

RELATIONSHIPS OF SEX HORMONE LEVELS WITH ACTIVITY OF DAILY LIVING IN CHINESE FEMALE CENTENARIANS

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Abstract: *Background:* Activity of daily living declines in female elderly, which not only increases hospitalization and mortality rates, but also aggravates individual and societal burden. Large samples are needed to elucidate the relationships of plasma sex hormone levels with activity of daily living in Chinese female centenarians to better understand the effects of hormone-replacing therapy. *Objective:* As the first time in the world, the current study was designed to investigate the relationships of plasma sex hormone levels with activity of daily living in Chinese female centenarians. *Participants:* China Hainan Centenarian Cohort Study was carried out in 18 cities and counties of Hainan Province. *Main measures:* Home interview, physical examination and blood analysis were carried out in 583 female centenarians following standard procedures. Barthel Index was used to assess the activity of daily living. *Key results:* Median age of all female centenarians was 102 years, with the range from 100 to 115 years. Median values of Barthel Index were 85(60-90). In multivariate linear regression analyses, Barthel Index values were inversely associated with plasma luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone, progesterone and estradiol levels ($P < 0.05$ for all). *Conclusion:* Plasma sex hormone levels, including LH, FSH, testosterone, progesterone and estradiol, had significant relationships with activity of daily living in Chinese female centenarians.

Key words: Activity of daily living, Chinese female centenarians, estradiol, follicle-stimulating hormone, luteinizing hormone, progesterone, testosterone.

Introduction

Activity of daily living declines in female elderly, which not only increases hospitalization and mortality rates, but also aggravates individual and societal burden (1). Scarce studies have analyzed the relationships of plasma sex hormone levels with activity of daily living (2, 3). One study has realized that plasma estrone levels were inversely related to activity of daily living in female elderly (3). However, another study has suggested that plasma testosterone and estrone levels showed no correlation with activity of daily living in female elderly (2). These studies have observed only a few kinds of sex hormones rather than the whole spectrum of sex hormones (2, 3). Moreover, these studies have been performed mainly in general adults or elderly in Western countries (2, 3). Ethnicity may affect the relationships of sex hormone levels with activity of daily living, which remain unclear in Chinese female elderly, especially in female centenarians. Thus, large samples are needed to elucidate these relationships in Chinese female centenarians to better understand the effects of hormone-replacing therapy and promote the development of medical tourism and health technology of Hainan, China. Hainan is a longevity area with the highest population density of centenarians in China, and China Hainan Centenarian Cohort Study (CHCCS) provides a considerably population-based sample of Chinese female centenarians. As the first time in the world, the current study was designed to investigate the relationships of plasma sex hormone levels with activity of

daily living in Chinese female centenarians.

Methods

Study population

As a population-based study, CHCCS was carried out in 18 cities and counties of Hainan Province, China. Based on National Civil Registry, 811 female centenarians aged 100 years or older participated in the current study from July 2014 to December 2016. Age was ascertained from national identification cards. The centenarians were excluded because they did not receive the analysis of sex hormone levels. The final analysis consisted of 583 female centenarians with complete information. All centenarians did not receive any exogenous steroid and other treatment which could affect plasma levels of sex hormones. There was no centenarian with oophorectomy in the current study. The current study was carried out based on the approval of Ethics Committee of the Hainan branch of Chinese People's Liberation Army General Hospital (Sanya, Hainan; Number: 301hn11201601). All centenarians provided written informed consent prior to the start of investigation.

Standard procedures

Home interview, physical examination and blood analysis were carried out following standard procedures by the research team and the central laboratory of the Hainan Branch of Chinese People's Liberation Army General Hospital. The

SEX HORMONE AND ACTIVITY OF DAILY LIVING

Table 1
 Features of Chinese female centenarians categorized by median values of Barthel Index

Features	All (n=583)	Barthel Index>85 (n=232)	Barthel Index≤85 (n=351)	P value
Age (year)	102(101-104)	102(101-104)	102(101-104)	0.557
Barthel Index	85(60-90)	95(90-100)	65(45-80)	<0.001
WC (cm)	74(68-80)	76(70-82)	74(68-80)	0.016
CAD (%)	13(2.2)	6(2.6)	7(2.0)	0.636
Hypertension (%)	432(74.1)	172(74.1)	260(74.1)	0.986
Dyslipidemia (%)	240(41.2)	89(38.4)	151(43.0)	0.263
Diabetes mellitus (%)	66(11.3)	21(9.1)	45(12.8)	0.160
SBP (mmHg)	151(137-170)	150(137-171)	151(136-170)	0.614
DBP (mmHg)	76(67-83)	76(67-84)	77(67-83)	0.743
Triglyceride (mmol/L)	1.05(0.82-1.41)	1.08(0.81-1.46)	1.03(0.82-1.38)	0.383
HDL-C (mmol/L)	1.41(1.18-1.67)	1.46(1.23-1.73)	1.37(1.14-1.65)	0.013
LDL-C (mmol/L)	2.76(2.31-3.33)	2.78(2.33-3.38)	2.74(2.28-3.26)	0.307
FBG (mmol/L)	4.77(4.20-5.76)	4.65(4.14-5.50)	4.94(4.22-5.90)	0.007
LH (mIU/ml)	35.87(28.13-46.93)	33.41(25.92-43.91)	37.55(29.36-48.50)	0.001
FSH (IU/L)	78.99(59.52-99.07)	73.25(57.06-95.48)	81.36(61.58-102.10)	0.016
Testosterone (nmol/L)	0.39(0.17-0.69)	0.31(0.10-0.54)	0.45(0.24-0.75)	<0.001
Prolactin (ug/L)	13.87(10.60-19.84)	13.99(10.48-19.61)	13.82(10.62-20.32)	0.839
Progesterone (nmol/L)	0.66(0.34-1.04)	0.55(0.27-0.93)	0.69(0.39-1.07)	0.001
Estradiol (pmol/L)	33.80(18.40-59.80)	24.50(18.40-43.10)	39.70(18.40-69.10)	<0.001

