Serum Adinopektin Düzeylerinin İskemik İnmedeki Rolü

The Role of Serum Adiponectin Levels on Ischemic Stroke

Dilcan Kotan[1], Yalçın Yılıkoglu[2], Ahmet Kızıltunç[3], Hızır Ulvi[2], Recep Aygül[2], Vefa Yanmaz[3]

[1] Sakarya University Medical Faculty, Neurology Department, Sakarya

[2] Ataturk University Medical Faculty, Neurology Department, Erzurum

[3] Ataturk University Medical Faculty, Biochemistry Department, Erzurum

Özet

Amaç: Ateroskleroz, iskemik inmede majör risk faktörlerindendir. Yağ dokudan üretilen, aterosklerozu gerileten adiponektinin; obezite, hipertansiyon, diyabet, hiperlipidemi gibi ateroskleroz risk faktörlerinin varlığında serum düzeylerinin azaldığı ortaya konulmuştur. Bu çalışmada, iskemik inmeli hastalarda serum adiponektin ve şuur düzeyleri ile olan ilgisini incelemeyi amaçladık.

Gereç ve Yöntem: Çalışmaya inme sonrası ilk 24 saati içerisinde başvuran, 45 yaş üstü akut iskemik inmeli 17 hasta alındı ve benzer yaştaki 22 sağlıklı kontrol grubu ile karşılaştırıldı. Hastaların ilk 24-48. saatlerinde alınan serum örneklerinde adiponektin düzeyleri ölçüldü ve bilinç düzeyleri Glaskow koma skoru ile değerlendirildi.

Sonuçlar: Sağlıklı olgularda adiponektin düzeyleri 17.16 ± 0.9 microg/mL iken iskemik inme grubunda 8.80 ± 0.7 microg/mL tespit edildi ve aralarındaki fark istatistiksel olarak anlamlı idi ($p<0.001$). İnmeli hastaların şuur düzeyleri ile adiponektin düzeyleri arasında ise istatistiksel olarak anlamlı bir ilişki saptanmadı ($p<0.1$).

Tartışma: İskemik inme varlığında adiponektin düzeyleri anlamlı olarak azalmaktadır. Düşük adiponektin düzeylerinin arttırılmasına yönelik çabalar, iskemik inmenin tedavi hedeflerinden biri olabilir.

Anahtar Kelimeler: İskemik inme, ateroskleroz ve adiponektin

Başvuru Tarihi: 04.07.2011 **Kabul Tarihi:** 05.09.2011

Abstract

Purpose: Atherosclerosis is among the major factors in ischemic stroke. It has been set forth that serum levels decline of adiponectin, which is produced from adipose tissue and downgrades atherosclerosis, in the presence of atherosclerosis risk factors such as obesity, HT, DM, and hyperlipidaemia. In this study, we aimed at examining the relation between levels of the serum adiponectin and consciousness in patients with ischemic stroke.

Method: 17 patients with acute ischemic stroke, who applied within the 24 hours after stroke and who are above the age of 45, were involved in the study and compared to the 22 healthy control group of similar age. The levels of adiponectin were measured in the serum samples of the patients taken within the first 24-48th hours of the patients and their levels of consciousness were evaluated with Glasgow coma score.

Results: While adiponectin levels are 17.16 ± 0.9 microg/mL in healthy cases, 8.80 ± 0.7 microg/mL has been found in ischemic stroke group and the difference between them was statistically significant ($p<0.001$). No statistically significant relation between consciousness and adiponectin levels of the patients with stroke were found ($p<0.1$).

Conclusion: The levels of adiponectin significantly declines in the presence of ischemic stroke. Efforts aimed at raising low levels of adiponectin can be one of the treatment objectives of ischemic stroke.

