

Human Growth Hormone Use in Age Related Therapies

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Objectives

- Understand the Physiological Function of Growth Hormone and its Role in Age Related Disorders
- Debate the Current Claims of HGH Use in Age Related Therapies Circulating in the Mass Media
- Interpret the Results of Current Clinical Trials in Order to Provide Evidence Based Recommendations

History

- **Prior to 1985**
 - Derived from Pituitary Glands of Cadavers
 - Limited Quantities Available
 - Productions ceased following studies implicating the impurities in pituitary HGH with development of Creutzfeldt-Jacob disease in treated patients
- **1985 to Present**
 - Biosynthetic HGH became available (Somatropin)
 - Minimal impurities, relatively safe, readily available

Indications – FDA Approved (Children)

- **Growth failure due to:**
 - Inadequate endogenous secretion
 - Turner syndrome
 - Prader-Willi syndrome
 - Chronic renal insufficiency
- **Born small for gestational age and fail to catch-up by 2 years**

Indications – FDA Approved (Adult)

- **HIV patients with wasting syndrome or cachexia**
- **Replacement of endogenous GH in patients with:**
 - Subnormal response to a standard growth hormone stimulation test
 - Hormones deficiencies as a result of single or multiple organ failure
- **Treatment of Short Bowel Syndrome**

Off Label / Investigational Use

- Chronic Heart Failure
- Pediatric HIV patients with wasting /cachexia
- **Age Related Therapies**

Physiological Effects

- **Promotes Linear Growth**
 - Partially through stimulation of Insulin-Like Growth Factor 1 (IGF-1)*
- **Positive Metabolic Actions**
 - Anabolic
 - Stimulates protein synthesis
 - Increases lean body mass
 - Increases bone density
 - Lipolytic
 - Most dramatic effect
- **Negative Metabolic Effects**
 - Increases total body water
 - Induces insulin resistance

**See next slide*

HGH and IGF-1

- **Hormonal Axis**
 - GH stimulates IGF-1 production
 - High levels of IGF-1 decrease HGH synthesis
- **Opposing Effects on lipids and glucose**
 - HGH stimulates lipolysis and decreases insulin sensitivity
 - IGF-1 stimulates lipogenesis and decreases serum glucose
- **Synergic Effects on Lean Muscle and Bone Density**

HGH Life Cycle

- **Declines with Age**
 - “Somatopause” term used to describe the decline in GH and associated physiologic responses with age
 - Optimal physiologic and age-adjusted ranges of normal values for HGH and IGF-1 are not currently defined

Total daily HGH declines with age so that “elderly” levels are reached by age 35-40

Adapted from: The Journal of NIH Research, April 1995

Marketing of HGH in the Media

- **In 1990, a study by Rudman, D. was published titled, “Effects of Human Growth Hormone on Men Over 60 Years Old”**
 - The study involved 21 men aged 61 to 81 who were apparently healthy but with IGF-1 levels below those found in normal young men
 - 12 men were given HGH injections, 9 received placebo for a treatment period of 6 months
 - Results were decrease in adipose tissue, increase in lean body mass and lumbar spine density in the treatment group (P < 0.05)
 - The study became the “Gold Standard” referenced as the study supporting most claims by marketed by manufactures

Marketing of HGH in the Media

- **Anti-Aging Movement Began**
 - Physicians began marketing themselves as age-specialist
 - Clinics were created with the premise ordering expensive test to determine “biological age” followed by treatment with the expensive course of injections

www.antiagingandvitality.com/
www.mdlongevity.com/
www.centerforantiaging.com/
www.antiagingclinic.com.au/

Growth Hormone and Sex Steroid Administration in Healthy Aged Women and Men: A Randomized Control Trial

JAMA. 2002, 288(18):2282-2292

- **Objectives:**
 - Evaluate the effects of recombinant HGH and/or sex steroids on body composition, strength, endurance, and adverse outcomes in aged persons
- **Design:**
 - 26-week randomized, double-blind, placebo controlled parallel-group trial in healthy, ambulatory, community-dwelling US women (n = 57) and men (n = 74) aged 65 to 88

