HUMAN CHORIONIC GONADOTROPIN TREATMENT OF NONORGANIC ERECTILE FAILURE AND LACK OF SEXUAL DESIRE:

A Double-Blind Study

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ABSTRACT—Forty-five cases of nonorganic failure (n = 39) or lack of sexual desire (LSD, n = 6) were treated for one month, either with human chorionic gonadotropins (HCG, 5,000 IU I.M. twice per week) or with placebo using a double-blind method. HCG gave better results than placebo (47% vs 12%, $p < 0.05$) and improved a higher number of sexual parameters (6/7) than placebo (2/7). HCG effect on sexual behavior did not correlate with the increase in plasma testosterone level: it seems HCG is a useful option in sexologic treatment of erectile failure and LSD.

Studies in hypogonadal men show that testosterone has an important part in the stimulation of their sexual behavior.[1,2] Hypogonadal men present less spontaneous erections, as has been well demonstrated in nocturnal penile tumescence monitoring,[1] and they engage less often in sexual activity than do normal men. However, their erectile response to erotic psychic stimuli is the same as in normal men.[3] In hypogonadal men oral administration of testosterone undecanoate[2,3] or testosterone esters injections[1,4] significantly increase sexual interest,[1,2,4] frequency of fantasies,[1,4] frequency of spontaneous erections,[1,4] frequency of erections induced by fantasies,[3] and frequency of ejaculations.[1,2,4] This stimulation of sexual behavior is proportional to the increases in plasma testosterone levels obtained with HCG treatment until a threshold level is reached, ranging from 2 to 4.5 ng/mL.[4] Beyond this threshold, the correlation between the degree of sexual activity and the plasma testosterone level is not definite. These data have been the basis for androgen therapy in erectile failure.

Though androgen therapy is often administered, its rationale can be questioned for several reasons: (1) The plasma testosterone level is decreased only in a minority of impotence cases (15 to 30%)[5-7]; therefore, theoretically, most impotent males have a plasma testosterone level sufficient for optimal sexual behavior. (2) The plasma testosterone decrease observed in some impotent patients is only moderate (2 to 4 ng/mL). However, many men have satisfactory sexual behavior with a level of 2.5 ng/mL.[4] (3) The decrease of plasma testosterone level can be the consequence rather than the cause of impotence because reduction of sexual activity[8,9] and stress in general (and particularly psychologic stress)[10-12] can decrease the plasma testosterone level.

Moreover, except in hypogonadotropic hypogonadism, the beneficial effect of androgens on sexual behavior of the potent patient has not been confirmed.[13] Also no controlled study has been performed where inapparent organic causes of impotence were excluded. Stenosis of sexual arteries or syndromes of venous leakage or some sexual neuropathies impair sexuality without any clinical symptom.[14] These etiologic factors were not known some years ago, and it is possible that some impotent patients tested

for the androgen therapeutic effect suffered from these defects, thus reducing the real efficacy of androgen therapy.

This reservation led us to perform a new controlled study in a more selected population of nonorganic impotent patients. We preferred to use human chorionic gonadotropin (HCG) which stimulates testicular secretion of testosterone rather than androgens.

The results of an unpublished preliminary study of our group suggest that HCG is superior to androgens in stimulating sexual behavior. This study concerned 29 cases of carefully selected nonorganic impotence. In each patient, we compared the effects of HCG intramuscular injections given twice a week (Chorionic Gonadotropins Endo, 5,000 IU) with the effects of intramuscular injections of testosterone propionate given twice a week (Sterandryl,[5] 50 mg). Each treatment was administered for four weeks, and assigned in a randomized way. Of the patients treated with HCG 46 per cent improved versus 28 per cent of the patients treated with testosterone propionate.

Material and Methods

There were 45 males, aged twenty-two to sixty-three years, with erectile failure (inability to obtain an erection sufficient for intromission or to maintain it until ejaculation in at least 50% of the attempts in 39 cases and lack of sexual desire leading to less than two sexual attempts per month in 6 cases). No organic cause was detected in the history, clinical examination, and the following investigations[14]: penile blood pressure measurement by ultrasonography and penile brachial index measurement (≥ 0.9); bulbocavernosus reflex latency time measurement (≤ 42 msec); artificial erection test associated with dynamic cavernosography in order to search a possible venous leakage syndrome[15]; normal blood sugar and serum prolactin; normal or slightly decreased level of plasma testosterone.

In every case, findings on prostatic examination were normal, excluding the existence of a prostatic carcinoma. Every patient had a regular sexual partner, and was able to fill the questionnaires.

Treatment

Each patient received a pack of 8 ampules for intramuscular (IM) injections. Each of these 8 ampules contained either 5,000 IU chorionic gonadotropins (Endo) or placebo. Organon laboratories performed a double-blind randomization of the packs. The patients received the intramuscular injections twice a week for four weeks. This frequency of injections allows a maximum increase of the testosterone levels in response to HCG: more frequent injections could produce a phenomenon of testicular desensitization.[16]

Evaluation of results

Each patient was asked to record daily the frequency of nine types of sexual events four weeks prior to the beginning of the treatment and four weeks during treatment. Seven of these nine events are listed in Table II. Two other items, "desire for sexual activity" and "satisfactory sexual intercourse" were not included because the observations were not reliable. The patients were also interviewed three times at one-month intervals: one month before the beginning of the treatment, just before treatment, and at the end of the treatment.

Plasma testosterone was assayed in every case before treatment, then seventy-two hours after the last eighth injection.[17]

Statistical comparisons

The results obtained with HCG and placebo treatments were classified as good, nonsignificant, and null. The distribution of these different groups were compared by means of chi-square test. The mean values of the plasma testosterone levels and of the frequencies of each sexual event were calculated before and during treatment. These values were compared by means of paired and unpaired Student's *t* tests.

