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The Effect of Trace Elements in the Development of Ascending Aorta Aneurysm

Asendan Aort Anevrizma Gelişiminde Eser Elementlerin Etkisi

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Abstract

Introduction: Ascending aorta aneurysm is a serious condition with an undetermined pathophysiology. Trace elements are essential for the effective performance of the body's multiple systems, including the immune system and relevant information to inflammation and infections. Since inflammation may contribute to the etiology of ascending aortic aneurysm, we investigated whether trace element alterations associated with inflammation occur in blood and tissue samples over the course of the condition.

Materials and Methods: We compared 32 individuals who underwent coronary artery bypass grafting and 23 patients who underwent surgery for an ascending aortic aneurysm. During surgery, samples of the ascending aorta's anterior portion removed from the aortic wall. The tissue's iron (Fe), copper (Cu), and zinc (Zn) levels measured.

Results: There were no statisticaly significant differences between the groups in the Zn averages of the cases divided by groups. Individual Cu mean values of the study group were statistically significantly lower than those of the control group. The mean Fe levels of the participants in the study group identified to be statistically substantially higher than those of the control group.

Conclusion: In this study, we aimed to find out more about the relationship between changes in the levels of trace elements in the tissue of the ascending aorta and aneurysm development. We believe that changes in trace element levels may involve a role in the progression of aortic aneurysms.

Keywords: Ascending aorta aneurysm; inflammation; trace elements; zinc; copper; iron.

Özet

Amaç: Asendan aort anevrizması patofizyolojisi bilinmeyen ciddi bir durumdur. Eser elementler, bağışıklık sistemi, iltihaplanma ve enfeksiyonlarla ilgili bilgiler dahil olmak üzere vücudun çoklu sistemlerinin etkili performansı için gereklidir. İnflamasyon asendan aort anevrizmasının etiyolojisine katkıda bulunabileceğinden, kan ve doku örneklerinde inflamasyonla ilişkili eser element değişikliklerinin oluşup oluşmadığını araştırdık.

Gereç ve Yöntem: Bu çalışmada koroner arter baypas greftlemesi yapılan 32 hasta ile asendan aort anevrizması nedeniyle ameliyat edilen 23 hastayı karşılaştırdık. Asenden aort ön kısmından ameliyat esnasında doku örnekerli aldık. Dokularda demir (Fe), bakır (Cu) ve çinko (Zn) seviyeleri ölçüldü.

Bulgular: Gruplar arasında Zn ortalamalarında istatistiksel olarak anlamlı fark bulunmadı. Çalışma grubunun Cu ortalama değerleri, kontrol grubununkinden istatistiksel olarak anlamlı derecede düşüktü. Çalışma grubundaki katılımcıların ortalama Fe düzeylerinin kontrol grubuna göre istatistiksel olarak önemli ölçüde yüksek olduğu belirlendi.

Sonuç: Bu çalışmada,asendan aort dokusundaki eser element seviyelerindeki değişiklikler ile anevrizma gelişimi arasındaki ilişki hakkında daha fazla bilgi edinmeyi amaçladık. Eser element seviyelerindeki değişikliklerin aort anevrizmalarının ilerlemesinde rol oynayabileceğine inanıyoruz.

Anahtar Kelimeler: Asendan aort anevrizması; İnflamasyon; eser elementler; çinko; bakır; demir.

Introductıon

Ascending aorta aneurysm (AAA) is clinically due to the potential for life-threatening complications, notably acute aortic syndromes such as aortic dissection and rupture (1,2). The occurrence of combined AAA and aortic dissection has been reported to be 6 to 13 per 100.000 per year, despite this overlooked clinically undetected AAA (3-5). Since there are currently no reliable prevention methods for TAA, early discovery, surveillance, and treatment are essential to enhancing outcomes (1,6). According to research, ascending aortic aneurysms are most frequently caused by idiopathic cystic medial degeneration. Aging is a typical process that causes the elastic fibers in the vascular wall to fragment and degrade. The etiology of the formation of ascending aortic aneurysm, as many diseases still

