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The effect of human chorionic gonadotropin (HCG) in the treatment of obesity by means of the Simeons therapy: a criteria-based meta-analysis

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1 A meta-analysis was conducted to assess if there is scientific ground for the use of human chorionic gonadotropin (HCG) as adjunctive therapy in the treatment of obesity.
2 Published papers relating to eight uncontrolled and 16 controlled trials that measured the effect of HCG in the treatment of obesity were traced by computer-aided search and citation tracking.
3 The trials were scored for the quality of the methods (based on four main categories: study population, interventions, measurement of effect, and data presentation and analysis) and the main conclusion of author(s) with regard to weight-loss, fat-redistribution, hunger, and feeling of well-being.
4 Methodological scores ranged from 16 to 73 points (maximum score 100), suggesting that most studies were of poor methodological quality. Of the 12 studies scoring 50 or more points, one reported that HCG was a useful adjunct. The studies scoring 50 or more points were all controlled.
5 We conclude that there is no scientific evidence that HCG is effective in the treatment of obesity; it does not bring about weight-loss or fat-redistribution, nor does it reduce hunger or induce a feeling of well-being.

Keywords HCG human chorionic gonadotropin Simeons weight-loss fat distribution appetite obesity diet meta-analysis

Introduction

Papers on the Simeons therapy have been published regularly since 1954. The Simeons therapy is a slimming therapy in which the patient, over a period of 3.5 to 6 weeks, keeps to a fat-free diet of 500 kilocalories (kcal) day^{-1}, as prescribed by Simeons. At the same time the patient receives daily an intramuscular injection of 125 International Units (iu) of human chorionic gonadotropin (HCG) [1–3]. HCG is a hormone that occurs in the body in large quantities during pregnancy. It is obtained from the urine of pregnant women and is used to make a drug for the treatment of certain infertility problems.

Simeons developed the therapy on the basis of his experience of using HCG to treat young boys suffering from the Fröhlich syndrome (Dystrophia adiposito-genitalis) [1]. It is claimed that overweight patients who follow the Simeons therapy will a) lose weight quickly, b) not feel weak, c) not be hungry, and d) lose fat from those parts of the body where it tends to remain longest during normal dieting (i.e. stomach, hips, thighs, upper arms) [1].

The therapy is controversial. Various mechanisms that could explain the above-mentioned effects of HCG in diet therapy have been described in the literature [1, 4–6]. None of these theories has a sound scientific basis [7–11]. Therefore, several authors have drawn attention to the need for a well-designed, well-executed, double-blind investigation into the effect of HCG in the Simeons therapy [12–14]. As long as there is no proof that HCG has a beneficial effect some doctors are unwilling to recommend the therapy [10, 15, 16]. According to others, however, since so few reduction-therapies are successful, the Simeons therapy should be used because—whatever its real effect may be—patients do lose weight with it, even if HCG itself is not effective [17]. In two review papers,

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one of which compares 20 investigations and the other six investigations, it is concluded that, as an adjunct to diet, HCG does not achieve any effects [18, 19].

On the basis of the data contained in the literature the Simeons therapy seems to have won general acceptance in many countries [4, 12, 18–23]. In the Netherlands, for instance, the therapy is recommended regularly in the popular press, particularly when 'it's bathing-costume time' or when 'the festive season' is over. The Medical Inspectorate in the Netherlands, an independent governmental body which monitors the quality of health-care, frequently receives questions and complaints about the Simeons therapy. For this reason and because the above-mentioned literature studies are out-of-date and of a narrative character we performed a meta-analysis in order to obtain an answer to the following question: What are the results of the investigations, reported in the literature, into the effect of HCG in the treatment of obesity by means of the Simeons therapy?

Methods

Data collection

Via Medline and using various combinations of keywords we searched for papers published between 1966 and 1993 (keywords: gonadotropins, chorionic, HCG, obesity, diet, reducing, caloric intake, appetite, Simeons). We were able to trace more publications from the references in the papers we found by this method.

Inclusion criteria

Investigations were included in this study if they:

- concerned the effect of HCG in the treatment of obesity by means of the Simeons therapy;
- were written in English, French, German or Dutch.

