LETTER TO THE EDITOR

Effects of short-term treatment with insulin-like growth factor-I and growth hormone on serum lipoprotein (a) in growth hormone-deficient adults

In their recent article, Laron et al. (1) reported that serum lipoprotein (a) Lp(a) concentrations were increased in response to 6–9 months treatment with growth hormone (GH) in GH-deficient patients and diminished after long-term insulin-like growth factor-I (IGF-I) treatment in children with GH insensitivity (Laron syndrome). They conclude that the two peptide hormones have opposite effects on serum Lp(a).

Lp(a) is a complex lipoprotein particle containing apolipoprotein (a) disulphide-linked to apolipoprotein B100, and is considered to be a strong and independent risk factor for the development of atherosclerotic cardiovascular diseases in humans (2). It has been shown that octreotide treatment (3) and transsphenoidal adenectomy (4) significantly reduced the (increased) serum concentrations of Lp(a) in acromegalic patients, whereas GH therapy increased the (normal) Lp(a) concentrations in GH-deficient adults (5,6). Short-term studies have shown that GH increases (7), whereas IGF-I decreases (8), serum Lp(a) concentrations in healthy adult humans. Because of their lack of functional GH receptors, patients with Laron syndrome offer the unique opportunity to test the effects of IGF-I in the absence of GH action, but they do not allow a meaningful comparison between the effects of IGF-I and GH in the same individuals. As IGF-I inhibits GH secretion by way of feedback control, GH-deficient patients are also of particular interest in the investigation of the effects of IGF-I without the interference of GH and in comparisons of the actions of both peptide hormones. To date, no studies have addressed the question whether IGF-I-administration influences Lp(a) concentrations in GH-deficient patients.

After the protocol was approved by the ethics committee of the University Hospital of Zürich and written informed consent had been obtained from the patients, eight GH-deficient patients (five women and three men, 48±14 years of age, body mass index 25.2±3.7 kg/m², IGF-I concentrations 7.5±0.9 nmol/l, mean±S.E.M.) were treated with IGF-I (5 µg/kg per hour in a continuous s.c. infusion) or with GH (0.03 U/kg per day by s.c. injection at 2000 h) for 5 days in a crossover fashion. Fasting venous blood samples were drawn daily for determination of serum concentrations of Lp(a) by a solid-phase, two-site IRMA (Pharmacia, Uppsala, Sweden).

Lp(a) concentrations ranged between 9 and 517 U/l at baseline (mean±S.E.M. 142±59 U/l), and decreased in every patient during IGF-I administration, to a nadir of 74% of baseline at day 3 (P<0.02) (Figs. 1 and 2). This effect was more pronounced in the four patients with the greatest initial concentrations of Lp(a). In contrast, Lp(a) increased after GH to a nadir of 122% of baseline at day 6. Because the increase was observed only in six of the eight patients, this effect was not statistically significant. Remarkably, each individual started at a comparable baseline Lp(a) value before treatment with IGF-I or GH, indicating that there is little intra-individual variation and that values returned to baseline during the observation period in this crossover trial.

The findings of our well-controlled, short-term crossover study corroborate and strengthen the long-term data of Laron et al. (1) in children with GH insensitivity syndrome. The results provide strong evidence that the decreasing effect of IGF-I cannot be explained by the suppression of GH secretion, and that circulating IGF-I does not mediate the potentially deleterious effects of GH on Lp(a) concentrations, as suggested previously (5). As reported elsewhere, IGF-I treatment led to a decrease of serum C-peptide concentrations without changing plasma glucose, whereas GH therapy caused an increase in C-peptide concentrations and a slight increase in plasma glucose in this study of GH-deficient adults (9). The decreased serum Lp(a) may reflect reduced hepatic production of Lp(a), possibly as a consequence of suppressed insulin secretion during IGF-I administration. It appears that Lp(a) is an additional parameter (apart from blood glucose and serum triglyceride concentrations)
that is regulated by GH at the level of classical insulin target tissues by mechanisms of action not mediated by IGF-I.

Our results show that short-term IGF-I treatment, unlike GH treatment, diminishes serum concentrations of Lp(a) in GH-deficient patients, possibly by way of partial inhibition of insulin secretion.

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