Keywords: Ischemic stroke, atherosclerosis, and adiponectin

Aplication: 04.07.2011 **Accepted:** 05.09.2011

Yazışma Adresi/Corresponding to: Dr. Dilcan Kotan, Sakarya University Medical Faculty, Neurology Department,Sakarya
Tel: 02642751010, e-mail: dkotan@sakarya.edu.tr

Introduction:

The stroke expresses a focal, sudden localized neurologic syndrome developing in parallel to cerebrovascular disease. World Health Organization defines stroke as "findings depending on the focal or global disorder of cerebral functions and developing rapidly, lasting 24 hours or more, or that may result in death"[1]. 80-85% of stroke cases are ischemical, whereas 15-20% are hemorrhagical[2]. Acute stroke is the third most frequent cause of death after cardiac diseases and cancer, and it is among the frequent causes of morbidity and mortality in Turkey and worldwide. Stroke is the most important cause of morbidity and long term disability. In Turkey, 40.6% of all deaths result from cardiac diseases, whereas 6.8% of them result from cerebrovascular diseases. With this rate, cerebrovascular diseases are the third most frequent cause of death in Turkey[3]. Every year, 700.000 new stroke cases develop in the USA and 20% of these patients die within the same year[4].

Various risk factors such as HT, smoking, obesity, DM, high LDL cholesterol level have been described for stroke until today. However, it has been found that none of these factors were present in approximately 23% of the patients that have had a stroke attack. And this implies that currently used risk classifications are insufficient and some other factors also take part in stroke. With a multifactorial approach, protection against all of these risks has caused an explicit decline in ischemic stroke incidence[5,6]. For this reason, proper determination of the risk factors that cause ischemic stroke and taking of the required measures are considerably important in terms of the prevention of the damages that they may cause. However, possible risk factors that may be the cause of stroke must also be explored.

Adiponectin is a recently discovered adipocytokine, also referred to as gelatin-binding protein-28[7]. Adiponectin is a plasma protein with anti-atherosclerotic properties, secreted from the adipose tissue. It indicates anti-atherosclerotic property by blocking the effects of inflammation mediators that cause atherogenesis by cumulating on damaged blood vessel wall[8]. Adiponectin is a protein with anti-inflammatory and anti-atherogenic properties[9]. Inflammatory processes play a fundamental role in atherosclerotic cerebrovascular disease and stroke, which is the second leading cause of death worldwide and a major cause of long-term disability[10]. It is speculated that low adiponectin levels are related to the increase in infarct risk independently from other risk factors. Testing these hypotheses is a challenge for future clinical research. In this study of ours, we aimed at examining the relation between the adiponectin levels and acute ischemic stroke and its impact on consciousness.

Matreıals and Methods:

In total, 17 patients above the age of 45 with acute ischemic stroke, 11 of which were male (64.7%) and 6 of which were female (35.3%), that applied to the emergency service within the first 24 hours of the stroke were involved in the study and compared to the 22 healthy control group of the same age group, 13 of which were male (59%) and 9 of which were female (41%). Ages of the stroke group varied between 50-83 (average: 67.8; standard deviation: (6.83), whereas age range varied between 48-73 in the control group (average: 63.3; standard deviation:[7.17].

Approval was obtained from the local ethics committee for the study. After the participants were provided with the information regarding the study, their verbal and written permission were taken. Demographic properties of the cases were recorded. Anamnesis was taken and physical examination was performed. Temporary ischemic attacks and hemorrhagic strokes were excluded in the study.

Blood samples taken from the patients with stroke within the first 24-48th hours of their hospitalization were centrifuged and the serum obtained was kept at-20 °C until the day of the study. On the day of study, adiponectin levels were measured by using ELISA kit (BioVendor Research and Diagnostic Product, Czech Republic) and compared to the healthy control group. Consciousness levels of the patients were evaluated via Glasgow coma score. The results were examined under SPSS statistics

program with Mann-Witney U-test. P<0.05 values were considered significant.

Results

In total, 39 patients were involved in this study, organized in case-control type. Anamnesis of the 17 patients with known acute cerebral ischemia and 22 healthy individuals were taken, their physical examinations were performed, and systolic-diastolic blood pressures, glucose, HbA1c, triglyceride, total cholesterol, HDL, LDL, and adiponectin levels were checked.

