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Towards a novel marker of insulin resistance in obesity: S100A4 in girls along the puberty. The longitudinal study "PUBMEP"

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Abstract

Introduction: Insulin resistance (IR) is the major driver for the development of obesity-associated metabolic and cardiovascular complications. It is well known that IR increase physiologically during puberty; hence, pubertal maturation might favour this metabolic risk in obese children. Recently, a study carried out in adult women with obesity has identified a new adipokine, known as S100A4, strongly associated with IR and inflammation in adipose tissue. On the contrary, little is known about the implication of S100A4 in the development of such metabolic disturbances during the onset and course of pubertal development.

Materials and methods: A longitudinal study was conducted on 53 Spanish girls distributed in six experimental conditions according to their obesity and IR status (before (T_0) and after (T_1) the onset of puberty). Anthropometric and biochemical parameters were evaluated in all samples and time points. Classification of pubertal stage was made according to the Tanner scale. S100A4 protein levels were quantified by ELISA CSB-EL02032HU in plasma samples (Cusabio Biotech, Wuhan, China). The statistical analysis of the results was carried out with the "nlme" package in R v3.4.4, using a mixed-effects linear model with random intercept and slope.

Results: At a significance level of alpha = 0.05, a linear mixed-effects model reported a significant association (P = 0.03) between the interaction term "time*experimental group" and S100A4 levels. Post-hoc pairwise comparisons between experimental groups revealed a strong association between a worsening/improvement of the IR status and the increase/decrease of S100A4 levels (yielding significant results for 5 of the 15 comparisons (P = 0.008, P = 0.04, P = 0.02, P = 0.04 and P = 0.02)). Furthermore, a multiple linear regression model reported a positive correlation between the increase in S100A4 levels and the increase in HOMA values during the course of puberty (B = 6.03, SE = 2.66 and P = 0.028).

Discussion: The S100A4 protein is strongly associated with the development of IR in girls with childhood obesity and this association is accentuated during pubertal development. Increase in S100A4 levels could be one of the molecular mechanisms by which pubertal maturation favour an increased metabolic risk in children with obesity.

Conflict of Interest

There is no conflict of interest