

Introduction

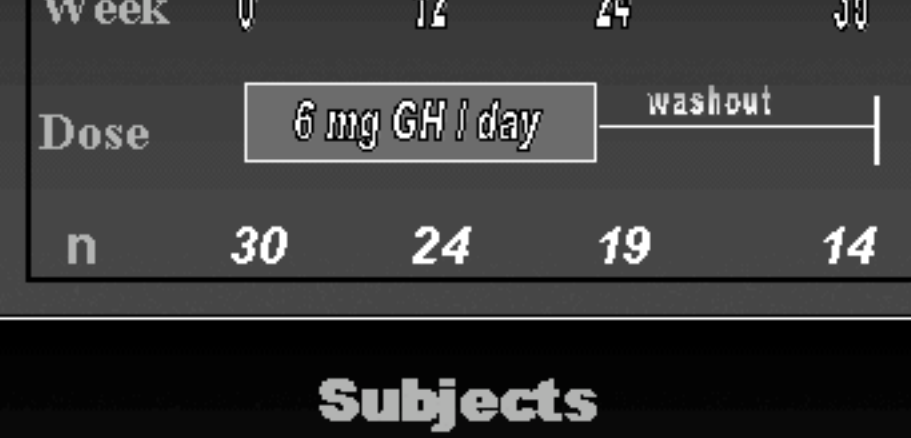
- Fat redistribution in HIV-infected individuals includes accumulation of excess visceral adipose tissue (VAT) (Engelson *et al* AJCN 1999)
- Recombinant human growth hormone (GH) promotes fat loss through increased lipid oxidation (Mulligan *et al*, JCE&M 1993)
- Two published reports suggest that GH (6 mg/day) reduces VAT in HIV fat redistribution
 - Torres *et al* AIDS 1999: 10 case studies
 - Wanke *et al* AIDS 1999: short-term (12 weeks), n=10
 - Study design limitations include the small number of subjects and body composition methods that do not measure VAT

Specific aims

- To determine the effect of recombinant human growth hormone (GH) on body composition in HIV-infected individuals with fat redistribution including excess visceral adipose tissue
- To assess the safety of GH treatment
- To determine the effect on body composition of discontinuing GH treatment

Study Design

Prospective, open-label trial of recombinant human growth hormone (GH; Serostim)



Subjects

- HIV+
 - 44.7 ± 8.6 years old (range 30 - 67)
 - 26 men, 4 women
 - 28 Caucasian, 2 African-American
- enlarged abdomen
 - self-report
 - visual confirmation by 2 CRIA physicians
- 10 also had visible lipoatrophy
- clinically stable on antiretrovirals
- no history of diabetes, carpal tunnel syndrome, or conditions with edema
- fasting glucose < 120 mg/dL

Measurements

- Whole body MRI (Engelson *et al*, AJCN 1999)
 - visceral and subcutaneous adipose tissue
 - skeletal muscle
- DXA scan
 - regional body fat
 - lean mass
- Total body potassium (TBK)
 - whole body counting of 40K
 - body cell mass = TBK x 0.0083
- 2 hour GTT
 - glucose
 - insulin
- Fasting lipids
 - triglycerides
 - cholesterol

Body Composition Results - Lean (all subjects)

		Baseline	Week 12	Week 24	Week 36 (after washout)
MRI	SM	29.6 ± 5.7	31.2 ± 6.3*	30.4 ± 6.5*	28.7 ± 5.7
DXA	Arm Lean	6.7 ± 1.4	7.4 ± 1.5*	7.5 ± 1.7*	6.7 ± 1.2
	Leg Lean	20.1 ± 3.7	21.3 ± 3.7*	21.0 ± 4.0*	19.4 ± 2.9
	Trunk Lean	30.1 ± 4.8	33.1 ± 5.8*	33.5 ± 5.8*	30.8 ± 4.8
TBK	Body Cell Mass	31.3 ± 5.5	32.4 ± 6.2*	32.8 ± 6.4*	32.1 ± 6.1

*Data analysis by paired t-test (only subjects with data from both visits)
 *All p values represent comparison with baseline

† p < 0.05 * p < 0.01 † p < 0.001 † p < 0.0001

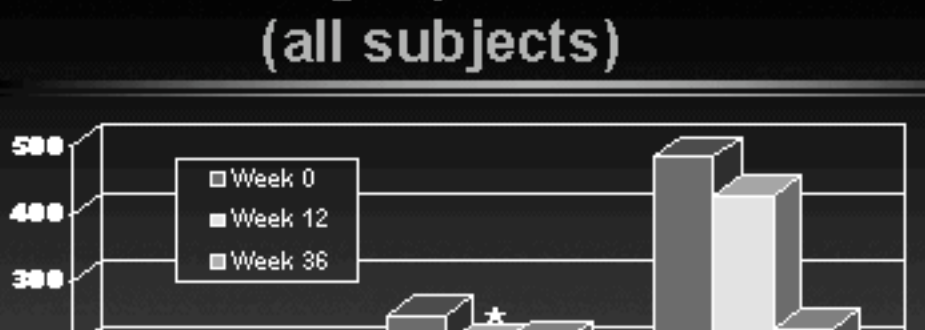
Body Composition Results - Fat (all subjects)

