

ASSOCIATION OF SERUM FIBROBLAST GROWTH FACTOR 21 AND IRISIN WITH INSULIN SENSITIVITY MARKERS AND SERUM LIPIDS IN 12-YEAR-OLD CHILDREN

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Satu Seppä^a, Sirpa Tenhola^{a,b} and Raimo Voutilainen^a

^aDepartments of Pediatrics, Kuopio University Hospital and University of Eastern Finland, Kuopio

^bDepartment of Pediatrics, Kymenlaakso Central Hospital, Kotka, Finland

The authors have nothing to disclose

BACKGROUND

Among other cytokines, the hepatokine fibroblast growth factor 21 (FGF21) and the myokine irisin have been considered potential biomarkers for insulin sensitivity (IS). In adult studies, both of them have been found elevated in insulin resistant states.

OBJECTIVE AND HYPOTHESES

Our aim was to study whether serum FGF21 and irisin associate with markers of IS and serum lipids in 12-year-old children.

METHODS

A total of 192 children (109 girls) were studied at the mean age of 12.25 years (range 12.01-12.73). Seventy eight of them had been born appropriate for gestational age (AGA), 70 small for gestational age (SGA), and 44 from preeclamptic (PRE) pregnancies as AGA (Table 1). Fasting serum FGF21, irisin, insulin, HDL cholesterol (HDL-C), triglycerides (TG), high-sensitivity (hs)-CRP, gamma-glutamyltransferase (GGT) and leptin were measured. IS was estimated by Quantitative Insulin Sensitivity Check Index (QUICKI).

RESULTS

The means of serum FGF21 and irisin did not differ between the sexes or between the children born SGA, AGA or from PRE pregnancies ($p > 0.05$ for all). In the whole study population,

Table 2. Associations between serum FGF21, irisin and other metabolic variables

Variable	n	FGF21		Irisin	
		beta ^a	p	beta ^a	p
FGF21	192	-	-	0.088	0.001
Irisin	192	0.630	0.001	-	-
Insulin	192	0.093	NS	0.341	<0.001
QUICKI	192	-0.501	NS	-2.516	0.001
HDL-C	192	-0.602	0.043	-0.020	NS
TG	192	0.236	NS	0.154	0.041
hs-CRP	188	0.022	NS	0.072	0.003
GGT	191	0.510	NS	0.536	0.003
Leptin	192	-0.262	0.024	0.003	NS
Age- and sex-adjusted BMI	192	-0.003 ^b	NS	0.020 ^b	NS
Waist-to-height ratio	192	-0.232 ^b	NS	0.103 ^b	NS

Skewed variables were logarithmically or square root -transformed before testing
^a General linear model adjusted for sex, pubertal developmental stage (G/B 1-5), birth weight SDS, maternal PRE pregnancy history and age- and sex-adjusted BMI
^b General linear model adjusted for sex and pubertal developmental stage (G/B 1-5)

Table 1. Anthropometric measures at birth and at the examination. The means (SD) are presented

Variable	All (n=192)	AGA (n=78)	SGA (n=70)	PRE (n=44)
At birth				
Gestational age (wk)	37.7 (3.2)	38.0 (3.3)	37.6 (3.1)	37.2 (3.2)
Weight (g)	2769 (754)	3158 (696)	2238 (507)	2926 (698)
Weight (SDS)	-1.14 (1.34)	-0.23 (0.97)	-2.52 (0.57)	-0.57 (0.92)
Length (cm)	47.3 (3.8)	48.9 (3.5)	44.9 (3.0)	48.2 (3.3)
Length (SDS)	-0.88 (1.47)	-0.02 (1.05)	-2.30 (0.94)	-0.14 (0.98)
At the examination				
Age (yr)	12.25 (0.17)	12.28 (0.16)	12.23 (0.18)	12.24 (0.15)
Weight (kg)	44.2 (10.64)	47.3 (11.98)	40.3 (8.17)	44.8 (9.80)
Age- and sex-adjusted BMI (kg/m ²)	21.5 (3.85)	22.1 (4.25)	20.4 (3.56)	21.9 (3.24)
Waist-to-height ratio	0.43 (0.06)	0.44 (0.06)	0.42 (0.05)	0.44 (0.05)
Height (cm)	153.1 (7.6)	155.9 (7.2)	150.1 (7.1)	153.1 (7.4)
Height (SDS)	0.26 (1.03)	0.63 (0.96)	-0.19 (0.96)	0.33 (0.98)

serum FGF21 had a positive association with irisin (beta=0.630, $p=0.001$) and negative associations with leptin (beta=-0.262, $p=0.024$) and HDL-C (beta=-0.602, $p=0.043$) [general linear model (GLM) analysis adjusted for sex, pubertal developmental stage, age- and sex-adjusted BMI, birth weight SDS and maternal PRE pregnancy history] (Table 2). Apart from FGF21, serum irisin associated positively with insulin (beta=0.341, $p < 0.001$), hs-CRP (beta=0.072, $p=0.003$), GGT (beta=0.536, $p=0.003$) and TG (beta=0.154, $p=0.041$), and negatively with QUICKI (beta=-2.516, $p=0.001$) (Table 2). In a ROC curve analysis, irisin was able to weakly discriminate the children in the lowest QUICKI tertile [area under the ROC curve (AUC) 0.624 (95% CI 0.541-0.708), $p=0.005$], whereas neither irisin nor FGF21 could identify the children with the highest TG/HDL-C ratio.

CONCLUSION

In 12-year-old children, serum irisin was associated with triglycerides and markers reflecting reduced IS, whereas FGF21 was associated negatively with HDL-C and leptin independently of BMI. In ROC curve analyses, irisin could weakly distinguish the children with the lowest IS, whereas neither irisin nor FGF21 could detect the children with markers of dyslipidemia.

