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Premenopozal Dislipidemik Kadın Hastalarda Atorvastatin Tedavisi Sonrası Ana Karotid ve Femoral Arter IMK ve Kompliyansının Ultrasonografik Olarak Değerlendirilmesi

Ultrasonographic Evaluation of Common Carotid and Femoral Artery IMT and Compliance After Atorvastatin Treatment in Premenopausal Dyslipidemic Female Patients

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Özet

GİRİŞ ve AMAÇ: Bu çalışmada dislipidemik premenopozal kadın hasta grubunda ultrasonografi (US) ile atorvastatin tedavisinin ana karotid arter ve femoral arter intima media kalınlığı (IMK) ile arteriyel kompliyans üzerine etkisini değerlendirmeyi amaçladık.
YÖNTEM ve GEREÇLER: Bu çalışmada dislipidemi tanısı bulunan 40 premenopozal kadın yer aldı. Katılımcılar 60 gün boyunca 80 mg / gün atorvastatin aldı; bazal ve tedavi sonrası ölçümleri adet döngüsünün olası etkisini önlemek için adetin ilk günü yapıldı. Ölçümler non-invazif olarak yüksek çözünürlüklü bir ultrasonografi cihazı ile yapıldı. Arteriyel kompliyans kesitsel kompliyans, kesitsel esneklik, diyastolik duvar basıncı ve elastik modül gibi çeşitli göstergeler kullanılarak değerlendirildi. Başlangıçta ve iki aylık tedavi sonrası elde edilen veriler Wilcoxon testi ile karşılaştırıldı, p<0,05 değerleri istatistiksel olarak anlamlı kabul edildi.
BULGULAR: Sekiz haftalık atorvastatin tedavisi sonrasında ana karotid arter (p=0,025) ve femoral arter (p<0,001) IMK'da anlamlı incelme saptandı. Ana karotid arter'den 8 haftalık atorvastatin tedavisi sonrası arteryel kompliyans göstergelerinden kesitsel kompliyans, kesitsel esneklik, diyastolik duvar basıncında istatistiksel olarak anlamlı farklılık saptandı (sırasıyla p<0,05, p<0,001, p<0,05). Femoral arter'den yapılan ölçümlerde kesitsel esneklik, diyastolik duvar basıncı ve elastik modül değerlerinde de istatistiksel olarak anlamlı farklılık saptandı (p<0,05, p<0,001, p<0,001).
TARTIŞMA ve SONUÇ: Yüksek çözünürlüklü US cihazı ile IMT ve arteriyel kompliyansın belirlenmesi dislipidemili hastalarda atorvastatin tedavisine cevabın non-invazif izlemi için nicel veri sağlar.

Anahtar Kelimeler: Arteriyel kompliyans, Atorvastatin, dislipidemi, intima-media kalınlığı, sertlik

Abstract

INTRODUCTION: In this study we aimed to evaluate the effect of atorvastatin treatment on common carotid artery (CCA) and femoral artery (FA) intima media thickness (IMT) and arterial compliance by using ultrasonography (US) in premenopausal females with dyslipidemia.
METHODS: The current study consisted of 40 premenopausal women with a diagnosis of dyslipidemia. The participants received 80 mg/day atorvastatin for 60 days, baseline and post-treatment measurements were performed on the first day of menstruation to avoid the possible effect of the menstrual cycle. Ultrasonographic measurements were non-invasively taken using a high resolution US system. Arterial compliance was evaluated using several indicators, such as cross-sectional compliance (CSC), cross-sectional distensibility (CSD), diastolic wall stress (DWS), and elastic modulus (EM). Data obtained at baseline and in the second post-treatment month were compared via a Wilcoxon test, p values of <0.05 were accepted as statistically significant.
RESULTS: A significant thinning in IMT was detected in the CCA (p=0.025) and FA (p<0.001) after 8 weeks' atorvastatin treatment. Measurements taken from the CCA revealed a statistically significant difference in CSC, CSD, and DWS arterial compliance indicators after 8 weeks' atorvastatin treatment (p<0.05, p<0.001, p<0.05, respectively). Statistically significant differences were found in CSD, DWS, and EM values obtained from the FA (p<0.05, p<0.001, p<0.001, respectively).
DISCUSSION AND CONCLUSION: Determination of IMT and arterial compliance by high resolution US provides quantitative data for non-invasive monitoring of the atorvastatin treatment response in patients with dyslipidemia.