Measuring instrument

The basis for the measuring instrument was a list of criteria that the methodology of a good scientific study had to satisfy. Chalmers compiled a list of such criteria [24]. This was later modified by Koes *et al.* [25]. These criteria (based on four main categories: study population, interventions, measurement of effect, and data presentation and analysis) were adapted for this study and were provided with a new weighting factor. In cases where a certain criterion was not met, a study received a score of zero on this item. The maximum score for a study was 100 (Table 1). The details about how the criteria were applied are given in the Appendix.

Procedure

We took great trouble to ensure that we traced all the published investigations into the effect of HCG in weight reduction. In addition, the validity and reliability of our work was enhanced because we further sharpened the application of several criteria as a result of a pilot study based on two randomly selected investigations to make the descriptions in the Appendix more explicit [29, 30]. Two non-blinded assessors (GKS L, I T) first scored all the studies independently. Thereupon they compared their scores, looking particularly at the criteria for which they had awarded different scores. During their consultation they generally came to an agreement; if they could not agree, then a third investigator made the decision (G vd W).

Table 1 Methodological criteria for assessing articles on the effectiveness of the Simeons therapy

*Criteria**		*Weighting factor*
Study population (30)		
A)	homogeneity	2
B)	comparability of the groups as far as important characteristics are concerned	5
C)	randomisation procedure	4
D)	drop-outs described for each group separately	3
E)	<20% drop-out during intervention**	2
	<10% drop-out during intervention**	2
F)	number of persons in the smallest study group	12
Interventions (30)		
G)	interventions described	14
H)	co-interventions not allowed	4
I)	pragmatic study	4
J)	placebo-controlled study	4
K)	measuring instruments reliable and valid	4
Effect (30)		
L)	patients blinded (or naive)	5
M)	investigator blinded	10
N)	relevant variables measured	10
O)	adequate follow-up	5
Data-presentation and analysis (10)		
P)	adequate data analysis	5
Q)	outcomes of the important variables given for the groups separately	5

*More details in the Appendix.
**In cross-over studies the first treatment-period before cross-over took place was scored.

Definitions

An investigation was judged to be positive if the authors of the study concerned concluded that the treatment with HCG had led to weight-loss compared with the starting weight in an uncontrolled study or in a controlled study compared with the weight-loss in a control group.

Analysis

The conclusions of the studies were analysed according to the scores awarded for methodological quality. It was decided that studies that scored less than 50 points were unsatisfactory as far as their methods were concerned.

Results

Twenty-four studies satisfied the inclusion criteria [23, 26–46] (Table 2). Of these, nine studies were traced via the Medline search.

In the first instance the two assessors disagreed about 51 of the 984 subcriteria (41 subcriteria × 24 studies) (5.2%). In their subsequent consensus meeting it became apparent that the disagreements were often due to a misreading. No agreement could be reached with regard to seven subcriteria; in these cases the third researcher made the decision.

Low scores were awarded particularly for the following criteria (Table 2):

B agreement between the groups with regard to the degree and duration of obesity and with regard to the use of medicines,
F size of the study population,
H avoidance of medicines or treatments other than the Simeons therapy used for weight reduction,
K reliability and validity of measuring instruments,
N the measurement of fat-distribution and well-being,
O results after 6 months.

Total scores per study varied from 16 to 73 (Table 2). The 14 randomised clinical trials (RCTs) had the highest ranking methodological scores, 12 having scored higher than 50. Two of the RCTs had a positive outcome (Table 3). Seven of the ten non-randomised trials had a positive outcome (data not in Table 3).

The particulars of the RCTs included in the meta-analysis are reported in Table 3. Only six of the 14 RCTs used a standard Simeons regimen only [29, 31, 35, 36, 37, 39]. Only a small minority reported on all four major outcomes (weight-loss, fat-redistribution, hunger, feeling of well-being) [23, 31, 33, 34, 38].

In Table 4 more quantitative data on the effectiveness of HCT treatment RCTS are presented.

