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Potential Effect of Several Heavy Metals with Alzheimer's Disease Infection

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ABSTRACT

Alzheimer's disease is the most common form of dementia and gradually affects the elderly. The disease is associated with toxic chemicals of industrial origin. Based on neurotoxic studies showing that heavy metals induce Alzheimer's disease, this paper discusses potential effect of several heavy metals with Alzheimer's disease infection. Where the study included 42 patients suffering from Alzheimer's disease after confirming their diagnosis of the disease and 30 cases as health controls. Concentrations of many heavy metals (lead, cadmium, mercury, iron, zinc and aluminum) were determined in the blood samples of patients and healthy subjects, as the detection of the content of the concentration of these minerals showed high levels in patients compared to healthy controls, and the analysis of the variance of the mineral content of the patients showed high significant effects ($P < 0.01$) Compared to healthy people.

Keywords: Alzheimer's disease,Heavy metals,Lead,Cadmium,Mercury,Iron,Zinc,Aluminum

INTRODUCTION

Alzheimer's disease (AD), which was described by Alois Alzheimer in 1906, is a neuropsychiatric disorder affecting elderly patients that results in cognitive impairment and dementia [1]. Factors of lifestyle affect the risk of an individual developing AD, including dietary habits and exposition to environmental and occupational threats [2]. Evidence shows in particular that the dysregulation in the homeostasis of essential metal and exposures to non-essential metals has a significant influence on AD pathogenesis [3]. Associations between AD and exposure to lead (Pb) have been extensively studied at the molecular level by generating oxidative DNA damage. Oxidative damage to the DNA during an aging process was identified in the brain and this damage could also lead to AD pathogenesis[4]. The potential neurotoxicity of cadmium has been identified due to high concentrations detected in brain tissues, liver, and plasma of Alzheimer's disease patient compared to healthy individuals [5]. Mercury has also

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been known to be a risk factor for Alzheimer's disease. As high levels of mercury have been detected in the blood of Alzheimer's patients and was also observed in brain tissue according to several studies, mercury in the nervous system has been shown to cause memory loss, attention deficits and dementia a symptom of Alzheimer's disease [6] .Notably, disruptions of iron brain homeostasis have been linked to several diseases, its excessive accumulation in adults has been linked to neurodegenerative diseases, including AD [7]. In AD individuals, inconsistent findings have been observed with the levels of zinc. As many studies reported increased zinc levels in the CSF and brains of AD individuals [8]. Early on 1976, high levels of aluminum have been found in brain lesions, such as plaques and tangles, in patients with AD [9].

MATERIAL & METHODS

The present study was carried out from September 2020 to June 2021.The materials of study comprised (42) patients suffering from Alzheimer's disease distributors in the governorates of Iraq .They were diagnosed with Alzheimer's disease by a consultant psychiatrist and neurologist consultant, their ages were range between (50 - 95 years) and the duration of the disease are different. The control group consisted of 30 healthy participants, ranging from (37 - 75 years) old. Serum samples were collected to measure heavy metals (Al - Zn - Cd - Hg - Fe - Pb) in the two groups. An Atomic Absorption Spectrometry (AAS) technique was used to determine the mineral concentration in samples [10].

STATISTICAL ANALYSIS

The Statistical Analysis System(SAS/ version 9.1) program was used to detect the effect of difference factors in study parameters.Statistical presentation and analysis of the present study was conducted, using the mean with the standard error (Mean ± SE).T-test was used for comparison between different groups (patients and control) .P values ≤ 0.01 wereconsidered significant.

RESULTS

The bioavailability of heavy metals (Pb, Cd, Hg, Fe, Zn and Al) was determined in AD patients and healthy controls by determining the concentration of this elements in the blood serum (Table1& 2). In table 3 the mean values data for each of the heavy elements in AD patients are also presented and compared with the healthy controls.

