

Evidence/Safety for weight loss using alternative therapies such as hCG injections

Objectives

1. Describe the usual role of human chorionic gonadotropin (hCG) in the body.
 2. Explain the Simeons method of weight loss using hCG injections.
 3. Recognize the adverse events associated with the use of hCG as therapy.
 4. Evaluate hCG's role in weight loss therapy based on existing evidence.
-

Usual Role of hCG

I. Structure

- A. Produced by the human placenta.
- B. Structurally similar to luteinizing hormone (LH), follicle-stimulating hormone (FSH), and thyroid-stimulating hormone (TSH)
 - i. Composed of an alpha chain and a beta chain
 - a. Alpha chains are identical among hCG, LH, FSH, and TSH
 - b. Beta chains vary slightly
 - c. Beta chain of hCG is more similar to LH

II. Function

- A. The primary function of hCG is maintenance of the corpus luteum
 - i. Corpus luteum
 - a. Produces the estrogen and progesterone needed to prevent menstruation and maintain pregnancy for the first 8 weeks of pregnancy
 - b. LH maintains the corpus luteum for the first few weeks of pregnancy
 1. LH concentrations fall due to increasing concentrations of progesterone (negative feedback) and hCG takes over to maintain the development and functionality of the corpus luteum .
- B. hCG exerts its effects through LH receptors
 - i. G protein coupled receptors
- C. LH and FSH
 - i. Due to structural similarities, hCG's activity is identical to LH and to a small extent FSH.
 - a. LH
 1. Women- stimulate androgen production and maintains corpus luteum.

2. Men- Primary stimulus for the production of testosterone
- b. FSH1
 1. Women- Primarily directs ovarian follicle development, and stimulates conversion of androgens to estrogen.
 2. Men- Primary regulator of spermatogenesis, maintains high androgen concentrations in the vicinity of developing sperm, and stimulates conversion of testosterone to estrogen.

III. Indications1,2

- A. Prepubertal cryptorchidism
 - i. Undescended testes.
 - ii. hCG can cause testicular descent which is usually temporary but can sometimes be permanent.
- B. Hypogonadism
 - i. Hypogonadotropic hypogonadism secondary to a pituitary deficiency
 - ii. LH and FSH are produced by the pituitary
 - iii. hCG supplementation gives direct application of the end hormone
- C. Ovulation induction
 - i. Second line to other therapies (clomiphene, aromatase inhibitors, metformin, etc...)

Simeons Method

I. Background

- A. Dr. ATW Simeons was a British endocrinologist that published his findings on the hCG diet in 1954 in the *Lancet*
 - i. Discovered hCG's potential benefits while working with children with Froelich's Syndrome in India
 - a. Froelich's Syndrome is most common in males and is characterized by delayed puberty, small testes, and obesity⁴
 - b. Most likely to a result of damage to the hypothalamus
- B. Used injections of hCG obtained from pregnant women's urine to help treat these patient's.
 - i. The patients commonly had an increased appetite and their appetite was found to be decreased when given injections
 - ii. The patients diets were not restricted and they did not lose weight, but the circumference of their hips decreased
 - iii. hCG was thought to mobilize "abnormal" fat deposited on the hips
- C. These patients with Froelich's Syndrome were put on a restricted diet and given daily injections of hCG.
 - i. Diet consisted of 500 kCal per day
 - ii. Patients were comfortable on such a diet

- iii. “Perfectly Evident that only abnormal fat was being consumed, as there were no signs of any depletion of normal fat.”
 - a. Skin was “fresh and turgid”
 - b. Figures eventually became “normal”
 - iv. Injections did not seem to have any deleterious side effects
 - v. Used this method in a few hundred obese patients not necessarily affected by Froelich’s Syndrome and was successful
 - D. Dr. Simeons postulated that hCG allows the hypothalamus to regulate fat storage in such a way that abnormal stores are available for use as energy
 - i. He states that once excessive fat is stored, it is no longer accessible for use
 - ii. Normal fat is used for energy demands thus leaving the excess, or “abnormal,” fat deposited in the body

II. Mobilized Fat

- A. Dr. Simeons stated that the high hCG levels during pregnancy allows high levels of circulating fat from abnormal stores.
 - i. “Normal” stores are maintained to carry out natural functions and hCG allows the mobilization of the abnormal fat for energy use
 - ii. Allows proper growth of the fetus by supplying adequate nutrition to meet demands of pregnancy
- B. In obese patients, under treatment with hCG, there are similar high levels of circulating fat from abnormal stores
 - i. Allows the patient to adhere to a restricted diet without feeling hungry

