Association of miR-34a and mir-149 with obesity and insulin resistance in obese children and adolescents

Mitra Nourbakhsh[1], Fatemeh Ahmadpour[1], Shahnaz Khaghani[2] , Maryam Razzaghy Azar[3,4]

[1]Department of Biochemistry, School of Medicine, Iran University of Medical Sciences, Tehran, Iran; [2]Department of Biochemistry, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran; [3]Metabolic Disorders Research Center, Endocrinology and Metabolism Research Institute, Tehran University of Medical Sciences, Tehran, Iran; [4]H. Aliasghar Hospital, Iran University of Medical Sciences, Tehran, Iran

Introduction

Obesity is a major public health problem and its rate is increasing worldwide. Obesity accompanies perturbations in metabolism, conferring substantial excess risk for insulin resistance and Type 2 diabetes. Various genetic and epigenetic factors contribute to the development of obesity. MicroRNAs (miRNAs) are short noncoding RNAs involved in post-transcriptional regulation of gene expression and influence many cellular functions including glucose and lipid metabolism and adipocyte differentiation. miRNAs have been shown to be involved in obesity but their role in this regard is not clearly defined.

Objective and hypotheses

The aim of this study was to evaluate the levels of miR-34a and miR-149 and their association with metabolic parameters in obese children and adolescents.

Methods

Seventy children (35 obese and 35 control) (8–18 years) were included in the study. The miRNA fractions were isolated from plasma and elongated by poly A tailing using E. Coli poly A polymerase. The resulting miRNA was reverse transcribed into cDNA, amplificated by Real time PCR using miRNA-specific primers and detected by SYBR green. Data were normalized with cel-miR-39 and compared with ΔCt method . Concentrations of visfatin and insulin in plasma were measured by ELISA method. Glucose and lipid profile were determined colorimetrically. HOMA-IR was calculated and used as an index of insulin resistance.

Results

miR-34a levels was significantly lower in children with insulin resistance compared to those without insulin resistance (Fig.1). There was an inverse relationship between miR-34a levels and both insulin (Fig.2) and HOMA-IR (Fig.3). On the other hand, miR-149 was significantly correlated with visfatin. There was no significant difference in miR-34a and miR-149 between obese and normal weight subjects. Visfatin was significantly elevated in obese children compared to control subjects and was correlated with glucose, insulin and HOMA-IR.

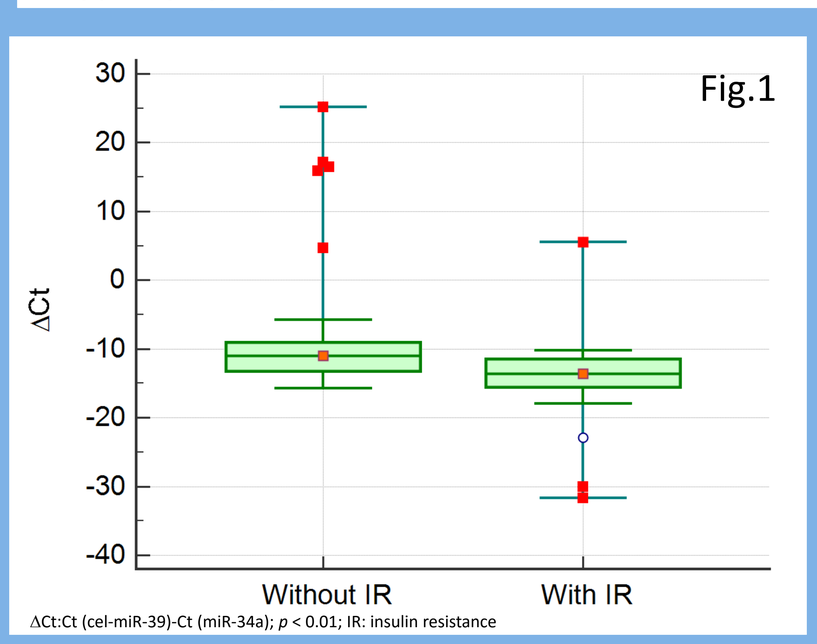
Table 1- anthropometric and biochemical characteristics

	Control	Obese	P value
Female/male	21/14	20/15	n.s.
Age (years)	11.42 ± 2.18	10.95 ± 2.73	n.s.
BMI	18.41 ± 2.64	28.12 ± 5.7	< 0.001
BMI z-score	0.683 ± 0.91	2.09 ± 0.45	< 0.001
WC (cm)	61.65 ± 6.57	84.80 ± 13.45	< 0.001
W/H ratio	0.78 ± 0.47	0.87 ± 0.89	< 0.001
SBP (mmHg)	95.43 ± 11.96	101.14 ± 14.50	< 0.001
DBP (mmHg)	68.57 ± 8.7	72.57 ± 12.21	< 0.001
FPG (mg/dl)	90.0 ± 4.9	92.05 ± 6.54	< 0.001
TG (mg/dl)	73.94 ± 31.9	126.6 ± 69	0.001
TC (mg/dl)	148.65 ± 19.1	171.54 ± 24.9	0.001
LDL-C (mg/dl)	75.80 ± 13.1	92.48 ± 16.8	0.024
HDL-C (mg/dl)	54.60 ± 7.5	47.65 ± 95	0.036
Insulin (µIU/dl)	7.74 ± 10.1	19.77 ± 9.6	< 0.001
HOMA-IR	1.75 ± 2.4	4.50 ± 2.2	< 0.001
visfatin	1/49 ± 0/9	2/08 ± 1/03	< 0.001