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Table 1:The concentration of heavy metals in the blood of Alzheimer's disease patients

Case No.	Concentration of heavy metals (ppm)					
	AL	Zn	Hg	Fe	Cd	Pb
1	0.902	1.52	0.051	2.022	0.025	0.012
2	1.22	1.25	0.043	2.167	0.027	0.011
3	1.24	1.76	0.072	2.654	0.031	0.023
4	2.51	1.13	0.112	3.654	0.029	0.013
5	2.77	2.66	0.081	2.987	0.033	0.012
6	2.31	2.99	0.034	3.118	0.043	0.033
7	2.56	1.87	0.056	3.543	0.034	0.034
8	2.87	1.93	0.059	2.765	0.031	0.038
9	3.11	2.85	0.049	2.876	0.051	0.031
10	3.54	2.22	0.064	3.943	0.065	0.013
11	2.67	3.98	0.075	3.888	0.055	0.015
12	3.97	3.90	0.079	4.132	0.041	0.019
13	2.76	3.23	0.055	5.765	0.077	0.031
14	4.11	3.67	0.081	2.412	0.063	0.035
15	2.42	3.22	0.087	5.101	0.069	0.027
16	4.97	3.77	0.092	4.712	0.073	0.028
17	4.77	3.69	0.054	3.911	0.075	0.038
18	4.04	5.88	0.095	3.884	0.081	0.037
19	3.79	5.12	0.145	5.771	0.093	0.029
20	3.86	4.77	0.119	2.971	0.048	0.031
21	3.98	4.53	0.114	2.199	0.047	0.039
22	3.77	6.11	0.120	4.944	0.058	0.041
23	4.99	3.76	0.097	5.106	0.051	0.051
24	4.63	3.64	0.127	5.204	0.059	0.011
25	3.98	3.81	0.123	4.456	0.055	0.032
26	3.89	3.75	0.135	4.651	0.074	0.043
27	3.76	2.76	0.139	3.742	0.061	0.022
28	3.99	2.99	0.099	3.917	0.085	0.034
29	3.66	2.87	0.145	2.003	0.075	0.044
30	4.98	5.11	0.156	2.012	0.085	0.033
31	4.11	3.66	0.096	2.555	0.044	0.011
32	4.43	3.78	0.157	2.652	0.039	0.019
33	3.76	5.66	0.088	3.670	0.076	0.029
34	2.88	5.43	0.068	5.114	0.089	0.027
35	1.65	5.13	0.091	3.876	0.049	0.022
36	4.09	6.01	0.151	5.004	0.033	0.028
37	3.55	2.88	0.079	4.898	0.039	0.031
38	2.77	2.11	0.077	3.797	0.049	0.026
39	3.90	2.44	0.069	3.878	0.051	0.019
40	4.17	2.54	0.011	3.666	0.055	0.018
41	4.87	2.31	0.056	3.791	0.056	0.025
42	4.76	3.24	0.075	4.009	0.066	0.024

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Table2 : The concentration of heavy metals in the blood of healthy controls.