Study Protocol

- **Participants were randomized to receive:**
 - HGH (starting dose, 30 µg/kg, reduced to 20 µg/kg SQ 3 times/wk) + sex steroids
 - **Men:** testosterone 100 mg biweekly IM injections
 - **Women:** transdermal estradiol, 100 µg/day + oral medroxyprogesterone, 10 mg/d, during the last 10 days of each 28-day cycle (HRT)
 - GH + placebo sex steroid
 - sex steroid + placebo GH
 - Placebo GH + placebo sex steroid

Study Results

Men

- **LBM¹ Increased by:**
 - 0.1 kg with placebo
 - 1.4 kg with Testosterone (P = 0.06)
 - 3.1 kg with GH (P < 0.001)
 - 4.3 kg with GH + Testosterone (P < 0.001)

Women

- **LBM¹ Increased by:**
 - 0.4 kg with placebo
 - 1.2 kg with HRT (P = 0.09)
 - 1.0 kg with GH (P = 0.001)
 - 2.1 kg with GH + HRT (P < 0.001)

*Lean Body Mass (LBM)
¹Measured by dual energy x-ray absorptiometry (DXA) scans

Study Results

Men

- **Fat Mass Decreased***
 - Significantly in **both** the GH and GH + Testosterone groups

Women

- **Fat Mass Decreased***
 - Significantly in **both** the GH and GH + HRT groups

*Measured by dual energy x-ray absorptiometry (DXA) scans

Study Results

Men

- **Strength**
 - ↑ in placebo group
 - ↑ in the testosterone group (P=0.86)
 - ↑ in the GH group (P = 0.29)
 - ↑ in the testosterone + GH group (P = 0.05)

Women

- **Strength**
 - ↓ in placebo group
 - ↑ in the HRT group (P=0.09)
 - ↑ in the GH group (P = 0.29)
 - ↑ in the HRT+GH group (P = 0.14)

Study Results

Men

- **Endurance (VO₂max)**
 - ↑ with GH (P=0.11) and GH + testosterone (P < 0.001)

Women

- **Endurance (VO₂max)**
 - ↑ with GH (P=0.07) and GH + HRT (P = 0.06)

Study Results- Comparative Adverse Effects

- **Diabetes or Glucose Intolerance**
 - Most Significant Adverse Effect
 - Occurred in 18 GH-treated men vs 7 not receiving GH (P = 0.006%)

	Patient with New Onset Glucose Intolerance and Diabetes by Treatment Group							
	Men				Women			
	Placebo	Test.	GH	GH+Test.	Placebo	HRT	GH	GH+HRT
Impaired Glucose (110-126 mg/dL)	3	3	7	6	2	2	2	2
Diabetes (>126 mg/dL)	0	1	2	3	0	0	0	0

Study Results- Comparative Adverse Effects

- **Edema**
 - Significantly more common in women taking GH (39% vs 0%) and GH + HRT (38% vs 0%)
- **Carpal Tunnel Symptoms**
 - More common in men taking GH + testosterone (32% vs 0%)
- **Arthralgias**
 - More common in men taking GH (41% vs 0%)

Conclusions

- In this study, GH with or without sex steroids in healthy, aged men and women improved body composition as demonstrated in earlier studies
- GH and GH + Sex steroid has varied responses in functionality between men and women. The authors concluded that the functionality correlated with the changes in LBM
- Due to frequent adverse effects encountered, especially diabetes and glucose intolerance, the authors concluded GH should currently be confined to use in controlled studies

Critique-

Strengths

- Strongest study type limits confounders
- No previous testosterone replacement in men
- Consistent diet and level of activity during study period documented
- Evaluated the effects of similar hormones used in combination or alone

Weaknesses

- Limitations of DXA scan for LBM measure
- 18 women had taken HRT previously
- Small number of participants, especially women
- Findings limited to relatively "healthy" older adults
- Study length

Overall Recommendations

- A summation of the literature to date demonstrates significant improvement in body composition but no significant improvement in functional status with short term use of GH
- There is still not enough data to make recommendations for long term GH use for "anti-aging" purposes
- For patient's who are prescribed such therapy, close monitoring for adverse effects especially glucose intolerance and diabetes should be conducted
- The current level of literature does show promise following larger and longer term studies

Questions

True or False:

1. The most dramatic effect following GH use is lipolysis.
2. Results from the most current RCT discussed demonstrated a significant increase in lean body mass, decreased fat mass, and increase in strength and endurance in both men and women treated with GH monotherapy.
3. The most frequent adverse effect of growth hormone use is hyperglycemia.

References

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