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Effects of growth hormone therapy and estrogen therapy on improvement of age-related clinical symptoms

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Abstract

Objective: Aging-related symptoms are closely related with perceived quality of life and an important target in the field of anti-aging medicine. This study was aimed to evaluate the effects of growth hormone therapy (GHT), estrogen therapy (ET) or their combined effects on the symptom score of ten major sets of symptoms.

Methods: One hundred and fifty-five volunteers were recruited. Ten of the study subjects received GHT and ET, 28 subjects received GHT only, 101 subjects received ET only and 16 subjects received general anti-aging therapy without hormone treatment. The ten major age-related symptoms were assessed using clinical symptom improvement index (CII) at baseline and after treatments. Symptom score improvements were compared among four treatment groups.

Results: Fatigue showed the highest symptom score (4.2 ± 0.4 for GHT+ET group, 4.1 ± 0.9 for GHT group, 4.0 ± 0.9 for ET group, 3.6 ± 0.5 for control group) before treatment. The improvement (2.1 ± 0.3 for GHT+ET group, 1.5 ± 1.2 for GHT group, 0.8 ± 0.8 for ET group, 0.7 ± 0.5 for control group) was the highest among the ten major aging-related symptoms. As for fatigue, GHT+ET group showed the highest improvement, GHT group was the second highest, and ET and control group showed similar improvement, which were statistically significant *($P<0.05$)*. CIIs were 7.3 ± 2.3 for GHT+ET group, 5.7 ± 2.8 for GHT group, 4.0 ± 2.45 for ET group and 1.9 ± 1.5 for controls. All of CII were statistically significantly different from zero and the CIIs of four groups were statistically different.

Conclusions: Fatigue was the most frequent and most improved symptom in the subjects who were looking for anti-aging medicine. Mental depression, sleep disturbance and memory disturbance were also relatively easily improvable symptoms that are closely related with aging. GHT combined with ET was the most effective in the control of aging-related symptoms and GHT was the second. ET and general anti-aging therapy had also showed significant improvement.

Key words: aging, growth hormone therapy, clinical symptom

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Introduction

Chronological age means the duration of survival after birth, and differs from biological age or functional age. Some people can be really younger than their chronological age in terms of biological functions.[1-3] The measurement of biological age is of utmost important in the field of anti-aging medicine. In order to assess the efficacy, if any, of an age-retarding protocol, it is essential to accurately measure biological age and aging rates. Though numerous methods to measure biological age have been developed,[4-5] there still needs a refined biological age measurement from a clinical point of view. Aging process raises many changes in human body that accompany subjective symptoms. Many age-related symptoms have been studied and Anti-Aging Quality of Life Common Questionnaire is widely used.[6] One major theory of aging is neuroendocrine theory, which posits that with age, human being experience a decline in circulating levels of hormones. From this point of view, hormone therapy has been widely used to prevent or reverse age-related symptoms or to retard biological aging.

This study was aimed to evaluate the effects of growth hormone therapy (GHT), estrogen therapy (ET) or combined treatment on the symptom score of ten major set of symptoms, which are closely related with aging.

Materials and Methods

Recruitment of the study subjects

One hundred fifty five volunteers took part in this study. The study participants took part in their own will and gave informed consent.

Hormone therapy and other general anti-aging therapies

Growth hormone was administered subcutaneously on abdominal skin area with 0.5 to 1.0 IU/day once daily. The frequency was five times a week. The duration of GHT was from six months to a year. For estrogen therapy, conjugated equine estrogen (CEE) was given at 0.3-0.625 mg orally for a day and continued for six months to a year. All of the subjects, including controls, received general anti-aging therapy including appropriate exercise, diet control and nutritional supplements.

Measurement of clinical symptoms

The ten major age-related symptoms were assessed by one to one interview manner. The symptoms were chosen among the items of Anti-Aging Quality of Life Common Questionnaire. The symptoms were evaluated before treatment and after from six months to a year of treatment. The ten major age-related symptoms were fatigue, lumbago, knee joint discomfort, neck stiffness, dry eye, depressive mood, sleep disturbance, decreased libido, memory decline and inability to concentrate. These symptoms were measured by an ordinal scale with the following value: 1=none, 2=almost none, 3=slightly, 4=moderately, 5=severely. These scales were regarded as ratio scale for the purpose of statistical analysis. The sum of score of these symptoms was defined as clinical symptom index (CI) and the difference between CI after treatment and before treatment was defined as clinical symptom improvement index (CII).

