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ORIGINAL PAPER

Correlation between Hair Zinc Level and Cognitive Function in Elderly Population

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Abstract

Introduction: Neurodegenerative disease is the most common problem in elderly. Amyloid β (Aβ) accumulation is the major cause of cognitive impairment. Zinc has an important role in antioxidant and Aβ accumulation process. This study aimed to evaluate the correlation between hair zinc level and cognitive function in elderly.

Methods: A cross sectional study was conducted involving 58 subjects of elderly at Kartini Regency, Central Jakarta in January 2019. Hair zinc level was measured by inductively coupled plasma emission spectrometer (ICPS) and cognitive function assessed by abbreviated mental test (AMT). Data analysis was done by spearman rank correlation test and p-value less than 0.05 were considered statistically significant.

Result: The mean of age was 65.4 ± 4.4 years old and 56.9% of subjects were female. The mean of hair zinc level was 123.23 ± 69.71 μg/gram hair and 32.8% subjects had hair zinc deficiency. There was 91.4% subjects had normal cognitive function. The study showed no correlation between hair zinc level and cognitive function in elderly (p=0.871 ; r=-0.022).

Conclusions: There was no correlation between hair zinc level and cognitive function in elderly. Further research is expected to be performed with different level of cognitive function.

Keywords cognitive, elderly, hair zinc level, zinc

Introduction

Raising of elderly population is a global phenomenon, not only in developed country with high income but also in low and medium income.[1] Population survey in 2010 showed that Indonesia is one of the five highest elderly population country in the world.[2] Elderly population have many health problems, mainly neurodegenerative disease.[3] In 2015, there are 9.9 million new case of dementia and 46.8 million people with dementia.[4]

Aging process causes physiological changes in musculoskeletal, sensory, gastrointestinal and nervous system which are related to health problems in the elderly.[1] Cognitive impairment risk factors in elderly include genetic, age, family history, and degenerative diseases.[5] Degenerative diseases such as hypertension, diabetes mellitus and atherosclerosis are related to Aβ accumulation. It is the major cause of cognitive impairment.[6] Cognitive function can be assessed by abbreviated mental test

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(AMT). Abbreviated mental test is a simple assessment which does not need capability of reading, writing or drawing skill and isn't depended to education level.[7]

Oral problem, like loose teeth and dry mouth (xerostomia) are also the most common problem in elderly which can disturb chewing and swallowing process thus cause low nutrient intake.[1] Zinc deficiency is one of nutrient deficiencies in elderly.[8] According to Briefel et al[9] study, only 44% people aged >70 years old had adequate zinc intake. Zinc mineral has many role in more than 2.000 transcription factors and 300 enzymes. Therefore, zinc is important for cellular mechanism such as DNA synthesis, protein synthesis, wound healing, immunity, and cognitive.[10] Zinc also plays an important role in antioxidant and Aβ accumulation process.[11-13]

Zinc level can be assessed by hair sample. Hair sample is a potential biomarker. Hair follicles can reflect zinc intake by 4-8 weeks before sample collection. Some advantages of hair sample are higher zinc concentrations than blood and urine, thus making the measurement easier. Hair sample can be collected, transported, and stored at room temperature. There is no rapid fluctuations seen in serum zinc produced by a recent meal, diurnal and circadian variation, or inflammation. Hair zinc levels are affected by biological factors such as age, sex and hair growth rate.[14]

The association between zinc level and cognitive impairment is a controversial issue. The aim of this study is to determine the correlation between hair zinc level and cognitive function in elderly.

Methods

A cross sectional study was conducted in January 2019 at Kartini Regency, Central Jakarta. Sample size was determined based on the correlation analysis (α=0.05; β=0.20; r=0.38), with estimated 10% drop out. The sum of samples was 60 subjects. Subjects were recruited by consecutive sampling. We disseminate this research information and those who wish to participate in the research can register themselves. If the number of subjects has been met then the recruitment of subjects was stopped.

Inclusion criteria were elderly (aged ≥60 years old), could communicate in Indonesian language (can hear and speak), had hair in the scalp near their necks and willing to participate by signing the informed consent. Exclusion criteria were not willing to participate, suffering from acute disease and was hospitalized, suffering chronic diarrhea and using benzodiazepine drugs in the last 3 months before this study.

