

노화의 신체적 개념과 노화방지 호르몬인 성장호르몬

Body Changes with Aging and GH Replacement as Antiaging Therapy

/

1

Sung - Woon Kim, M.D.

Department of Internal Medicine / GH Clinic

Kyunghee University College of Medicine & Hospital

E - mail : igf1@unitel.co.kr

Abstract

Aging is a very natural and mandatory process of human life. Aging processes mean physical and psychological declining as well. These declines include hormonal deficiencies compared with in one's young adult life. From an academic point of view, aging originates from the shortening of the telomere length, attacking oxidative radicals and accumulations of toxic materials. Antiaging treatment stems from the following concept : ' aging is a kind of disease, not a natural process, so we can handle it for a better and longer life. ' Growth hormone (GH) is the first - line treatment of aging, because the GH secretion declines by 14%/decades through the adult life, leading to a functional GH deficiency in the elderly. It may increase the fat mass inside the abdomen and decrease the bone mass. It may also involve other negative changes in the body composition. Recently, many studies showed that GH replacement therapy may restore negative changes in the body composition from aging. We predict the human being's life span will reach up to 100 years in this century. Until about 80 years of age, one can maintain his or her life with the inborn health ; however, after that age, medical modifications should be needed for restoring their well beings.

Keywords : **Aging; Antiaging; Growth hormone**

: ; ;

‘ ,

. 가

가

2 . ,

가

. ()

20 1%

(1).

20

가 50%

가

70 가

가

80

20

가

21

14.4%

human genome project가

60 가 50% 65

2001

1/3 DNA 가 1990

(menopause), 10 1 DNA 1953

(Androgen Deficiency in Aging Male, ADAM)

가 (

(somatopause)) human genome project

가

가

가 2

LH/ 2001 , 5

FSH가 가

10

IGF - I(3 5

I ; insulin - like growth factor - I) 가 (2).

가

가

가 ? DNA

mRNA가

가 , DNA

가

50%

가

100

10 DNA

80 (bioproduct)

80

ERT or HRT)

(3~5).

20%

가 10%

가

2 가 .

가

(8).

가

2.

1)

FDA

가

가

(mela-

가

,

tonin)

(6),

, ,

7%

가

. 가

(7).

CT MRI

가

가

6

1.

1

,

4~6 kg

(9~14).

