

Effective Anti-aging Strategies in an Era of Super-aging

Saerom Park¹, Min-Ji Yang¹, So-Nyeong Ha¹, Jeong-Sang Lee^{1,2,3}

¹Department of Health and Functional Food, College of Medical Science, ²Food Industry Research Institute, ³The Health and Science Research Institute, Jeonju University, Jeonju, Korea

The societies of the world in the 21st century have faced challenges arising from an aging population as the fertility rate has dropped dramatically and medical advances have extended the average human life span. The elderly aged 65 years or older make up at least 20% of the population in Korea, making the country a super-aging society as defined by the United Nations. The number of elderly women is higher than that of elderly men and women live longer than men. Based on the analysis of recent trends in previous studies, this study aimed to suggest practical strategies to utilize isoflavones, substances chemically similar to the female hormone estrogen, and to search for effective anti-aging strategies using this substance for women to be prepared to reach the elderly stage in good health. (**J Menopausal Med 2014;20:85-89**)

Key Words: Anti-aging, Estrogen, Female, Hormone replacement therapy, Isoflavone, Quality of life

Introduction

1. Population of aging

After entering into the 21st century, our aging population is one of the greatest challenges facing society with a growing elderly population along with industrialization, an increase in the number of working-women, a decreasing fertility rate, and an extended human life span with improvements in medicine. The elderly aged 65 years or older make up more than 20% of the Korean population, making the country a super-aging society according to the standard defined by the United Nations. Korea is projected to become one of the most aged nations among the Organisation for Economic Co-operation and Development (OECD) countries in next 50 years. The OECD report, pension at a glance 2013, has predicted that the support ratio is projected to drop to 1.2 by 2062 and Korea will be one of the oldest OECD countries.¹

In the 1960's and 1970's, the national family planning program of the Planned Population Federation of Korea under the Ministry of Health and Welfare achieved its primary objectives to reduce the fertility rate. However, the decreased fertility rate became apparent over the past 3-4 decades that Korea would have to shift its population policy directions to pro-natalism, indicating that Korea's population is aging very rapidly.²

The population of aging in Korea has reached a serious level. Building a sound society requires about 70% of the working population in a society. A decrease in the number of working age people of followed by aging population poses serious threat to workforce. An increase in expenditure on welfare facilities and welfare-related cost for the aged imposes tax burden on people and government budget as well.³ Therefore, in addition to the implementation of pro-natal policies, the development of practical strategies is crucial for high quality and stable elderly lives of growing

Received: July 7, 2014 Revised: November 12, 2014 Accepted: November 25, 2014

Address for Correspondence: Jeong-Sang Lee, Director of Food Industry Research Institute, Assistant Professor of Department of Health and Functional Food, College of Medical Science, Jeonju University, Jeonju 560-759, Korea
 Tel: +82-63-220-4660, Fax: +82-63-220-2054, E-mail: jslee11@jj.ac.kr
 Saerom Park, Min-Ji Yang, So-Nyeong Ha contributed equally to this work.

Copyright © 2014 by The Korean Society of Menopause

© This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>).

elderly population.

2. Increase in women population

According to the 2006 Future Population Projection by Statistics Korea, the male to female ratio for the population aged 65 years or over was 69.2 increased by 7.2 females from 2000 to 2010.⁴ However, the number of elderly women is still noticeably greater than that of elderly men.

Aging along with a rapid growth of elderly population and extended life span, the number of elderly women is greater than that of elderly men and their average life span and life expectancy are much longer. In the process of industrialization, urbanization and nuclear family trend in modern societies, the number of one-person household of older individuals has grown largely after the increase in residential separation between elderly parents and their adult children, and the number of widowed elderly women has increased after spouse's death.

Nevertheless, 92.2% of elderly women and 77.4% of elderly men are suffering from chronic diseases lasting more than 3 months. The lifetime duration of a disease or impairment is found to be 12.7 years in women and 7.3 years in men on average, indicating that elderly women live longer, but not healthier lives.⁵ Moreover, the incidence of depression was higher and the level of emotional satisfaction became lower in elderly women than in elderly men.⁶ A non-participation rate in leisure activities was 16.7% in elderly men and 26.6% in elderly women.⁷ Elderly women live longer than their spouses, but severely experience a variety of problems including financial difficulties, health problems unique to women, and adaptations to isolation from family and society in old age.

Poverty of elderly women is a much more serious problem. Moreover, current policies for the elderly have focused on the conditions of elderly men, and the problems and needs of elderly women have been rarely recognized.⁸

3. Future direction of research

Life expectancy has been increased markedly with advances in modern science. However, living unhealthy lives will lead to the rise in economic deprivation and mental and physical suffering. Thus, it is humanity's desire and aspiration to lead a healthy life in their old age, at the

same time, a challenge to be tackled in the era of aging population.