Keywords: Arterial compliance, Atorvastatin, dyslipidemia, intima-media thickness, stiffness

INTRODUCTION

Studies have shown that common carotid artery (CCA) stiffness was strongly related to atherosclerosis and cardiovascular risk factors (1-3) and it was an independent risk factor for ischemic stroke (4). Endothelial dysfunction is the first step in the cascade of atherosclerosis.

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Determination of endothelial dysfunction by non-invasive methods may provide useful information for treatment. Intima-media thickness (IMT) and arterial stiffness are the most commonly used methods in non-invasive measurement of the presence and the extent of atherosclerosis. Statin group drugs are used in high demand in destiffening treatment for their pleiotropic effects (5-7).

The aim of this study was to evaluate the effect of atorvastatin treatment on CCA and femoral artery (FA) IMT and arterial compliance in premenopausal female patients with dyslipidemia, sonographically.

METHODS

Ethics

Ethical approval was taken from the local ethics committee. Informed consent was obtained from all patients.

Study Design

Current study consisted of 40 premenopausal women with the diagnosis of dyslipidemia (mean age 41 years). The patients were given 80 mg/day atorvastatin for 60 days. Baseline and post-treatment measurements were performed on the first day of menstruation to avoid possible effect of menstrual cycle. Exclusion criteria of the study were as follows: Underlying diabetes mellitus, hypertension, overt obesity, pregnancy, breast feeding, presence of active malignancy, concomitant use of antiplatelet, anticoagulant, vasoactive or non-steroidal anti-inflammatory drugs, narcotic substance use, Burger's disease, bleeding tendency or thrombocyte count less than 130,000/cm3 or hematocrit lower than 30%. Blood pressure was measured via automated sphygmomanometry (Vitagnost 2015 OC, MARS, Taiwan) after 15 minutes rest. Ultrasonographic measurements were non-invasively performed by a high resolution US system (Aplio MX (Toshiba Medical Systems, Corp.) after 12 hours fasting and at least 48 hours rest after strenuous physical activity. US probe was placed 2 cm proximal to the right CCA bifurcation and 2 cm distal to the origin of the deep branch of the right FA than IMT, systolic and diastolic vessel diameter measurements were taken in the same session (8). Arterial compliance was evaluated by using some indicators such as cross-sectional compliance (CSC), cross-sectional distensibility (CSD), diastolic wall stress (DWS) and elastic modulus (EM). CSC, CSD, DWS and EM were calculated according to the previously described formulas from CCA and FA as following (8-9).

$CSC = (\pi.(Ds2-Dd2))/(4.\Delta P)$

$CSD = (Ds2-Dd2)/ (Dd2.\Delta P)$

Lumen cross-sectional area= $\pi.Dd2/4$

Wall cross-sectional area= $\pi.((Dd/2)+IMT)2-\pi.(Dd/2)2$

$DWS = (Dd/ (2.IMT)).((Ps+Pd)/2)$

EM = (3/ (1+ (lumen cross-sectional area/wall cross-sectional area)))/CSD

Data obtained at baseline and in the second post-treatment month were compared by Wilcoxon test by means of computer software (Statistical Package for Social Sciences version 15.0, SPSS Inc., Chicago, Illinois, USA); p values <0.05 were accepted as statistically significant.

RESULTS

Baseline characteristics of the patients were shown in Table 1. Descriptive values of measurements obtained from FA and CCA at baseline and after two months atorvastatin treatment were demonstrated in Table 2. A significant thinning in IMT was detected in CCA ($p=0.025$) and femoral artery ($p<0.001$) after 8 weeks atorvastatin treatment (Figure 1). When compared to baseline values, measurements

Tablo 1. Baseline characteristics of the patients

Female	Mean	SD
Age (yrs)	41.75	14.026
High (cm)	156.75	6.107
Weight (kg)	61.81	8.563
Waist (cm)	81.63	7.289
Hip (cm)	99.75	5.051
BMI (kg/m²)	25.15	3.07
WHR	0.82	0.06
BP S (mmHg)	137.38	19.718
BP D (mmHg	84.13	18.924
Pulse (beats per min)	87.13	13.514
Cholesterol (mg/dl)	281.2	75.9
HDL (mg/dl)	59.3	24.4
LDL (mg/dl)	189.1	71.7
TG (mg/dl)	111.2	80.1

SD: Standard Deviation, **BMI**: Body Mass Index, **WHR**: Waist Hip Ratio, **BPS**: Blood Pressure Systolic, **BPD**: Blood Pressure Diastolic, **HDL**: High Density Lipoprotein, **LDL**: Low Density Lipoprotein, **TG**: Triglycerides

