Effects of human recombinant Growth Hormone (rhGH) treatment on plasma extracellular vesicles in GH-deficient children: a preliminary report.

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Background: Recombinant human growth hormone (rhGH) replacement therapy, administered to children with growth hormone deficiency (GHD), exerts pleiotropic effects on growth, metabolism, and tissue functions. Extracellular vesicles (EVs) are emerging mediators of inter-organ communication, but the effects of rhGH therapy on EV release in humans have not yet been investigated.

Methods: In a preliminary prospective clinical study, children with GHD (n = 10; F/M = 5/5; age: 11.0 ± 2.7 years) were treated with rhGH for 6 months. Plasma samples were collected at baseline (T0) and after treatment (T6) to characterize the size distribution and tissue-derived composition of circulating EVs. Total EVs and EV subpopulations derived from monocytes/macrophages (CD14+), adipose tissue (FABP+), skeletal muscle (SCG+), endothelium (CD62E+), and platelets (CD42A+) were analyzed. Clinical, auxological/auxometric, and biochemical/metabolic parameters were assessed in parallel. Statistical methods included longitudinal analyses, interaction models, and adjustments for relevant covariates, including insulin-like growth factor 1 (IGF-1) and osteocalcin. Results: After 6 months of rhGH therapy, significant improvements in height velocity (cm/year and SDS) were observed, accompanied by increased circulating IGF-1 and osteocalcin levels. Hormone therapy induced no size-dependent changes in (total) EVs. Significant increases in CD14+ and FABP+ EVs were observed after treatment, without affecting the other tissue-derived EVs. Interaction analyses revealed that children with more severe GHD exhibited a stronger vesiculogenic response to rhGH. Furthermore, specific tissue-derived EVs were associated with metabolic/biochemical and auxological/auxometric parameters, including lipids, insulin resistance, and growthrelated measures

Conclusions: When administered for six months, rhGH therapy seems to selectively change tissue-derived composition of circulating EVs in GHD children, particularly those derived from immune cells and adipose tissue. These preliminary findings suggest that EVs might represent an adjunctive component of GH-dependent inter-organ communication and might serve as biomarkers of treatment response and disease severity in pediatric endocrinology.