Data collection was conducted after obtaining approval from Ethics Committee of the Faculty of Medicine, Universitas Indonesia. Baseline characteristics of subjects, including age, gender, educational level, working status and medical history, were collected by interview. Educational level was categorized into three groups according to Indonesian constitutional law No. 20, 2003.[15] Emotional status was assessed by geriatric depression scale-5 items (GDS-5 items).[7,16,17] Nutritional screening was done by mini nutritional assessment-short form (MNA-SF).[18]

Anthropometric measurements such as height, weight, and calf circumference were performed twice and the average results were used. Measurement of height was done by calculating knee height (0.1 cm accuracy) with Chumlea formulation. Weight measurement was done using the digital scale "SECA" (0.1 kg accuracy). From height and weight measurements body mass index (BMI) were calculated. If BMI could not be assessed, it was then replaced by calf circumference measurements.[19,20] Zinc, protein, and total calorie intakes were obtained from semi-quantitative food frequency questionnaire (SQ-FFQ) and then the data was processed using Nutrisurvey 2007 program. Hair sample as much as 0.5-1 gram of hair was collected for hair zinc level assessment which used inductively coupled plasma spectrometer (ICPS).[21,22] Cognitive functions were assessed by abbreviated mental test (AMT).[23,24]

Data were analyzed by using SPSS version 20.0 program. Normality test was done by Kolmogorov Smirnov. Spearman rank correlation test was used to determine correlation between hair zinc level and cognitive function in elderly.

Results

Subject characteristics

Based on the inclusion and exclusion criteria, 60 subjects were willing to join in this study and signed an informed consent. Subjects who followed this study and the data could be analysed were 58 subjects. Baseline characteristics of the subjects can be seen in Table 1.

Table 1. Characteristic of subjects (n=58)

Variable	Frequency n(%)	Mean ± SD or Median (min-max)
Age (year)		65.36 ± 4.40
60-69	48 (82.8)	
≥ 70	10 (17.2)	
Gender		
Male	25 (43.1)	
Female	33 (56.9)	
Education level		
Low	42 (72.4)	
Moderate	13 (22.4)	
High	3 (5.2)	
Occupation		
Employee	20 (34.5)	
Unemployment	38 (65.5)	
Disease history		
No	32 (55.2)	
Yes	26 (44.8)	
Hypertension history		
No	34 (58.6)	
Yes	24 (41.4)	
Diabetes mellitus history		
No	53 (91.4)	
Yes	5 (8.6)	
Stroke history		
No	58 (100)	
Yes	0 (0)	
Emotional status		
Without depression	58 (100)	
Depression	0 (0)	
Nutritional assessment screening		
Normal	45 (77.6)	
Malnutrition risk	13 (22.4)	
Malnutrition	0 (0)	

The average age was 65.4±4.4 years old. The number of people aged <70 years old (82.8%) was more than those of the elderly ≥70 years. In this study, 56.9% subjects are female, 72.4% had low level education and 65.5% did not work.

A total of 44.8% of subjects had a history of disease. Based on the type of disease, 41.4% of subjects had history of hypertension, 8.6% had history of diabetes mellitus, and none of the subjects had history of stroke. Based on the assessment of mental status, there was no subject suffering from depression, according to GDS-5. Based on nutritional assessment screening with the MNA-SF instrument, 77.6% had normal nutritional status and 22.4% had risk of malnutrition.

Zinc, protein and total calorie intakes

The mean value of zinc intake data was 5.65 (3.2 - 13.3) mg/day. There was 87.9% of subjects who had less zinc intake than *angka kecukupan gizi* (AKG/Indonesian recommended daily intake) 2013. Average value of protein intake per-kg body weight (BW) was 1.09±0.47 gram/kgBW/day. From the analysis of protein intake obtained, as many as 46.6% of subjects had protein intake of less than 1 gram/kg BW/day. The average value of total calorie intake per-kg BW was 29.61±8.86 kcal/kgBW/day. From the analysis of total calorie intake, 56.9% of subjects had a total calorie intake less than 30 kcal/kg BW/day. (Table 2)

Table 2. Characteristic distribution based on zinc, protein, and total calorie intake

Variable	Frequency n(%)	Mean ± SD or Median (min-max)
Zinc intake (mg/day)		5.65 (3.2 – 13.3)
Adequate	7 (12.1)	
Inadequate	51 (87.9)	
Protein intake		1.09 ± 0.47
Adequate	31 (53.4)	
Inadequate	27 (46.6)	
Total calorie intake		29.61 ± 8.86
Adequate	25 (43.1)	
Inadequate	33 (56.9)	

Hair zinc levels

The average hair zinc level was 123.23±69.71 µg/gram of hair (Table 3). There were 34 subjects (58.6%) who had normal zinc levels (80-200 µg/ gram of hair), 19 subjects (32.8%) had zinc hair deficiency, and 5 subjects (8.6%) had high hair zinc levels.