Women generally live longer than men. To investigate this tendency, early investigators paid attention to overproduction of pro-inflammatory cytokines in post-menopausal women, but recent studies have focused on the roles of estrogen.⁹ This study aims to propose practical strategies using isoflavones chemically similar to estrogen, and to provide a reference base for exploring effective measures for women to be prepared to live in a super-aged society in good health based on the analysis on the recent studies.

Main Body

1. Estrogen and anti-aging: verification of the relationship between

1) Trends of recent studies

Persisting weak inflammatory responses deteriorate ability to restore cell damages and homeostasis, and the repetition of this process generate cellular aging.⁹ For this reason, many studies are investigating other functions of estrogen, in addition to the role of female sex hormone.

Along with a recent rise in the number of patients with non-alcoholic fatty liver disease (NAFLD), the prevalence of NAFLD is noticeably high in both men and post-menopausal women. This provides an indicator for the correlation between estrogen and liver that estrogen is associated in inhibiting trans-differentiation of activated hepatic stellate cells to myofibroblasts.¹⁰ In a previous study,¹¹ when HeLa cells (cervical cancer-derived cell lines) were treated with estrogen, progesterone and tamoxifen, estrogen treated for 2.5-6 days at a high concentration of 10 g/mL had an effect on inhibiting proliferation of cancer cells and this effect increased with time-dependent manner.

2. Anti-aging strategies using estrogen

1) Aerobic exercise

The active secretion of growth and sex hormones is known to have a profound relationship with muscle development and aging.¹² Aging-related symptoms progress rapidly in women

at menopause including sarcopenia, an increase of body fat, a change in body fat distribution, a decrease of bone mineral density (BMD) and skin thickness and others, and postmenopausal women experience several other physical symptoms, in addition to aging, due to reduced ovarian function and estrogen levels.¹³ Aerobic exercise at an age-appropriate intensity combined with hormone therapy has positive effects on estrogen levels of midlife women.¹⁴

Han¹⁵ performed a combined aerobic and resistance exercise program in healthy elderly women. They verified that there was a significant difference in the increase of aging-related hormones such as dehydroepiandrosterone (DHEA), growth hormone, estrogen and others having significance as aging parameters for the endocrine system, and proved that the combined workouts were effective in inhibiting and delaying aging process by declining the levels of aging-related hormones.

A significant impact of aerobic exercise on aging-related hormones including growth hormones and estrogen was identified by performing Qi-gong exercise for mental and physical training and basic breathing and gait training in midlife women.¹⁶ To explore the effect of Taekwondo forms and Taekwon gymnastics on aging-related hormones and obesity index, Kim¹⁷ conducted Taekwondo forms, Taekwon gymnastics and weight training each in three groups of elderly women without previous exercise experience. Consequently, the level of estrogen showed a significant increase in all three groups.

In addition, Ham and Park¹⁸ applied a 12-week dance sport program to midlife women and analyzed hormone responses at the 4th, 8th and 12th weeks of the study. As a result, a significant increase was found in both estrogen and growth hormone levels, suggesting the positive effect of exercise on the increase in these hormone levels.

2) Intake of soybeans and their products (isoflavone intake)

(1) What are isoflavones

Isoflavone is a type of phytoestrogens having similar physiological effects as estrogen by binding to estrogen receptors within cells. Isoflavone glycosides are hydrolysed by the action of glucosidase, and then converted into aglycone forms such as genistein and daidzein having

estrogenic properties.

Isoflavone consumption reduces menopausal symptoms without side effects, thus isoflavones can be substituted for estrogenic agents. Moreover, this compound is reported to improve serum lipid profiles and BMD, and to lower cardiovascular risk and serum lipid hydroperoxides in women.¹⁹

(2) Side effect and its prevention

Men who consumed isoflavones, chemically similar to estrogens, on a regular basis have complained of side effects in some cases. An elderly man with regular daily intake of soybean milk about 3 L/day experienced gynecomastia, impotence, declined sexual responsiveness, an increase in female hormone levels, and he recovered from these symptoms after discontinuation of soybean milk intake.²⁰ In addition, a 19-year old man also experienced declined sexual responsiveness and impotence by consuming soybean milk consistently.²¹

Other research shows that there is no effect on male hormone levels in men who consumed soy foods and isoflavone agents in a placebo trial.²² Research on the effects of isoflavones has found that isoflavone agents have no correlation with sperm counts and survival rates and semen volume.²³ The above findings suggest that despite no correlation of isoflavones with male sex hormones, sperm density, numbers and survival rate, and semen amount, isoflavones may increase the levels of female sex hormones in men and lead to impotence, declined sexual responsiveness and other symptoms.

