EXPRESION OF MIR-576-5p IN UMBILICAL CORD AS A NOVEL BIOMARKER FOR THE IDENTIFICATION OF CATCH-UP GROWTH IN SMALL-FOR-GESTATIONAL-AGE INFANTS

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BACKGROUND

Early catch-up growth, between birth and age two years, in infants born small-for-gestational-age (SGA) is a risk factor for the development of cardiometabolic diseases in adulthood. The basis and mechanisms underpinning catch-up growth in SGA newborns are unknown.

RESULTS

The miRNA profile showed 12 miRNAs deregulated in SGA-CU vs SGA-nonCU children, 6 of which were validated in all study children (Table 1). Among them, the miR-501-3p, miR-576-5p, miR-770-5p and miR-876-3p associated with increased weight, height, weight catch-up and height catch-up at 1 year of age (all p<0.05; Table 2); and the miR-374b-3p, miR-548c-5p and miR-576-5p associated with increased weight, height, waist circumference and renal fat at 6 years of age (all p<0.05; Table 3). Multivariate analysis showed that miR-576-5p was predictor of weight catch-up (β= 0.286, p=0.003; R²=63.1) and height catch-up (β= 0.301, p=0.001; R²=64.6) at 1 year of age; and waist circumference (β = 0.459, p=0.01; R²=65.2) and renal fat (β = 0.455, p=0.03; R²=20.7) at 6 years of age. In silico studies showed that miR-576-5p targets genes of the insulin, IGF-1, PDGFR-B and mTOR signaling pathways (Table 4).

OBJECTIVES

We aimed to investigate the catch-up predictive ability of umbilical cord tissue miRNAs in SGA infants.

METHODS

MicroRNA PCR Human Panels (Exiqon) were used to study the miRNA profile in umbilical cord tissue of 5 SGA infants with catch-up (SGA-CU), 5 SGA infants without catch-up (SGA-nonCU) and 5 control infants (appropriate-for-gestational-age, AGA). The miRNA with differential expression between the study groups were validated in a cohort of 64 infants (24 SGA-CU, 18 SGA-nonCU and 22 AGA) and correlated with anthropometric and metabolic parameters (weight and height, body composition and fat distribution) at 1 and 6 years of age.

Table 1: Clinical characteristics of the study subjects at birth and at 1 year and 6 years follow-up.

Table 2: Pearson correlation analysis of miRNAs at 1 year follow-up.

Table 3: Pearson correlation analysis of miRNAs at 6 years follow-up.

Table 4: Predicted signaling pathways and genes targeted by miR-576-5p.

CONCLUSION

miR-576-5p could be a novel biomarker for the early identification of catch-up growth in SGA infants. miR-576-5p may also contribute to the regulation of postnatal growth and influence the risk for cardiometabolic diseases associated with postnatal growth.