Homocysteine Levels in Acute Ischemic Stroke Patients

Akut İskemik İnmeli Hastalarda Homosistein Düzeyleri

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Abstract

Objective: The aim is to investigate the relationship between plasma homocysteine levels and acute ischemic stroke in Turkish patients.
Materials and Methods: Our study included 41 patients with acute ischemic stroke and 20 controls. All patients were examined within 24 h after symptom onset. Stroke was defined as acute onset of focal neurological deficits and then confirmed by computed tomography findings. Homocysteine was measured on admission.
Results: The mean homocysteine levels in patients with ischemic stroke and controls were 22.92±17.49 micromol/L and 11.18±4.68 micromol/L, respectively, the difference being statistically significant (p<0.02).
Conclusion: The results of the present study showed that Hcy levels were significantly higher in patients admitted with acute ischemic stroke. Therefore, we consider that high plasma Hcy levels should be further evaluated as a risk factor. *(JAEM 2010; 9: 169-71)*
Key words: Homocysteine, ischemic stroke, risk factor

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Özet

Amaç: Amaç Türk toplumunda akut iskemik inme ve plazma homosistein düzeyleri arasındaki ilişkiyi araştırmaktır.
Gereç ve Yöntemler: Çalışmaya 41 akut iskemik inmeli hasta ve 20 kişilik kontrol grubu alındı. Semptomlar başladıktan sonraki 24 saat içinde tüm hastalar muayene edildi. İnme fokal nörolojik defisitlerin akut başlaması olarak tanımlandı ve sonra bilgisayarlı tomografi bulgularıyla teyit edildi. Homosistein düzeyi başvuru esnasında ölçüldü.
Bulgular: Akut iskemik inmeli hastalarda ve kontrol grubunda sırasıyla Ortalama homosistein düzeyleri 22.92±17.49 micromol/L and 11.18±4.68 micromol/L idi ve istatistiksel olarak farklıydı (p<0.02).
Sonuç: Bu çalışmanın sonuçları homosistein düzeylerinin akut iskemik inme ile başvuran hastalarda anlamlı olarak daha yüksek olduğunu göstermektedir. Bu yüzden yüksek plazma homosistein düzeylerinin risk faktörü olarak araştırılması gerektiğini düşünmekteyiz. *(JAEM 2010; 9: 169-71)*
Anahtar kelimeler: Homosistein, iskemik inme, risk faktörü

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Introduction

Stroke is a leading cause of mortality and has a subsequent serious long-term disability among survivors. In the elderly, ischemic stroke accounts for more than 80% of all stroke cases and atherosclerosis is a major risk factor (1). Recently, homocysteine (Hcy) has been recognized as a risk factor for atherosclerosis (2).

Hcy is a sulfhydryl amino acid, structurally similar to cysteine, with an additional methylene group. The normal Hcy level in blood plasma is 5-12 mmol/L. Hcy exists in the blood predominantly in a protein bound form (70-80%), a reduced form (5%), and an oxidized form. Hyperhomocysteinemia (hhcy) leads to a wide variety of human diseases, ranging from mental retardation to renal diseases. The vitamin B6-dependent cysthathionine b Synthase (CBS) gene is involved in the breakdown of hcy in the mammalian system. Hhyc originates from a deviation in the methionine-hcy metabolism including disturbances of enzymes, vitamin deficiencies and various other factors. Observational studies, genetic polymorphism studies and several meta-analyses already implicate a causal relation between homocysteine and cerebrovascular diseases (3). Elevated total Hcy is reported to be associated with a higher risk of cerebrovascular disease (4-8).

The purpose of this study was to examine the relationship between plasma Hcy levels and ischemic stroke (IS) in Turkish population.

Material and Methods

Included in this study were consecutive patients with acute IS, within 24 h of stroke onset. Stroke was defined as acute onset of focal neurological deficits combined with relevant CT findings. Inclusion criteria were: presence of acute IS, no prior history of IS, hospitalization for more than 24 h after the appearance of neurological symptoms and CT confirmed diagnosis of IS. Patients with hemorrhagic stroke or transient ischemic attack and patients with subacute or chronic IS were excluded. Age and gender matched controls were included for comparison. Hcy was measured by HPLC (Agilent 1100

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Series, Agilent, Germany) with fluorescence detection using a commercial kit (Immundiagnostik, Germany). The reference intervals were 5-12 µmol/L for hcy.

Statistics

The software package SPSS 15.0 was used for statistical evaluation, and a probability value of less than 0.05 was accepted as statistically significant. As the data were normally distributed and independent, groups were compared using Student's t-test. The results are given as the mean±standard deviation (SD).

Results

A total of 41 patients and 20 healthy controls were included in this study. The mean age of the patients and the control group were 71.05±13.92 and 56.35±17.61 years respectively. There was a significant difference between the plasma hcy levels of the patients (22.92±17.49 micromol/L) and those of the healthy controls (11.18±4.68 micromol/L) (p<0.002) (Figure 1). Table 1 shows the concentrations of plasma Hcy for both groups. In this study, 56.4% of the patients were male and 43.6% were female. History of patients included hypertension in 41.1%; diabetes mellitus in 14.6%; coronary artery disease in 17.1% and hyperlipidemia in 9.8%.

