Exercise Screening of Short Children for Growth Hormone Deficiency in a Family Practice Setting

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Exercise stimulation tests for growth hormone were performed in two groups of children: 163 patients aged 4 to 20 years had growth hormone measured before and after exercise, and 28 children had growth hormone checked only after exercise. Of 180 exercise stimulation tests performed in the first group, 124 showed an adequate growth hormone response as did 23 of 29 such tests in the second group. Careful instruction and preparation of patients for exercise screening of growth hormone leads to an accuracy for this test of nearly 80 percent.

In children with extremely short stature or a falling growth rate, it is often necessary to investigate a diagnosis of growth hormone deficiency. A variety of stimuli exist for eliciting growth hormone response.

Exercise is a physiologic stimulus to growth hormone release.[1] A peak response in normal individuals occurs 20 to 30 minutes after the onset of strenuous exercise.[2] Several investigators[2-6] in academic settings have reported the results of screening children for growth hormone deficiency by means of exercise stimulation, and found adequate growth hormone responses in 64 to 92 percent of patients studied. The authors have reviewed the results of exercise screening for growth hormone in a family practice setting.

Methods

Group I

Between July 1972 and December 1976, exercise stimulation tests for growth hormone were performed on 163 children aged 4 to 20 years. The patients were all members of the Northern California or Oregon Kaiser-Permanente prepaid medical care program. All patients had growth hormone testing requested by their own physicians for evaluation of short stature and/or declining growth rate. Patients to be tested for growth hormone response were instructed by their physician to come to their local hospital or clinic laboratory following an overnight fast. A pre-exercise sample of blood for growth hormone was drawn, after

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Table 1. Growth Hormone (GH) Responses to Exercise Screening

Category	Number of Patients	Number of Tests	Mean and (Range) of Pre-Exercise GH (ng/ml)	Mean and (Range) of Postexercise GH (ng/ml)
Group I				
Adequate response to exercise GH>6 ng/ml	121*	124	3.7 (0.1-52.0)	16 (6.0-80.0)
True GH deficiency	1	1	1.5	1.7
Falsely low GH response to exercise	42*	46	1.5 (0-4.9)	2.6 (0-5.6)
Undiagnosed low GH response	8	9	1.7 (0.3-5.1)	2.7 (0.2-5.6)
Total	172*	180		
Group II				
Adequate response to exercise	23	23		21.4 (6.6-46.2)
Falsely low GH response to exercise	5	6		3.6 (0.8-5.7)
Total	28	29		

*The total number of patients in Group I=163. Nine patients with falsely low growth hormone responses subsequently showed adequate growth hormone response on repeat testing

which the patient was told to exercise for 20 minutes, either by jogging or by continuous walking up and down stairs. After exercise, the patient returned to the laboratory for a second, postexercise blood sample for growth hormone.

Group II

From January 1977 through October 1979, an additional 28 children in the same age group had 29 exercise stimulation tests for growth hormone, having only a postexercise blood sample taken.

All samples were assayed in duplicate by a double antibody radioimmunoassay based on the method of Morgan and Lazarow.[7] A standard curve was constructed to measure growth hormone to 10 ng/ml. Sera with growth hormone levels greater than 10 ng/ml were diluted and reassayed. The interassay variability measured with a "low pool sample" was 3.4 ± 0.3 ng/ml standard deviation (SD) and with a "high pool sample," 7.6 ± 0.7 ng/ml SD. The intra-assay variability determined on 30 samples was 3.7 ± 0.24 ng/ml SD. A growth hormone level greater than 6 ng/ml was considered evidence of adequate growth hormone response.

Results

Group I

Of 180 growth hormone stimulation tests performed, 124 tests (69 percent) in 121 patients showed an adequate growth hormone response (Table 1). One hundred twenty-three of these 124 satisfactory tests (99 percent) showed a growth hormone value greater than 6 ng/ml on the postexercise sample; only one showed a growth hormone value greater then 6 ng/ml on the preexercise sample.

Fifty-six tests in 51 patients resulted in growth hormone values less than 6 ng/ml. One patient was diagnosed as having true growth hormone deficiency after further growth hormone provocative testing. Twenty-nine patients were shown to have falsely low growth hormone responses to exercise: in nine cases, a repeat exercise screening test was normal, and in 20, growth hormone response was normal after provocative testing with a stimulus other than exercise. Thirteen additional patients were considered on clinical grounds to have falsely low growth hormone responses although their growth hormone was not retested. Eight of these children had growth rates greater than 2 inches/year, two had chromosomal gonadal dys-

genesis, and three sexually mature adolescents, of normal height, were obese. Eight other patients who had low growth hormone responses on nine tests were lost to follow-up.

Seventeen patients had repeat exercise testing for growth hormone. Three responded adequately on both the first and second trial, and 9 of the remaining 14 (64 percent) had an adequate response on the second test.

Group II

Twenty-three of 29 growth hormone stimulation tests performed showed an adequate growth hormone response (79 percent). Three tests in two patients were shown to be falsely low when a growth hormone response was obtained with a stimulus other than exercise. In three patients, the growth hormone value below 6 ng/ml was considered a falsely low test when continued follow-up revealed a growth rate greater than 2 inches/year.

Comment

Although the patients screened for growth hormone deficiency received instructions from many different physicians and laboratories, our growth hormone results after exercise stimulation are similar to those of other investigators,[2-6] who studied their patients in university settings. Of short children screened as outpatients, 77 percent (72 percent on the first and 5 percent on the second trial) showed satisfactory growth hormone levels. Because 99 percent of the patients with positive growth hormone responses showed growth hormone levels above 6 ng/ml in the postexercise blood sample, the authors agree with Johanson and Morris[6] that a single postexercise sample is satisfactory for growth hormone screening. The achievement of an adequate growth hormone level on repeat exercise testing in 64 percent of a small group of patients whose initial growth hormone response was below 6 ng/ml suggests that a repeat screening test is worthwhile in the patient who initially fails to respond. The authors suspect that falsely negative growth hormone responses to exercise are usually due to food ingestion before testing or to insufficient exercise.

The 13 Group I and 3 Group II children judged on clinical grounds not to have growth hormone deficiency demonstrate the importance of appropriate clinical screening of those patients in whom growth hormone testing is considered. Patients with severe short stature or a declining growth rate of undiagnosed cause can be evaluated easily in a clinical setting with a single postexercise blood sample for growth hormone. Careful instruction and preparation of the patient leads to an accuracy for this test of close to 80 percent.

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