# GROWTH HORMONE RESPONSE TO CLONIDINE IN OBESE CHILDREN

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## ABSTRACT

*Basal and stimulated serum growth hormone (GH) levels after exercise, insulin induced hypoglycemia (IIH) and oral clonidine were evaluated in 20 (16 M, 4 F) normal statured obese (body mass index ≥25 kg/M$^2$) children. Basal serum GH levels (mean ± SEM, 2.0 ± 0.38 ng/ml) were not different from basal levels in non-obese children. The mean peak levels were 3.16 ± 1.17 ng/ml, 2.15 ± 0.36 ng/ml and 3.15 ± 1.12 ng/ml (±SEM) after exercise, IIH and oral clonidine, respectively. The positive responses (peak level of serum GH >7 ng/ml) were seen in 10% with exercise, in 10% with clonidine and in none with IIH test. These observations suggest that GH response to oral clonidine is subnormal in obese children.*

**Key words:** *Growth hormone, Obesity, Clonidine stimulation test.*

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Basal growth hormone (GH) level is not a good method to study GH secretory reserve(1). Investigation for GH reserve is based on the use of different tests including insulin induced hypoglycemia (IIH), arginine and L-dopa. Since these tests release GH through different mechanisms, a single test may fail to elicite a GH response in a patient who has normal responses to other stimuli(2). The GH response to exercise, IIH and arginine have been found to be subnormal in obese subjects(3,4). Oral clonidine is a potent stimulator for GH release(5,6) but GH response to clonidine in obese subjects has not been adequately studied. This study was designed to find out the effect of obesity on GH response to clonidine. This would have an impact on clonidine stimulation while evaluating pituitary function in children with obesity.

## Material and Methods

After taking informed consent from parents, 20 obese children (16 M and 4 F with body mass index ≥ 25 kg/M$^2$) aged 9 to 14 years and of height above 50th centile (Tanner's growth chart) were included in the study. They had no systemic, endocrine or central nervous system diseases impairing GH release. Blood samples from antecubital vein were collected after an overnight fast at 0800 h for estimation of basal serum GH, tri-iodothyronine ($T_3$), thyroxine ($T_4$) and thyrotropin (TSH).

All the subjects underwent GH provocative tests allowing a wash out period of 72 hours in between each test. Exercise test was commenced at 0800 a.m. after an overnight fast by walking up and down a flight of stairs (10 steps) at moderate speed for 20 minutes (blood samples were collected at 0, 20 and 40 minutes after exercise). Insulin hypoglycemia test was done using 0.1

unit of crystalline insulin per kg body weight after an overnight fast at 0800 a.m. (blood samples were collected for blood sugar and serum GH at 0, 30, 45, 60 and 90 minutes). More than 50% fall in pretest blood sugar level or symptomatic hypoglycemia was considered adequate for GH stimulation. Glucose infusion to counteract hypoglycemia did not invalidate the test. Oral clonidine test was carried out with a dose of 4 $\mu$g/kg body weight (blood samples were collected 0, 45, 60, 90 and 120 minutes). Basal serum GH levels in obese children were compared with the basal values in non-obese children. Statistical analysis was done using Student 't' test and SEM (standard error of mean).

Serum samples were stored at –20°C till assay by standard radio-immunoassay technique using commercially obtained RIA kit (Bhabha Atomic Research Centre, Bombay, India). The Inter- and intra-assay coefficient of variations were 6.5 and 5.3%, respectively with minimum limit of detection of serum GH being 0.5 ng/ml.

**Results**

Mean values of basal serum GH (average of basal GH levels taken at various occasions) was 1.26 ± 0.26 ng/ml (range 0.5-3.9 ng/ml) in obese children. It was identical to basal levels in non-obese children (*Table I*).

Mean (±SEM) peak level of serum GH after exercise was 3.6 ± 1.17 ng/ml while a positive response (peak serum GH level >7 ng/ml) was seen in 10% (2/20) only. After insulin induced hypoglycemia (IIH) the mean (± SEM) serum GH level was 2.15 ± 0.36 ng/ml but none of the subjects had a positive GH response. After clonidine, mean (± SEM) serum GH level was 3.15 ± 1.12 ng/ml, and a positive response was seen in 10% (2/20) of the subjects who also had normal response to

**TABLE I**—*Mean (±SEM) Basal and Peak GH Levels After Provocative Test in Obese and non-Obese Children. Per cent Positivity Rate of GH Response to Provocation is Also Shown in the Two Groups.*

| Groups | Serum GH ng/ml levels (mean ± SEM) | | | |
|---|---|---|---|---|
| | Basal | Peak after stimulation (Positivity rate in per cent) | | |
| | | Exercise | IIH | Clonidine |
| Obese children (n=20) | 1.6 ± 0.26 | 3.60 ± 1.17 (10%) | 2.15 ± 0.36 (None) | 3.15 ± 1.12 (10%) |
| Non-obese* children (n=20) | 2.0±0.42 | 11.0±2.19 (70%) | 9.82±2.81 (80%) | 15.2±2.54 (85%) |
| 'P' value | Not significant | <0.001 | <0.001 | <0.001 |

*Collected from our previous study(9).

exercise test. In none of these subjects any serious side effects to the insulin hypoglycemia or clonidine test was seen except for mild drowsiness in two subjects after clonidine.

The growth hormone profile studied in normal statured non-obese children were also compared with our study (*Table*).

## Discussion

Basal GH level in obesity has been reported to be abnormal. However, in our study, basal GH level was within the normal range as was observed in normal weight children ($p > 0.05$). This finding has been reported earlier and has been attributed to lack of sensitivity of GH assay to differentiate between the two groups at lower level of serum GH(7).

Oral clonidine test was found to be safer, easier to perform and equally potent as insulin induced hypoglycemia(6). Provocative tests are reliable in establishing the diagnosis of GH secretory reserve and more than one test is required for this purpose(8). Oral clonidine may substitute IIH test in combination with others(6). Similar to exercise and insulin test, it has limitation when used for the study of GH secretory dynamics in overweight or obese subjects. We had selected obese children with BMI more than 25 kg/M$^2$ in our study and only 10% showed significant GH response (peak more than 7 ng/ml) to oral clonidine and exercise test but none with insulin induced hypoglycemia. This suggests that GH secretory abnormality to oral clonidine and exercise was more common with higher grade of obesity. It is difficult to explain the lack of GH responses to insulin in children who had normal response to clonidine and exercise.

In conclusion, our study underlines the importance of body weight with BMI more than 25 kg/M$^2$ and GH response with oral clonidine. The GH response to oral clonidine is subnormal in obese children. Oral clonidine test has the same limitation as other GH provocative tests when applied to an obese child for study of the GH secretory dynamics. A correlation between degree of obesity and abnormality of GH response to oral clonidine requires further study on groups of children with different grades of obesity.

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## NOTES AND NEWS

### UPDATE ON SEVERE INFECTIONS IN PEDIATRIC PRACTICE

An Update on Severe Infections in Pediatric Practice is being organized by the Indian Academy of Pediatrics, Baroda Branch at Baroda on *September 29, 1991.*

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