Statistical analysis

After establishing a computerized database, the CIIs were tested in each group by paired t-test. In the comparison of CIIs between groups, ANOVA test with Duncan's multiple comparison was applied. SAS for windows ver 8.1 was used in the statistical analyses. Four treatment groups (GHT+ET, GHT only, ET only, no hormone treatment) were compared.

Results

The mean age of GHT only group was 63.5±9.5 years, which was higher than other groups. There were only female subjects in ET group. There were 19 males and 9 females in GHT group, and 5 males and 11 females in non-hormone therapy group. The distribution of age, height, weight, body mass index (BMI) is presented at Table 1.

Ten major aging-related symptom scores are presented at Table 2. Fatigue showed the highest symptom score (4.2 ±0.4 for GHT+ET group, 4.1±0.9 for GHT group, 4.0± 0.9 for ET group, 3.6±0.5 for control group) before treatment. The improvement (2.1±0.3 for GHT+ET group, 1.5±1.2 for GHT group, 0.8±0.8 for ET group, 0.7±0.5 for control group) was the highest among the ten major aging-related symptoms. As for fatigue, GHT+ET group showed the highest improvement, GHT group was the second highest and ET and control group showed similar improvement, all of which were statistically significant. Other symptoms showed a similar pattern to that of fatigue with lesser improvement, most of which were statistically significant. Depressive mood, sleep disturbance and

memory disturbance showed a little more improvement than other symptoms.

CIs before treatment were 19.8±2.6 for GHRT+ERT group, 20.2±3.2 for GHRT group, 20.2±4.2 for ERT group and 18.2±2.1 for control group. CIs after treatment were 12.5±0.7 for GHRT+ERT group, 14.5+2.3 for GHRT group, 16.3±3.4 for ERT group and 16.3±1.7 for control group. CIIs were 7.3±2.3 for GHRT+ERG group, 5.7±2.8 for GHRT group, 4.0±2.45or ERT group and 1.9 ±1.5 for controls. All of CII were statistically significanlty differenct from zero. ANOVA with Duncan's multiple comparison revealed that all four groups showed significantlyl differenct CIIs (Table 3).

Table 1. General characteristics of study participants

	N	Age (Years)	Height (Cm)	WT (kg)	BMI (Height/weight2)	Sex (male/female)
GHRT+ERT	10	55.0±5.8	156.5±4.7	56.9±6.6	23.3±2.7	0/10
GHRT only	28	63.5±9.5	162.9±.5	65.7±9.4	24.8±2.9	19/9
ERT only	101	55.0±8.2	156.4±4.6	6 59.0±7.0	24.9±2.7	0/101
Control	16	55.3±7.2	162.3±7.5	65.9±12.8	24.9±3.8	5/11

Values are means±standard deviation

Table 2. Major age related symptoms of each group

		Before	After	Improvement	p-value
Fatigue					
	GHRT+ERT	4.2±0.4	2.1±0.3	2.1±0.3	<0.001
	GHRT only	4.1±0.9	2.6±0.7	1.5±1.2	<0.001
	ERT only	4.0±0.9	3.2±0.9	0.8±0.8	<0.001
	Control	3.6±0.5	2.9±0.7	0.7±0.5	<0.001
Lumbar pain					
	GHRT+ERT	1.7±0.7	1.2±0.4	0.5±0.5	0.0150
	GHRT only	1.8±0.8	1.4±0.5	0.4±0.5	0.0003
	ERT only	1.9±0.9	1.5±0.7	0.4±0.9	<0.001
	Control	1.8±0.7	1.5±0.5	0.3±0.6	0.1038
Knee pain					
	GHRT+ERT	1.6±0.5	1.1±0.3	0.5±0.5	0.0150
	GHRT only	1.5±0.6	1.3±0.4	0.3±0.5	0.0087
	ERT only	1.7±0.8	1.4±0.8	0.3±0.9	0.0012
	Control	1.3±0.4	1.3±0.4	0.0±0.0	1.0000
Neck stiffness					
	GHRT+ERT	1.4±0.5	1.0±0.0	0.4±0.5	0.0368
	GHRT only	1.5±0.5	1.2±0.4	0.3±0.5	0.0028
	ERT only	1.7±0.8	1.4±0.7	0.3±0.8	0.0002
	Control	1.5±0.5	1.7±0.5	0.2±0.4	0.0825