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referred to be idiopathic, is that metabolic issues in the presence of risk factors (older age, male, sex, smoking, hypertension, atherosclerosis, Hyperlipidemia, etc) induce rapid aortic wall deterioration. What this metabolic issue is, or issues that speed up the process, are not yet known (7,8). One of the less uncommon but still significant genetic diseases relating to AAA is Marfan syndrome, which differs in prognosis and treatment choices. Some of these conditions or risk factors increase medial degeneration, whereas others enhance wall stress. Even though only 5% of instances of AAA are linked to genetic disorders, 20% of patients with AAA have a family history (9). The trace elements Fe and Cu participate in the fenton reaction, which occurs in tissue. The process's free electron furthers lipid peroxidation and damages to cell membranes. Fe and Cu are thus involved in the peroxidative process of lipid peroxidation. Considerable amounts of Fe and Cu both point to greater lipid peroxidation and hence increased oxidative stress on the cell (10). Zn functions as a cofactor for the antioxidant superoxide dismutase. By modifying the quantities of collagen and elastin in experimental models, researchers investigated the causes of aneurysm formation. Cu, a co-factor of lysyl oxidase that is essential to produce elastin, played a role. Hereditary Cu deficiency in rats resulted in the formation of aortic aneurysms (11). Therefore, trace elements (Fe, Cu, and Zn) affect the artery wall directly or indirectly because of oxidative stress, either by accelerating up or reducing the atherosclerotic process. All forms of life, from basic microorganisms to complex ones like humans, depend on these iron (Fe), copper (Cu), and zinc (Zn) ions (Zn). This article's goal is to discuss aortic aneurysm causes based on the trace elements Fe, Cu, and Zn. This paper seeks to offer additional research directions and practical applications to known diseases. Investigating alterations in trace element levels as one of the factors that may affect the development of an ascending aortic aneurysm is the goal of our study. Therefore, we chose to compare the trace element levels in the aortic tissue of patients who received elective aortic aneurysm surgery in our clinic to the trace element levels in the aortic tissue of patients who underwent coronary artery surgery but had a normal ascending aortic diameter.

Material and Method

Patients and samples: The study, planned prospectively over two years in a cardiovascular hospital, included 53 participants, divided into two groups: those with isolated coronary artery disease and normal aorta (ICA, n=32; m/f=19/13) and ascending aortic aneurysms (AAA, n=23; m/f=13/10). The levels of iron, copper, and zinc in the specimens of aortic tissue from the 23 patient groups who underwent surgery for an ascending aortic aneurysm and the 32 control group patients who underwent coronary artery bypass grafting were compared. Patients with congenital valve disease (bicuspid, unicuspid aortic valve), genetically inherited connective tissue disease (Marfan, Ehlers Danlos, Loeys-Dietz syndrome, etc) redo cases and dissecting aortic aneurysm were excluded from the study. Standard on-pump cardiopulmonary bypass and standard sternum incision were performed on all patients.

Aortic wall tissue sample collection: Patients in the study group had their aorta tissue removed following an aortotomy, and the control group's aortic tissue was removed from the punching site during proximal anastomosis. Both samples were taken for evaluation.

Samples analysis: In graded and heat-resistant glass tubes, 0.5 g of tissue from each sample was introduced to 1 ml of 65% HNO3 (Nitric acid). Tissue samples were maintained in a 100–120°C oven for two hours. The samples were removed out of the oven, allowed to cool to room temperature, and then wet burned. To this, 1 ml of 65% HC104 (perchloric acid) was added, and it was heated for two hours at 150–180°C. The samples were prepared for element measurement by cooling them first, adding deionized water, mixing it in until it reached a volume of 5 ml, and then removing it. The elements of the aortic tissues subsequently analysed using an atomic absorption spectrophotometer. From atomic absorption prepared standard solutions of the elements Cu, Zn, and Fe, stock solutions (1000 ug/ml) were created. Using deionized water, working standards of 1.2 g/ml for Cu and Fe and 0.5 g/ml for Zn were extracted from the stock solutions. Water that has been deionized was utilized as a control. Atomic absorption spectrophotometers used hollow cathod lamps (HLC), which produced light with the optimum frequency for analyzing each element. It was decided to use a spectrum of 324.8 nm for Cu, 213.9 nm for Zn, and 248.3 nm for Fe. The elements concentrations of the prepared samples were determined, and a calibration chart was created in the atomic absorption spectrophotometer with the support of blank and standard solutions.

Table 1: Comparison of the Zn, Cu, and Fe levels in the Study and Control groups

Trace elements	Study group	Control group	+ p
	Ort ±SS	Ort ±SS	value
Cu	0.77±0.33	2.31±0.99	0.001**
Zn	21.13±7.68	19.43±8.85	0.473
Fe	51.25±46.16	25.15±14.87	0.015*

Student t test *p<0.05** p<0.01

Statistical analyses: SPSS (Statistical Package for Social Sciences) for Windows 15.0 program was utilized for statistical analysis for reviewing the study's findings. When analyzing the study data, the student's t test was applied to compare the parameters between the two groups. The correlations between the parameters were evaluated utilizing Pearson correlation analysis. All the patients were informed about the procedure in detail and provided written informed consent at enrollment.

Ethical approval: "The study protocol was reviewed and approved by Kartal Koşuyolu Education and Research Hospital Clinical Research Ethics Committee.