Table 3. Characteristic distribution based on hair zinc level

Variable	Frequency n(%)	Mean ± SD or Median (min-max)
Hair zinc level		123.23 69.71
Deficiency	19 (32.8)	
Normal	34 (58.6)	
High	5 (8.6)	

Cognitive function

The median value of cognitive function was 9 (minimum and maximum value: 3 and 10, respectively) which can be seen in Table 4.

A total of 53 subjects (91.4%) had normal cognitive function, 4 subjects (6.9%) had moderate cognitive impairment (AMT score 4-7) and 1 subject (1.7%) had severe cognitive impairment (AMT sore 0-3).

Correlation between hair zinc level and cognitive function

The correlation between hair zinc level and cognitive function in elderly was assessed by Spearman rank correlation test. The study found that there was no correlation (p=0.871; r=-0.022) between hair zinc levels and cognitive function in the subjects who were assessed by the AMT instrument.

Table 4. Characteristic distribution based on cognitive function

Variable	Frequency n(%)	Mean ± SD or Median (min-max)
Cognitive function		9 (3-10)
Normal	53 (91.4)	
Moderate cognitive impairment	4 (6.9)	
Severe cognitive impairment	1 (1.7)	

Discussion

The average age of this study was 65.4±4.4 years old with 82.8% subject were <70 years old. Rahmawati's research[25] showed that there was more subject (72.8%) less than 70 years old and average age was 66.34±5.34 years. Based on Indonesian population pyramid data in 2016, most of elderly people are ≥70 years old of age. The pyramid shows that the mortality rate is still high in the elderly population, because 70 years old of age is categorized as high-risk elderly.[26] There are various risks of degenerative diseases such as high blood pressure, diabetes mellitus, coronary heart disease, kidney disease and nutritional problems that can affect the elderly.[27]

The average value of hair zinc in this study was 123.23±69.71 µg/gram of hair. The normal zinc level reference in this study was 80-200 µg/gram of hair.[14] Subjects with normal hair zinc levels were 58.6%, subjects with zinc deficiency were 32.8%, and subjects with high hair zinc levels were 8.6%. A research was conducted by Yasuda, et al.[28] in the Japanese population aged 0-100 years old to determine zinc levels through hair specimens using the ICP-MS method. Reference to control of hair zinc levels in the study was 86.6-193 µg/gram hair (ppm). The lowest zinc concentration of 9.69 ppm was found in women aged 51 years old. The prevalence of zinc deficiency in the male group in the 6th decade age was 11.6% and in the 7th decade was 15.1%. However the prevalence of zinc deficiency in the female group in the 6th decade age was 8.5% and in the 7th decade was 15.4%. There is a significant negative correlation (p<0.001) between zinc concentration and age (r=-0.12 in the male group and r=-0.14 in the female group). This study shows that elderly population is susceptible to zinc deficiency. In this study there were 8.6% of subjects who had high hair zinc levels. According to a study by Lee,[29] excess zinc levels can occur due to excess exogenous zinc, excessive oxidants resulting in zinc release from metallothionein (MT), and dysregulation of zinc homeostasis systems related to the expression or function of MT, Zrt- and Irt-like protein (ZIP), and zinc transporter (ZnT). The subjects who had high zinc hair levels in this study had zinc intake pattern that was less than the recommendation. Therefore it is possible that this study subject had high hair zinc levels due to dysregulation of the zinc homeostasis system or the presence of excess oxidant resulting in zinc release from MT.

