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TRACE ELEMENT LEVELS IN THE ELDERS OVER 80 FROM THE HAINAN PROVINCE OF CHINA

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Abstract: Trace elements are key regulators of metabolism and physiological pathways, and their levels change during aging. Hair, as a biological sample, has attracted much attention due to its ease of collection and slow substance metabolism. Also, trace elements in hair can reveal the distribution of essential nutrients and toxic elements in the body pools. Therefore, we investigated the lifestyle and dietary status by questionnaire and measured 8 trace elements in hair and 6 elements in blood of a sample of elders over 80 residing in Hainan province of China. Our data showed that the concentration of Se, Fe and Pb dropped as people grow older, but Mn rose. Changes in trace elements may affect enzyme activity and biological pathways, and are associated with many diseases, including cancer and chronic diseases. In addition, association between age-related diseases and trace elements are increasingly being reported, suggesting that approaches of combining nutrition with longevity studies in the further study will help us to identify the mechanisms whereby trace elements affect the aging process.

Key words: Trace elements, hair, dyslipidemia, anemia, hypertension.

Abbreviations: BMI: body mass index; Ca: calcium; Cr: chromium; Cu: copper; DBP: diastolic blood pressure; Fe: iron; Hb: haemoglobin; HDL-C: high-density lipoprotein cholesterol; K: potassium; LDL-C: low-density lipoprotein cholesterol; Mg: magnesium; Mn: manganese,; Na: sodium; P: phosphorus; Pb: lead; SBP: systolic blood pressure; Se: selenium; Sr: strontium; TC: total cholesterol; TG: triglyceride; Zn: zinc.

Introduction

Aging is a period of decline in body health and function, and is accompanied by changes in human trace elements (1, 2). Studies have reported age-related changes in trace element content (3-5). However, there are some differences among the data, which may be related to region, ethnicity and physical status. Trace element analysis of hair helps to understand diseases, metabolic disorders, environmental exposure and nutritional status. Besides, the greatest advantage of hair sampling is non-invasive, and it is easy to store and transport. Therefore, it is used as a tool for mineral measurement in various scientific studies (6). For the elderly, trace elements can be used as a helpful biomarker to reflect the state of the body over a period of time. In addition, trace element data from longevity can provide new indicators for healthy aging.

This study assessed 8 trace elements in hair and 6 elements in blood of a sample of elders over 80 residing in Hainan province of China. Trace elements measured were selenium (Se), chromium (Cr), copper (Cu), iron (Fe), manganese (Mn), strontium (Sr), zinc (Zn) and lead (Pb). Other elements were magnesium (Mg), phosphorus (P), calcium (Ca), sodium (Na), potassium (K). The data is used to examine some potential determinants of trace element status including diet, plasma lipid, and trace element interactions.

Methods

Study Population

The sample consisted of 152 elderly people living in Changjiang, Wanning, Chengmai, Wuzhishan and Sanya in Hainan Province, where there are more centenarians. Age ranged from 80-112 years old. The subjects were divided into three groups according to the age, named group 80-89 (n=54), group 90-99 (n=52) and group 100+ (n=46). The number of each group is basically consistent in each region. All participants did not use drugs to regulate blood lipid, blood pressure and blood sugar in the recent three months. The study was approved by the Ethics Committee of Hainan Hospital of PLA General Hospital and informed consent was obtained from each subject.

The exclusion criteria were: (1) metallic implants; (2) use of synthetic hair dyes; (3) vegetarian diet; (4) cancer; (5) Parkinson and Alzheimer; (6) receiving trace element preparations or hormonal preparations at present; (7) acute surgical diseases and traumas.

Dietary Pattern

Data regarding lifestyle characteristics and dietary habits were obtained by a questionnaire, just as we did in the previous articles (7).

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Table 1
General information of study subjects

Variables	Total (n=152)	80-89 (n=54)	90-99 (n=52)	100+ (n=46)	P-value
Age, years	92.9±8.8	83.3±2.5	93.3±3.3	103.8±2.8	<0.001
Women,%	82.2	74.1	94.2	78.3	0.018
Illiterate,%	88.8	75.9	92.3	100	<0.001
Han ethnic,%	92.8	90.7	88.5	100	0.069
Heavy manual work,%	27.6	29.6	28.8	23.9	0.793
BMI	19.8±3.6	20.4±3.7	20.2±3.7	18.6±3.2	0.043
SBP	151.3±26.0	147.8±25.5	152.5±24.8	154.0±28.0	0.556
DBP	80.0±13.5	83.1±13.2	80.5±12.0	75.7±14.6	0.027
TC	5.1±1.1	5.3±1.3	5.2±1.1	4.7±1.0	0.069
TG	1.3±0.8	1.5±0.8	1.2±0.8	1.2±0.6	0.087
HDL-C	1.5±0.4	1.4±0.4	1.6±0.5	1.5±0.4	0.129
LDL-C	3.1±0.9	3.3±1.1	3.1±0.9	2.8±0.8	0.194
Hb	118.7±16.9	126.1±16.6	117.83±12.5	111.02±18.2	<0.001