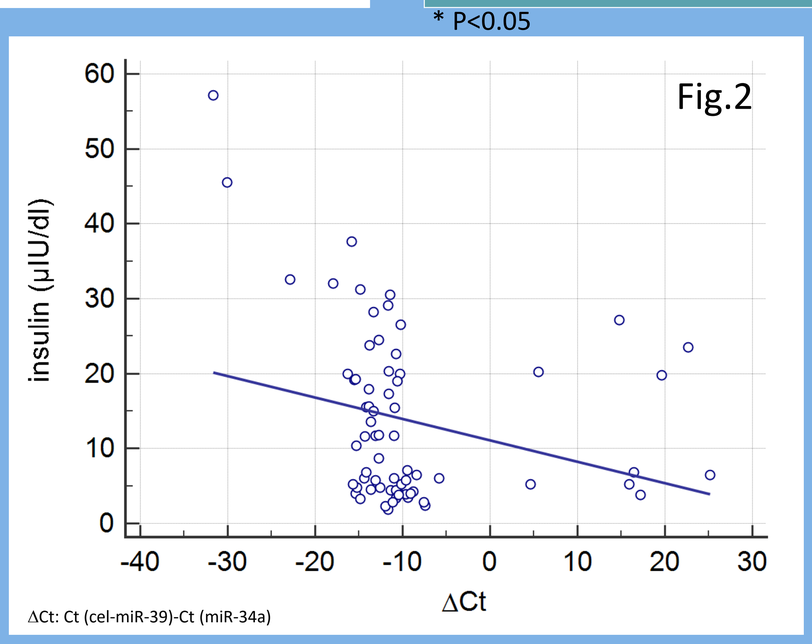
Table 2- correlations of miR-34a and miR-149 with metabolic parameters.

	miR-34a	miR-149
BMI (kg/m²)	-0.117	-0.049
BMI z-score	0.05	0.035
FPG (mg/dl)	-0.105	0.352
TG (mg/dl)	-0.097	-0.073
TC (mg/dl)	-0.039	-0.126
LDL-C (mg/dl)	-0.085	0.085
HDL-C (mg/dl)	-0.238	-0.025
Insulin (µIU/dl)	-0.285*	-0.201
HOMA-IR	-0.281*	-0.19
Visfatin (ng/ml)	-0.162	-0.302*

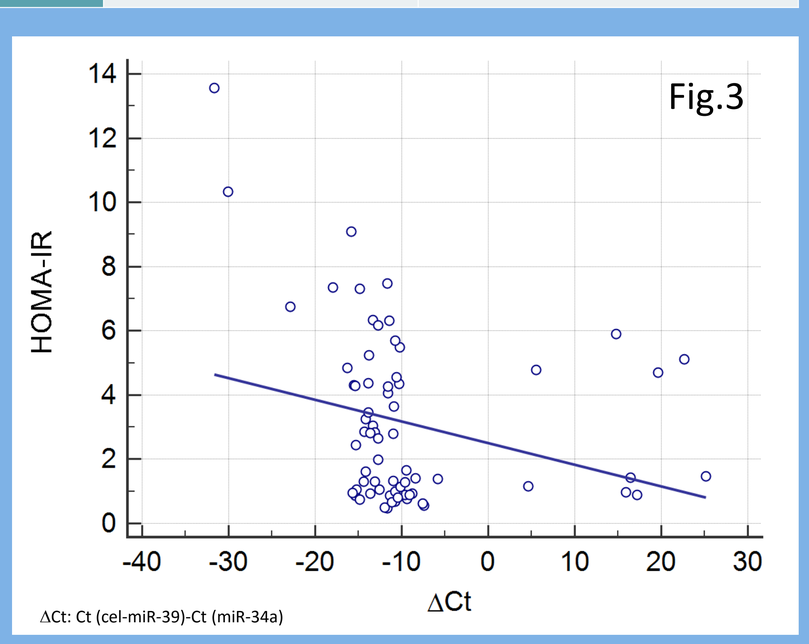
* P<0.05



ΔCt:Ct (cel-miR-39)-Ct (miR-34a); $p < 0.01$; IR: insulin resistance



ΔCt: Ct (cel-miR-39)-Ct (miR-34a)



ΔCt: Ct (cel-miR-39)-Ct (miR-34a)

Conclusion

miR-34a is associated with insulin and HOMA-IR and thus seems to be involved in insulin resistance. miR-149 is inversely associated with visfatin levels which could be indicative of anti-inflammatory effect of this miRNA.

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Mitra Nourbakhsh

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