Case No.	Concentration of heavy metals (ppm)					
	AL	Zn	Hg	Fe	Cd	Pb
1	0.010	3.44	Nil	4.22	Nil	Nil
2	Nil	3.65	Nil	4.27	Nil	Nil
3	Nil	3.87	Nil	5.65	Nil	Nil
4	0.011	3.73	Nil	3.44	Nil	Nil
5	Nil	3.88	Nil	2.44	Nil	Nil
6	Nil	4.99	Nil	2.65	Nil	Nil
7	Nil	4.71	Nil	4.11	Nil	Nil
8	0.002	3.89	Nil	4.75	Nil	Nil
9	0.001	4.87	Nil	3.65	Nil	Nil
10	0.002	5.98	Nil	4.88	Nil	Nil
11	0.002	3.98	Nil	5.10	Nil	Nil
12	0.015	4.66	Nil	4.66	Nil	Nil
13	0.012	5.21	Nil	4.33	Nil	Nil
14	0.021	4.11	Nil	4.76	Nil	Nil
15	0.011	4.89	Nil	5.66	Nil	Nil
16	0.003	4.99	Nil	5.11	Nil	Nil
17	0.009	5.76	Nil	5.54	Nil	Nil
18	0.010	6.10	Nil	5.78	Nil	Nil
19	0.011	5.25	Nil	4.88	Nil	Nil
20	0.015	5.76	Nil	4.89	Nil	Nil
21	0.022	4.66	Nil	4.33	Nil	Nil
22	0.021	4.91	Nil	5.62	Nil	Nil
23	Nil	4.96	Nil	5.66	Nil	Nil
24	0.011	5.55	Nil	4.99	Nil	Nil
25	Nil	5.82	Nil	4.53	Nil	Nil
26	0.020	5.87	Nil	4.57	Nil	Nil
27	0.033	4.77	Nil	5.12	Nil	Nil
28	0.021	4.98	Nil	5.76	Nil	Nil
29	0.011	5.22	Nil	5.33	Nil	Nil
30	0.023	5.33	Nil	5,21	Nil	Nil

Table 3 : Comparison between AD patients and healthy control in Concentration of Heavy metals

Group	Mean ± SE (PPM)					
	Aluminum	Zinc	Mercury	Iron	Cadmium	Lead
Patients	3.49 ±0.16	3.47 ±0.20	0.0899 ±0.005	3.75 ±0.16	0.0557 ±0.003	0.0271 ±0.0015
Control	0.0099 ±0.001	4.86 ±0.14	0.00 ±0.00	4.72 ±0.15	0.00 ±0.00	0.00 ±0.00
T-Test	0.3843 **	0.5350 **	0.0130 **	0.4654 **	0.0068 **	0.0037 **
P-value	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
** (P≤0.01).						

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In the tables above, the highest value of lead (0.051 ppm) and the lowest value (0.011 ppm) were recorded in AD patients. A statistical analysis of these values was carried out where it was found that the mean value of lead levels (0.0271 ±0.0015 ppm) While no concentration of lead was recorded in the healthy controls. In AD patients, the highest value recorded for cadmium concentration in the blood was (0.093 ppm) and the lowest value (0.025 ppm), while the mean values of cadmium concentration in the blood of AD patients (0.0557 ±0.003 ppm) compared to healthy controls that did not record any cadmium concentration. Of the heavy metals whose concentration was measured in this study is mercury, as it was found that the highest value of mercury concentration in the blood of AD patients (0.157 ppm) and the lowest value (0.011 ppm) . A statistical analysis of these values was carried out, and it was found that the mean values for the level of mercury concentration in AD patients (0.0899 ±0.005 ppm), while it did not record any concentration of mercury in healthy controls. In the case of the total iron content in the blood, the highest value was recorded in AD patients (5.771 ppm) and the lowest value (2.003 ppm), while were recorded (5.78 ppm) and (2.44 ppm) as a higher and lowest values, respectively in healthy controls. We note the mean values of iron concentration in AD patients (3.75 ±0.16 ppm), as they were statistically less than the mean values in healthy controls (4.72 ±0.15 ppm). Zinc concentration was explained in the blood of AD patients and healthy controls, where the highest value of zinc concentration was recorded in patients (6.11 ppm) and the lowest value (1.13 ppm), while the highest value was recorded in healthy controls (6.10 ppm) and the lowest value (3.44 ppm). The mean values of zinc concentration in AD patients (3.47 ±0.20 ppm) statistically less compared to healthy controls (4.86 ±0.14 ppm). It was observed that the highest and lowest value of Aluminum concentrations in the patients' blood serum (4.99 ppm) and (1.22 ppm) , respectively, but the highest value (0.033 ppm) and lowest (0.001 ppm) had been in healthy controls. The mean values of aluminum concentration in patients (3.49 ±0.16 ppm) were statistically higher than mean values for Al concentration in healthy controls (0.0099 ±0.001ppm), The results of the statistical analysis of all minerals showed high significant differences ($P \leq 0.01$).