P<0.05 indicated statistical significance.

Physical Examination

Weight and height were measured twice with a scale (Seca, Germany). The blood pressures were obtained from the right arm of the sitting participants using electronic sphygmomanometers (Omron Hem-7200, Japan). If the difference between the first and second measurement was more than 5 mmHg, then repeated measurements were taken. The average of two measurements was used.

Blood samples were transported in cold storage (4°C) to the Laboratory within 4 hours. Colorimetry was used to detect Ca, Mg, P and Fe in serum using Calcium Gen.2 kit, Magnesium Gen.2 kit, Phosphate ver.2 kit and Fe kit, respectively (Cobas C 702). The plasma concentrations of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) were measured by enzyme colorimetry (Cobas C701) using Cholesterol Gen.2 kit, HDL-Cholesterol plus 3rd generation kit, and LDL-Cholesterol Gen.3 kit respectively. The plasma triglyceride (TG) was determined by colorimetry (Cobas C701) using Triglycerides kit (Roche). Blood autoanalyzer was used to detect hemoglobin (Hb) (SYSMEX XS-800I).

SBP/DBP≥140/90 mmHg was considered hypertension (8). TG ≥1.7 mmol/L or TC ≥5.18 mmol/L or LDL-c ≥3.37 mmol/L or HDL-c <1.04 mmol/L was considered dyslipidemia (9). Anemia was defined as an Hb level <12 g/dL in women and <13 g/dL in men according to the WHO criteria (10).

Trace Elements in Hair

5 mg hair samples were collected for trace elements analysis. First, the samples were cleaned with different solvents, acetone, deionized water and 0.5% Triton X-100 solution respectively. Then the samples were digested with nitric acid, hydrogen peroxide and deionized water, and finally the solutions were used for detection of trace elements using inductively coupled plasma mass spectrometer (ICP-MS, ELAN DRC II, Perkin-Elmer Norwalk, USA).

Statistical Analysis

The data have been documented in EpiData 3.0 software and carried out by SPSS 19.0 software (IBM Corporation, Armonk, NY, USA). The data were described as mean values and standard deviations for normally distributed variables. The counts and percentages were reported for the categorical variables. Differences in the categorical variables were explored using the Chisquare test, while differences in the continuous variables were informed using nonparametric K-W test. The associations between variation of laboratory index and trace elements in hair were firstly examined using Pearson correlation analysis. Binary logistic analysis was then used among hypertension, dyslipidemia, anemia and trace elements in hair. p<0.05 indicated statistical significance.

Results

General Information of Study Subjects

There are 54 the elderly in the 80-89 group, 52 in the 90-99 group, and 46 in the 100+ group. As shown in table 1, the female accounted for over 70 percent in each group. Moreover, the majority of the participants were Han ethnic and illiterate. Surprisingly, the proportion of heavy manual workers is less than 30%. However, with the increase of age, BMI, DBP, TC, TG, LDL-C and Hb were downward trend, from 20.4±3.7

