

POSTER PRESENTATION

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Association of change on insulin-like growth factor (IGF)-i and IGF-binding protein 3 with genetic markers after a month of growth hormone (GH) therapy on Chinese children born with GH deficiency

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Aims

To identify genetic markers associated with changes in IGF-I and IGFBP3 standard deviation score (SDS) after 1 month of r-hGH treatment in Chinese GHD children either born Appropriate for Gestational Age (AGA) or Small for Gestational Age (SGA).

Methods

This phase IV open-label interventional study was performed on samples from 205 GHD children (175 subjects born AGA and 30 subjects SGA) of Chinese Han origin, recruited at 8 centers. All the subjects were given r-hGH for 4 weeks (0.033mg/kg/d). 1536 SNPs were selected from 100 Candidate Genes involved in the GH-IGFI axes, growth plate and other short stature-related diseases. We genotyped Single nucleotide polymorphism (SNP) using Illumina GoldenGate™ Assays. Linear regression was used to identify single SNPs significantly associated with changes, from baseline to week 4, in serum IGF-I SDS and IGFBP3 SDS. Gestational age (GA) was also included in the model. The significance threshold was set as a corrected P-value<0.05. Multiple linear regressions with interaction effect were used to identify significantly associated genes with changes, from baseline to week 4, in serum IGF-I SDS and IGFBP3 SDS. The significance threshold was set as a corrected P-value<0.1.

Results

(1) 6/19 SNPs which correspond to 4/17 genes were significantly associated with IGF-I SDS change/IGFBP3 SDS change separately from baseline to Week 4 in all samples (AGA+SGA) with a corrected P-value<0.05. Among them, 3/10 SNPs showed significant interaction effects, suggesting that the pattern of SNPs associated with IGF-I SDS change/IGFBP3 SDS change was different between two groups.

(2) 14/14 genes which significantly associated with IGF-I SDS change/IGFBP3 SDS change at Week 4 were identified in all samples (AGA+SGA). Among them, 6/12 genes showed significant interaction effects, suggesting that IGF-I SDS change/IGFBP3 SDS change have different effect on these genes expression between two groups. We also found that 5 genes in common associated with both IGF-I SDS change and IGFBP-3 SDS change.

Conclusions

The results of our study demonstrate the genetic association between polymorphic variations of some candidate genes and serum IGF-I and IGFBP3 SDS changes after r-hGH therapy in children with GHD born SGA and AGA, suggesting that these genetic markers could be used into clinical practice in order to optimize efficacy, safety and cost of r-hGH therapy.

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