Discussion

In our study, Hcy concentrations in stroke patients were significantly higher than healthy individuals. Hhyc can cause vascular injury and atherosclerotic plaque instability. Elevated plasma Hcy may be a causal and modifiable risk factor for ischemic stroke, but the results of previous studies have been conflicting. The relationship between high plasma Hcy levels and stroke outcome remains controversial, as some studies have found an association while others have not (1, 7, 9-11). This conflict of results could be due to underlying genetic polymorphisms in different ethnicities. The aim of our study was to evaluate the significance of serum Hcy levels in Turkish patients diagnosed with acute ischemic stroke. Our study supports the fact that raised Hcy levels are seen in patients with acute IS.

Stroke is the third leading cause of death and disability in adults even in industrialized countries. Early detection and control of risk factors is thought to be crucial in reducing the risk of stroke and providing effective care (1). Stroke is a heterogeneous, multifactorial disease regulated by modifiable and nonmodifiable risk factors. Modifiable factors include a history of high blood pressure, diabetes mellitus and coronary heart disease. Nonmodifiable factors include age, sex and race. Other less well documented risk factors include geographic location, socioeconomic status and alcoholism (12). However, it has become increasingly apparent that apart from the traditional risk factors associated with stroke, there are several newly studied independent modifiable risk factors, such as Hhcy (13, 14).

Mc Cully first reported the association of Hhcy and vascular wall changes. Hcy has been shown to be responsible for both arterial changes and damage; moreover, extensive research has proved that Hhcy is an independent risk factor for cardiovascular, neurovascular and renal diseases. Hhcy has also been causally associated with stroke, a disease of the blood vessels in the brain that typically results in a reduction or disruption of blood flow to the brain. The physiological parameters used to describe cerebrovacular physiology include the permeability of the blood brain barrier, cerebral blood flow, and blood pressure. Hhcy has been reported to increase vascular resistance, vascular injury and remodeling in animals; this is the basis for Hhcy acting as a risk factor for coronary, cerebral, and peripheral arterial occlusive disease (6).

Table 1. Homocysteine levels (mean±SD)

	Homocysteine (micromol/L)
Group 1 (stroke patients)	22.92±17.49
Group 2 (control)	11.18±4.68
Group 1 and 2 p<0.02	

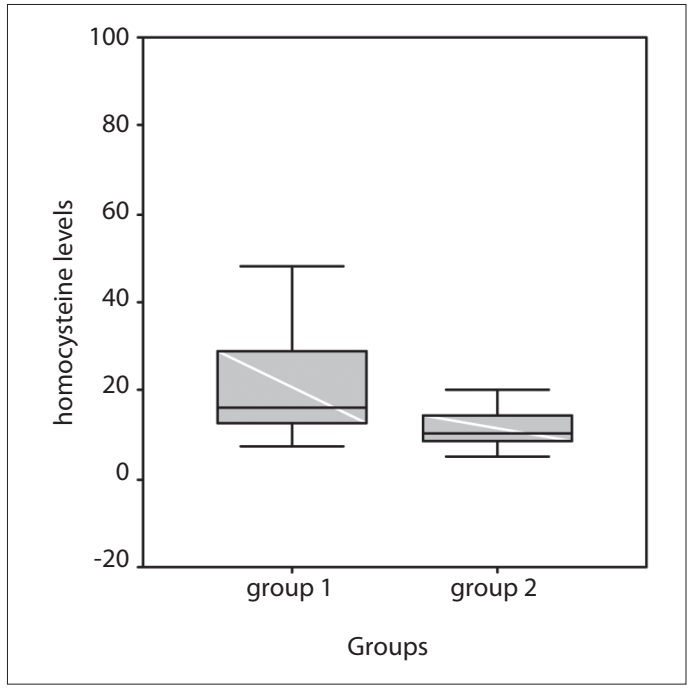

Figure 1. Diagram showing the results of homocysteine levels in groups 1 and 2

Hcy is an intermediate for the conversion of methionine to cysteine. It is metabolized through vitamin B6, folic acid and vitamin B12 dependent pathways. Hhcy can be seen with enzymatic defects (cystathionine beta-synthase, methylentetrahydrofolate reductase, methionine synthase) or vitamin deficiencies (vitamin B12, vitamin B6, folate) in one or more of the Hcy metabolising pathways (14). Hhcy is generally regarded as a treatable risk factor for atherothrombotic disease. Observational studies, genetic polymorphism studies and several meta-analyses implicate a causal relation between Hcy and cerebrovascular diseases in certain populations. It is useful to determine Hcy levels in acute stroke when no other risk factor is present, or in young patients who have a family history of premature atherosclerosis. Because of the low cost and safety of the therapy, the American Heart and Stroke Association advises physicians to treat patients with a stroke and Hhcy with 0,4 mg folic acid, 2,4 microg vitamin B12 and 1,7 mg vitamin B6 daily. However, a significant benefit in secondary prevention is not yet proven (3). Also, several studies have reported important benefits in reduction of the stroke risk and improvement in the post-stroke-associated functional deficits in patients who consume foods rich in micronutrients, including B vitamins and antioxidant vitamins E and C. Higher consumption of fruits and vegetables appears to protect against stroke (15).

Conclusion

In conclusion, our findings suggest that elevated Hcy concentrations may be a sign of increased risk of IS in the Turkish population. We consider that the prevention of Hhcy may reduce the incidence of IS, therefore evaluation of Hhcy as a risk factor should further be studied in the Turkish population.

Conflict of Interest

No conflict of interest is declared by the authors.

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