Diurnal Variation of Serum Insulin-like Growth Factor Binding Protein-1 in Three Boys and Fasting Insulin-like Growth Factor Binding Protein-1 Levels in Normal Children

Toru Yasunaga, Toshiaki Tanaka, Noriyuki Katsumata, Ayako Tanae and Itsuro Hibi

Department of Endocrinology and Metabolism, National Children's Medical Research Center, (TY, TT, NK), Division of Endocrinology and Metabolism, National Children's Hospital, (AT, IH), Tokyo, Japan

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Introduction

It is reported that insulin-like growth factor binding protein-1 (IGFBP-1) is one of the IGFBPs and modulates the IGF action (1). Since IGFBP-1 is reported to be regulated by insulin, it is speculated that meals and nutritional condition influence IGFBP-1 secretion from the liver (2). We measured the 24 hour secretion of serum IGFBP-1 to study the diurnal variation and the relation with calorie intake. We also measured IGFBP-1 levels in fasting normal children to study the age dependent reference value.

Patients and Methods

Blood was sampled every 20 minutes for 24 hours from 3 males (glycogen storage disease type 1, partial growth hormone (GH) deficiency, idiopathic precocious puberty aged 11.9, 18.0 and 12.8 years old, respectively) before treatment. Total calories per day were approximately 2,400 kcal.

Blood samples were also drawn from 82 normal children (42 male and 40 female) aged from 8.0 to 14.9 years after overnight fasting. Mean height standard deviation (SD) was -0.42 ± 0.84 (mean ± SD) SD. Mean body mass index (BMI) was 17.39 ± 1.71.

Serum IGFBP-1 was measured by immuno enzymometric assay (IEMA) kit (Medix Biochemica) and serum insulin was measured by radioimmunoassay (RIA) kit (Eiken).

Results

24 hour levels of serum IGFBP-1 in the three patients are shown in Fig. 1-3. There was a great variation in serum IGFBP-1 levels during 24 hours which showed a high level at early morning and tended to decrease after meals. Maximum level of IGFBP-1 is at early morning (8:40, 6:40, 7:40, respectively). Minimum level of IGFBP-1 is at evening to night (17:40, 20:00, 23:00, respectively). The serum
IGFBP-1 levels in the patient with glycogen storage disease type 1 were very high compared with the others. There was a time interval between change in insulin levels and change in IGFBP-1 levels. It was shown that serum IGFBP-1 levels decreased slowly after insulin secretion. Although IGFBP-1 levels greatly changed during a day, the levels were significantly different among the 3 boys.

Serum IGFBP-1 levels decreased with age ranging from 8.0 to 14.9 years (Fig. 4). Females showed significantly lower levels than males at 10.0 to 10.9 and 12.0 to 12.9 years. IGFBP-1 showed a significant negative correlation with age, height, body weight, height SD score and BMI, respectively (Table 1).

**Discussion**

It is considered that serum IGFBP-1 is chiefly influenced by endogenous insulin secretion and hepatic insulin sensitivity, and participates in glucose counterregulation to
Serum IGFBP-1

Table 1 Correlation with IGFBP-1 in normal children

| Age (years) | -0.688 |
| Height (cm) | -0.710 |
| Body weight (kg) | -0.71 |
| Height SDS | -0.336 |
| BMI | -0.619 |

p<0.01

Inhibit IGF action (3). The IGFBP-1 levels in patients with partial GH deficiency and precocious puberty at early morning before breakfast were within normal levels, but that of the patient with glycogen storage disease type 1 was very high. He had frequent hypoglycemia and liver dysfunction. It is reported that serum IGFBP-1 levels were high in patients with liver cirrhosis (4). High levels of serum IGFBP-1 may contribute to prevent hypoglycemia by modulating IGF action in our case.

In our 24 hour study there is a time interval between change in insulin levels and change in IGFBP-1 levels. Lee et al. (5) reported that the half-life of IGFBP-1 is from 60 to 120 min. Since there was a great diurnal variation in serum IGFBP-1 levels during 24 hours, sampling time is important. It is better to sample the blood for IGFBP-1 measurement in the early morning after overnight fasting when IGFBP-1 is most stimulated, for the reference value.

Although it is unclear which is the main regulator among age, height, body weight, BMI, and insulin in normal fasting children, one of the reasons why serum IGFBP-1 decreases with puberty is that insulin secretion increases with puberty (6, 7). As the female begins puberty earlier than the male, IGFBP-1 levels of the female might be lower than the levels of the male at 10 and 12 years. It is speculated that decreased IGFBP-1 increases free IGF-I, and promotes growth.

References