Table 2 Methodological item scores of studies on the effectiveness of human chorionic gonadotropin (HCG) in the treatment of obesity by means of the Simeons therapy

First author [reference]	*Methods-criteria‡*																
	Score per item																*Total*
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	
	2	5	4	3	4	12	14	4	4	4	4	5	10	10	5	5	5	100
RCTs:																		
Stein [29]	2	2	4	3	2	4	14	2		4		5	8	10	3	5	5	73
Young [30]	1	4	4	3	2	12	10			4		5	5	10	3		5	68
Shetty [31]		2	4	3	4		10			4		5	10	10	3	5	5	65
Mens [32]	1	1	4	3	4		12			4		5	5	10	5	5	5	64
Richter [33]	2	4	4	3	4	4	12	2	4				10		3	5	5	62
Bosch [23]	2	1	4	1	2		14			4		5	10	10	3		5	61
Greenway [34]	2	2	4	1			6	2		4		5	10	10	3	5	5	59
Asher [35]	2	2	4	1			14	2		4		5	7	10	3		5	59
Craig [36]	1	2		1	4		10	4		4		5	2	10	5	5	5	58
Richter [33]	2	3	4	3	4		12	2	4				10		3	5	5	57
Miller [37]	2	2	4	1			10			4		5	7	10	3		5	53
Frank [38]		1	4	1		4	10	2		4		5	8	10	3			52
Lebon [39]	1	2	4	1	2		10			4		5	2	10	3		5	49
Carne [26]		2		1	2		10			4		5	2	10	3		5	44
Non-RCTs:																		
Sohar [40]	2	3		3	2		12			4		5	2		3		5	41
Veuilleux [42]				3	4	4	8						7		3	5	5	39
Gianoli [43]				3	4	12	10						2		3	5		39
Lebon [27]				3	4	4	10						2		3	5	5	36
Gusman [44]	2				4	12	10						2		3			33
Hastrup [41]	2	3		1	2		8			4			2		3		5	30
Simeons [45]	2					12	8						2		3			27
Harris [46]						12	8						2		3			25
Lebon [39]	1						8						2		3		5	19
Kalina [28]				1		4	6						2		3			16

‡For specifications per item see Table 1 and Appendix.

Table 3 Simeons therapy for treatment of obesity; particulars of the available randomised clinical trials

(First) author [ref.]	*Regime†*	*Loss to follow-up HCG* %*	*control %*	*Results on main outcome measures‡ a*	*b*	*c*	*d*
Stein [29]	standard	0	0	neg	neg	neg	
Young [30]	+ lectures on diet and behaviour twice a week	20	10	neg	neg		
Shetty [31]	standard	0	0	neg	neg	neg	neg
Mens [32]	+ daily group sessions	0	0	neg		neg	
Richter [33]	250 iu HCG daily, control group got no injections, only diet; weekly supporting interview	4	4	neg	neg	neg	neg
Bosch [23]	+ lectures on obesity and behaviour once a week	15	20	neg	neg	neg	neg
Greenway [34]	HCG dose not mentioned	10	35	neg	neg	neg	neg
Asher [35]	standard	0	0	pos			pos
		0	10			pos	
Craig [36]	standard	0	0	neg			
Richter [33]	all patients used contraceptives; 250 iu HCG daily, control group got no injections, only diet; weekly supporting interview	13	6	neg	neg	neg	neg
Miller [37]	standard	0	0	neg		neg	neg
Frank [38]	1030 kcal. daily + 3 times weekly 200 iu HCG subcutaneously	0	0	neg	neg	neg	neg
Lebon [39]	standard	0	0	pos			
Carne [26]	+ daily group sessions, used CG instead of HCG	8	17	neg			

*HCG = Human chorionic gonadotropin.
†In so far as it differs from standard which is: 500 kcal day^{-1} plus one intramuscular injection of 125 iu HCG or placebo daily over a period of 3.5 to 6 weeks.
‡a = weight-loss; b = fat-redistribution; c = hunger; d = feeling of well-being; pos = positive, neg = negative; positive and negative are results as reported by the authors in the article.