(total

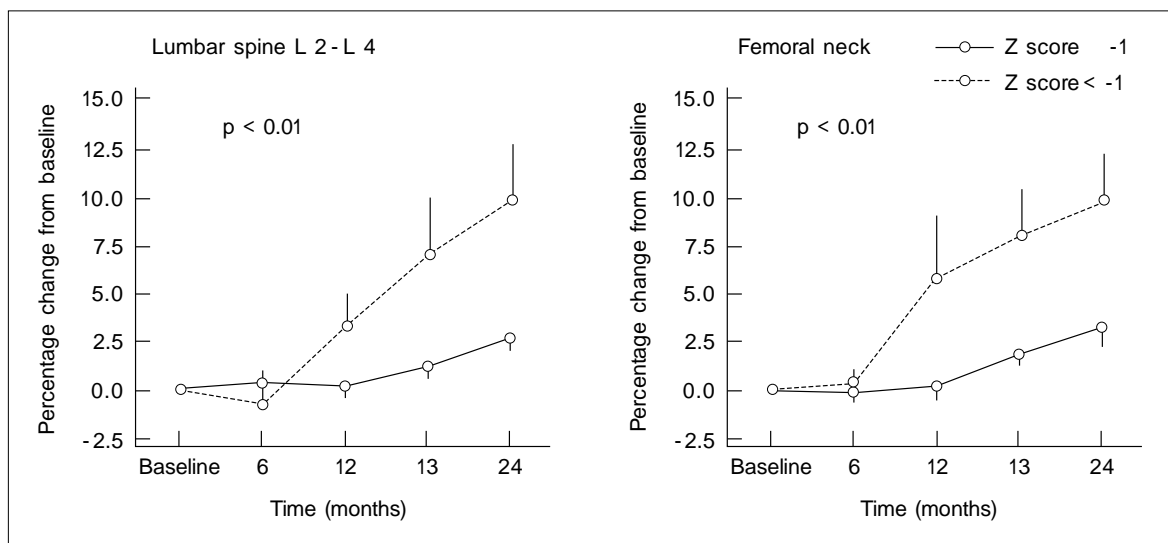
cholesterol, TC),

(triglyceride, TG),

(estrogen or hormone replacement therapy,

(LDL - cholesterol, LDL - C),

B(apolipoprotein B, ApoB) , 가, (ejection fraction) 가
 가가 , tion fraction) 가
 (HDL - cholesterol, HDL - C) 가 .
 . 6
 0.25 IU/kg week 가(18%), 1 (stroke volume)
 (12.5 0 µg/kg/day) TC, LDL - 가(28%), (cardiac output) 가
 C, ApoB TG, ApoA 가 (43%), .
 (15~23).
 가 (餘命 ; (32~35).
 life expectancy) ,
 2 가 . 2)
 344 가
 가 (stan- 가 가,
 dardized mortality ratio, SMR) 1.74 가,
 . (腦卒中 ; .
 SMR=3.39) (SMR=4.91) 가 (double blind placebo controlled
 . study) open trial .
 (premature atherosclerosis) 0.25 IU/kg/week(12.5 µg/kg
 day) .
 [body mass index, BMI(kg/m²)], 3~6 가
 가 , PAI - 1(plasminogen 가 가
 activator inhibitor - 1), , 6 12
 (HDL - cholesterol) . , 1
 4~10% 가
 가 가
 - (intima - media thickness, IMT), 가 6
 .
 20 가
 , 가가 6
 , 가 2 가
 . 3 가 (24 ~



1.

24

가

30)(1).

2~3

4. (Quality of Life, QoL)

가 가

가

가

가

, 5

2

, , -

QoL

3.

T , B , NK(natural

가

killer) ,

IGF - I 가

QoL

Nottingham

IGF - I

Health Profile(NHP)

(cell - mediated immunity)

86

86

(humoral immunity)

(less energetic),

(Snell dwarf mouse)

(12.5 $\mu\text{g}/\text{kg}/\text{day}$)

(38~45).

NK

(36, 37).

, libido 가,

(short - term

memory) open trial

가 . 0.5~1.0 /

1 6~7

5. (46, 47). 3~4 IGF - I

, , IGF - I

, Sheehan ,

가 가

1997 Port .

Stephen

(insulin toler-

ance test, ITT insulin induced hypoglycemic 3~6 , 2 3

test, IHT) 3 µg/L0(=ng/

mL) (46, 47). 47 (LG , 4

GHRH , , L - DOPA /), - II(, 4 /),

(- , 4 /),

L - DOPA (, 16 /) .

500 mg L - DOPA 1

90 , 120 3 . 1

. ,

L - DOPA 가

L - DOPA metoclopramide 가 4

. 1

가

6. 30%

가

(48~51).

가

carpal tun-
nel (1%)
base 4,000
6
3 가
가

1999 2 26
GHRH, L - DOPA,
3 ng/mL
3
3
가
2000 UN 65
가 7% 가
가
가(aged nation) 가 . 100
가

1. Zumoff B, et al. Age variation of the 24 - hour mean plasma concentrations of androgens, estrogens, and gonadotropins in normal adult men. J Clin Endocrinol Metab 1982 ; 54(3) : 534 - 8
2. Birney E, et al. Mining the draft human genome. Nature 2001 ; 409(6822) : 827 - 8
3. Christiansen JS, et al. Effects of growth hormone on body composition in adults. Horm Res 1990 ; 33 (Suppl 4) 61 - 4
4. Holcombe JH, et al. Biosynthetic human growth hormone in the treatment of growth hormone deficiency. Acta Paediatr Scand Suppl 1990 ; 367 : 44 - 8
5. Shi YF, et al. Treatment of growth hormone deficient patients with recombinant somatotropin for 1 year : results of a Chinese multicentre trial. Acta Paediatr Scand Suppl 1990 ; 370 : 212 - 5
6. Huether G. Melatonin as an antiaging drug : between facts and fantasy. Gerontology 1996 ; 42(2) : 87 - 6
7. Raben M. The clinical use of growth hormone. NEJM 1962 ; 266 : 82 - 6
8. Rosen T, BA Bengtsson. Premature mortality due to cardiovascular disease in hypopituitarism. Lancet 1990 ; 336(8710) : 285 - 8
9. Bengtsson BA, et al. Treatment of adults with growth hormone(GH) deficiency with recombinant human GH. J Clin Endocrinol Metab 1993 ; 76(2) : 309 - 17
10. Snel YE, et al. Adipose tissue assessed by magnetic resonance imaging in growth hormone - deficient adults : the effect of growth hormone replacement and a comparison with control subjects. Am J Clin Nutr 1995 ; 61(6) : 1290 - 4

