

Study Plasma Homocysteine Level in Alzheimer's Disease Andits Relationship with the Folic Acid and Vitamin B12 in Alshamaiah Baghdad Hospital

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Abstract: Objectives: To investigate homocysteine levels in Alzheimer's disease and its relationship with folic acid and Vit-B12. Methods: This investigation was performed as a case control study for two groups as 40 Alzheimer patients and 25 non- Alzheimer patients for one group in Baghdad, Iraq from May 2013 to April 2015. Alzheimer patients were selected based on the criteria of the American Psychological Association. Mental status of the patients was evaluated by Mini Mental State Examination (MMSE). The plasma levels of homocysteine were measured by HPLC method at UV detector 338nm the folic acid and B12 was measured by enzyme-linked immunosorbent assay method. Results: The average plasma homocysteine level in the 40 patient group in group 1 was $24.01 \pm 9.21 \mu\text{mol/L}$, and in the 25 control group was 10.31 ± 4.25 ($p=0.003$). The average plasma homocysteine level in the group 2 of patients was $27.34 \pm 10.52 \mu\text{mol/L}$, in the control group $10.36 \pm 4.01 \mu\text{mol/L}$, ($p=0.438$). Conclusion: The average plasma homocysteine level in Alzheimer patients was higher than in the control group; however, it shows a significant relationship with the folic acid and B12.

Keywords: Homocysteine, Alzheimer's disease, Iraq

1. Introduction

Alzheimer's disease (AD) is the most common and important degenerative disease of the brain, and is also the most common cause of dementia. Earlier symptoms are impairment of near memory, and awareness of time and place. In the advanced stage of the disease one could point to psychosis, paranoia, and delirium (1). One of the probable mechanisms of Alzheimer is vascular disorders, and for this reason the risk factors of vascular disorders increase the appearance and development of AD (2,3). So, the relationship and some studies have been carried out in this area (4,7).

Homocysteine (Hcy) is an intermediate formed during the catabolism of essential sulphur containing amino acid methionine (9,10,11). Increased Hcy is associated with endothelial dysfunctions in healthy human. (It is found either as free homocysteine, cysteine-homocysteine mixed disulfide or protein bound homocysteine. The one that is bound with protein in plasma reflects total plasma homocysteine (tHcy) (8). Gender, age and circulating levels of folate and B12 effect plasma tHcy level and also by oestrogen status possibly (12). Elevated concentration of homocysteine (Hcy) in human tissues, defined as hyperhomocysteinemia has been correlated with some diseases (13).

Unbalanced diet, leading to significant deficiency of vitamins B2, B6, B12 and folic acid may cause an increase in plasma Hcy concentration. Additionally, alcohol, tobacco smoking and coffee also lead to increased plasma Hcy level. Also alimentary tract disorders connected with impaired absorption of vitamins B2, B6, B12 and folic acid may play an important role. In some countries, e.g. in the U.S.A., supplementation of food with folic acid is a common

occurrence. In Poland, however, the food is not supplemented with folic acid and therefore the levels of total plasma homocysteine should be decreased (14). Plasma homocysteine level depends among other things on sex, age, smoking, function of the liver and kidneys, physical activity and diet, and optimal physical activity may influence the level of this amino acid. There are also various compounds which lead to the reduction of Hcy levels. Folic acid, vitamins B6 and B12 should be mentioned, because some pathways of Hcy metabolism are correlated with the level of these vitamins and antioxidant. Due to its antioxidant action, significantly attenuated the oxidative stress Fig(1) (15).

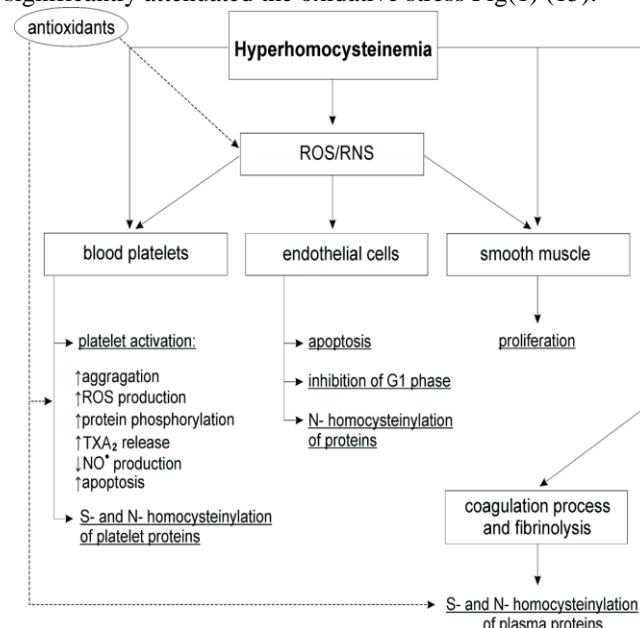


Figure 2: Proposed model for the protective role of phenolic antioxidants on selected elements of hemostasis during hyperhomocysteinemia.(16)