	Before	After	Improvement	p-value
Sleep disturbance				
GHT+ET	2.0±0.8	1.1±0.3	0.9±0.7	0.0039
GHT only	2.0±0.7	1.1±0.4	0.9±0.7	<0.001
ET only	2.0±1.2	1.5±0.8	0.5±0.8	<0.001
Control	1.8±0.7	1.1±0.3	0.7±0.5	<0.001
Decreased libido				
GHT+ET	2.5±0.5	2.0±0.2	0.5±0.5	0.0150
GHT only	2.8±0.8	2.4±1.0	0.4±0.6	0.0013
ET only	2.4±1.1	2.0±1.0	0.3±0.7	<0.001
Control	2.4±0.6	2.2±8	0.3±0.4	0.0410
Memory disturbance				
GHT+ET	1.8±0.6	1.0±0.0	0.8±0.6	0.0031
GHT only	1.7±0.7	1.2±0.4	0.5±0.7	0.0007
ET only	1.6±0.9	1.4±0.7	0.2±0.6	<0.001
Control	1.6±0.5	1.5±0.5	0.1±0.3	0.3332
Inability to concentrate				
GHT+ET	1.1±0.3	1.0±0.0	0.1±0.3	0.3434
GHT only	1.6±0.6	1.1±0.4	0.4±0.6	0.0013
ET only	1.4±0.6	1.3±0.6	0.1±0.5	0.0087
Control	1.2±0.4	1.1±0.3	0.1±0.3	0.1639

Table 3. Clinical symptom index of 3 treatment groups and control group

	CI before treatment	CI after treatment	CII	p-value	Multiple comparison
GHT+ET (GE)	19.8±2.6	12.5±0.7	7.3±2.3	<0.001	GE > G, E, C
GHT only (G)	20.2±3.2	14.5±2.3	5.7±2.8	<0.001	G > E, C
ET only (E)	20.2±4.2	16.3±3.4	4.0±2.4	<0.001	E > C
Control (C)	18.2±2.1	16.3±1.7	1.9±1.5	0.0001	-
p-value of ANOVA	<0.001				

Discussion

GHRT has been confirmed to be effective in body status, lipid profile and age related symptom improvement.[8-11] In the results of the present study, GHRT combinded with ERT was most effective modality of improving aging related symptoms. This result implies that ERT combined with GHRT is most effective treatment method for old females. GHRT only was the second best and ERT only was the third. Without hormone replacement therapy, general anti-aging treatment including excercise, diet control and nutritional supplements showed significant effect on the control of aging related symptoms.

Among ten major aging related symptoms, fatigue was most frequent and severe symptom before treatment in the subjects who were looking for anti-aging medicine, and most improved symptom by treatments. Mental depression, sleep disturbance and memory disturbance were also relatively frequent and easily improvable symptoms that are closely related with aging, which was compatible with previous report.[12] The other symptoms (lumbar pain, knee pain, neck stiffness, eye dryness, sexual disturbance, inability to concentrate) were improved by GHRT+ERT, GHRT, ERT and general anti-aging therapy, which, most of them, were statistically significant. These results imply

that most aging related symptoms can be effectively controlled by anti-aging medicine, with or without hormone replacement therapy.

There are some limitations in the present study. The different age of different groups might affect the result of the present study. The age of GHRT only group showed significantly higher than the other groups. This can affect the results of our present study. However, the symptom score before and after treatment is comparable to those of other groups, which implies that the age difference pose no major effect on the results. Inevitable sex distribution mismatch another limitation, because man cannot receive ERT. There ar more than one hundred ERT only subjects in contrast to only ten to twenty eight subjects in the other treatment group. In the field of anti-aging practice, GHRT is one of the most useful treatment method, which has practical limitations. To recruit more GHRT partients, the long duration of research is needed. The imbalance of sample size weakens statistical power, which mean the increased chance of 'toward the null bias'. This implies that there are more than observed differences in the effectiveness among four treatment groups. Symptoms scores which is an ordinal scale, is converted to ratio scale. The difference between 'severe' and 'moderate' should be different from the difference between 'none' and 'almost none'. However, this measurement has long been used in other researches and the consistent tendency in our results imply that this limitation hardly pose a major effect in our results.

