POLYMORPHISM AFFECTS GH THERAPY

A common polymorphism in the growth hormone receptor (GHR) gene may influence the metabolic response to recombinant human growth hormone (rhGH) therapy in adults with growth hormone deficiency, report an Italian team of researchers.

The exon 3-deleted polymorphism of the GHR gene (d3-GHR) confers increased activity to the receptor and seems to increase response to rhGH therapy in children with or without growth hormone deficiency. Effects of the polymorphism in adults with growth hormone deficiency are less clear and prompted Giavoli *et al.* to compare the metabolic effects of short-term (1 year) and long-term (5 years) rhGH therapy in individuals with or without at least one d3-GHR allele.

Of the 100 adults with growth hormone deficiency included in the prospective study, 52 were either heterozygous or homozygous for the d3-GHR allele; only 50 patients were evaluated after long-term therapy.

After long-term therapy, total and LDL-cholesterol levels decreased in the whole cohort, but analysis of the effects in the separate genetic groups revealed that the decrease was only significant in patients with at least one d3-GHR allele. Furthermore, therapy seemed to worsen insulin sensitivity in the short term in the whole cohort, but was restored in the long term. By contrast, long-term restoration seemed to be thwarted in patients with at least one d3-GHR allele, who had a tendency to develop impaired glucose tolerance at both 1 year and after 5 years. Importantly, therapeutic normalization of insulin-like growth factor 1 levels and body composition was not effected by the d3-GHR polymorphism.

Lead researcher Claudia Giavoli of the University of Milan says the team now hope to enlarge the cohort to strengthen the results.

Carol Wilson

Original article Giavoli, C. *et al.* Influence of the d3GH receptor polymorphism on the metabolic and biochemical phenotype of GH-deficient adults at baseline and during short- and long-term recombinant human GH replacement therapy. *Eur. J. Endocrinol.* **163**, 361–368 (2010)