The basics of Homocysteine:

- Byproduct of protein metabolism• Metabolized/detoxified in the liver
- Risk factor for cardiovascular disease• Necessary nutrients include B-12, folate, B-6, di or trimethylglycine
- Normal values Homocysteine in human body:
- Male: 6.3-15.0 $\mu\text{mol/L}$ • female: 4.6-12.4 $\mu\text{mol/L}$
- Comment – optimal levels are generally considered to be $< 9 \mu\text{mol/L}$ with some calling for $< 7 \mu\text{mol/L}$.
- Hyperhomocysteinemia can be categorized clinically as:
- Moderate: upper limit of normal to 30 $\mu\text{mol/L}$ • Intermediate: $>30-100 \mu\text{mol/L}$
- Severe: $>100 \mu\text{mol/L}$ (17,18,19).

The aim of this study

Is assessing the Plasma homocysteine level in Alzheimer's disease , and comparing it with a control group, and also determining the relationship of homocysteine level with biochemical markers as Folic acid and Hb.

2. Materials and Methods

Eighty patient and 50 control healthy human categories for two groups depended to period age (60-74)year and (75-93)yearForty patients with Alzheimer's disease and 25 healthy people.As were studied in Alshamaeahhospital-Baghdad , Iraq, from May2013 to April 2015.This study was performed with patients consent and approved by the Ethics Committee all patients and control samples carried out in College of Medicine Al-Nahran UniversityLaboratories. The diagnosis of Alzheimer's disease was based on the diagnostic criteria of American Psychological Association(20).

Blood collection and assessment of biomarkers: Measurements of plasma tHcy, folate, vitamin B12 have been described previously (21). In brief, tHcy was determined by HPLC; by used UV detector at 338nm assay; and folate and B12 were measured by an ultrasensitive ELISA assay (R&D Systems, Minneapolis, MN), with CVs of 10.3%, 6.1%, and 4.1%, respectively (22).

3. Results

The mean age in group 1 patients was 72.1 ± 7.9 and control group 1 was 70.8 ± 7.7 . There were males and females in the case and control groups. Both groups were equal regarding age and gender, and similar risk factors(Table 1).The number of patients according to global deterioration scale is shown in Figure 1. The average level of plasma homocysteine in patients was $24.01 \pm 9.21 \mu\text{mol/l}$,and in the control group 1 was $10.31 \pm 4.25 \mu\text{mol/lit}$. The difference of plasma homocysteine level in patients and control group was significant ($p=0.001$). The average plasma homocysteine level of patients group 2 was $27.34 \pm 10.52 \mu\text{mol/lit}$ in the control group 2 was $10.36 \pm 4.01 \mu\text{mol/l}$ The difference of plasma homocysteine level in patients and control group 2 was significant ($p=0.438$).There was a significant For estimating the homocysteine cut point. The average level of serum Folicacid in patients was $6.58 \pm 2.00 \text{ ng/ml}$,and in the control group 1 was $8.87 \pm 3.88 \text{ ng/ml}$. The difference of

serum Folic acid level in patients and control group 1was significant ($p=0.39$). The average serum Folic acid level of patients group 2 was $7.03 \pm 2.96 \text{ ng/ml}$ in the control group 2 was $10.91 \pm 4.55 \text{ ng/ml}$ The difference of plasma homocysteine level in patients and control group 2 was significant ($p=0.511$).There was a significant For estimating the Folic acid.The average level of serum B12 in patients was $200 \pm 69 \text{ pmol/l}$,and in the control group 1 was $236 \pm 76 \text{ pmol/l}$. The difference of serumB12 level in patients and control group1 was nosignificant ($p=0.11$). The average serum B12 level of patients group 2 was $7.0 \pm 2.96 \text{ pmol/l}$ in the control group 2 was $10.36 \pm 4.01 \text{ pmol/l}$ The difference of serum B12 level in patients and control group 2 was significant ($p=0.094$).There was a significant For estimating the B12.All results showed in Table 1, Fig 2 and Table 2, Fig 3

Table 1: Comparison of all measured parameters between control andAlzheimer's Patient group1(Data presented as Mean \pm SD).Based on age(60-74)year.

