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Original Contributions

Chorionic Gonadotropin in Weight Control

A Double-Blind Crossover Study

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• Two hundred two patients participated in a double-blind random crossover study of the effectiveness of human chorionic gonadotropin (HCG) vs placebo in a weight reduction program. Serial measurements were made of weight, skin-fold thickness, dropout rates, reasons for dropping out, and patient subjective response. There was no statistically significant difference between those receiving HCG vs placebo during any phase of this study ($P > .1$).

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SINCE human chorionic gonadotropin (HCG) was first proposed as an aid in weight reduction programs, a controversy has arisen regarding its efficacy.[1-13] Much of the literature on its use has been observations from uncontrolled studies or editorials.[1-5] Previous controlled studies have been done but suffered either from small numbers of patients or deviation from the injection schedule originally proposed by Simeons.[6-13]

This report details the results of a double-blind controlled crossover study of 202 patients treated with HCG and saline placebo.

METHODS

Informed consent was obtained from all patients after the nature of the study had been fully explained.

Patients were numbered sequentially as they volunteered for the study. The patient identification numbers were supplied to the Wilford Hall USAF Medical Center pharmacy, who prepared the HCG and placebo. Patients were allocated to receive either HCG or placebo during the first phase of the program according to a table of random numbers, and the investigators received the samples in vials identified with only the patient's number. A separate vial was prepared for each patient. The vials were kept refrigerated at all times after preparation. New vials were prepared every two weeks.

The diet program was designed to follow as closely as possible that originally designed by Simeons.[1,2] Patients were given oral and written instructions on a 500-calorie diet. During the first two days of injections, patients were allowed to eat anything they wanted and began the 500-calorie diet on the third day. They ate two meals a day of weighed portions of protein and specific amounts of fruit, vegetables, and carbohydrates. Fats were excluded except for that contained in the small amount of meat allowed in the protein portion. Lectures were given on diet and behavior modification twice weekly.

The patients received injections of either 125 units HCG or placebo for six days of each week and were weighed daily. After the first six weeks of injections, the patients were provided specific oral and written instructions on a gradual increase in calories, with the goal of maintaining weight stability for six weeks. They received no injections and no scheduled visits during the six-week maintenance phase. They then underwent another six weeks of injections wherein those who received HCG the first time received placebo and vice versa. This was followed by another six-week maintenance phase.

All patients had a detailed history of duration of obesity, a general medical history, a physical examination, and measurements of height and weight. Percent body fat was estimated from skin-fold measurements of triceps, biceps, subscapular, and suprailiac areas. Percent body fat was calculated from an anthropometric model, using the arithmetic sum of these four measurements.[14] In addition, circumferences of upper arm, chest, waist, hip, and thigh were measured.

In order to be entered into the study, a patient had to have a calculated excess of 18.2 kg or more of fat. This figure was derived by assuming a normal percent fat of 17% in men and 23% in women. For example, a woman who weighed 91 kg and had a calculated percent fat of 43% would have exactly 18.2 kg of excess fat. This calculation actually underestimates the degree of overweight since it assumes all weight loss would be fat. Patients less than 18 years old were excluded as were those with major medical illnesses or diabetes requiring therapy other than diet.

In addition to objective measurements, an attempt was made to evaluate the patients' subjective responses to the injections. They filled out questionnaires regarding their general satisfaction with the program and noted the presence of any specific symptoms they attributed to the

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injections. They were also asked to guess whether they had received HCG during each treatment phase.

RESULTS

For clarity of presentation, those who received HCG during the first series of injections have been designated as group 1 and those who received the placebo first, group 2 (Table 1).

Using a one-way analysis of variance, we determined that there was no statistically significant difference ($P>.1$) in the HCG and placebo groups prior to the start of the study in age, duration of obesity, change in weight over the last six months, weight, height, percent body fat, triceps, or subscapular skin folds (Table 2). There were 25 men in group 1 and 29 in group 2 ($P>.1$). Statistical analysis of all the factors in Table 2 plus each skin-fold and circumference measurement was carried out separately for men and women. No statistical differences were found between group 1 and group 2 ($P>.1$ for all).

We recognize that percent body fat determined from skin-fold thickness is an estimation, but it does correlate well with other methods of determining total body fat.[14] To our knowledge, there have been no studies evaluating whether changes in skin-fold thickness correlate exactly with changes in percent body fat by other independent measurements of fat mass. It is reasonable to assume that changes in skin fold reflect largely changes in fat, and we have used them as an objective measurement in addition to changes in total weight. Comparison of standard height and weight tables showed mean values in both groups to be more than 27.3 kg over standard weight for height and age.

In those patients who completed the first series of injections, there was no difference ($P>.1$) between the two groups in weight loss or change in percent body fat, nor did changes during the subsequent maintenance phase differ between the two groups ($P>.1$) (Table 3). Likewise, there was no difference ($P>.1$) between the HCG and placebo groups during these periods in the change of any single skin-fold thickness or circumference measured. No difference in changes of any of these indicators was noted between the HCG and placebo groups in the second treatment or maintenance phases ($P>.1$). There was, however, a significantly greater weight and percent body fat loss in the first treatment phase vs the second treatment phase in both groups ($P<.001$).

Using the crossover aspect of the study and analyzing only those patients who completed all phases of the protocol, an analysis of variance was used to eliminate the order effect and, in essence, use the patient as his own control. The overall mean weight loss

Table 1.—Designation of Groups and Time Periods for Human Chorionic Gonadotropin (HCG) vs Placebo (PL)

	Group 1 (n=100)*	Group 2 (n=102)*
Treatment period 1	HCG 6 times/wk for 6 wk	PL 6 times/wk for 6 wk
Maintenance period 1	No therapy; keep weight stable 6 wk	No therapy; keep weight stable 6 wk
Treatment period 2	PL 6 times/wk for 6 wk	HCG 6 times/wk for 6 wk
Maintenance period 2	No therapy; keep weight stable 6 wk	No therapy; keep weight stable 6 wk

*Number of patients in each group at the start of the study.