III. The Diet

- A. The diet is said to allow rate of loss of approximately 1 pound daily
- B. The physician takes medical history and the patient is weighed and measured
 - i. The amount of weight needed to be lost is determined
 - a. Used a chart for average weight based on height, age, and build
- E. The patient begins IM injections of 125 IU of hCG
 - i. During this time, the patient eats excessively for three days to regain normal fat stores that may have been used
 - ii. Currently, a homeopathic oral solution is available for sublingual use as well as
- F. After the the third day, the patient continues the injections and starts a very strict 500 kCal diet.
 - i. Restricted to certain foods
 - ii. Patient must adhere to this diet, or the diet will not be successful
 - iii. Drink approximately 2 liters of water (plain or mineral) or unsweetened coffee/tea per day.
 - iv. Must avoid cosmetics containing lipid emulsions
 - a. Due to restricted fat intake, the body will absorb the lipids from topical application
- G. The patient comes in daily for weighing, consultation, and injections
 - i. If a gain occurs the consultation is to ascertain the cause
- H. The duration is based on the amount of weight loss needed

- i. Never less than 23 days
 - a. If less than 23 days are needed to meet “normal weight,” the patient will continue injections, but will be placed on a higher kCal diet (800-1000kCal)
 - ii. Never more than 40 days in a row
 - a. If more than forty days needed, the patient must wait 6 weeks before beginning the next cycle.
- I. When the patient finishes the injections, he/she must continue the restricted diet for 3 days.
 - i. The patient must avoid sugars and starches for the first 3 weeks post treatment.
 - ii. The patient is then free to eat whatever he/she chooses
 - a. The patient must weigh in daily and report any changes above 2 pounds
- J. Menstruation
 - i. Therapy should start immediately after or, alternatively, 10 days before the start of menstruation
 - ii. Injections cease during menstruation, but dieting continues
 - iii. If the end of therapy will coincide with menstruation
 - a. The last three injections should be given before menstruation
 - b. Alternatively, the last three injections could be given following menstruation with continuing the diet
 - 1. Not applicable if the patient has reached desirable weight and is on increased kCal intake

Adverse Effects/Safety

- I. Simeons
 - A. Dr. Simeons states that hCG has no “stimulating effect whatsoever on normally developed and normally functioning sex-glands.”
 - i. Only indirectly improves abnormal sex function and can cause the onset of puberty to occur more quickly in young people.
 - B. He also states that there are no undesirable sexual changes in men or women
 - i. Gynecomastia in men
 - ii. Voice changes or beard development in Women
 - C. Dr. Simeons believed that the body will only burn the unwanted fat, and leave all the vitamins and minerals that were stored with the fat
 - i. Therefore hCG injections will not cause vitamin/mineral deficiencies
 - D. Does state that hCG injections can cause:
 - i. Fluid retention
 - ii. Gout exacerbations upon initiation, but states that these do not occur with continued therapy
 - iii. Gallstone complications in those that have previously had them
 - E. Possible hair loss
- II. Present Day

A. *Black Box Warning*

- i. “Human chorionic gonadotropin (hCG) has no known effect on fat mobilization, appetite, sense of hunger or body-fat distribution. Human chorionic gonadotropin (hCG) has not been demonstrated to be effective adjunctive therapy in the treatment of obesity. There is no substantial evidence that it increases weight loss beyond that resulting from caloric restriction, that it causes a more attractive or “normal” distribution of fat or that it decreases the hunger and discomfort associated with calorie-restricted diets.”

B. Contraindications

- i. Use in:
 - a. Precocious puberty
 - 1. Use of hCG can also induce precocious puberty and should be discontinued if this occurs
 - b. Pregnancy
 - 1. Category X
 - c. Prostatic carcinoma
 - d. Androgen-dependent neoplasm
 - e. Allergy to hCG

C. Menstruation

- i. Overstimulation of the ovaries during ovulation can lead to
 - a. Self-limiting ovarian enlargement that spontaneously resolves
 - b. Ovarian hyperstimulation syndrome (OHSS)
 - 1. More serious than general overstimulation of ovaries
 - 2. Characterized by ascites, ovary enlargement, pleural effusions, hypothorax, fever and hypovolemia which can result in shock
 - 3. enlargement/rupture of preexisting ovarian cysts resulting in hemoperitoneum, multiple births, and arterial thromboembolism
 - c. Multiple pregnancies
 - 1. This and OHSS is more common when being treated with hCG and other gonadotropins (LH/FSH) for fertility

D. Edema

- i. Use in caution in patients with
 - a. Cardiac disease
 - b. Renal disease
 - c. Epilepsy
 - d. Asthmea
 - e. Migraine