The ten major age related symptom were chosen by authors in the basis of Anti-Aging Quality of Life Common Questionnaire and the authors' experience and data. Other symptoms, including blurry eye, dyspnea, lethargy, anorexsi, headache and so on, should be considered if the standardized set of aging related symptoms. More data and informations are indispensible to formulate the golden standardized set of aging related symptoms in the field of anti-aging medicine. Our results might play a role in the establishment of the standard. As the subjective feeling or symptom is closely related with biological age, our result also implies that the symptom score can possibly be applied as a biological age measurement tool. The subjective feeling or symptom is closely related with biological age. To develope a standardized biological age measurement tool, more data and results are needed. The research in this *field is just beginning and should be more and more* important in the future, especially due to the rapidly increasing need of anti-aging medicine.

Conclusions

Fatigue was the most frequent and most emproved symptom in the subject who were looking for anti-aging medicine. Mental depression, sleep disturbance and memory disturbance were also relatively easily improvable symptoms that are closely related with aging. GHRT combined with ERT was most effective in the control of aging related symptoms and GHRT was the second best. ERT and general anti-aging therapy were also showed significant improvement.

The standardized lists of aging related symptoms are indispensible in the field of anti-aging medicine and the symptom score possibly applied as a biological age measurement tool if more data and results are available.

References

1. Borkan G. Assessment of biological age using a profile of physical parameters. *J Geront* 1980;35:177-84.
2. Nakamura E. The aged people and its physiological ages in the relation to work capacity. *Kyoiku Igaku* 1982;28:2-11.
3. Webster IW. Subjective good health and biological impairments in female subjects. Comunity Health Studies 1982;4:39-46.
4. Hochschild R. Improving the precision of biological age determinants. Part 1: A New Approach to Calculating Biological Age. *Experi Gerontol* 1989;24:298-300.
5. Hochschild R. Improving the precision of biological age determinants. Part 2: Automatic Human Tests, Age Norms and Variability. *Experi Gerontol* 1989;24:301-16.
6. Yonei Y, Mizuno Y, Togari H, Sato Y. Muscular resistance training using applied pressure and its effects on the promotion of growth hormone secretion. *Anti-Aging Medical Research* 2004;1:13-27.
7. Morgan R. Hormone Replacement Therapy: A Primer - DHEA, Estrogen, HGH, Melatonin, Progesterone, Testosterone, Thyroid. In Klatz R, Goldman R (eds), Anti-Aging Therapeutics, Volume V, A4M Publicatoins, Chicago, pp. 360-9.
8. Rudman D, Felter AG, Nagraj HS et al. Effects of human growth hormone in men over 60 years old. *N Engl J Med* 1990;5:1-6.
9. *Albert SG, Mooradian AD. Low-dose recombinant* human growth hormone as adjuvant therapy to lifestyle modifications in the management of obesity. *J Clin Endocrinol Metab* 2004;89:695-701.

10. Pavel ME, Lohmann T, Hahn EG, Hoffmann M. Impact of growth hormones on central nervous activity, vigilance, and tiredness after short-term therapy in growth hormone-deficient adults. *Horm Metab Res* 2003;35:114-9.
11. Blum WF, Shavrikova EP, Edwards DJ et al. Decreased quality of life in adult patients with growth hormone deficiency compared with general populations using the nwe, validated, self-weighted questionnaires, questions on life satisfaction hypopituitarism modul. *J Clin Endocrinol Metab* 2003;88:4158-67.
12. Mesa J, Gomez JM, Hernandez C, Pico A, Ulied A; Grupo Colaborador Espanol. Growth hormone deficiency in adults: effects of replacement therapy on body composition and health-related quality of life. *Med Clin (Barc)* 2003;120:41-6.