Table 2
Lifestyle characteristics and dietary habits of the participants

Variables	Total	80-89 (n=54)	90-99 (n=48)	100+ (n=54)	P-value
Smoking,%					0.326
Yes	8.6	11.1	3.8	10.9	
No	91.4	88.9	96.2	89.1	
Alcohol drinking,%					0.433
Yes	12.5	14.8	7.7	15.2	
No	87.5	85.2	92.3	84.8	
Tea drinking,%					0.281
Yes	9.9	14.8	5.8	8.7	
No	90.1	85.2	94.2	91.3	
Betel quid consumption,%					0.414
Yes	2.0	3.7	1.9	0.0	
No	98.0	96.3	98.1	100	
Passive smoking,%					0.228
Yes	19.1	22.2	11.5	23.9	
No	80.9	77.8	88.5	76.1	
Red meat consumption,%					0.485
Frequent	71.1	75.9	65.4	71.7	
Occasional	28.9	24.1	34.6	28.3	
Never	----	----	----	----	
Poultry consumption,%					0.157
Frequent	64.5	72.2	55.8	65.2	
Occasional	28.3	16.7	38.5	30.4	
Never	7.2	11.1	5.8	4.3	
Seafood consumption,%					0.126
Frequent	59.8	66.7	57.7	54.3	
Occasional	25.7	14.8	26.9	37.0	
Never	14.5	18.5	15.4	8.7	
Vegetable consumption,%					0.887
Frequent	89.5	88.9	85.5	91.3	
Occasional	10.5	11.1	11.5	8.7	
Never	----	----	----	----	
Fruit consumption,%					0.144
Frequent	53.9	64.8	50.0	45.7	
Occasional	38.2	25.9	40.4	50.0	
Never	7.9	9.3	9.6	4.3	
Egg consumption,%					0.248
Frequent	63.2	63.0	65.4	60.9	
Occasional	25.0	18.5	25.0	32.6	
Never	11.8	18.5	9.6	6.5	
Milk consumption,%					0.638
Frequent	61.8	63.0	59.6	63.0	
Occasional	20.4	14.8	23.1	23.9	
Never	17.8	22.2	17.3	13.0	
Nut consumption,%					0.240
Frequent	63.2	61.1	61.5	67.4	
Occasional	15.8	11.1	15.4	21.7	
Never	21.0	27.8	23.1	10.9	

Chisquare test for categorical variables. P<0.05 indicated statistical significance.

Table 3
Trace elements in hair and other elements in blood in the elderly in relation to age

Characteristics	Total	80-89	90-99	100+	P-value
Elements In Blood (mmol/L)					
Mg	0.88±0.08	0.87±0.06	0.88±0.07	0.91±0.10	0.065
P	1.12±0.25	1.07±0.24	1.15±0.28	1.15±0.24	0.083
Ca	2.26±0.11	2.26±0.12	2.31±0.09	2.22±0.09	<0.001
Fe	13.61±5.16	14.92±5.23	13.38±5.06	12.34±4.93	0.008
Na	140.64±3.84	141.71±2.64	141.67±4.36	138.22±3.34	<0.001
K	4.29±0.66	4.14±0.60	4.14±0.69	4.63±0.57	<0.001
Trace Elements in Hair (ug/L)					
Se	0.57±0.30	0.78±0.21	0.65±0.21	0.24±0.19	<0.001
Cr	0.34±0.25	0.33±0.14	0.27±0.15	0.43±0.38	<0.001
Mn	4.71±7.60	4.45±7.67	4.82±7.71	5.35±8.12	0.614
Sr	3.62±5.58	3.97±4.95	5.32±8.26	1.85±1.78	0.012
Pb	4.21±6.99	5.52±8.87	4.55±7.40	2.31±1.95	0.405
Fe	33.10±34.25	39.73±39.43	34.76±38.65	23.44±16.13	0.143
Cu	8.93±7.00	8.76±3.57	9.20±6.72	8.82±9.18	0.264
Zn	121.49±65.36	142.91±91.38	109.32±36.95	110.11±45.81	0.209

Nonparametric K-W test for continuous variable. P<0.05 indicated statistical significance.

Table 4
Pearson correlation analysis between variation of laboratory index and trace elements in hair

Variables	SBP	DBP	TC	TG	HDL-C	LDL-C	Hb
Se	-0.067	0.139	0.209*	0.086	-0.034	0.156	0.282***
Cr	0.076	-0.002	0.008	0.087	0.047	-0.015	-0.102
Mn	0.112	-0.041	-0.113	0.057	-0.090	-0.106	-0.131
Sr	0.065	0.009	0.012	0.021	0.009	-0.011	0.092
Pb	0.023	0.040	-0.020	-0.004	-0.040	-0.014	0.047
Fe	-0.054	0.057	0.026	0.197*	-0.094	0.037	-0.051
Cu	-0.035	-0.066	0.044	0.074	-0.008	0.037	-0.091
Zn	-0.093	-0.035	0.010	0.043	0.038	-0.003	0.101

*p<0.05,**p<0.01,***<0.001

to 18.6±3.2, from 83.1±13.2 to 75.7±14.6, from 5.3±1.3 to 4.7±1.0, from 1.5±0.8 to 1.2±0.6, from 3.3±1.1 to 2.8±0.8, from 126.1±16.6 to 111.02±18.2, respectively. While SBP gradually elevated from 147.8±25.5 to 154.0±28.0. As for HDL-C, it fluctuated among groups.