E. Possible tumor development

- i. Testicular and ovarian tumors have been reported
 - a. When used for fertility
 - 1. Dose range of 500 IU to 10,000 IU based on indication

F. Injections

- i. Possible injection site reactions
- ii. Diluent contains benzyl alcohol
 - a. Gasping syndrome in premature infants
 - b. Inconclusive evidence regarding hCG excretion during lactation

G. Others

- i. Gynecomastia
- ii. Testicular and penile enlargement
- iii. Headache
- iv. Arterial thromboembolism
- v. Irritability
- vi. Restlessness
- vii. Depression
- viii. Fatigue
- ix. Aggressive behavior
- x. Signs/symptoms of androgen excess
 - a. Hirsutism, virilization, masculinization, acne, excess hair, menstrual irregularity, obesity, and infertility

H. Drug Interactions

- i. Interacts with radio-immunassay of gonadotropins
 - a. Especially LH

Evidence

I. Lipolytic effects

- a. hCG has not been found to have direct control of lipolysis (or lipogenesis)
 - i. Adipose tissue does appear to have receptors for hCG/LH
 - a. However hCG was not found to influence glycerol release from adipose tissue (*in vitro*)
 - 1. i.e. does not affect lipolysis
 - b. hCG was not found to affect biochemical markers of lipogenesis

II. Leptin

- a. hCG has been shown to enhance leptin secretion in the body
 - i. This correlation is actually thought to lead to increased fat deposition
 - a. Increases the capacity of preadipocytes to proliferate and differentiate
- B. However, exogenous leptin administration has been shown to facilitate weight loss
 - i. Studies show that obese patients have an increase in circulating leptin proportionate to the degree of excess weight
 - b. Similar to insulin resistance
 - c. Implications on hCG efficacy?
- C. Leptin also has a role in inducing satiety when the body has received enough nourishment.
 - i. Further implications on hCG efficacy?

III. Human Growth Hormone

- A. hCG has also been reported to stimulate the secretion of HGH
 - i. HGH is important in lipid and carbohydrate metabolism
 - a. Possesses lipolytic effects
 - b. Further implications on hCG efficacy?
- IV. Speculative Relationships
 - A. Research is lacking that directly links hCG to most of the ?'s above
- V. Randomized Studies
 - A. Most Randomized double-blind studies were performed from the early 1960's to the late 1970's
 - i. Only 4 trials have been performed since 1977
- VI. Meta-Analysis
 - A. Sabine and colleagues showed that the trials conducted regarding hCG:
 - i. Were considered to be poorly designed or reported
 - a. Scored trials based on reviewer established criteria
 - 1. Out of 100 points possible the scores ranged from 16 – 73
 - B. 24 studies were reviewed
 - i. 14 were randomized controlled trials
 - a. 12 of these reported weight loss with hCG plus 500 kCal diet did not differ from placebo plus diet
 - ii. One of the RCT's that did show that hCG caused a greater reduction in weight versus placebo (Asher and Harper) has been criticized due to the design of their trial
 - a. The physician who performed the clinical work had an active hCG assisted weight loss practice
 - b. The authors also performed an initial trial that showed no difference in weight loss for hCG vs. placebo
 - a. Reported this in the positive trial
 - b. Yet findings from initial trial were unpublished
- VII. Position statement
 - A. Due to the continual use of hCG as an adjunct in weight loss therapy, the American Society of Bariatric Physicians approved this position statement:

“Numerous clinical trials have shown HCG to be ineffectual in producing weight loss. HCG injections can induce a slight increase in muscle mass in androgen-deficient males. The diet used in the Simeons method provides a lower protein intake than is advisable in view of current knowledge and practice. There are few medical literature reports favorable to the Simeons method; the overwhelming majority of medical reports are critical of it. Physicians employing either the HCG or the diet recommended by Simeons may expose themselves to criticism from other physicians, from insurers, or from government bodies.”

“It is the position of the American Society of Bariatric Physicians that:

- 1. The Simeons method for weight loss is not recommended.*
- 2. The Simeons diet is not recommended.*
- 3. The use of HCG for weight loss is not recommended.”*

Conclusion

- I. hCG is a naturally occurring substance that is primarily responsible for the maintenance of the corpus luteum during pregnancy
- II. Because of its function as a sex hormone, hCG has utility as medicinal therapy.
- III. It was due use of hCG as therapy in patients with Froelich's Syndrome that he created his restricted calorie, hCG diet.
- IV. Use of hCG comes with inherent risks
- V. Due to lack of evidence, hCG should not be recommended as an aide in weight loss therapy.