

CASE REPORT

Growth hormone and insulin-like growth factor I in a Sydney Olympic gold medallist

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Br J Sports Med 2002;**36**:148–149

An Italian athlete who won a gold medal at the Sydney Olympic Games was studied. She was accused of doping after the finding of high levels of plasma growth hormone (GH) before the Games. She was studied firstly under stressed and then under unstressed conditions. In the first study, GH was measured every 20 minutes for one hour; it was above the normal range in all blood samples, whereas insulin-like growth factor I (IGF-I) was normal. In the second study, GH progressively returned to accepted normal levels; IGF-I was again normal. It was concluded that the normal range for GH in athletes must be reconsidered for doping purposes, because athletes are subject to stress and thus to wide variations in GH levels.

The interest of the medical and general press in doping in sport has increased since the recent cases of suspected abuse of erythropoietin, nandrolone, and growth hormone (GH), with a number of athletes involved.

In October 2000, an Italian daily magazine cited 61 top Italian athletes, among them five gold medallists from the Sydney Olympics, as having abnormal levels of plasma GH before the Games.¹ This news became a national and international cause celebre and was the object of discussion on television and in weekly magazines. The discussion was focused on the fact that high GH levels cannot be physiological in these athletes, and GH administration was thus suspected. However, the currently used methods for measuring GH are not reliable enough to confirm or exclude doping. Wu *et al*² recently described a new method for the detection of recombinant GH abuse, a method criticised by Jenkins.³ GH tests were not conducted at the Sydney Games, but no Italian athlete failed any other drug test and all athletes denied taking GH.

Table 1 Hormone and serum glucose concentrations in athlete under stressed (A) and unstressed (B) conditions

Time (min)	Glucose (mmol/l)	Insulin (pmol/l)	GH (μ g/l)	IGF-I (μ g/l)	IGFBP-3 (μ g/l)
A					
0	4.4	21.5	16.9	315	
20	4.7	21.6	18.6	305	
40	4.6	21.6	14.5	298	
60	4.6	21.5	11.2	284	
B					
0	4.5	50.2	9.9	262	3881
30	4.6	28.6	7.8	214	3647
60	4.6	21.5	5.7	235	3942
90	4.9	14.3	3.3	244	3782
120	5.2	28.6	1.9	239	3895
Normal range	3.8–6.6	43–186	0.06–5	100–400	1700–4000

GH, Growth hormone; IGF-I, insulin-like growth factor I; IGFBP-3, IGF binding protein 3.

We decided to study one of these gold medallists (a female cyclist, aged 32 years). The subject was healthy, and no clinical evidence of acromegaly or other diseases was found. She denied taking any substances banned by the International Olympic Committee. The sample in question was obtained in August 2000 as part of a programme called "I don't risk my health", organised by the Italian Olympic Committee. The programme was not intended to screen for doping, and the athlete was advised 15 days before the test. Measurement of insulin-like growth factor-I (IGF-I) was not included in this programme. On the day of blood sampling, she drove 150 km under stressful conditions from her home to the collecting venue. The plasma concentration of GH was 10.6 μ g/ml, whereas the upper limit of normal is 5 μ g/ml.

The athlete denied taking any GH or other banned substance and asked to be studied.

PROTOCOL

The athlete was studied under two different experimental conditions after giving informed written consent. The first experiment reproduced the situation of the original test. The athlete arrived by car at our centre at 9 am in a fasted state, and four blood samples were obtained at 20 minute intervals by repeated venepuncture in the sitting position, for measurement of fasting GH, IGF-I, insulin, and glucose. The same variables and IGF binding protein 3 (IGFBP-3) were measured two weeks later, while the athlete was fasting and resting; a venous cannula was used to obtain blood samples under unstressful conditions.

RESULTS

Serum GH was high and IGF-I values normal in all the samples in the first experiment. The GH level in the first blood sample was 16.9 μ g/l; after one hour it was 11.2 μ g/l (table 1A). Serum glucose concentration was normal and insulin levels were lower than normal over the test.

In the second experiment, while the athlete was not stressed, the first GH concentration was lower than in the first study, but it was still above the normal range (9.9 μ g/l). It progressively declined to 3.3 μ g/l after 90 minutes and 1.9 μ g/l after two hours. Serum IGF-I and IGFBP-3 levels were always within the normal range, while the insulin concentration was again decreased (table 1B).

DISCUSSION

These results are not consistent with an exogenous source of GH because the hormone remains in the bloodstream for only a few minutes, and if this had been the case, the serum GH concentration would have declined progressively during both tests. In addition, there was no increase in IGF-I and IGFBP-3

Abbreviations: GH, growth hormone; IGF-I, insulin-like growth factor I; IGFBP-3, IGF binding protein 3

Take home message

GH levels can be elevated in athletes, but IGF-I levels are always normal. Be cautious of making accusations of doping, when dealing with substances that are also produced endogenously.

as would be seen after injection of GH or long acting GH preparations. In a recent study, Wallace *et al*⁸ showed that recombinant human GH treatment increases serum IGF-I and IGFBP-3, which return to baseline in three to four days. In our athlete, these variables were normal in all determinations. It is thus inappropriate to use a random blood sample of GH for clinical or doping purposes, because GH shows sharp peaks, and exercise is a powerful stimulus to its secretion. In addition, the hormone is very sensitive to stress, especially in women.⁵⁻⁷ The action of GH is mediated by IGF-I, which remains in the bloodstream for 24–36 hours and is thus more appropriate as a marker of GH secretion or exogenous administration for doping purposes. Serum insulin was reduced in all samples, consistent with the reported insulin hypersensitivity of athletes.⁸ The moral of the story is to exercise caution when accusing an athlete of taking illegal substances, when the substances are also produced endogenously—for example GH, 19-nor-testosterone, and erythropoietin.

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Accepted 11 November 2001

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