Abbreviations: WC: waist circumference; CAD: coronary artery disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; FBG: fasting blood glucose; LH: luteinizing hormone; FSH: follicle-stimulating hormone.

Table 2
 Features of Barthel Index in Chinese female centenarians

Features	All (n=583)	Barthel Index>85 (n=232)	Barthel Index≤85 (n=351)	P value
Barthel Index	85(60-90)	95(90-100)	65(45-80)	<0.001
Grooming	1(0-1)	1(1-1)	1(0-1)	<0.001
Bathing	1(0-1)	1(1-1)	0(0-1)	<0.001
Toilet use	2(1-2)	2(2-2)	1(1-2)	<0.001
Bowel movement	2(2-2)	2(2-2)	2(2-2)	<0.001
Urinary incontinence	2(2-2)	2(2-2)	2(2-2)	<0.001
Dressing	2(1-2)	2(2-2)	2(1-2)	<0.001
Feeding	2(1-2)	2(2-2)	2(1-2)	<0.001
Stair climbing	0(0-1)	1(1-2)	0(0-1)	<0.001
Transferring	2(2-3)	3(3-3)	2(1-2)	<0.001
Walking	3(2-3)	3(3-3)	2(1-2)	<0.001

research team included internists, geriatricians, cardiologists, endocrinologists, nephrologists and nurses. All examiners of research team were well trained in a unified standard. Activity of daily living was assessed by trained doctors without knowledge of laboratory results. Barthel Index was used to

assess the activity of daily living through 10 items (grooming, bathing, toilet use, bowel movement, urinary incontinence, dressing, feeding, stair climbing, transferring and walking) (4). Barthel Index has been validated in various populations, and was widely used with good reliability (5). Waist circumference

Table 3
 Relationships of Barthel Index with plasma sex hormone levels in Chinese female centenarians

Features	Models	Standardized β	Standard error	t	P value
LH (mIU/ml)	1st	-0.084	0.002	-2.043	0.042
	2nd	-0.084	0.003	-2.036	0.042
	3rd	-0.098	0.002	-2.421	0.016
FSH (IU/L)	1st	-0.083	0.001	-1.999	0.046
	2nd	-0.083	0.001	-1.999	0.046
	3rd	-0.096	0.001	-2.331	0.020
Testosterone (nmol/L)	1st	-0.130	0.046	-3.171	0.002
	2nd	-0.130	0.046	-3.160	0.002
	3rd	-0.147	0.045	-3.641	<0.001
Prolactin (ug/L)	1st	-0.029	0.003	-0.703	0.482
	2nd	-0.030	0.003	-0.712	0.477
	3rd	-0.018	0.003	-0.449	0.654
Progesterone (nmol/L)	1st	-0.154	0.059	-3.766	<0.001
	2nd	-0.154	0.059	-3.760	<0.001
	3rd	-0.151	0.058	-3.739	<0.001
Estradiol (pmol/L)	1st	-0.233	0.001	-5.763	<0.001
	2nd	-0.232	0.001	-5.742	<0.001
	3rd	-0.193	0.001	-4.628	<0.001

Notes: Linear regression analyses were carried out following these models: model 1 with no adjustment; model 2 adjusted for age; and model 3 adjusted for age, waist circumference, coronary artery disease, hypertension, dyslipidemia, diabetes mellitus, systolic blood pressure, diastolic blood pressure, triglyceride, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and fasting blood glucose; Abbreviations: LH: luteinizing hormone; FSH: follicle-stimulating hormone.

