SIRT1 and SIRT2 gene expression in peripheral blood mononuclear cells of obese children and adolescents and their relationship with metabolic parameters and insulin resistance

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Introduction

Sirtuins are highly conserved NAD^+-dependent protein deacetylases and/or ADPribosyl transferases that target histones, transcription factors, co-regulators, as well as metabolic enzymes to adapt gene expression and metabolic activity in response to the cellular energy state. SIRT1 and SIRT2 are two of seven sirtuin enzymes that are poised at the center of regulation of metabolism. SIRT1 has an important role in glucose metabolism and improves glucose homeostasis. It can also regulate fatty acid oxidation and hepatic cholesterol and bile acid homeostasis. SIRT2 has an antioxidant activity and negatively regulates insulin resistance.

Methods

60 children and adolescents (30 obese and 30 age and gender matched control subjects), between the ages of 8 and 15 years, were selected and clinically evaluated. PBMCs were separated and their total RNA were extracted. After cDNA synthesis, SIRT1 and SIRT2 gene expression were analyzed by real-time PCR. Relative difference in gene expression was calculated by ΔCt method using β-actin as a normalizer. Serum insulin was measured using ELISA, and insulin resistance (IR) was calculated by the Homeostasis Model of Assessment of Insulin Resistance (HOMA-IR). Fasting plasma glucose (FPG), triglyceride (TG), total cholesterol (TC), LDL-C and HDL-C were also measured. Metabolic syndrome (MetS) was determined according to IDF criteria.

Results

Expression of SIRT1 gene was significantly diminished in obese subjects compared to control one. It was also significantly lower in obese children with IR compared to obese children without IR (0.33± 0.079 vs. 0.97± 0.17, respectively) (P=0.008). There was a trend toward a lower SIRT2 expression in obese subjects but the difference was not significant. SIRT1 expression was significantly correlated with BMI and waist circumference as well as insulin and MOMA-IR. SIRT2 was significantly correlated with SIRT1 and HDL-C.

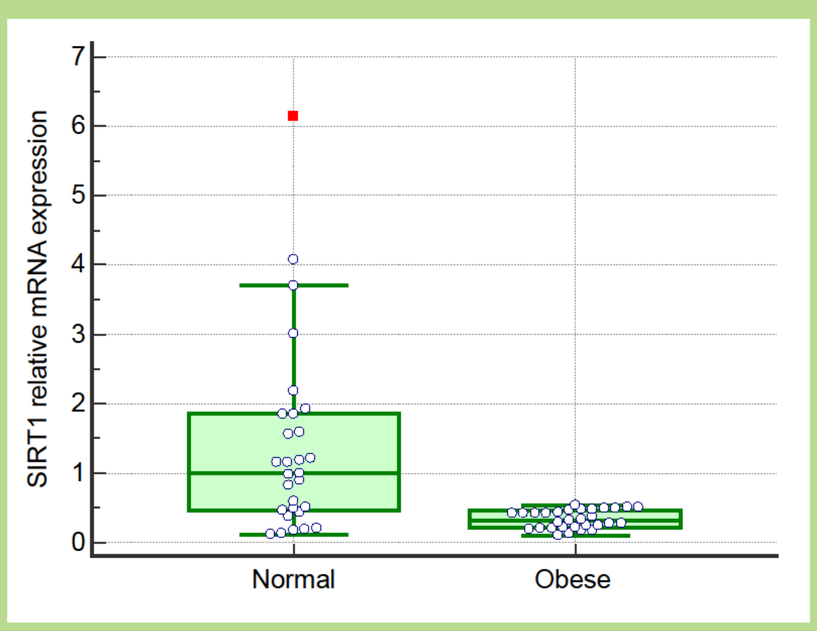
Table 1- anthropometric and biochemical characteristics