Average serum adiponectin levels in the group with ischemic stroke were 8.80 ± 0.7 microg/mL, whereas 17.16 ± 0.9 microg/mL in the control group. A statistically significant relation was found between the serum adiponectin levels of the patients with stroke (p<0.001) in comparison to the control group.

Table 1: Demographic data

	Control (n=22)	Stroke group (n=17)
Age (years)	48-73 (av.: 63.3)	50-83 (av.: 67.8)
Male	13 (%59)	11 (%64.7)
Female	9 (%41)	6 (%35.3)

Level of consciousness was evaluated as open in 4 (23.5%) patients, somnolence in 6 (35.2%) patients, stupor in 4 (23.5%) patients, and coma in 3 (17.6%) patients. No statistically significant relation was found between the consciousness levels and adiponectin levels of the patients with stroke (p<0.1). No statistically significant relation was found between adiponectin level and sex, systolic-diastolic blood pressure, DM history, stroke history in the family, regular exercise history, drug utilization history, HbA1c level, HDL-LDL cholesterol level (p<0.5).

Discussion:

Atherosclerosis has an important place in the development in ischemic stroke. Atherosclerosis emerges due to genetic and environmental factors. With the prevention of the environmental risk factors and the development of the factors known to possibly cause atherosclerosis, the rate of ischemic stroke in parallel to atherosclerosis would decline. HT, DM, hyperlipidaemia, and smoking are the known risk factors for atherosclerosis and there has been a decline in atherothrombotic strokes by the measures taken against these factors[11]. However, in order to struggle with atherosclerosis, the risk factors that have not yet become definite must be studied and clarified.

Table 2: Data of control and stroke groups

	Control group (n=22)	Stroke group (n=17)
Systolic blood pressure (mm Hg)	135±25	170±30
Diastolic blood pressure (mm Hg)	75.3±9.8	87.0±9.2
Glucose (mg/dL)	89.0±15.0	115.0±13.0
HbA1c	4.3±2.1	4.7±1.9
TG (mg/dL)	178.0±51.0	201.0±69.0
TChol (mg/dL)	184.0±45.0	238.0±38.0
HDL (mg/dL)	49.0±8.0	47.0±11.0
LDL (mg/dL)	126.0±29.0	129.0±24.0
Adiponectin (µg/mL)	17.16 ± 0.9	8.80 ± 0.7

Adiponectin is an adipocytokine synthesized from the adipose tissue. Serum adiponectin level in human beings is between 10-30 µg/ml. In clinical and experimental studies, it has been set forth that plasma adiponectin level is negatively correlated with age, body mass index, total cholesterol, triglyceride, and fasting glucose; positively correlated with HDL cholesterol; and the level of serum adiponectin is low at older ages, in male sex, obeses, type 2 DM, and cardiovascular disease[12].

Although the physical role of adiponectin has not yet been precisely set forth, it has been found that it has anti-atherogenic and anti-inflammatory effects in particularly endothelial cells and macrophages. Due to these properties, adiponectin plays a protective role in early period atherosclerosis[13].

It has been indicated that adiponectin cumulates on atherosclerotic blood vessel wall in parallel to dose and inhibits inflammatory cell migration induced by tumor necrosis factor alpha (TNF-alfa)[14]. We have found that serum adiponectin level is lower than control in the individuals with ischemic stroke. Decline in serum adiponectin level may be dependent on probably present athesclerotic lesion. In some publications, it has been stated that men have a two or three times lower serum adiponectin level than women[15]. In our study group, adiponectin levels in the two sexes did not indicate a statistically significant difference.