(WC) was measured with a soft tape midway between the lowest rib and the iliac crest. Systolic and diastolic blood pressures (SBP and DBP) were measured twice on the right arm of centenarians with 1-minute interval. The average of these measurements was used for the final analysis. Blood samples were collected to analyze plasma sex hormone levels and transported in chilled bio-transport container (4°C) to our Central Laboratory within 4 hours. Plasma levels of sex hormones, triglyceride, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and fasting blood glucose (FBG) were analyzed with the enzymatic analyses (Roche Products Ltd, Basel, Switzerland) on a fully automatic biochemical autoanalyzer (Cobas c702; Roche Products Ltd, Basel, Switzerland). All analyses were carried out by qualified technicians who were blinded to clinical data. Hypertension was defined as SBP \geq 140 mmHg, DBP \geq 90 mmHg or using anti-hypertensive drugs (6). Diabetes mellitus was defined as FBG \geq 7.0 mmol/L or using anti-diabetic drugs/insulin (7). Dyslipidemia was defined as triglyceride \geq 1.7 mmol/L, LDL-C \geq 3.37 mmol/L, HDL-C \leq 1.04 mmol/L or using lipid-regulating drugs (8).

Statistical analyses

Data were assessed using Statistic Package for Social Science (SPSS) version 17 (SPSS Inc., Chicago, IL, U.S.). Data were described using mean and standard deviation (continuous variables with normal distribution), median and interquartile range (continuous variables with skewed distribution), and number and percentage (categorical variables). Data were compared between female centenarians categorized by median values of Barthel Index, using Student's t-test for continuous variables with normal distribution, Mann-Whitney U test for continuous variables with skewed distribution and Chi-square test for categorical variables. Linear regression analyses were used to assess the relationships of plasma sex hormone levels with Barthel Index (normal transformation) following three models: model 1 with no adjustment; model 2 adjusted for age; and model 3 adjusted for age, WC, coronary artery disease, hypertension, dyslipidemia, diabetes mellitus, SBP, DBP, triglyceride, HDL-C, LDL-C and FBG. Two-tailed P<0.05 was regarded statistically significant.

SEX HORMONE AND ACTIVITY OF DAILY LIVING

Results

Median age of all female centenarians was 102 years, with the range from 100 to 115 years. Median values of Barthel Index were 85(60-90). Plasma levels of sex hormones were described in Table 1. Features of Barthel Index in Chinese female centenarians were described in Table 2. Female centenarians with Barthel Index values >85 had lower plasma levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone, progesterone and estradiol than those with Barthel Index values ≤85 (P<0.05 for all). In the first, second and third models of linear regression analyses (Table 3), Barthel Index values were inversely associated with plasma LH, FSH, testosterone, progesterone and estradiol levels (P<0.05 for all).

Discussion

Female elderly generally have abnormal activity of daily living, leading to not only increased hospitalization and mortality rates, but also aggravated individual and societal burden (1). One study has proved that plasma estrone levels were inversely related to activity of daily living in female elderly (3). However, another study has considered that plasma testosterone and estrone levels showed no correlation with activity of daily living in female elderly (2). In Chinese female elderly, especially in female centenarians, there have been limited studies evaluating the relationships of plasma sex hormone levels with activity of daily living (2). The current study confirmed that plasma sex hormone levels, including LH, FSH, testosterone, progesterone and estradiol, had significant relationships with activity of daily living in Chinese female centenarians.

Previous studies have put forward the hypothesis that hormone-replacing therapy, such as testosterone and estrone, might have beneficial effects on activity of daily living in elderly men (9, 10). Moreover, in terms of mechanisms, sex hormones have been presumed to not only have neurotrophic and neuronal remodeling activity, but also be related to better endothelial function, all which get an chance to improve activity of daily living (11-13). Also studies have indicated significant relation of sex hormones with muscle mass and strength, but not with physical activity (14-16). In different studies, plasma sex hormone levels have been proposed to be positively or inversely related to muscle mass and strength, as well as physical activity (17-19). Given the mixed and contradictory results, the current study was not in support of applying these sex hormones to improving activity of daily living in Chinese female centenarians.

Previous studies have found that hormone replacement therapy significantly reduced the incidence of climacteric symptoms, suggesting it effective, safe and well tolerated treatment in Chinese postmenopausal women (20). However, the current study did not obtain positive relationships between hormone replacement therapy and activity of daily living in

Chinese female centenarians. Moreover, the current study provided the evidence that these sex hormones had an independent linkage to activity of daily living, and reminded us that these sex hormones might have inverse relationships with activity of daily living in Chinese female centenarians. These studies have many differences, such as age group, living area and observed indicators, and more studies are needed to understand the effects of hormone replacement therapy on activity of daily living in Chinese females. Meanwhile, in a future study, the relationships of sex hormones with activity of daily living should be analyzed in Chinese female centenarians with steroid therapy.

Conclusion

As the first time in the world, the current study demonstrated that plasma sex hormone levels, including LH, FSH, testosterone, progesterone and estradiol, had significant relationships with activity of daily living in Chinese female centenarians. The current study could better understand the effects of hormone-replacing therapy and promote the development of medical tourism and health technology of Hainan, China.

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Consent for publication: Not applicable.

Ethical approval: All the patients were informed about the purposes of the study and consequently have signed their "consent of the patient". All investigations conformed to the principles outlined in the Declaration of Helsinki and were performed with permission by the responsible Ethics Committee of the Hainan Branch of the Chinese People's Liberation Army General Hospital (Sanya, Hainan; Number: 301hn1201601).

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