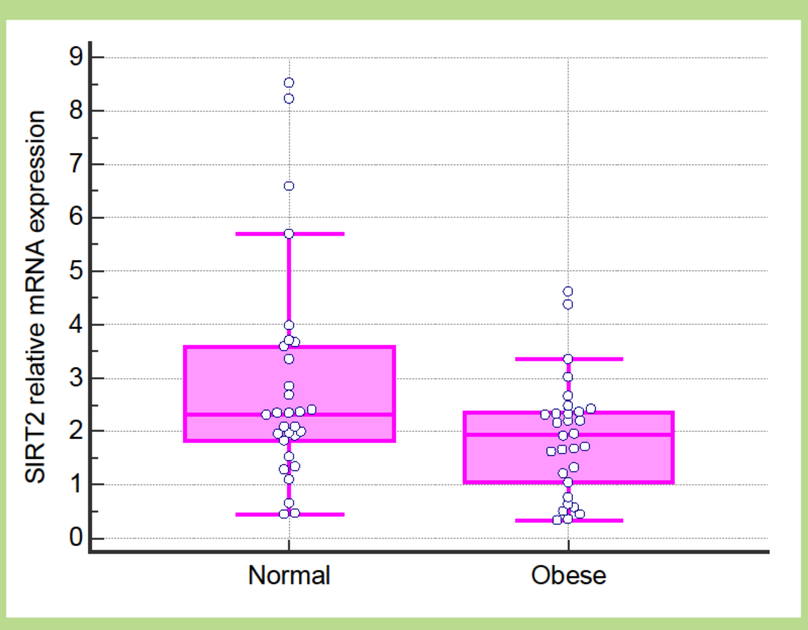
	Control	Obese	P value
Age (years)	11.19 ± 2.43	11.22 ± 2.41	n.s.
BMI z-score	0.02 ± 0.14	2.25 ± 0.05	< 0.001
WC (cm)	66.93 ± 7.9	93.65 ± 12.34	< 0.001
W/H ratio	0.85 ± 0.01	0.94 ± 0.01	< 0.001
SBP (mmHg)	111.4 ± 10	127.2 ± 16	< 0.001
DBP (mmHg)	72.4 ± 7.6	79.7 ± 9.9	< 0.01
FPG (mg/dl)	86.93 ± 10.55	93.86 ± 5.65	< 0.001
TG (mg/dl)	81.5 ± 42.5	110.06 ± 42.91	0.002
TC (mg/dl)	155.3 ± 27.6	164.93 ± 25.64	0.167
LDL-C (mg/dl)	75.43 ± 13.79	83.56 ± 16.61	0.044
HDL-C (mg/dl)	54.73 ± 13.15	47.13 ± 9.35	0.038
Insulin (µIU/dl)	6.34 ± 3.29	14.55 ± 9.82	< 0.001
HOMA-IR	1.39 ± 0.81	3.37 ± 2.25	< 0.001
SIRT1	1.37± 0.25	0.33± 0.02	< 0.001
SIRT2	1.88± 0.19	2.83± 0.36	0.057

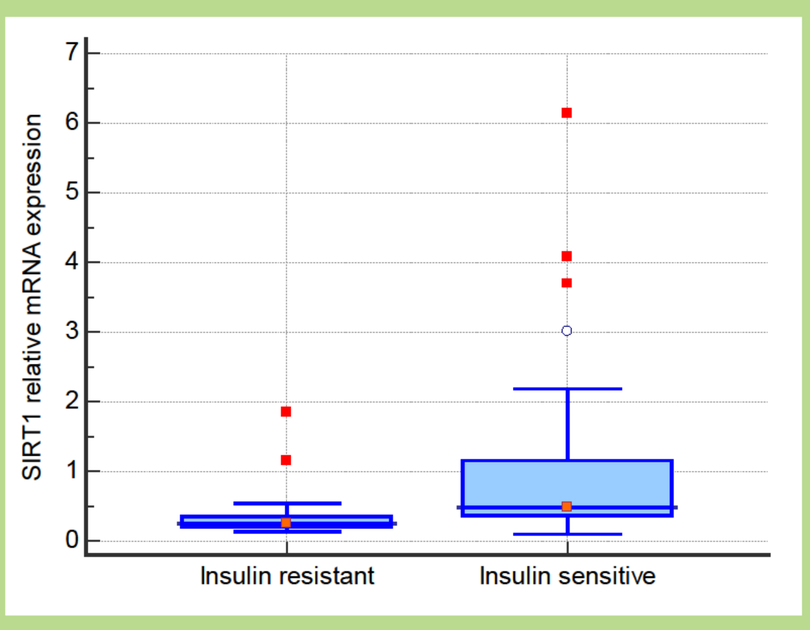
Table 2- correlations of SIRT1 and SIRT2 with metabolic parameters.

	SIRT1	SIRT2
BMI (kg/m²)	0.41**	-0.16
BMI z-score	0.35**	-0.10
FPG (mg/dl)	0.10	0.04
TG (mg/dl)	0.04	-0.03
TC (mg/dl)	0.15	0.18
LDL-C (mg/dl)	0.18	0.04
HDL-C (mg/dl)	0.01	0.39*
Insulin (µIU/dl)	-0.31*	-0.201
HOMA-IR	-0.31*	-0.19

* P<0.05; ** P<0.01







Conclusion

SIRT1 but not SIRT2 gene expression is decreased in obesity and is associated with insulin resistance in children and adolescents. Targeting SIRT1 can be valuable in treating obesity and insulin resistance in childhood and adolescence.

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