A SIMPLE CLINICAL TEST FOR MEASURING THE SERUM TESTOSTERONE RESPONSE TO INTRAVENOUS INFUSION OF HUMAN CHORIONIC GONADOTROPHIN (HCG)

By F. Vivanco, P. Gonzalez-Gancedo and F. Ramos

ABSTRACT

A simple clinical test for measuring the blood testosterone response to intravenous infusions of HCG is described. Testosterone was measured in serum by a competitive protein-binding method at 0, 4, 12 and 24 h after the iv infusion of 5000 IU of HCG. Normal men showed a maximal increase of serum testosterone of about 2.5 times the basal levels at 12–24 h after starting the HCG infusion. Normal women did not respond at all to HCG stimulation. Four cases of proven Klinefelter syndrome (XXY) had basal testosterone values higher than in women but significantly lower than in normal men and did not show any response to HCG stimulation. In two orchidectomized patients with very low basal levels of serum testosterone the response to iv HCG was also negative. The test appears to measure specifically the testosterone secretion of the Leydig cells and may be very useful for the differential diagnosis of male hypogonadal syndromes.

The need for clinical purposes of a simple, accurate and standardized technique for studying the blood testosterone response to HCG stimulation is widely recognized. Several attempts have been made recently in this connection. Two of them involve the use of im administration of 2000–3000 IU of HCG for two (Ettinger et al. 1971) or three days (Winter et al. 1972) and one involves iv infusion of 100 or 500 IU of HCG (Maurer et al. 1971). In these three studies,
blood testosterone was measured by plasma competitive protein-binding methods. Although valuable and specific results have been obtained, a standardized, simple and useful technique has not yet been developed. The aim of this paper is to describe a simple, safe and accurate procedure for measuring serum testosterone response to iv HCG stimulation in human subjects.

MATERIAL AND METHODS

Basal serum testosterone determinations were made in 70 normal males and in 36 normal females, aged from 15 to 40 years. The iv HCG test (ivHCG-T) was performed in 10 normal males, 12 normal females, 4 patients with a cytogenetically proven Klinefelter syndrome (XXY males) and in two orchidectomized patients suffering from prostatic carcinoma. The ivHCG-T was carried out as follows: 5000 IU of HCG (Pregnyl®, Organon) was dissolved in 400 ml of a 5% glucose solution and intra¬venously administered during 4 h at a rate of about 33 drops/min. Blood samples were drawn at 0, 4, 12 and 24 h respectively after starting the HCG infusion. All tests were performed at 9 a.m. with the subjects fasted for 12 h and remaining recumbent throughout the whole test period. The samples were allowed to clot at room temperature for 1 h and the sera kept frozen at −20°C until analysis.

Serum testosterone was measured in duplicate by a competitive protein-binding method (Gonzalez-Gancedo et al. 1971) which is essentially a modification of Mayes & Nugent (1968) and Maeda et al. (1969). The sensitivity of this method was 5 ng per 100 ml and the coefficient of variation of duplicate samples was ±9.7%. The testosterone assays were performed in serum instead of plasma only for technical reasons. We observed that when plasma is used, the ammonium sulphate precipitation is rather inconstant, whereas with serum a bulky and consistent precipitate is consistently obtained. Therefore, serum has been used instead of plasma in all the tests.

RESULTS

The average values (±SEM) of serum testosterone and their respective ranges, in both normal males and females can be seen in Table 1. These values agree essentially with those published in the literature. The results of the ivHCG-T

<table>
<thead>
<tr>
<th>Basal serum testosterone levels.</th>
<th>ng/100 ml</th>
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<tbody>
<tr>
<td>No.</td>
<td>Age: Years</td>
</tr>
<tr>
<td>----</td>
<td>------------</td>
</tr>
<tr>
<td>Normal men</td>
<td>70</td>
</tr>
<tr>
<td>Normal women</td>
<td>36</td>
</tr>
</tbody>
</table>

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Table 2.
Serum testosterone levels during the ivHCG-T.
ng/100 ml

<table>
<thead>
<tr>
<th>No.</th>
<th>Age: Years</th>
<th>Hours after starting the infusion</th>
</tr>
</thead>
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<tr>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Normal men</td>
<td>10</td>
<td>14–36</td>
</tr>
<tr>
<td>Normal women</td>
<td>12</td>
<td>14–36</td>
</tr>
<tr>
<td>Klinefelter</td>
<td>4</td>
<td>22–47</td>
</tr>
<tr>
<td>Orchidectomized</td>
<td>2</td>
<td>66–69</td>
</tr>
</tbody>
</table>

± = SEM

are summarized in Table 2 and Fig. 1. All normal male subjects respond to the ivHCG-T with a rise in serum testosterone which attains its maximum at 12–24 hours after starting the HCG infusion. The average maximal increase represents approximately 2.5 times the basal values. Females did not respond at all.

Fig. 1.
Serum testosterone response to the intravenous infusion of 5000 IU of human chorionic gonadotrophin (HCG).
to the HCG stimulation. The four cases of Klinefelter's syndrome showed basal levels of serum testosterone higher than in females but significantly lower than in normal males, and they did not show any significant response to the ivHCG-T. Orchidectomized subjects had even lower values than normal females and their response to HCG stimulation was also negative. The test has been well tolerated in all cases and there have been no significant side effects.

DISCUSSION

The intravenous HCG stimulation test here proposed seems to fulfil at least three of the criteria essential for all functional tests to be used for clinical purposes. a) It is carried out in a relatively short period of time (24 h) and it needs only four blood samples for the analysis. b) The test is sufficiently accurate for detecting the changes in the serum testosterone levels induced by HCG stimulation. c) It specifically measures the rise in testosterone secretion by the Leydig cells since the typical response of normal males is not observed either in orchidectomized subjects or in the Klinefelter patients. These last patients showed, however, intermediate basal values between normal males and normal females but significant higher values than orchidectomized men. These data confirm previous observations of Coppage & Cooner (1965).

It it also worthwhile emphasizing that the minute amounts of testosterone present in the serum of normal females are not increased during the ivHCG-T. This finding demonstrates that HCG has no stimulating effect on the ovary and/or adrenal testosterone production, which are the only known sources of blood testosterone in females.

The data presented in this study led us to conclude that the present test may be very useful in the differential diagnosis of the several clinical syndromes found in male testicular dysfunction.

REFERENCES


Received on December 14th, 1972.

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