Table 2.—Baseline Data in Patients Entered Into Chorionic Gonadotropin vs Placebo Study

	Group 1 n=100		Group 2 n=102	
	Mean	SD	Mean	SD
Age, yr	32	9.8	33	10.5
Duration of obesity, yr	14	10.7	14	11.5
Change in weight over last 6 mo, kg	0.9	8.6	0.1	7.7
Weight, kg	89	17	90	15
Height, cm	30	1.7	30	1.8
Body fat, %	40	6.4	40	6.2
Triceps skin fold, mm	30	7.9	29	8.6
Subscapular skin fold, mm	34	10.1	36	10.2

Table 3.—Mean Changes (±SD) in Weight and Percent Body Fat for Each Period*

	No. of Patients	Weight, kg		Body Fat, %	
		Mean	SD	Mean	SD
Treatment period 1					
HCG	80	−8.5	3.3	−4.2	3.5
Placebo	92	−9.0	3.8	−4.0	3.1
Maintenance period 1					
HCG	73	1.8	2.5	0.4	3.0
Placebo	83	1.8	2.9	0.2	2.5
Treatment period 2					
HCG	62	−4.5	2.6	−2.3	2.1
Placebo	49	−4.2	3.3	−2.6	2.3
Maintenance period 2					
HCG	53	2.0	2.0	0.4	1.6
Placebo	43	1.7	2.1	0.6	2.1

*Only those patients completing the entire period are included in each group. $P>.1$ for all comparisons of human chorionic gonadotropin (HCG) vs placebo.

Table 4.—Dropout Ratio for Patients Who Left Program Because of Dissatisfaction*

	HCG	PL
Treatment period 1, %	14	8
Maintenance period 1, %	6	6
Treatment period 2, %	21	25
Maintenance period 2, %	12	9

*Percents are based on number of patients beginning each period. $P>.1$ for human chorionic gonadotropin (HCG) vs placebo (PL) for all periods.

while receiving HCG was 6.8 kg, vs 7.0 kg while receiving placebo ($P>.1$). Overall percent body fat loss while receiving HCG was 3.2, vs 3.4 while receiving placebo ($P>.1$). Similar analysis for the two maintenance periods showed no significant differences between groups ($P>.1$).

The overall dropout rate from all causes over the entire protocol was 57 patients during HCG therapy or the following maintenance period and 49 during placebo therapy or subsequent maintenance period ($P>.1$).

Eighteen in the HCG group and 15 in the placebo group dropped out for reasons considered beyond their control. The remaining patients dropped out because of dissatisfaction with the program; either it was too inconvenient to continue or weight loss was unsatisfactory. There was no significant difference ($P>.1$) in dropout rates at any time period in the HCG group compared to the placebo group (Table 4).

One patient received only 26 shots during the placebo period, and one received only 28 shots during the HCG period. All others received 30 or more injections during each period. No patient missed more than three injections in a row. Analysis of weight loss for those who did not complete the first phase showed a mean weight loss of 3.4 kg in the HCG group and 3.9 kg in the placebo group ($P>.1$).

The patient questionnaire responses showed no significant clinical differences during the HCG or placebo injections. The patients could not guess when they received the HCG ($P>.1$).

COMMENT

In a randomly assigned HCG vs placebo crossover study of 202 patients, we could not demonstrate by any objective indicator that HCG was beneficial in promoting weight loss, nor was there any significant difference in fat loss or body circumference measurements ($P>.1$).

There was no evidence that those receiving HCG were more satisfied with the program. Analysis of dropout rates showed no tendency for those receiving HCG to finish the program more frequently than the control group ($P>.1$). Whether analyzed as total dropout rate or dropout at any given phase of the study because of dissatisfaction with the program, there was never a significant difference between the groups ($P>.1$).

The two major tenets of those advocating the use of HCG in weight control are that it specifically promotes weight loss or in some way improves the feeling of well-being in the patient, allowing easier adherence to the diet.[1-5,13] With the exception of one study, all previous controlled studies on the use of HCG have found no more than a .90 kg difference in HCG and control groups.[6-12] The maximum number of patients in previous controlled studies has been 50. As such, none of the previous studies has been able to make truly adequate adjustment for dropout rates.

Asher and Harper[13] found a 4-kg greater weight loss in their HCG group as compared to control. They initially included the weight loss in seven placebo and three HCG patients who received less than 30 injections.[15] Reevaluation of their data, including only patients who had received 36 injections, showed a 3-kg greater weight loss in the HCG group, with a P value of .02.[16] The resultant population size was 22 patients.

Contrasting with their results, the dropout rate of patients receiving HCG for the first time in our study was almost twice that of the placebo group ($P>.1$). The range of weight loss in both groups in both studies was quite large. The randomization of patients was based only on whether they were to receive HCG or placebo. This does not assure that other factors that could account for weight loss were also randomized. We attribute the difference between our results and those of Asher and Harper[13,16] to their sample size, which was not sufficient to assure that factors other than HCG and placebo were equally distributed in the two groups. The most important such factor was probably individual patient motivation.

Other claims regarding the use of HCG are that it allows the patients to maintain the weight loss better than patients who have not received it and that a second course is as effective as the first. We found no evidence of better weight loss maintenance as a result of HCG, and a second course of therapy was less effective regardless of the injection received during the first course.

Nonproprietary Name and Trademarks of Drug

Chorionic gonadotropin—*Antuitrin-S, APL, Follutein, Pregnyl, Riogon.*

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