DISCUSSION

In this study, the risk of heavy metals (Pb, Cd, Hg, Fe, Zn and Al) contamination was estimated by measuring the concentrations of their in the blood of AD patients, and these were compared

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with health controls. Through the results, it was found that the lead values exceeded the values of the limits (0.01 ppm) suggested by the WHO[11], as the statistical analysis of these values showed differences of high statistical significance. These results were consistent with those of several study [12]. Lead is well known to cause Alzheimer's disease [13].Humans are constantly exposed to lead from natural sources as well as humanity, for example. Drinking water, soil, industrial emissions, automobile exhaust, polluted food and beverages. Higher concentrations of lead in air may occur in working environment, for example mining, storage battery plants, etc. Several other studies have shown a relationship between socioeconomic status and Pb levels [14]. The results of the cadmium concentration in the patients showed high values that exceeded the limits values (0 – 0.003 ppm) suggested by the WHO [11], as the statistical analysis showed differences of high statistical significance. These results are consistent with the studies that have found levels of cadmium in the blood were significantly associated with AD-related mortality among older adults [15]. There is a pronounced influence on blood cadmium concentration from the inhalation of tobacco smoke. Among non-smokers, a slight increase with age in the blood cadmium concentration can usually be seen [16]. The values of mercury concentration were high in the patients' blood, that exceeded the limits values (0.01 ppm) suggested by the WHO [17], as the statistical analysis showed values of high statistical significance compared to healthy controls that did not record any concentration. These results are consistent with studies that have showed an almost twice as significant increase in plasma and blood Hg levels in AD patients when compared to the respective values from age matched controls [18]. Potential sources of mercury in AD patients may arise from the presence of dental amalgam restorations, the diet (fish and seafood) and the environment. The findings from epidemiological and demographical studies, the frequency of amalgam application in industrialized countries, clinical studies and the dental state of Alzheimer patients in comparison to controls suggest a decisive role for inorganic mercury in the etiology of Alzheimer's disease [19]. It was also found that the total iron content in Alzheimer's patients was different from the acceptable values for total iron according to the WHO [17], where the values showed differences of high statistical significance compared to healthy controls. These results are consistent with the study in which the meta-analysis revealed that there is a significant decreased level of iron in the serum of AD individuals as compared to healthy controls [20]. In this study, high differences were observed in the zinc content according to limit values (0.8 – 1.5 ppm) proposed by the WHO [11], and the values showed high statistically significant differences. This study agreed with the decreasing in AD patients with

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several studies, which their results indicated that AD patients overall had lower levels of zinc than healthy controls [21]. The high heterogeneity found among the studies is mostly explained on the basis of the method used for zinc measurements, zinc supplement intake, and the age of the control individuals [22].It was noticed that the concentrations of Aluminum in blood serum of patients were exceed the limit value (0.001 – 0.003 ppm) which was suggested by ATSDR [23], as there were highly statistically significant differences. The results of this study are consistent with many of the studies that have reported a higher incidence of AD or AD mortality in areas with high levels of aluminum in the drinking water [24].The high concentration of aluminum in patients is attributed to several reasons, including that Aluminum is a versatile metal , e.g. in packing and building materials, paint pigments, cosmetics and cooking utensils. By far the most important contribution to aluminum intake comes from antacid medications that can provide several grams of the metal per day [25].

CONCLUSION

Due to the use of products that contain heavy metals, exposure to these minerals is increasing and it has become a serious danger to the nervous system, as neurotoxic activities resulting from mineral imbalance are associated with reduced enzymatic activities, increased protein accumulation and oxidative stress, which in turn lead to cell death and many degenerative diseases, including In it Alzheimer's disease. The environmental component of Alzheimer's disease is also related to living conditions in industrial areas, where the prevalence of Alzheimer's disease and cases of infection increase in populations exposed to high concentrations of heavy metals compared to those exposed to low levels.

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Conflict of Interest – Non.

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