Experimental Gerontology 108 (2018) 28–34

Contents lists available at ScienceDirect

Experimental Gerontology

journal homepage: www.elsevier.com/locate/expgero

Blood zinc levels and cognitive and functional evaluation in non-demented older patients

Tobías E. Rivas-García[a], Marta Marcelo-Pons[b], Francisco Martínez-Arnau[c,d], Nuria Serra-Catalá[e], Yolanda Santamaría-Carrillo[e], Omar Cauli[b,*]

[a] Enfermería, Escuela de Tecnología Médica, Facultad de Medicina, Universidad de El Salvador, El Salvador
[b] Department of Nursing, University of Valencia, Valencia, Spain
[c] Department of Physiotherapy, University of Valencia, Spain
[d] Department of Nursing, Catholic University of Valencia San Vicente Martir, Spain
[e] Geroresidencias, La Saleta, Valencia, Spain

ARTICLE INFO

Editor: T Foster

Keywords:
Zinc
Barthel Index
Mini-Mental State Examination
Sleep
Depression

ABSTRACT

A complete battery of geriatric and psychometric tests was used to determine whether plasma-borne zinc (Zn), a key ion in neuroplasticity, can be associated with the severity of functional, psychological and cognitive impairment in non-demented older individuals. There was a significant positive correlation between plasma Zn levels and the concentration subcategory measured with the Mini-Mental State Examination (MMSE) test ($p < 0.001$), but not the total MMSE score, and the levels were significantly reduced in polymedicated patients (defined as concurrent administration of > 5 drugs). No correlations were found between plasma Zn levels and depressive symptoms measured with the Yesavage scale for geriatric depression or the Barthel Index - a measurement of the ability of individuals to perform the activities of daily living. Depressive symptoms were associated with poor sleep quality and polymedication ($p < 0.001$ and $p < 0.05$, respectively). Our results suggest that peripheral Zn concentration may play a role in the physiopathology of some domain of cognitive function. No correlation to depressive symptoms in the geriatric population under antidepressant drug treatment was observed. However, further studies are needed to understand the relationship between circulating Zn and concentration deficits in order to determine whether Zn represents a candidate early biomarker for cognitive impairment.

1. Introduction

Zinc (Zn) ions are important neuromodulators and signaling molecules in the central nervous system, with an influence upon the monoaminergic, endocrine and immune systems (Marger et al., 2014; Maywald et al., 2017). A body of evidence indicates that Zn plays a role in the physiopathology of depression (Schefft et al., 2017; Swardfager et al., 2013). However, some discrepancies are found in the literature regarding Zn deficiency in depression or the association between plasma Zn levels and the severity of depression (Narang et al., 1991; Maes et al., 1997; Crayton and Walsh, 2007; Irmisch et al., 2010; Salustri et al., 2010; Swardfager et al., 2013). A decrease in blood Zn concentration has been associated to impaired cognitive function (Portbury and Adlard, 2017, for review). However, the existence of an association between Zn ions and specific dimensions of cognitive function in non-demented individuals is not clear, since no systematic clinical data are available on Zn levels in older individuals subjected to psychogeriatric evaluations.

It is estimated that nearly one quarter of the world population is at risk of Zn deficiency (Maret and Sandstead, 2006). Older individuals have a higher risk of Zn deficiency, as demonstrated in the context of the third United States National Health and Nutrition Examination Survey, where 35–45% of all adults aged 60 years or older were seen to have an inadequate or low Zn intake (Ervin and Kennedy-Stephenson, 2002). Recent research has shown an association between low dietary intake of Zn and depression in men and women (Vashum et al., 2014; Yary and Aazami, 2012). Moreover, two recent meta-analysis of studies with psychiatric inpatients revealed an impact of low plasma Zn levels on depressive disorders (Swardfager et al., 2013) and the high dietary zinc intake represents a protective factor for depression with a pooled relative risk of 0.67 (95% CI: 0.58–0.76) (Li et al., 2017). However, there is a lack of data concerning plasma Zn levels in older patients. Moreover, the association between Zn levels in blood and psychogeriatric variables from complete clinical assessments has not been

* Corresponding author at: Department of Nursing, University of Valencia, c/Jaume Roig s/n, 46010, – Valencia, Spain.
E-mail address: Omar.Cauli@uv.es (O. Cauli).

https://doi.org/10.1016/j.exger.2018.03.003
Received 27 January 2018; Received in revised form 22 February 2018; Accepted 5 March 2018
Available online 20 March 2018
0531-5565/

established. Furthermore, most studies do not control for known psychogeriatric determinants of depression such as poor sleep quality, cognitive function, functional impairment or polymedication. A case-control study analyzed Zn concentration in older non-demented patients with depression, or subjects with mood disorders of some kind, in order to determine whether and to what extent plasma Zn levels are correlated to psychopathological features, including severity of depressive symptoms, functional impairment and cognitive function.

The main objectives of the present study were:

(1). To evaluate peripheral Zn concentration in blood in relation to depression and the severity of depressive symptoms in non-demented older individuals.
(2). To assess the relationship between Zn and different geriatric assessment tool measurements (the Mini-Mental State Examination [MMSE] test for cognitive function, the Barthel Index for basic activities of daily living, the Norton scale for the risk of pressure ulcers, the Lawton index for instrumental activities of daily living, and the Athens scale for sleep quality).