11. de Boer H, et al. Changes in subcutaneous and visceral fat mass during growth hormone replacement therapy in adult men. *Int J Obes Relat Metab Disord* 1996 ; 20(6) : 580 - 7
12. Marcus R, AR Hoffman. Growth hormone as therapy for older men and women. *Annu Rev Pharmacol Toxicol* 1998 ; 38 : 45 - 61
13. Cummings DE, GR Merriam. Age - related changes in growth hormone secretion : should the somatopause be treated? *Semin Reprod Endocrinol* 1999 ; 17(4) : 311 - 25
14. Wang Z. Growth hormone deficiency in adults and clinical use of recombinant human growth hormone. *Chin Med J (Engl)* 1999 ; 112(3) : 195 - 201
15. Eden S, et al. Growth hormone treatment of growth hormone - deficient adults results in a marked increase in Lp(a) and HDL cholesterol concentrations. *Arterioscler Thromb* 1993 ; 13(2) : 296 - 301
16. Garry P, P Collins, JG Devlin. An open 36 - month study of lipid changes with growth hormone in adults : lipid changes following replacement of growth hormone in adult acquired growth hormone deficiency. *Eur J Endocrinol* 1996 ; 134(1) : 61 - 6
17. O'Halloran DJ, et al. Increased serum lipoprotein(a) concentrations after growth hormone (GH) treatment in patients with isolated GH deficiency. *Ann Clin Biochem* 1996 ; 33(Pt 4) : 330 - 4
18. Hassan HM, et al. Body composition, atherogenic risk factors and apolipoproteins following growth hormone treatment. *Acta Paediatr* 1996 ; 85(8) : 899 - 901
19. Lucidi P, et al. A dose-response study of growth hormone (GH) replacement on whole body protein and lipid kinetics in GH - deficient adults. *J Clin Endocrinol Metab* 1998 ; 83(2) : 353 - 7
20. Leese GP, et al. HDL - cholesterol reductions associated with adult growth hormone replacement. *Clin Endocrinol(Oxf)*, 1998 ; 49(5) : 673 - 7
21. Bengtsson BA, et al. The effects of treatment and the individual responsiveness to growth hormone(GH) replacement therapy in 665 GH - deficient adults. KIMS Study Group and the KIMS International Board. *J Clin Endocrinol Metab* 1999 ; 84(11) : 3929 - 35
22. Chrisoulidou A, et al. Effects of growth hormone treatment on very - low density lipoprotein apolipoprotein B100 turnover in adult hypopituitarism. *Metabolism* 2000 ; 49(5) : 563 - 6
23. Wieringa G, et al. Changes in lipoprotein(a) levels measured by six kit methods during growth hormone treatment of growth hormone - deficient adults. *Growth Horm IGF Res* 2000 ; 10(1) : 14 - 9
24. Johannsson G, et al. Two years of growth hormone (GH) treatment increases bone mineral content and density in hypopituitary patients with adult - onset GH deficiency. *J Clin Endocrinol Metab* 1996 ; 81(8) : 2865 - 73
25. Baum HB, et al. Effects of physiologic growth hormone therapy on bone density and body composition in patients with adult - onset growth hormone deficiency. A randomized, placebo - controlled trial. *Ann Intern Med* 1996 ; 125(11) : 883 - 90
26. Burman P, et al. Growth hormone(GH) - deficient men are more responsive to GH replacement therapy than women. *J Clin Endocrinol Metab* 1997 ; 82(2) : 550 - 5
27. Janssen YJ, et al. Skeletal effects of two years of treatment with low physiological doses of recombinant human growth hormone(GH) in patients with adult - onset GH deficiency. *J Clin Endocrinol Metab* 1998 ; 83(6) : 2143 - 8
28. Johannsson G, C Ohlsson, Growth hormone therapy and fracture risk in the growth hormone - deficient adult. *Baillieres Clin Endocrinol Metab* 1998 ; 12(2) : 233 - 50
29. Sartorio A, et al. Effects of 12 - month GH treatment on bone metabolism and bone mineral density in adults with adult - onset GH deficiency. *J Endocrinol Invest* 2001; 24(4) : 224 - 30
30. Gotherstrom G, et al. A prospective study of 5 years of GH replacement therapy in GH - deficient adults : sustained effects on body composition, bone mass, and metabolic indices.