Investigation of Dietary Habits

The data of the dietary habits of the elderly were investigated among three groups (Table 2). Specifically, the proportion of smokers (8.6%), drinkers (12.5%), tea drinkers (9.9%) and betel nut users (2.0%) were lower, while passive smoking (19.1%) was relatively higher. Vegetable consumption level ranked on the top, up to 89.5%, followed by red meat with 71.1%, and then poultry, egg , nut, milk, seafood and fruit.

Elements Characteristics Analysis

Analyses on elements and different age were carried out (Table 3). The content of Fe and Na in blood decreased slowly with the increase of age, while Mg, P and K slightly increased. On the other hand, trace elements in hair showed that the concentration of Se, Fe and Pb dropped as people grow older, but Mn rose. Compared with other groups, Cr was the highest in group 100+, whereas Sr was the lowest.

Table 5
Binary logistic analysis between hypertension and trace elements in hair

Variables	B	SE	OR	95%CL	P
Se	-0.486	0.660	0.615	0.169-2.241	0.461
Cr	-0.704	0.809	0.495	0.101-2.414	0.384
Mn	-0.102	0.047	0.903	0.823-0.991	0.031
Sr	-0.044	0.048	0.957	0.871-1.052	0.365
Pb	0.030	0.034	1.030	0.965-1.100	0.377
Fe	0.009	0.006	1.009	0.997-1.021	0.157
Cu	-0.018	0.032	0.983	0.923-1.046	0.584
Zn	0.006	0.003	1.006	1.000-1.013	0.044

P<0.05 indicated statistical significance.

Table 6
Binary logistic analysis between dyslipidemia and trace elements in hair

Variables	B	SE	OR	95%CL	P
Se	1.026	0.621	2.789	0.825-9.421	0.099
Cr	0.076	0.688	1.079	0.280-4.153	0.912
Mn	-0.017	0.026	0.983	0.934-1.034	0.501
Sr	-0.024	0.036	0.976	0.909-1.049	0.510
Pb	-0.017	0.030	0.984	0.928-1.034	0.577
Fe	0.000	0.006	1.000	0.989-1.011	0.984
Cu	0.008	0.026	1.008	0.958-1.061	0.768
Zn	-0.004	0.003	0.996	0.990-1.002	0.184

P<0.05 indicated statistical significance.

Table 7
Binary logistic analysis between anemia and trace elements in hair

Variables	B	SE	OR	95%CL	P
Se	1.189	0.659	3.284	0.903-11.944	0.071
Cr	-0.895	0.874	0.409	0.074-2.264	0.306
Mn	-0.021	0.030	0.979	0.923-1.039	0.491
Sr	0.064	0.054	1.066	0.959-1.185	0.233
Pb	0.081	0.042	1.085	0.996-1.178	0.055
Fe	-0.014	0.007	0.986	0.972-1.000	0.058
Cu	-0.102	0.052	0.903	0.815-1.000	0.051
Zn	0.004	0.003	1.004	0.998-1.010	0.215

P<0.05 indicated statistical significance.

Spearman's coefficients for the correlations between the laboratory index and trace elements in hair are shown in Table 4. TC and Hb were well-correlated with Se content, and TG was associated with Fe. Binary logistic analysis was used to evaluate the association between hypertension and trace elements in hair, as shown in table 5. The incidence of hypertension was related to Mn and Zn, but Mn was a protective factor for hypertension, while Zn was a risk factor. According to the results, the incidence of dyslipidemia and anemia was not related to trace elements in hair (Table 6 and Table 7).

Discussion

Chemical elements play an important role in enzymatic action, electrolyte balance, nerve impulse transmission, muscle contraction, and bone formation. Also, the absorption and utilization of elements are related to individual physical status and age. In this study, we investigated the lifestyle and dietary status of the elderly by questionnaire. Hair trace elements and blood analysis were measured, and the relationship among trace element levels and dyslipidemia, anemia, and hypertension was evaluated to provide basic data for clinical application of trace element analysis for the elderly.