The median value of cognitive function in this study is 9 (3-10). The number of subjects with normal cognitive function was 91.4%, subjects had moderate cognitive function impairment as much as 6.9% and subjects who experienced severe cognitive impairment were 1.7%. This result is different from Markiewicz-Zukowska's research. The Markiewicz-Zukowska's study was conducted on elderly subjects who lived in the nursing home and it was found that 48% of subjects showed symptoms of depression.[7] While in this study performed on elderly subjects who stayed at home, and did not find subjects who showed symptoms of depression. According to a meta-analysis cohort study shows that depression history increases the risk of dementia.[5] Wherever subjects with dementia often exhibit neuropsychiatric symptoms such as depression, anxiety, agitation, sleep disturbances, and apathy. This increases the risk of progression to dementia in individuals with mild cognitive impairment (MCI).[30]

In this study, there was no correlation between hair zinc level and cognitive function in elderly people. Research on zinc levels with cognitive function is still controversial because it shows different results. The Rabia, et al[21] study showed a significant difference (p=0.02) of hair zinc levels between the Alzheimer's group (75 ± 29 µg/gram) compared to the control group (98 ± 54 µg/gram). AMT and GDS-5 items were a simple instrument to screen the cognitive function and mental status. In future study, we recommend to use other examination to diagnose the real of cognitive function and mental status. There are many tools to evaluate the cognitive function and mental status with strengths and weaknesses. We need to consider with the characteristic of the elderly population and collaborate with other professionals like neurologist and psychiatrist doctor.

Zinc has an important role in cellular metabolism such as proliferation, differentiation, and apoptosis. In addition, zinc is an antioxidant element and maintains tissues against oxidative stress. Alzheimer's disease, MCI and the aging process are associated with Aβ deposits and cognitive decline.[31] Amyloid lesions or senile plaques consist of Aβ peptides originates from the APP proteolytic process. Zinc plays a role in Aβ degradation. In the healthy brain, there was a little production of Aβ and degraded by enzymes which degrades Aβ. The enzymes that play a role in Aβ degradation are also related with zinc.[11]

Zinc is an important micronutrient for various cellular processes especially immune system function. Zinc deficiency may cause a significant decrease of innate and adaptive immune responses which then trigger systemic inflammation.[32] Chronic inflammation is related to oxidative stress.[13] Zinc deficiency increases oxidative stress and resulting in the formation of pro-inflammatory cytokines such as IL-1β, IL-2, IL-6, and tumor necrosis factor-α (TNF-α).[32]

Cognitive function is not only influenced by zinc minerals. There are various kinds of factors that can affect cognitive function. Genetics and family history are unmodifiable risk factors. Modifiable risk factors include sleep patterns, physical activity/exercise, social activities, diets that are not limited to just one micronutrient. Older people also often experience degenerative problems such as hypertension, diabetes and stroke which are risk factors for decreased cognitive function. Psychological conditions and education of elderly people also have a role in cognitive function.[6,33].

In conclusion, there was no correlation between hair zinc level and cognitive function in elderly population. There are many other factors which can influence cognitive function in elderly population that should be assessed e.g. physical and social activity.

This study was the first cross sectional study aiming to find the correlation between hair zinc levels with cognitive function in elderly population who stayed at home. The strong points of this study was the use of hair sample to detect zinc level. In addition, measurement of anthropometric was using calibrated anthropometry tools. The assessment of cognitive function was performed by general physician.

There were several limitation in this study: utilization of SQ-FFQ that relies on the memory and assumptions of the intake portions, frequency, and type of foods by each subject. However, this had been anticipated by trained personnel, food photo book and household utensil to help the subject to remember and estimate the number and type of foods. There were other limitations in this study. Utilization of AMT and GDS-5 items were a simple instrument to screen the cognitive function and mental status however, they could not represent the real cognitive function and mental status. Nonetheless, it was anticipated in this study priory by the instrument's trial tests to some subjects performed by a general physician. We need to consider with the characteristic of the elderly population to choose the appropriate instrument to assess cognitive function and mental status. Besides that, we can collaborate with other professionals like neurologist and psychiatrist doctor.

Further research may be needed using hair sample to assess zinc level for it is simple, stable, and representable method. The researcher should be taking subjects from various cognitive levels and using random sampling method to avoid selection bias. Not only using screening tools but also other examination to diagnose cognitive function and mental status is recommended. Collaboration with other professionals and assessment of other risk factors that influence cognitive function in elderly likes sleep patterns, physical activity/exercise, social activities, diets that influence cognitive function in elderly are also suggested for future studies.

Conflict of Interest

Authors declared no conflict of interest regarding this study. No educational grant is provided to the authors.

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