Results

With a mean age of 63.08 + 7.63, 8 of the 23 aneurysm groups also had ascending aortic aneurysms. A sinus valsalva aneurysm was discovered in one patient. The ascending aorta tubular graft interposition procedure was performed on 14 of the patients. Four of these patients had their aortic valves replaced in addition to the tubular graft interposition of the ascending aorta, and two had their aortic valves replaced. Three patients underwent David procedure, whereas six patients underwent Bentall de Bono surgical procedure. The control group's patients with coronary artery disease had an average age of 59.15+9.66 years. All participants undergo a standard coronary bypass. The aortic Cu averages of the study group were statistically lower than those of the control group (p 0.001). The mean Zn level in the study group was higher than that in the control group. However, there was no statistically significant change in the Zn averages of the patients in either of the groups (p>0.05). The Fe averages of the study group's participants were statistically greater than those of the control group (p 0.05). The average results from the trace element analysis in the aortic tissue are compared each group in Table 1.

Discussion

Ascending aortic aneurysms (AAAs) increase the risk of serious aortic issues such aortic dissection and rupture. The actual incidence of ascending aortic aneurysm (AAA) is obscure since it commonly remains asymptomatic (12,13). A scientific method to determine one's risk of developing an aortic aneurysm is not yet available. Concerningly, the overall incidence of acute aortic dissection is not decreasing as projected due to the lack of technologies currently available to enable specific detection of those at higher risk of ATAs (14). Although severals recent, significant case studies that assessed the ascending aorta's histology, most cases in young people lacked a clear etiology. Aneurysms in young people typically happen in the context of an inherited illness, in contrast to aortic aneurysms in elderly individuals that are linked to hypertension, tobacco, and hyperlipidaemia. Nonetheless, no investigations in this cohort have clearly connected pathologic and pathophysiological diagnosis. A common final defect in inherited diseases is an increase in tumor growth factor (TGF) activity in the ascending aorta. The Marfan syndrome (MFS), the autosomal dominant polycystic kidney disease (ADPKD), the arterial tortuosity syndrome (ATS), the Loeys-Dietz syndrome (LDS), the Ehlers-Danlos syndrome type IV (EDS-IV), and the autosomal recessive cutis laxa type 1 (ARCL) are among these "TGF-Anomalous" conditions (15-17). Aortic aneurysm is caused by biomechanical reasons, which are highly crucial. The factors that are thought to have the greatest influence on aortic wall stress are hypertension, aortic size, and elasticity. Which element, nevertheless, has the most impact on shear load remains a conundrum.

To measure the stress in the aortic wall, a multifactorial examination is required because the anatomy of the proximal ascending aorta differs from person-to-person. Several studies assessed the impact of biomechanical factors, such as wall stiffness, aortic root motion, hypertension, flow shear stress, the shape of the aorta, and aortic valve type, on the stress of the ascending aorta wall. The maximum vascular size is typically regarded as the primary criteria for conservative ascending aorta replacement in patients with tubular ascending aorta. Ascending aortic aneurysms are more than a 50% expansion in the artery's normal diameter. Clinical investigations have investigated the potential health advantages of trace element supplementation for a variety of disorders. Dietary intake of Zn and Cu effects have been suggested to reduce the incidence or mortality of cardiovascular disease, but unclear issues are still being debated. Copper is required for physiological processes and has a catalytic role. Numerous inflammatory vascular disorders, such as atherosclerosis and AAA, are caused on by inadequate copper (18,19,20). The group's aortic Cu averages were statistically lower than those of the control group in our study. These findings are consistent with the literature's statement that Cu levels may contribute to the development of AAA. Elevated body Fe stores are considered as a risk factor for cardiovascular diseases. Previously found an increased level of Fe in the serum of thoracic aortic aneurysm patients (21). Our study Fe averages of the study group's participants were statistically greater than those of the control group. The ways through which zinc contributes to AAA formation are currently poorly understood. The pathogenic roles of oxidative stress and inflammation in AAA have been thoroughly demonstrated (22,23). According to studies, zinc inhibited the development of matrix metalloproteinases (MMP), reduced the release of pro-inflammatory cytokines, and reduced oxidative lipid damage. MMPs, which degrade extracellular matrix and are zinc-dependent enzymes, have a role in the pathophysiology of cardiovascular events as ascending aortic aneurysms (24,25). In contrast, there was no noticeable change in Zn levels between AAA and control individuals in our analysis. We suspect that the disagreement across published research may be due to the significant variability of the individual studies included in our analysis.

Study limitations: The study has a number of limitations. First, we evaluated at a small sample of cases. Additionally, the study was conducted at a single heart center. Real-world data would be more properly reflected by a multicenter trial. The rates of progression to clinical aortic aneurysm may differ between patients with normal and low levels of these trace elements, according to a prospective follow-up of these patients.

Conclusion

This study contributes to our knowledge in the development of ascending aortic aneurysm and can be perceived as a support point for a more detailed and in-depth analysis of ascending aortic diseases and revealing their histopathological formation. The pathology of degenerative aortic aneurysms is unknown. We assume that variations in trace element levels may contribute to the development of aneurysms.

Ethical consent: Kartal Koşuyolu Education and Research Hospital Clinical Research Ethics Committee granted approval for this study (date:09.05.2013, number: 538.38792./6013

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