2. Method

2.1. Sample

The study sample was recruited in 2015 and 2016 at different mental health centers and nursing homes in Valencia city and province (Spain). In accordance with the requirements established by the Declaration of Helsinki, written consent was obtained from each person participating in the study, after having been informed in a clear and simple way about the purpose of the study and the procedures involved. Confidentiality of all the provided data was also explained. The study protocol was approved by the Human Research Ethics Committee of the University of Valencia (Reference: 38417528).

2.2. Inclusion criteria

The following inclusion criteria were established: adults of both sexes aged 60 years and over; subjects diagnosed with major depression (DSM-IV-TR); outpatients or people living in a nursing home; stable drug treatment for at least three months; and the ability to understand the study procedures and provide written informed consent. Exclusion criteria were: current hospitalization; severe neurocognitive disorders (Alzheimer's disease or other problems characterized by severe cognitive impairment) or severe psychiatric disorders (schizophrenia or bipolar disorder); visual or hearing disabilities impeding understanding of the protocol; the inability to read or understand Spanish; current cancer disease; and current administration of Zn supplements or polyvitamin products containing Zn salts.

2.3. Sociodemographic variables

The independent variables were those variables that could influence or modify the dependent variable, i.e., Zn concentration in blood. The collected sociodemographic variables included gender, age, marital status, place of residence, body mass index (BMI), and polymedication.

2.4. Geriatric and psychological evaluation

Each individual was subjected to complete clinical, geriatric and functional assessment. Demographic, anthropometric, pharmacological and clinical variables were recorded.

Two validation scales were used to evaluate the functional area: the Barthel Index (Mahoney and Barthel, 1965) and the Mini-Mental State Examination (MMSE) (Folstein et al., 1975). The Barthel Index assesses the ability to perform activities of daily living, and measures independence with 10 items, with a score range of 0–100. The items assessed are: eating, washing, dressing, arranging, deposition, urination, going to the toilet, moving to the couch/bed, wandering and going up/down stairs. A lower score indicates greater dependence, while a higher score indicates greater independence - 0 representing total dependence and 100 total independence.

The Mini-Mental State Examination was used for the analysis of cognitive impairment (Spanish version adapted by Lobo et al., 2002, values 0-35). This scale scores 5 cognitive sub-domain items: orientation, fixation, concentration, memory, language and construction. A score of ≥ 30 points indicates that the subject probably does not have any type of cognitive impairment, while a score of ≤ 24 points indicates that the subject already has cognitive impairment.

Sleep and dreaming capacity was evaluated by the Athens Scale of Insomnia (Soldatos et al., 2003), composed of 8 items. The first four items analyze sleep in a quantitative way, the fifth item analyzes the quality of sleep, and the last three items analyze the daytime impact of sleep quality. The score ranges from 0 (no difficulty sleeping) to 24 (presence of insomnia).

Finally, the score obtained from the Yesavage scale was categorized to evaluate the mental state of the participants, namely the presence or absence of depression. This scale evaluates the depressive symptoms present in the elderly. We used the reduced version, composed of 15 dichotomous response (yes or no) items, with scores ranging from 0 to 15, where a score of over 5 indicates the probable presence of depression. The presence of depression was also dichotomized by reviewing the medical records for a clinical diagnosis of depression (including antidepressant and other psychotropic drug treatments).

The Norton scale was used to measure the risk of developing pressure ulcers (Norton et al., 1975).

2.5. Analysis of zinc

Blood samples were obtained from each subject between 7:30 a.m. and 9 a.m. 10 ml of blood was collected in two BD Vacutainer tubes containing EDTA. After extraction, the blood samples were allowed to stand for 15 min and were centrifuged at 1500 rpm for 10 min at room temperature. Subsequently the plasma samples were aliquoted and stored at −80 °C until analysis. Zinc concentration was determined by inductively coupled plasma mass spectrometry (ICP-MS) in the Central Experimental Research Supporting Service of the University of Valencia (SCSIE). The samples (100 µl) were subjected to acid digestion with 0.2 ml of concentrated nitric acid at 80 °C in a dry bath for 5 h. Then, 4 ml of ultrapure water was allowed to cool Zinc determination was performed by ICP-MS using an Agilent model 7900, with rhodium as internal standard. A plasma Zn concentration ≤ 11 µmol/l (719.5 µg/l) was defined as the cut-off point for Zn deficiency (Maret and Sandstead, 2006; Marcellini, 2006; Brown et al., 2004).

2.6. Statistical analysis

The quantitative variables were subjected to a descriptive analysis, using central tendency and dispersion measures. Likewise, a descriptive analysis was made of the qualitative variables, based on frequency distributions. The Kolmogorov-Smirnov test was used to estimate the normal distribution of quantitative variables and thus define the type of test to be used (parametric or nonparametric). The differences of means between two or more groups were analyzed using nonparametric tests (Mann-Whitney U test or Kruskal-Wallis test). The confidence level established in all the analyses was 95%, with statistical significance being defined for $p < 0.05$. The IBM SPSS version 22.0 statistical package was used throughout.