Adiponectin has anti-diabetic, anti-inflammatory, anti-atherogenic properties. Adiponectin has taken its place as a promising target in the studies to be carried out on the prevention of atherosclerotic disease. Today, the importance of adiponectin for human organism is not clearly known. Relation has been found between hypoadiponectinemia and body mass index, insulin resistance, type 2 DM, inflammation, endothelial dysfunction in various studies carried out[16]. When the situation is considered in terms of other risk factors effective on ischemic stroke; HT, DM, and high plasma LDL-cholesterol levels are the risk factors, effects of which have become definite[17]. In our study, p values that are considered to be in relation to the variables such as HT, DM, LDL-cholesterol, HDL-cholesterol did not reach the level of significance. However, in this study, a limited number of cases and a control group of similar age were present. There were patients with coronary artery disease and HT within the control group. For this reason, the effects of these risk factors might have been obscured.

Our prestudy results indicating low adiponectin levels have set forth a detectable risk factor for ischemic stroke. We think that the efforts aimed at raising low levels of adiponectin can be effective in the prevention of ischemic stroke.

Kaynaklar

1. Kumral E, Balkır K. Inme epidemiyolojisi. In: Balkan S, editör. Serebrovasküler hastalıklar. 1. baskı, Ankara: Güneş Kitapevi; 2002. pp. 38-40.
2. Lewandowski C, Barsan W. Treatment of acute ischemic stroke. Ann Emerg Med 2001;37:202-16.
3. Onat A., Keleş İ, Çetinkaya A, et al. On Yıllık TEKHARF Çalışması Verilerine Göre Türk Erişkinlerinde Koroner Kökenli Ölüm ve Olayların Prevalansı Yüksek. Türk Kardiyol Dern Arş 2001;29:8-19.
4. American Heart Association. Heart Disease and Stroke Statistics—2006 Update. Dallas, Tex: American Heart Association.
5. Marmot MG, Poulter NR: Primary prevention of stroke. Lancet 1992, 339: 344-347.
6. Zuber M, Mas JL: Epidemiologie des accidents vasculaires cerebraux. Rev Neurol 1992, 148: 245-255.
7. Maeda K, Okubo K, Shimomura I, Funahashi T, Matsuzawa Y &Matsubara K. cDNA cloning and expression of a novel adipose specific collagen-like factor, apM1 (adipose most abundant gene transcript 1). Biochemical and Biophysical Research Communications 1996 221 286–289.
8. Faraj M, Havel PJ, Phelis S,Blank D, Sniderman AD, Cianflone K, plasma acylation – stimulating protein adiponectin , leptin, and ghrelin before and weight loss induced by gastric bypass surgery in morbidly obese subjects.J Clin Endo.Metab. 2003; 88: 1594 – 1602.
9. M. Sasaki, T. Kawano and T. Saito et al., Hypoadiponectinemia in patients with cerebral infarction: comparison with other atherosclerotic disorders, Am J Med Sci 333 (2007), pp. 140–144.
10. Chamorro A. Role of inflammation in stroke and atherothrombosis. Cerebrovasc Dis. 2004; 17 (suppl 3): 1–5.
11. Rosenson RS. Statins in atherosclerosis: lipid-lowering agents with antioxidant capabilities. Atherosclerosis 2004; 173: 1-12.
12. Yang CY. Calcium and magnesium in drinking water and risk of death from cerebrovascular disease. Stroke 1998, 29(2): 411-414.
13. Kappanen H, Pennanen R, Passinen L. Minerals, coronary heart diseae and sudden coronary death. Adv Cardiol 1978, 25:9.
14. Ouchi N, Kihara S, Arita Y, Nishida M, Matsuyama A, Okamoto Y. Adipocyte-derived plasma protein, adiponectin, suppresses

lipid accumulation and class A scavenger receptor expression in human monocyte-derived macrophages. Circulation 2001; 103:1057–1063.

15. Shand BI, Scott RS, Elder PA, George PM. Plasma adiponectin in overweight, nondiabetic individuals with or without insulin resistance. DM Obes Metab 2003; 5:349-353.
16. Homoscysteine and risk of ischemic heart disease and stroke: a meta analyisis. JAMA 2002;288:2015. [PMID:12387654]
17. The Fifth Report of The Joint National Committee on detec¬tion evaluation and treatment of high blood pressure. Arch Intern Med 1993, 153-161.