- J Clin Endocrinol Metab 2001 ; 86(10) : 4657 - 65
31. Cuneo RC, et al. Growth hormone treatment in growth hormone - deficient adults. . Effects on exercise performance. J Appl Physiol 1991; 70(2) : 695 - 700
 32. Jorgensen JO, et al. Adult growth hormone deficiency. Horm Res 1994 ; 42(4 - 5) : 235 - 41
 33. Weaver JU, et al. The effect of low dose recombinant human growth hormone replacement on regional fat distribution, insulin sensitivity, and cardiovascular risk factors in hypopituitary adults. J Clin Endocrinol Metab 1995 ; 80(1) : 153 - 9
 34. Johansson JO, et al. Long - term treatment with growth hormone decreases plasminogen activator inhibitor - 1 and tissue plasminogen activator in growth hormone - deficient adults. Thromb Haemost 1996 ; 76(3) : 422 - 8
 35. Johannsson G, et al. Long - term cardiovascular effects of growth hormone treatment in GH - deficient adults. Preliminary data in a small group of patients. Clin Endocrinol(Oxf) 1996 ; 45(3) : 305 - 14
 36. Bozzola M, et al. In vitro and in vivo effect of growth hormone on cytotoxic activity. J Pediatr 1990 ; 117(4) : 596 - 9
 37. Benfield MR, et al. The effect of rhGH in vitro on donor - specific hyporesponsiveness in pediatric transplantation. Pediatr Transplant 1997 ; 1(1) : 90 - 7
 38. McKenna SPA, LC Doward. Quality - of - life assessment of adults with growth hormone deficiency. Implications for drug therapy. Pharmacoeconomics 1994 ; 6(5) : 434 - 41
 39. Beshyah SA, et al. Replacement treatment with biosynthetic human growth hormone in growth hormone - deficient hypopituitary adults. Clin Endocrinol(Oxf) 1995 ; 42(1) : 73 - 84
 40. Wallymahmed ME, et al. Quality of life, body composition and muscle strength in adult growth hormone deficiency : the influence of growth hormone replacement therapy for up to 3 years. Clin Endocrinol(Oxf) 1997 ; 47(4) : 439 - 46
 41. Wren LBA, Bengtsson G. Johannsson. Beneficial effects of long - term GH replacement therapy on quality of life in adults with GH deficiency. Clin Endocrinol (Oxf) 1998 ; 48(5) : 613 - 20
 42. Chrisoulidou A, et al. How much, and by what mechanisms, does growth hormone replacement improve the quality of life in GH - deficient adults? Baillieres Clin Endocrinol Metab 1998 ; 12(2) : 261 - 79
 43. Deijen JB, EA van der Veen. The influence of growth hormone (GH) - deficiency and GH replacement on quality of life in GH - deficient patients. J Endocrinol Invest 1999 ; 22(Suppl 5) : 127 - 36
 44. Monson JP, et al. Growth hormone deficiency and replacement in elderly hypopituitary adults. KIMS Study Group and the KIMS International Board. Pharmacia and Upjohn International Metabolic Database. Clin Endocrinol (Oxf) 2000 ; 53(3) : 281 - 9
 45. McGauley G. The psychological consequences and quality of life in adults with growth hormone deficiency. Growth Horm IGF Res 2000 ; 10 (Suppl B) : s63 - s68
 46. Sonksen PH, JS Christiansen. Consensus guidelines for the diagnosis and treatment of adults with growth hormone deficiency. Growth Hormone Research Society. Growth Horm IGF Res 1998 ; (Suppl 8) : 89 - 92
 47. de Boer H, et al. Monitoring of growth hormone replacement therapy in adults, based on measurement of serum markers. J Clin Endocrinol Metab 1996 ; 81(4) : 1371 - 7
 48. Verhelst J, et al. Two years of replacement therapy in adults with growth hormone deficiency. Clin Endocrinol (Oxf) 1997 ; 47(4) : 485 - 94
 49. Chrisoulidou A, et al. Effects of 7 years of growth hormone replacement therapy in hypopituitary adults. J Clin Endocrinol Metab 2000 ; 85(10) : 3762 - 9
 50. Hatrick AG, et al. Does GH replacement therapy in adult GH - deficient patients result in recurrence or increase in size of pituitary tumours? Eur J Endocrinol 2002 ; 146(6) : 807 - 11
 51. Murray RD, et al. Low - dose GH replacement improves the adverse lipid profile associated with the adult GH deficiency syndrome. Clin Endocrinol (Oxf) 2002 ; 56(4) : 525 - 32