and 44.2 (s.d. 14.9) in the LC group at IP. Mean protein intake (g/d) was 113.2 (21.4) 130.0 (s.d. 15.9) overall and in the LC group at IP. Mean FGF21 levels were 179.9 pg/mL (s.d. 144.9) in the overall group and 94.4 pg/ML (s.d. 48.6) in the LC group at IP.

	Total kcal r	%TE				Intake (g/d)					
		CHO r	NMES r	PROT r	FAT r	CHO r	GLU r	FRU r	NMES r	PROT r	FAT r
T	-.214	.623	.635	-.326	-.491	.448	.699*	.686*	.742*	-.606	-.496
LC	.143	.637	.937	.427	-.059	.722	.980*	.967*	.919	.998**	-.080

CHO-Total carbohydrates, FAT-Total fat, FRU-Fructose, GLUC-Glucose, LC-low-carbohydrate, high-fat group, NMES-non-milk extrinsic sugars, PROT-protein, T – total, %TE – percentage total energy, \* $p < .05$  \*\* $p < .005$ .

In conclusion, low-carbohydrate diets provide the opportunity to assess responses to even small amounts of CHO, which are likely to be replaced in part by proteins. Despite low overall intakes of fructose and glucose in the LC group, strong and positive correlations with FGF21 levels were observed. The lower levels of FGF21 in the LC compared to the overall group are in line with findings that FGF21 levels are elevated with high-carbohydrate, low-protein diets with dietary fats having only minor impact<sup>(3)</sup>. However, the majority of studies have still been undertaken using rodent models. The impact of dietary macronutrients on FGF21 levels as novel CMR marker in humans and the mechanism behind this relationship warrant further investigation.

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