

Insulin-Like Growth Factor-1 and IGF Binding Protein-3 Remain High After GnRH Analogue Therapy in Girls With Central Precocious Puberty

Kanety et al measured estradiol, insulin-like growth factor 1 (IGF-1), and IGF-binding protein 3 (IGFBP-3) prior to and after 1, 2, and 3 months of GnRHa (D-Trp⁶-GnRHa, Decapeptyl 3.75 mg, Ferring, Malmo, Sweden) in 10 girls, aged 7 to 8 years, with central precocious puberty (CPP). Results were compared to those from 7 prepubertal girls aged 8 to 10 years, with no known endocrine abnormalities. The results were analyzed using the nonparametric Wilcoxon signed rank tests and the Pearson χ^2 -test. The values were expressed as mean \pm SEM.

Pretreatment estradiol levels were in the pubertal range in all 10 patients, fell to levels below the detection limits 1 month after therapy, and remained depressed. Serum IGF-1 was significantly higher in CPP patients as compared to controls (48.8 ± 6.5 nmol/L vs 23.1 ± 4.9 nmol/L; $P < 0.01$). Although serum IGF-1 levels decreased after 1 injection of GnRHa, the decrease was not significant and no further decrease was noted after 2 to 3 months. The changes in IGF-1 levels, when analyzed individually, were heterogeneous and did not follow a specific pattern. Serum IGFBP-3 levels were also significantly higher in CPP patients than in controls (4.70 ± 0.37 mg/L vs 3.71 ± 0.42 mg/L, $P < 0.01$) at baseline and did not change significantly after 1, 2, or 3 months of GnRHa therapy. IGFBP-3 levels were also heterogeneous and did not fall into any specific category. Interestingly, IGF-1 and IGFBP-3 failed to correlate before or during the 3 months of therapy.

The authors review previous studies of the effects GnRHa in CPP on growth hormone (GH), IGF-1 and IGFBP-3. Variable results have been reported, including a decrease in basal and GRF-stimulated GH levels after 3 months of GnRHa

therapy without a decrease in serum IGF-1, and a decrease in IGF-1 only after a year of therapy. The authors conclude their data suggest that while estradiol has a role normally in increasing GH, IGF-1, and IGFBP-3, it may not be important in maintaining the levels of these hormones once the increases over the prepubertal state have been established. They speculate that the lack of change in IGF-1 and IGFBP-3 "with GnRHa therapy which has been proven to reduce growth velocity underscores the known effect of sex steroids in the growth process."

Kanety H, et al. *Clin Endocrinol* 1996;45:7-12.

Editor's comment: *This is an interesting article. When one looks at individual data, it would appear that 7 out of the 10 girls had reductions in IGF-1 by 3 months of therapy while 6 out of 10 had reductions in IGFBP-3 during the same period. The lack of consistent patterns and the fact that some girls' levels rose probably accounts for the inability of the data to be significant. It may be that statistical significance could be obtained by studying a larger number of girls. However, the speculation of the authors remains provocative. Should these findings be verified in studies of larger numbers of girls? This may account for the observation that bone age advanced in girls with CPP treated with GnRHa despite adequate suppression of gonadotropins. In addition, this may account for some of the lack of success in achieving significantly greater final heights in children treated with exogenous GH simultaneously with GnRHa therapy.*

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Increased Energy Expenditure in Growing Adolescents With Crohn's Disease

Growth failure is common in children and adolescents with Crohn's disease and may be the result of reduced energy intake, impaired absorption, or protein-losing enteropathy. In addition, patients with Crohn's disease may have increased energy requirements related to the increase in metabolic activity of their inflamed tissue. Zoli et al measured resting energy expenditure via indirect calorimetry in adolescents with inactive Crohn's disease, both those who were growing and those who had completed their growth. In addition, a control group of healthy growing adolescents was studied. Ten growing adolescents with inactive Crohn's disease (aged 17.8 ± 1.4 years) and 9 who had ceased growing matched for disease, site, and duration (aged 19.0 ± 1.3 years) participated. Subjects had to have histologically proven Crohn's

disease with onset prior to age 16, and to have been diagnosed a minimum of 2 years. Height was assessed every 3 months, and those whose height had increased by 2 cm or more during the previous 12 months were considered growing. Nutritional status was assessed by anthropometric measurements from which body mass index, percent body fat, and free fat mass were calculated. Food intake was assessed by 7-day food diary. No subjects were currently receiving corticosteroids and both interleukin 6 and C-reactive protein levels were in the normal range for all subjects.

Resting energy expenditure per kilogram of body weight was significantly higher in growing patients compared to disease controls (32.1 ± 1.6 kcal vs 27.6 ± 0.9 kcal; $P < 0.05$) or healthy controls (24.5 ± 1.0 kcal; $P < 0.001$).