Results

Table I shows the results of the two treatments on the frequency of "successful" sexual intercourses (intromission maintained until ejaculation, which was not judged as premature by the couple). The result was considered good when the frequency of successful sexual

TABLE I. *Effect of HCG treatment on frequency of successful sexual intercourse*

Result	HCG	Placebo
Good	10	3
Nonsignificant	2	5
Null	9	16
TOTALS	21	24

TABLE II. *Mean ± SEM of frequency of 7 sexual events and of plasmatic testosterone values during 4 weeks before and during treatment*

Parameter	Treatment			
	Placebo		HCG	
	Before	During	Before	During
Erection (whatever its rigidity)	11.6 ± 5.6	15.6 ± 10.6*	13 ± 8.6	18.6 ± 7.1†
Full rigid erection (less than 5 minutes)	3.3 ± 6.6	6 ± 8†	2.9 ± 4.7	8.3 ± 8.6†
Fully rigid erection (more than 5 minutes)	2.6 ± 7	3.8 ± 7.2	2.5 ± 3.5	6.5 ± 7.8*
Sexual attempts	5.4 ± 4.9	6.1 ± 3.8	4.8 ± 4.9	9.6 ± 2.2*‡
Vaginal intromission	2.4 ± 4	4 ± 3.9	3.9 ± 3.5	6.2 ± 3*
Ejaculation	2.3 ± 3.8	3.6 ± 4.6	6.3 ± 4§	7 ± 2.2§
Successful sexual intercourse	1.2 ± 2.5	2.2 ± 3.7	1.2 ± 1.6	3.8 ± 3.7
Plasma testosterone	5.43 ± 1.96	5.11 ± 1.81	6.09 ± 1.58	10.6 ± 4.12†§

*$p < 0.05$.
†$p < 0.01$ with respect to corresponding value before treatment.
‡$p < 0.05$.
§$p < 0.01$ with respect to corresponding value during treatment.

intercourse was at least doubled and when it reached at least twice per week under treatment. The result was considered null if there was no improvement, and nonsignificant in the intermediate cases. Forty-seven per cent of the patients treated with HCG obtained a good result versus 12 per cent of the patients treated with placebo (slightly significant difference: chi-square = 6.84, $p < 0.05$).

We could not evaluate if HCG treatment had any specific effect in the subgroup with slight decreased testosterone level (2 to 4 ng/mL). Five of these 7 patients received placebo (failure in the 5 cases). Of the 2 patients who received HCG, 1 was a failure and 1 had a nonsignificant result, in spite of definite increase in plasma testosterone levels in both.

Table II shows the mean frequencies of the seven sexual events before and during treatment. We could not take into account items as "desire for sexual activity" and "satisfactory sexual intercourse." Analysis of the daily responses during interviews showed that a great number of patients did not understand the meaning of the last two items. Particularly, the majority of patients confused the term "desire for sexual activity" with spontaneous erection.

With placebo treatment only the number of incomplete or short spontaneous erections increased in a statistically significant way. With HCG treatment, the frequency of every type of erection increased; the frequency of sexual attempts, of penetrations, and of successful sexual intercourse also significantly increased. The comparison of the two treatment groups showed that the frequency of sexual attempts and of ejaculations was significantly higher in the HCG group. However in regard to frequency of ejaculations, this was already higher in the HCG group before treatment.

TABLE III. *Mean ± SEM of plasma testosterone increases (ng/mL) following HCG treatment*

Results	HCG	Placebo
All cases	5.25 ± 3.29	−0.5 ± 2.35
Good	5.23 ± 4.12	. .
Null	5.47 ± 3.81	. .

Table II also shows that the mean values of plasma testosterone were similar in both groups before treatment and that these values significantly increased after HCG. Table III shows that among the patients treated with HCG, the increase of plasma testosterone in response to HCG treatment did not correlate with the results.

Comments

Our study shows that HCG injections given twice a week clearly improve sexual behavior in nearly 50 per cent of the cases of nonorganic erectile failure or LSD. Thus, this treatment could be a useful option in sexologic therapy. The difference of efficacy between HCG and placebo injections, however, reached only borderline significance ($p < 0.05$). Furthermore, the two treated groups were not strictly identical, i.e., the monthly frequency of ejaculations was significantly higher before treatment in the HCG group compared with the placebo group. The patients in the HCG group reported a more intense sexual activity; the possible role of

different psychologic factors such as less rigid sexual norms, more flexibility, lesser sexual inhibition, or stronger sexual interest has to be considered. Possibly, there was a placebo effect, derived from the injection or by the interviews.

Our results, however, suggest that HCG acts at least partially by increasing sexual interest. Indeed, the frequency of sexual attempts increased more under HCG than under placebo. This is consistent with what is known about effects of androgens on male sexual behavior.[1,2,4] The hypothesis that HCG would exert beneficial effects by an increase of testosterone levels has not been proved. We observed no difference in testosterone levels in our good and null results following HCG injections. One may wonder also why the oral administration of testosterone undecanoate did not differ from placebo in the experience of Benkert *et al.*[13] In their study, however, testosterone undecanoate did not clearly increase the plasma testosterone level of their patients, probably because of the getting up of the negative feedback of androgens on pituitary gonadotropins release. Another explanation would be either that HCG exerts a direct effect on sexual behavior, like that described for certain neuropeptides as LHRH,[18,19] or that HCG exerts its effects by stimulating the secretion of another testicular hormone distinct from testosterone.

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