Reliability of Clonidine Testing for the Diagnosis of Growth Hormone Deficiency in Children and Adolescents

Introduction
The diagnosis of growth hormone deficiency (GHD) is currently based on clinical, auxological, biochemical, and neuro-radiological investigation. Provocative tests of GH secretion using physiological/pharmacological stimuli are required to confirm GHD. The clonidine test (CT) is widely used to assess GH secretory status. In this retrospective study, we analyzed the reliability of CT and the effect of puberty in a large number of children with short stature who had been evaluated for suspected GHD.

Subjects And Methods
Data were collected retrospectively from 327 children and adolescents with short stature (table 1). All children underwent CT as the first GH stimulation test after exclusion of other known causes for their short stature. All children with a GH peak ≥7 μg/L, normal growth velocity for age, and no other recognizable cause for their shortness were considered as non-GHD. Steroid priming was never used in any of the subjects.

Children were subdivided into two groups based on pubertal stage according to Tanner (group 1, pre-pubertal Tanner 1; group 2, pubertal Tanner 2-5) (table 1) and into two groups according to diagnosis (GHD vs non-GHD) (table 2). We then analyzed separately prepubertal vs pubertal GHD children, and prepubertal vs pubertal non-GHD children (table 3, figure 1).

Results
Eleven subjects failed CT, but had normal GH responses to a second stimulation test independently of the pubertal status and the BMI (table 3). Thus, overall rate of false positives was 3.3% (figure 2).

The median (IQR) GH peak was similar between prepubertal and pubertal subjects either in the GHD and the non-GHD groups (figure 1). The median IGF-1 SDS was significantly higher in pubertal vs prepubertal non-GHD subjects while there was no difference between prepubertal and pubertal GHD patients (table 4).

Conclusions
The low rate of subnormal false positive responses observed in our study using a previously validated cut-off of 7 μg/L, in a large number of children suggests that CT is effective and reliable in both prepubertal and pubertal children and that steroid priming is probably not required.

The oral CT is safe and simple to perform and may well be used as the first GH stimulation test in the evaluation of short children and adolescents with suspected GHD.

References

Figure 1. Comparison of GH peak to GHD and non-GHD prepubertal and pubertal children (p < 0.001).

Figure 2. Comparison of GH peak to GHD and non-GHD prepubertal and pubertal children (p < 0.001).

Table 1. Main clinical and biochemical characteristics of the children studied. A GHD group was considered significant at p < 0.05. All values are reported as median and interquartile range (IQR).

Table 2. Main clinical and biochemical characteristics of the children studied. A GHD group was considered significant at p < 0.05. All values are reported as median and interquartile range (IQR).

Table 3. Main clinical and biochemical characteristics of the children studied. A GHD group was considered significant at p < 0.05. All values are reported as median and interquartile range (IQR).

Figure 3. Subject distribution according to the peak GH response to CT.