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Short Communication

Some Biochemical Markers in Patients with Alzheimer's Disease

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Abstract

Background: Metal ions effect on homeostasis of Alzheimer's disease (AD) patients. The aim of this study was to assess the metal ions (Iron, Zinc and Copper) and CBC in patients with AD in comparison with normal range.

Methods: The samples of study were 17 patients with AD in Tehran's aging centers in 2015, selected as an access sample. Blood samples were analyzed in a pathobiology laboratory. Data were analyzed by one sample *t*-test.

Results: According to the normal range, provided by laboratory, there is a significant difference between zinc in patients with AD and normal reference interval (α=0.01). The comparison of CBC of the AD patients with normal group showed also some decreases

Conclusion: Zinc value in AD patients is significantly lower than normal range. It should be repeated by a larger sample size.

Keywords: Iron, Copper, Zinc, Alzheimer's disease

Introduction

Alzheimer's disease (AD) is known as the most common form of dementia and degenerative disease (1). AD is related to the deposit of amyloid plaques and neurofibrillary tangles within the cortex. Several factors result in AD but there is no clear casual factor for AD. Most of studies assigned to genetic and biological structures.

As we know, the formation of signs and symptoms of AD are not only influenced by APOE and other genes, but also mediated by some environmental factors. Metals as mediated factors are studied in several studies.

The highlighted lesion in the brain of people with AD is the amyloid plaques that include Amyloid β (Aβ) peptides derived from Amyliod precursor protein (APP). Toxicity of Amiloid β is resulted from abnormal interaction with metals like zinc, copper and iron in Neocortex (2-4). Homeostasis of metals can be traced in the serum/plasma in AD patients. One study explained the effects of metals in AD (5). Copper, zinc and iron are elevated in AD-affected cortex, repeated in other studies (6, 7).

These metals are found in amyloid plaques and neurofibrillary tangles (8). They bind to the Aβ and deposit into the Aβ (9). Therefore, sequestration of these metals into senile plaques leads to the loss of cellular and synaptic metals. This synaptic loss is relevant to the maintenance of normal cognition.

ApoE isoforms bind to metals such as iron, zinc and copper (10). Some evidence focus on the ef-

fect of metals on expression levels of Apolipoproteins. The expression of Apo A and B has been regulated by zinc and copper (11). Altered metal rate in AD affect the expression of ApoE. Moreover, these metals play an important role in the regulation of the AD-related proteins (APP and tau) (12)

We do not know that the metal ions dyshomeostasis in AD is a cause or consequence of disease, the findings are controversial. There is an age-dependent decrease of serum zinc, approximately 0.4% per year (13). There is a direct relation between AD and metal ions, but other studies suggest that it is not significant (4).

The aim of this study was to assess the metal ions (Iron, Zinc and Copper) and CBC in patients with Alzheimer's disease in comparison with normal range.

Methods

Among a group of patients with AD, 17 patients who signed the testimonial, blood sample were collected. Samples were analyzed for zinc, Iron, copper and CBC in a pathobiological laboratory. According to the existing reference interval, data were analyzed by one sample *t*-test.

Lab methodology

- Iron in serum is analyzed by FreroZink method.
- Zinc in serum is analyzed by Photometric method.
- Copper in serum is analyzed by photometric method.
- CBC test was performed for all participants

Results

The results of CBC test showed a decrease for all participants; data are presented in Table 1 and Fig.1.

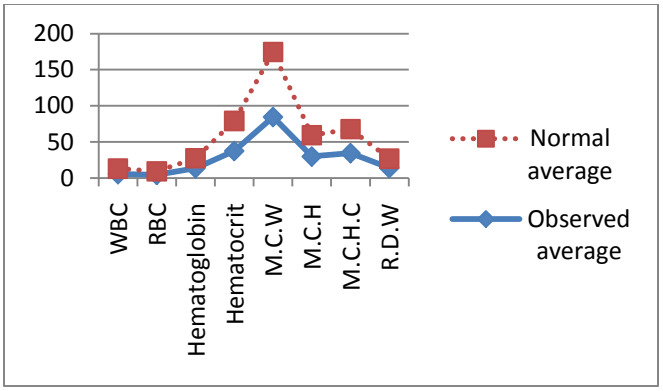

Fig.1: Results of hematology

Table 1: Descriptive analysis of hematology test

	WBC	RBC	Hemato globin	Hematocrit	M.C.W	M.C.H	M.C.H.C	R.D.W
Observed average	5.61	4.64	13.85	37.61	84.62	29.94	34.65	14.03
Normal average	7.5	4.65	13.5	41.5	90	29.5	33	12.8
Ref. interval	4-11	3.8-5.5	12-15	36-47	80-100	27-32	31.5-34.5	11.6-14

As it shows in Table 1, there was no significant deficit in CBC of the participants. Obtained data were categorized and descriptive analysis is presented in Table 2.

As it shows in Table 2, each variable was analyzed and descriptive data (Mean, standard deviation and standard error mean) are provided for analysis. Results of one sample *t*-test are presented in Table 3. According to the degree of freedom (df), *t* is achieved from table distribution and then compared with obtained *t*. There was a significant difference between obtained data and distribution range.

A reference interval was provided by laboratory as normal range for each variable. Iron, Zinc and Copper are 37-145, 80-120 and 80-155, subsequently. Therefore, according to the provided interval reference, only the Zinc shows a significant decrease.