Table 4 Results of randomised clinical trials on the effectiveness of human chorionic gonadotropin in the treatment of obesity by means of the Simeons therapy

First author [reference]	*Review score*	n†	*Duration of intervention*	*Follow-up**	*HCG‡: weight-loss in pounds (p) or kilograms (kg) (95% CI)*	*Control: weight-loss in pounds (p) or kilograms (kg) (95% CI)*	*Authors' conclusion on results of the study*
Stein [29]	73	51	4½ weeks	E	15.8 p (14.0–17.6)	15.5 p (13.7–17.3)	negative
Young [30]	68	202	6 weeks	E	8.5 kg (7.8–9.2)	9.0 kg (8.2–9.8)	negative
				E + 6 weeks	6.7 kg	7.2 kg	
Shetty [31]	65	11	4 weeks	E	9.3 kg (7.9–10.7)	9.4 kg (8.2–10.6)	negative
Mens [32]	64	11	6 weeks	E	9.0 kg (6.3–11.7)	12.8 kg (10.7–14.9)	negative
				E + 6 months	3.3 kg (−1.8–8.4)	3.5 kg (−1.9–8.9)	
Richter [33]	62	50	4 weeks	E	5.8 kg (5.1–6.5)	6.1 kg (5.5–6.7)	negative
				E + 7 days	6.0 kg	5.7 kg	
				E + 3–5 months	8.7 kg	11.0 kg	
Bosch [23]	61	40	6 weeks	E	3.2 kg	4.6 kg	negative
Greenway [34]	59	40	6 weeks	E	8.8 kg	8.1 kg	negative
Asher [35]	59	40	6 weeks	E	20.0 p (16.9–23.1)	11.1 p (8.6–13.6)	positive
Craig [36]	58	20	6 weeks	E	6.4 p (3.0–9.8)	8.9 p (6.4–11.4)	negative
				E + 6 months	10.9 p (4.6–17.2)	10.0 p (−0.2–20.2)	
Richter [33]	57	32	4 weeks	E	4.9 kg (4.2–5.6)	6.3 kg (5.5–7.1)	negative
				E + 7 days	4.9 kg	6.4 kg	
				E + 3–5 months	2.7 kg	−0.6 kg	
Miller [37]	53	19	4 weeks	E	12.0 p (10.4–13.6)	10.3 p (6.0–14.6)	negative
Frank [38]	52	40	21–25 injections in 7–8 weeks	E	12.3 p (9.2–15.4)	11.5 p (8.4–14.6)	negative
Lebon [39]	49	24	3 weeks	E	data inaccurate	data inaccurate	positive
Carne [26]	44	25	6 weeks	E	21.0 p	19.0 p	negative

‡HCG = Human chorionic gonadotropin. †*n* = total study size; because of randomisation: intervention groups comparable in size.
*E = end of intervention.

Discussion

We did our best to trace all publications relating to studies on the Simeons therapy. Nevertheless, it is possible that we have missed one. Furthermore, we do not know whether there have been studies that have not been published. Our review may be subject to publication-bias. For instance, it is fairly certain that small-scale clinical trials with negative results are less likely to be published [47]. But this does not make our main conclusion any less acceptable: the effect of HCG in the Simeons therapy is insufficiently proven from a scientific point of view. It is striking that since 1977 only four studies have been published on the Simeons therapy [23, 32, 33].

Although the maximum score is almost impossible to reach, the average score for the published studies is low. No study reached the full score for criterion B. Although difference between groups in a RCT should arise from chance we think such descriptions are necessary to check the comparability at baseline, especially in small studies. It is striking, but not surprising as far as the older studies are concerned, that not a single study scored any points for the reliability and validity of the measuring instruments (criterion K). For instance, there were no high scores for subjective concepts like hunger and well-being. Although K is a strict criterion, particularly in the case of older studies, we included it because nowadays considerable importance is attached to the reliability and validity of measuring instruments. A weakness in several studies is that potentially disturbing variables are not recognised as such (criterion G): for instance, when HCG is dissolved it may become less effective under the influence of environmental factors. In several studies the HCG solution was kept for a long time and sometimes there was no mention of the conditions under which it was kept [26, 37, 38]. In addition, few of the studies mention how much contact there was between the patient and the person administering the treatment (criterion G, see Appendix) or between the patient and other patients receiving the treatment (group sessions) (Table 3).

One study stands out because it is the only positive study that received a fairly high score [35]. Criticism has been levelled at this study [48], but the criticism has been largely refuted by the authors [49]. The study can be severely criticised on other grounds. Furthermore, the article mentioned that another study by the same investigators had negative results; however, this work has not been published.