Parameters	Controls Mean \pm SD N=25	Patient Mean \pm SD N=40	P value
Homocystiene $\mu\text{mol/L}$	10.31 \pm 4.25	24.01 \pm 9.21	0.001
Folic acid ng/ml	8.87 \pm 3.88	6.58 \pm 2.00	0.39
B12 pmol/L	236 \pm 76	200 \pm 69	0.11

Table 2: Comparison of all measured parameters between control and Alzheimer's Patient group 1(Data presented as Mean \pm SD).Based on age (75-93)year.

Parameters	Controls Mean \pm SD N=25	Patient Mean \pm SD N=40	P value
Homocystiene $\mu\text{mol/L}$	10.36 \pm 4.01	27.34 \pm 10.52	0.438
Folic acid ng/ml	10.91 \pm 4.55	7.03 \pm 2.96	0.511
B12 pmol/L	206 \pm 58	189 \pm 49	0.094

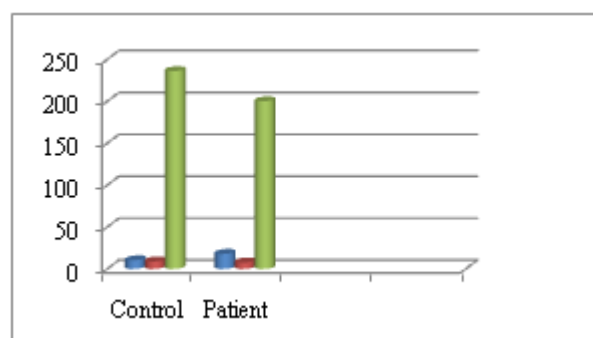


Figure 2: parameters in control and Alzheimer's Patient group1

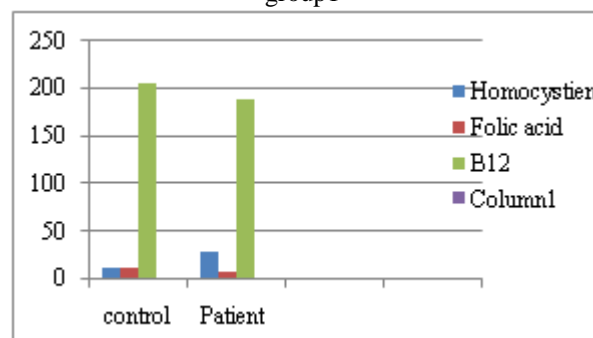


Figure 3: Parameters in control and Alzheimer's Patient group2

4. Discussion

Any interference for decreasing the risk of disease or to delay the beginning of the disease, has a very important influence on the costs of health care. One factor that has a supportive role for Alzheimer disease is nutrition. In this area, the relationship of the serum concentration of vitamins B12, folic acid, and homocysteine with Alzheimer disease has been shown in various studies.¹⁰ In a study carried out by Seshadri (23) 1092 non-dementia persons (667 females and 425 males with an average age of 65) were followed for 8 years, and 111 individuals were affected ultimately by dementia, with 85 having Alzheimer disease. They concluded that with a plasma homocysteine level higher than 14 mmol/l, the risk of Alzheimer disease would be approximately 2 times higher. Therefore, homocysteine was considered as a strong and independent risk factor for dementia, and Alzheimer disease. Ravaglia et al (24) concluded in their study that higher concentration of total plasma homocysteine, and lower concentration of serum folate are independent predicting factors for developing dementia and Alzheimer disease. It was shown by Gallucci et al's (25), study, that serum homocysteine level had a distinct increase in Alzheimer disease in comparison with the control group. It also showed that plasma homocysteine level in Alzheimer's patients had a distinct increase in comparison with the control group Selley (26). Against that, there is a considerable decrease in plasma adenosine concentration in Alzheimer's. This is in disagreement with other studies,^{8,11,12} which did not find a relationship between homocysteine level and Alzheimer disease. In summary, most studies showed that hyperhomocysteinemia is a risk factor for Alzheimer disease in agreement with ours. The probable mechanisms of effect of homocysteine in Alzheimer's include the cytotoxic effect, which results in damage of vascular endothelium, and accelerate the process of thrombosis, prevention of nitric acid function, which is a vasodilator, and decreasing of adenosine level.

In conclusion, this study showed that the serum homocysteine level in Alzheimer disease (AD) was significantly higher in comparison with the control group, however, there is no relationship between plasma homocysteine level and Folic acid and B12. We suggest that this study should be carried out on a large number of blood samples taken from AD patients, especially with severe disease.

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