Table 2: Descriptive analysis of data

	n	Observed Mean	Reference Interval	SD	Standard error mean
Iron	17	55.76	37-145	19.60	4.75
Zinc	17	64.35	80-120	13.50	3.27
Copper	17	119.29	80-155	23.12	5.60

Table 3: Results of one-sample *t*-test

	t	df.	Mean difference	99% confidence	
				Lower	Upper
Iron	11.72	16	55.76	41.87	69.65
Zinc	19.64	16	64.35	54.78	73.91
Copper	21.27	16	119.29	102.91	135.67

Discussion

Zinc as a metal in the brain, has various functions. Zinc has numerous functions in AD. Zinc is essential in processing of the APP (13, 14) and in the enzymatic degradation of the Aβ peptide (15, 16).

Zinc has a role in sustaining the adhesiveness of APP during cell-cell and cell-matrix interactions (17). APP can be processed by the Amiloidogenic pathway or Non-Amiloidogenic pathways. Amiloidogenic pathway leads to the production of Aβ and in healthy brain; the non-Amiloid pathway is predominant APP processing pathway (18, 19).

Zinc in patients with AD is lower than reference interval. Decrease in serum zinc is depended on aging and it decreases approximately 0.4% per year (15).

Overall, decrease of zinc is approved in most of studies but with different explanations. It needs to more accurate studies for presenting the relationship between zinc and AD.

Conclusion

Copper, zinc and iron show significant differences in AD patients and normal older adults. There is significant decrease in zinc serum of AD patients, but copper and iron did not show significant differences.

Ethical consideration

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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References

1. Khanahmadi M, Farhud DD, Malmir M (2015). Genetic in Alzheimer's disease-a narrative review article. *Iran J Public Health*, 44(7):892-901.

2. Squitti R, Lupoi D, Pasqualetti P, et al. (2002). Elevation of serum copper levels in Alzheimer's disease. *Neurology*, 59: 1153-61.
3. Markesbery WR (1997). Oxidative stress hypothesis in Alzheimer's disease. *Free Radic Biol Med*, 23: 134-47.
4. Aly WW, Elsaid SMS, Wahba HMF (2013). Copper, zinc and iron serum levels in patients with Alzheimer's disease. *Life Sci J*, 10(3): 2628-2632.
5. Bush AI, Pettingell WH, Multhaup G, et al. (1994). Rapid induction of Alzheimer Abeta amyloid formation by zinc. *Science*, 265:1464-67.
6. Hozumi I, Hasegawa T, Honda A, et al. (2011). Patterns of levels of biological metals in CSF differ among neurodegenerative disease. *J Neurol Sci*, 303: 95-99.
7. Vural H, dermirin H, Kara Y, Eren I, Delbias N (2010). Alterations of plasma magnesium, copper, zinc, iron and selenium concentrations and some related erythrocyte antioxidant enzyme activities in patients with AD. *J Trace Elem Med Biol,* 24:169-173.
8. Ayton S, Lei P, Bush AI (2013). Metallostasis in AD. Free Radic. *Free Radic Biol Med,* 62:67-89.
9. Altamura S, Muckenthaler MU (2009). Iron toxicity in diseases of aging: AD, Parkinson disease and atherosclerosis. *J Alzheimer's Dis*, 16: 879-895.
10. Miyata M, Smith JD (1996). Apolipoprotein E allele-specific antioxidant activity and effects on cytotoxity by oxidative insults and beta-amiloid peptides. *Nat Genet,* 14: 55-61.
11. Cui L, Schoene NW, Zhu L, Fanzo JC, Alshatwi A, Lei KY. (2002). Zinc depletion reduced Egr-1 and HNF-3beta expression and apolipoprotein A-I promoteractivityinHepG2cells. *Am J Physiol Cell Physiol*, 283: C623–C630.
12. Xu H, Finkelstein DI, Adlard PA (2014). Interactions of metals and apolipoprotein E in Alzheimer's disease. *Front Aging Neurosci*, 6: 121.
13. Bush AI, Multhaup G, Moir RD, et al. (1993). A novel zinc (II) binding site modulates the function of the βA4 amyloid protein precursor of Alzheimer's disease. *J Biol Chem,* 268(22): 16109–16112.
14. Bush AI, Pettingell WH, De Paradis M, Tanzi RE, Wasco W (1994). The amyloid β-protein precursor and its mammalian homologues. Evidence for a zinc-modulated heparin binding super family. *J Biol Chem,* 269(43): 26618–26621.
15. Rembach A, Hare DJ, Doecke JD, et al (2014). Decreased serum zinc is an effect of ageing and not alzheimer's disease. *Metallomics*, 6: 1216-1219.
16. Bateman RJ, Munsell LY, Morris JC, Swarm R, Yarasheski KE, Holtzman DM (2006). Human amyloid-β synthesis and clearance rates as measured in cerebrospinal fluid in vivo. *Nat Med*, 12(7): 856–861.
17. Multhaup G, Busha AI, Pollweina P, Masters CL (1994). Interaction between the zinc (II) and the heparin binding site of the Alzheimer's disease βA4 amyloid precursor protein (APP). *FEBS Letters*, 355(2): 151–154.
18. Chow VW, Mattson MP, Wong PC, Gleichmann M (2010). An overview of APP processing enzymes and products. *Neuromolecular Med*, 12(1): 1–12.
19. Edwards DR, Handsley MM, Pennington CJ (2008). The ADAM metalloproteinases. *Mol Aspects Med*, 29(5): 258–289.