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Relationship of Circulating Mirnas With Insulin Resistance and Metabolic Dysfunction in Adolescents

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Objectives: To evaluate the relationship of plasma expression of miR-122, -375, -139, 15-a and -let7c with insulin resistance and factors related to metabolic syndrome (MetS) in adolescents.

Methods: Data from 188 adolescents aged 12–19 years participating in a cross-sectional population-based study were analyzed, all non-smokers, without acute inflammatory diseases and cancer, and without the use of medication that would interfere in the outcome. The quantification of circulating miRNA was performed by RT-PCR, using the Fluidigm chip technique. The miRNA expression was compared among adolescents grouped by the absence ($n = 94$) or presence of insulin resistance ($n = 94$)—categorized according to with the HOMA-IR index -, and the absence ($n = 92$) or presence of 1 ($n = 59$), 2 ($n = 23$), 3 ($n = 10$) or 4 ($n = 4$) factors related to MetS. The comparison of means was performed using the Mann-Whitney test for two samples or

Kruskal-Wallis followed by Dunn's post-test to compare three or more samples.

Results: Insulin resistance was identified in 50% of the individuals (HOMA-IR > 2.7). In adolescents with insulin resistance, the plasma expression of miR-122 was higher in comparison to normoglycemic individuals and was positively associated with fasting insulinemia ($r = 0.157$; $P = 0.031$), HOMA-IR index ($r = 0.160$; $P = 0.028$) and plasma hepcidin ($r = 0.209$; $P = 0.005$) levels. When evaluating the expression according to the number of factors related to MetS, the expression of miR-let7c, -139 and -15a increased according to the increase of the factors related to MetS. The opposite effect was observed in relation to miR-375. Individuals with 3 or more factors differed from groups with 1 or 2 factors for plasma miR-375, -139, 15-a and -let7c expression. MiR-375 showed a negative association with body weight ($r = -0.169$; $P = 0.019$), while miR-139 was associated with systolic ($r = 0.153$; $P = 0.055$) and diastolic ($r = 0.193$; $P = 0.016$) blood pressure. Plasma miR-15a expression had a positive correlation with diastolic blood pressure ($r = 0.198$; $P = 0.0064$). MiR-let7c showed a positive correlation plasma TG ($r = 0.156$; $P = 0.029$).

Conclusions: Plasma miR 122 expression was related to insulin resistance, while plasma miR 375, 139, 15 a and let7c expressions were associated with MetS in adolescents.

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