Of the 14 randomised studies 12 reported that the weight-loss with the use of HCG was no greater than with the use of a placebo or with the use of a diet only. However, there was always some weight-loss (Table 4). It seems reasonable to conclude that the effect of the Simeons therapy can be attributed to a diet of 500 kcal, but that the HCG has no specific effect. One claimed effect of HCG is that patients no longer feel hungry and/or find it easier to keep to the diet because they feel well on it. Supporters of the therapy, including Simeons himself, say that a double-blind study of the therapy is not feasible, because persons in the control group will simply not persist with the therapy unless they are extremely motivated [50]. If this view is correct, then in the double-blind studies there should have been far more drop-outs in the control group than in the HCG group or less strict adherence to the diet in the control group, resulting in less weight-loss in that group than in the HCG group. However, according to the results of the studies investigated this does not seem to have been the case (Table 3).

In a meta-analysis, results of studies that score higher than a selected cut-off point and are sufficiently homogeneous are sometimes 'pooled' [51]. We did not engage in 'pooling' in our study because the study populations and outcome measurements are too heterogeneous and because the methodological quality of the studies identified is too low to warrant 'pooling'.

We conclude that there is no scientific evidence that HCG causes weight-loss, a redistribution of fat, staves off hunger or induces a feeling of well-being. Therefore, the use of HCG should be regarded as an inappropriate therapy for weight reduction, particularly because HCG is obtained from the urine of pregnant women who donate their urine idealistically in the belief that it will be used to treat an entirely different condition, namely infertility.

Pharmacists and physicians should be alert on the use of HCG for Simeons therapy. The results of this meta-analysis supports a firm standpoint against this improper indication. Restraints on physicians practising this therapy can be based on our findings.

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Appendix

Details about the criteria listed in Table 1

A Description of inclusion and exclusion criteria. (1)
Description of the way in which the study population was obtained. (1)

B The groups are comparable (i.e. similar) with respect to the following characteristics:
- distribution of men and women (1)
- distribution of age (1)
- distribution of the degree of obesity (1)
- distribution of the duration of obesity (1)
- distribution of the use of medicines (1)

C The randomisation procedure is described in sufficient detail. (4)

D The number of drop-outs per group is known. (1)
The reason for dropping out is known in each case. (2)

E The total number of patients dropping out before the end of the intervention divided by all patients is:
< = 20% (2)
< = 10% (4)

F The size of the smallest group at the start of the intervention in a controlled study is:
> = 25: (4)
> = 50: (8)
> = 75: (12)
and in an uncontrolled study:
> = 50: (4)
> = 100: (8)
> = 150: (12)

G Descriptions are given of:
- the number of injections per week (2)
- the dose of HCG per injection (2)
- the type of injection (subcutaneous or intramuscular) (2)
- keeping-time and keeping-quality of dissolved HCG (2)
- administration of the injections by the patient himself/herself or by someone else (2)
- the number of calories per day (2)
- the duration of the treatment (2)

H Other medicines (laxatives, diuretics, appetite depressants, amphetamines, thyroid drugs) (2) and other co-interventions (weighing sessions, group-meetings) (2), in as much as they are used for slimming purposes, are not allowed during treatment.

I Treatment with HCG is compared with another kind of regular treatment. (4)

J The study is placebo-controlled. (4)

K Information is given about the reliability and validity of the measuring instruments used to measure the following:
- weight reduction (1)
- an alteration in fat-distribution (1)
- degree of hunger (1)
- well-being (1)

L Placebo-controlled: patient is blinded. (5)
Pragmatic study: patient does not know which is intervention and which is control treatment. (5)

M During the intervention the most important variables are measured:
- weight (2)
- body-girth or skin-thickness (distribution of fat) (3)
- degree of hunger (3)
- well-being (2)

N The assessor(s) is(are) binded. (10)

O Values of one or more of the most important variables measured (see M) were measured during or very shortly after the end of the intervention (3)
Values of these variables were measured 6 months or more after the end of the intervention (2)

P If the drop-out during the intervention is less than 10%, then the calculations made on the basis of the most important variables for all patients minus the drop-outs are satisfactory. If the drop-out during the intervention is more than 10%, a calculation has to be made which takes the drop-outs into account. (5)

Q Outcomes for the variables are given at the beginning and end of the treatment; in the case of continuous variables, the following information is given: average values or medians and with standard anomalies, errors, deviations or percentages. (5)