Trace elements are involved in immune function (Se, Zn, Cu), oxidative stress (Zn, Se, Cu, Fe, Mn), insulin sensitivity (Se, Zn) and cognitive function (Se, Zn) to regulate the aging process (11-16). It can be seen that Se is closely related to aging. Data from the National Health and Nutrition Examination Survey (NHANES III) in the United States (http://www.ars.usda.gov/ba/bhnrc/fsrg) revealed that the elderly are generally short of Se. Similar results were obtained from the Epidemiology of Vascular Ageing (EVA) study, Se inadequacy was related to cognitive decline, and with low level of Se and an increased mortality and prevalence of chronic diseases in an age-dependent manner (17, 18). Moreover, Se, together with vitamin E, plays an important role in boosting the immune system and inhibiting oxidation in the body (19). If it is lacking, it may be a risk factor for cancer development and aging. Our study showed that Se noticeably decreased with age, and Se was well-correlated with TC and Hb, thus it is believed that nutritional intervention should be carried out to increase the concentration of Se in the elderly.

Cr is involved in carbohydrate metabolism and cholesterol synthesis, and transported by binding to proteins such as transferrin or albumin. In addition, it has a helpful effect on glucose regulation through insulin (1). Study have shown that an age-related Cr content in hair decreased both in men and women (20). While other reported a significant age-associated decrease in hair Cr content only in women (5). Our data presented concentration of Cr was the lowest in the group 90-99, which may be related to the high proportion of women in this group (94.2%).

Zn is an active component of hundreds of protein and DNA binding proteins, including P53 (21). It was reported that the Zn content decreased during aging (22). However, Zn did not

show significant differences by age in our data, whereas it still presented an obvious downward trend as the age increased from 80 to 90.

As one of the most important essential elements, Fe is particularly important in metabolic reactions, and it is closely related to hemoglobin and myoglobin. The gradual decrease of iron content during aging may be caused by several factors: (1) deterioration of tissue respiration and transcapillary metabolism; (2) reduction of the intensity of protein synthesis process regulated by Fe-dependent and Fe-containing proteins; (3) disturbance of intestinal absorption (23). In addition, a significant correlation was determined between Fe concentration in hair and Fe deficiency anaemia (24).

Surprisingly, toxic trace element Pb was reduced with the increase of age in our data, which may be related to gender, age, diet, and lifestyle (25-27). Research has shown that drinking of milk, tea, coffee or lemon resulted in decreased Pb in hair (26). Besides, Pb content of suburban population was significantly lower than that of urban area (28). In our survey, most of the elderly lived in the countryside, where there is less Pb pollution in the air and water.

Mn content in hair was accumulating with age in our study. As a naturally occurring element, Mn is found in water, food and air. Whole grains, green leafy vegetables and nuts are rich in Mn, and tea drinkers and smokers may intake more Mn than those who do not (29). Furthermore, high doses of Mn are associated with neurotoxicity, which is characterized by changes in the neurobiology of dopamine in the brain (30, 31). Studies have reported the relationship between high Mn exposure and neurological deficits (32, 33). Therefore, the increase of Mn in the elderly should be paid enough attention.

There are several limitations in this study. First, most participates (82.2%) were female. There are too few male participants, due to many are bald. Studies have shown that an age-related trace element changed related to gender (5, 20, 34). Second, Trace elements in hair may be affected by soil, air and water, but we didn't involve. Finally, the use of different shampoos may also affect the concentration of trace elements in the hair (35). It is necessary to further increase the number of subjects and expand other areas to confirm the observed association.

In conclusion, the obtained data indicated that the concentration of Se, Fe and Pb in hair dropped among the elderly over 80 years old, but Mn rose, and it is considered that nutritional intervention to control the imbalance of mineral nutrition is required. Also, as the results of this study showed some correlations between hair mineral levels and dyslipidemia, anemia, and hypertension, the possibility of utilizing hair mineral analysis for age-related diseases is suggested.

Ethics approval and consent to participate: Prior to investigation and physical examination, we have got the consent from the participants or from their family members such as sons and daughter-in-laws. If the participants could not sign their names because of illiteracy or being cognitive-impaired, their names were signed by their direct relatives after the consent of the participants. The Ethics Committee of the Hainan branch of PLA General Hospital (Sanya, Hainan) approved the study protocol (No. of serial: 301HNLL-2016-01).

Consent for publication: Not applicable.

Availability of data and material: The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests: On behalf of all authors, the corresponding author states that there is no conflict of interest.

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Author contributions: ZQ designed the study and drafted the manuscript. YY participated in the design of the study and performed the investigation. NCX performed the statistical analysis. ZYL conceived of the study, participated in its design and coordination, and helped to draft the manuscript. The authors declare that they have no conflict of interest. All authors read and approved the final manuscript.

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