		Baseline	Week 12	Week 24	Week 36 (after washout)
MRI	SAT	14.3 ± 6.0	12.6 ± 6.3*	11.7 ± 6.0	14.9 ± 8.3
	VAT	5.2 ± 2.0	3.3 ± 1.3*	2.8 ± 1.2*	4.4 ± 1.9*
DXA	Arm Fat	1.2 ± 0.7	1.0 ± 0.7*	0.9 ± 0.7	1.3 ± 0.9
	Leg Fat	3.0 ± 1.9	2.4 ± 1.6*	2.2 ± 1.6*	2.9 ± 1.9
	Trunk Fat	10.0 ± 3.3	7.0 ± 3.4*	6.1 ± 3.4*	9.2 ± 4.4

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 *All p values represent comparison with baseline

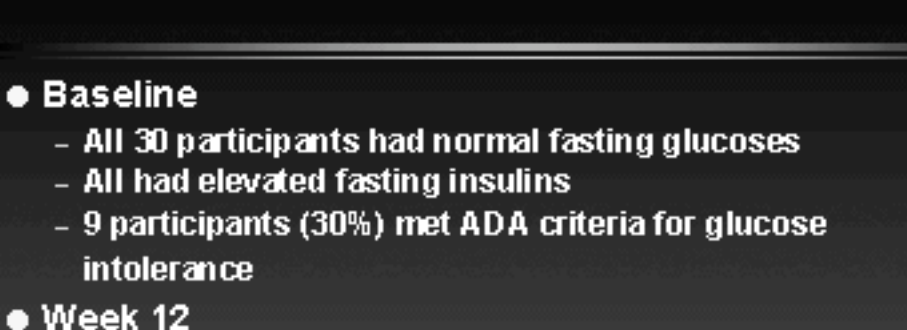
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MRI Adipose Tissue Results (n = 14)



*Statistics: Repeated Measures ANOVA and Scheffe pairwise comparisons
 *p values vs baseline † p < 0.05 † p < 0.01 † p < 0.0001

Fasting Lipid Results (all subjects)

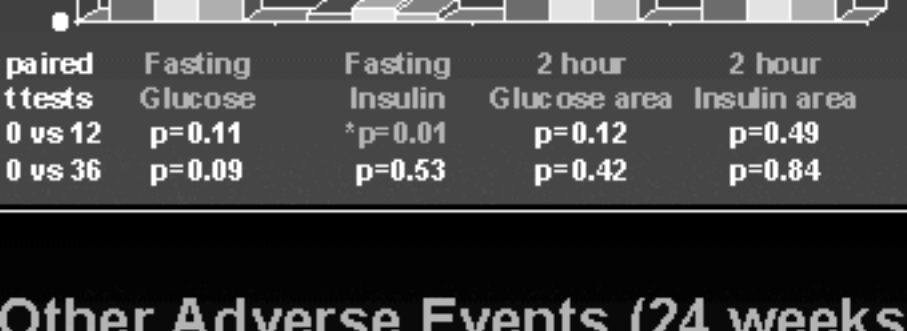


0 vs 12 p=0.38 p<0.01 p=0.57
 0 vs 36 p=0.64 p=0.06 p=0.17
 paired t-tests

Glucose & Insulin Results - 1

- Baseline
 - All 30 participants had normal fasting glucoses
 - All had elevated fasting insulins
 - 9 participants (30%) met ADA criteria for glucose intolerance
- Week 12
 - 3 participants (13%) met ADA criteria for diabetes
 - 2 began oral hypoglycemic agents
 - 9 (38%) met criteria for glucose intolerance
- Week 36 (after washout)
 - 1 participant remained glucose intolerant
 - 2 remained on oral hypoglycemic agents

Glucose & Insulin Results - 2 (all subjects)



paired ttests: Fasting Glucose p=0.11 Fasting Insulin † p=0.01 2 hour Glucose area p=0.12 2 hour Insulin area p=0.49
 0 vs 36 p=0.09 p=0.53 p=0.42 p=0.84

Other Adverse Events (24 weeks)



Discussion

- 24 weeks of growth hormone promoted fat loss
 - preferentially VAT (↓ 46%)
 - also SAT (↓ 18%)
- GH increased lean tissue
 - SM (↑ 3%)
 - also fat free mass and body cell mass
- After 12 weeks off drug:
 - all trunk fat and SAT returned
 - 85% of VAT returned
 - all gains in lean tissue reversed

Discussion 2

- Adverse events were common, and included diabetes and carpal tunnel syndrome.
- Most adverse events resolved after GH was discontinued.

Conclusions

- Growth Hormone is an effective treatment for excess visceral adipose tissue.
- In this population, which is likely to have a high prevalence of insulin resistance at baseline, it is important to monitor plasma glucose.
- The tolerability of GH may be improved with a dose of less than 6 mg/day.