Breast cancer incidence rates declined by 36% in the group with consumption of ≥ 10 mg isoflavones compared to the group with consumption of ≤ 4 mg isoflavones.²⁴ Although isoflavones are effective in preventing breast cancers, isoflavone consumption failed to reduce cancer cell proliferation according to a study performed on 9,514 cancer patients for 7.4 years.²⁵ On the contrary, isoflavone intake may hamper the management of estrogen-dependent cancers such as breast cancer or endometrial cancer, requiring anti-estrogen therapies.

(3) Isoflavone intake

Gwak et al.¹⁹ found out that a 12-week administration of isoflavone and gamma-linolenic acid is effective in reducing the oxidation of low-density lipoproteins (LDL)-

cholesterol from oxidative stress in post-menopausal women by identifying a decrease in oxidized LDL levels and a significant difference in the changes of plasma medroxyprogesterone acetate (MPA) levels. Furthermore, Kim et al.²⁶ reported that total cholesterol levels, very LDL (VLDL)+LDL cholesterol levels, and atherogenic index were significantly decreased in male Sprague-Dawley rats administered with extracted soybean isoflavones, while only VLDL+LDL levels were significantly lowered in the other group fed with a cholesterol added diet. In addition, total superoxide dismutase (T-SOD) activity of isoflavone group was significantly higher than that of non-isoflavone group with no cholesterol, and total antioxidant status (TAS) increased significantly higher in isoflavone group than non-isoflavone group. These outcomes imply that isoflavones act independently and improve serum lipid patterns and antioxidant ability.

Conclusion

The elderly aged 65 years or older make up more than 20% of the Korean population, making the country a super-aging society.¹ In 2010, the male to female ratio for the population aged 65 years or over was 69.2 females, markedly higher than the number of males. The purpose of study is to suggest practical strategies to utilize isoflavones, substances chemically similar to estrogen, and to provide a reference base for finding effective measures for high quality and stable elderly lives of growing elderly population.

The release of growth and sex hormones is known to be profoundly associated with aging.²⁷ Aging-related symptoms develop rapidly in women at menopause including sarcopenia, an increase of body fat, a change in body fat distribution, a decrease of BMD and skin thickness and others.¹³ Aerobic exercise at an age-appropriate intensity combined with hormone therapy has positive effects on estrogen levels of midlife women.¹⁴ There was a significant difference in the increase of aging-related hormones such as DHEA, growth hormone, estrogen and others having significance as aging parameters for the endocrine system in healthy elderly women performed with a combined aerobic and resistance exercise program.¹⁵ A significant impact of aerobic exercise

on aging-related hormones including growth hormones and estrogen was verified by performing Qi-gong exercise for mental and physical training and basic breathing and gait training in midlife women.¹⁶ The significant increase of estrogen levels was observed in all three groups performed with Taekwondo forms, Taekwon gymnastics and weight training.¹⁷ Moreover, a significant increase was found in both estrogen and growth hormone levels of midlife women when hormone responses were analyzed at the 4th, 8th and 12th weeks while applying a 12-week dance sport program, suggesting the positive effect of exercise on the increase in these hormone levels.

A large number of studies have investigated that isoflavones chemically similar to estrogen lower cholesterol levels, prevent cardiovascular diseases (by inhibiting the oxidation of LDL-cholesterol and acting as an agent changing activation of LDL-receptors), keep hormone homeostasis, and have effects on prevention and management of cancers and osteoporosis. A 12-week administration of isoflavone and gamma-linolenic acid reduced oxidized LDL levels and a significant difference was observed in the changes of plasma MPA levels, indicating that these substances are effective in preventing the oxidation of LDL-cholesterol from oxidative stress.¹⁹

Total cholesterol levels, VLDL+LDL cholesterol levels, and atherogenic index were significantly reduced in male Sprague-Dawley rats administered with extracted soybean isoflavones, and isoflavones act independently and enhance serum lipid patterns and antioxidant ability.²⁶

To sum up the above results of previous studies, moderate-intensity aerobic exercise facilitates the release of sex and growth hormones and isoflavone consumption boosts antioxidant effects, having positive effects on anti-aging in post-menopausal women. Based on these findings, exercise and isoflavone intake on a regular basis are expected to be beneficial in planning anti-aging strategies to maintain good health of elderly women living in an aging society.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

References

1. OECD. Pensions at a glance 2013: OECD and G20 indicators. Seoul: OECD/Korea Policy Centre; 2014.
2. Shin SJ. Problems and countermeasures of low birth rate and aging society. *J Korean Hosp Assoc* 2005; 34: 4–6.
3. Cho DH, Ma SR. Old age security pension policies and reverse mortgages. Paju: Jipmoon; 2007.
4. Suh HJ. Korea's aging society and its problems. *Minjok Yeonku* 2011; 48: 25–40.
5. Jang HJ. Industrial restructuring and women's labor market: focusing on the financial industry. *J Korean Women's Stud* 2000; 16: 35–74.
6. Lee HJ, Sung MO, Shin YA. A study on the psychological well-being and depression of urban elderly women. *J Well Aged* 2003; 22: 127–50.
7. Kwon JD. A study on the casual factors of elderly abuse. *J Korea Gerontol Soc* 2004; 24: 1–19.
8. Lee H. Current conditions and prospects of women's movements in community: a case study of Chinju area. *J Korean Women's Stud* 1999; 15: 103–52.
9. Cho BS, Kim H, Ku SY. Role of estrogen in sex dimorphism of longevity. *J Repord Med Popul* 2011; 24: 42–51.
10. Hyun J, Jung Y. Potential roles of hedgehog and estrogen in regulating the progression of fatty liver disease. *J Life Sci* 2011; 21: 1795–803.
11. Min G. Inhibitory effects of high concentrations of estrogen, progesterone and tamoxifen on proliferation of HeLa in culture. *J Life Sci* 2011; 21: 1746–51.
12. Ferry B, Roozendaal B, McGaugh JL. Basolateral amygdala noradrenergic influences on memory storage are mediated by an interaction between beta- and alpha1-adrenoceptors. *J Neurosci* 1999; 19: 5119–23.
13. Yeo E. Menopause, aging and obesity. *J Korean Soc Study Obes* 2002; 11: 289–98.
14. Kim MJ. The effects of aerobic exercise on the health-related physical fitness factors, bone mineral density, and estrogen for menopausal women with long-term HRT and menopausal women without HRT. *J Korea Sport Res* 2007; 18: 587–98.
15. Han JK. The impact of long term combined exercise on aging related hormone in elderly women. *Exerc Sci* 2008; 17: 23–30.
16. Kim EJ, Kim JS, Yoon JH. The impact of Gichejo for mental and physical training on middle-aged women's body composition and aging-related hormone. *Exerc Sci* 2013; 22: 239–47.
17. Kim JD. Effect of Takwondo training and resistance training difference on aging related hormones and obese index of elderly women. *J Sport Leis Stud* 2013; 51: 687–97.
18. Ham YG, Park BK. Effects of dance sports training on estrogen and growth hormone in middle-aged women. *Korean J Exerc Nutr* 2010; 14: 69–73.
19. Gwak JH, Kim JY, Kim HJ, Shin DH, Lee JH. The effect of isoflavone and gamma-linolenic acid supplementation on serum lipids and menopausal symptoms in postmenopausal women. *Korean J Nutr* 2010; 43: 123–31.
20. Martinez J, Lewi JE. An unusual case of gynecomastia associated with soy product consumption. *Endocr Pract* 2008; 14: 415–8.
21. Siepmann T, Roofeh J, Kiefer FW, Edelson DG. Hypogonadism and erectile dysfunction associated with soy product consumption. *Nutrition* 2011; 27: 859–62.
22. Hamilton-Reeves JM, Vazquez G, Duval SJ, Phipps WR, Kurzer MS, Messina MJ. Clinical studies show no effects of soy protein or isoflavones on reproductive hormones in men: results of a meta-analysis. *Fertil Steril* 2010; 94: 997–1007.
23. Mitchell JH, Cawood E, Kinniburgh D, Provan A, Collins AR, Irvine DS. Effect of a phytoestrogen food supplement on reproductive health in normal males. *Clin Sci (Lond)* 2001; 100: 613–8.
24. Nechuta SJ, Caan BJ, Chen WY, Lu W, Chen Z, Kwan ML, et al. Soy food intake after diagnosis of breast cancer and survival: an in-depth analysis of combined evidence from cohort studies of US and Chinese women. *Am J Clin Nutr* 2012; 96: 123–32.
25. Khan SA, Chatterton RT, Michel N, Bryk M, Lee O, Ivancic D, et al. Soy isoflavone supplementation for breast cancer risk reduction: a randomized phase II trial. *Cancer Prev Res (Phila)* 2012; 5: 309–19.
26. Kim SY, Kim SY, Chung CE, Yoon S, Park JH. Effects of isoflavone supplementation on lipid profiles and antioxidant systems in rats fed with cholesterol diet. *J Life Sci* 2000; 20: 1683–90.
27. Ferry B, Roozendaal B, McGaugh JL. Role of norepinephrine in mediating stress hormone regulation of long-term memory storage: a critical involvement of the amygdala. *Biol Psychiatry* 1999; 46: 1140–52.