Tablo 2. Descriptive values of measurements obtained from FA and CCA at baseline and after two months Atorvastatin treatment

N: 40	1st data (pretreatment)		2nd data (posttreatment)		Statistic
	Mean	SD	Mean	SD	p value
C IMT	0.563	0.187	0.513	0.226	0.025
C MDD	6.425	0.522	6.490	1.302	0.298
C MSD	7.113	0.536	7.140	1.155	0.600
RVFV	0.118	0.081	0.131	0,057	<0.001
LVFV	0.130	0.051	0.141	0.047	0.017
F IMT	0.550	0.229	0.475	0.164	<0.001
F MDD	5.838	0.935	5.850	1.784	<0.001
F MSD	6.413	0.997	6.525	2.056	<0.001
C CSC	0.145	0.073	0.150	0.049	0.040
C CSD	0.005	0.004	0.005	0.002	<0.001
C DWS	211.523	188.843	161.023	67.246	0.040
C EM	237.882	138.247	223.038	207.568	0.121
F CSC	0.111	0.054	0.154	0.147	0.121
F CSD	0.004	0.002	0.006	0.005	0.040

C IMT: Carotid Intima Media Thickness), **C MDD**: Carotid Mean Diastolic Diameter, **C MSD**: Carotid Mean Systolic Diameter, **RVFV**: Right Vertebral Artery Flow Volume, **LVFV**: Left Vertebral Artery Flow Volume, **C CSC**: Carotid Compliance, **C CSD**: Carotid Distensibility, **C DWS**: Carotid Diastolic Wall Stress, **C EM**: Carotid Elastic Modulus, **F IMT, F MDD, F MSD, F CSC, F CSD, F DWS, F EM**: Provisions in the femoral artery. **SD**: Standard Deviation

taken from CCA revealed statistically significant difference in CSC, CSD and DWS arterial compliance indicators after 8 weeks atorvastatin treatment ($p<0.05$, $p<0.001$, $p<0.05$, respectively). Statistically significant differences were found in CSD, DWS and EM values measured from FA ($p<0.05$, $p<0.001$, $p<0.001$, respectively).

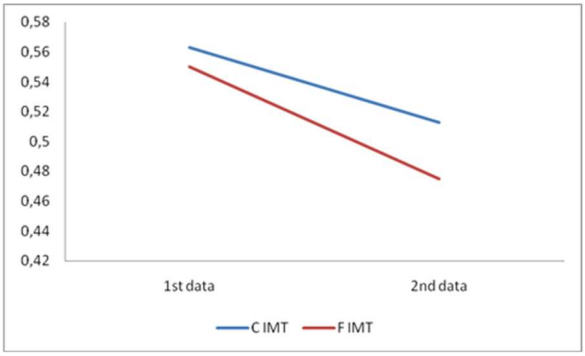

Figure 1. Demonstration of thinning in CCA and femoral artery IMT after 8 weeks atorvastatin treatment

DISCUSSION

The most important result of the present study is that 8 weeks atorvastatin treatment reduced IMT (morphologic) and arterial stiffness (dynamic) of FA and CCA in a premenopausal dyslipidemic women group when compared to baseline.

Atherosclerotic changes mainly occur in intimal layer of arteries. In addition to the contribution of the changes in arterial intima layer to vessel stiffness, these changes also cause changes in compliance by affecting muscle tone by means of vasoactive substance release to media layer (10). Arterial IMT is a non-invasive and reliable indicator showing the presence and extend of atherosclerosis. It is inversely proportional to compliance and used to monitor regression, cessation and progression of atherosclerosis. CCA IMT may predict future vascular events better for stroke than myocardial infarction (9).

Blood pressure is a source of mechanical stress on arteries. Strain is the change in diameter that occurs as a result of pressure, while the relationship between blood pressure and strain reflects elasticity and stiffness. Quantitative equivalent of elasticity is compliance, while quantitative equivalent of stiffness is distensibility. A high resolution US device is required to determine systolic and diastolic

vessel diameter or sectional area and a sphygmomanometer is used to measure blood pressure. Wall stress is defined as the pressure load exerted by blood pressure on unit vessel area. EM is a measure of vessel deformation under blood pressure. EM is inversely proportional to CSC and CSD (9). Arterial compliance is described as the change in volume caused by a certain change in pressure, while distensibility is baseline volume-to-compliance ratio (10). Among various indicators developed to measure arterial compliance, CSC, CSD and EM may be calculated more easily.
US is a cheap, easy to access and use device with no ionizing radiation, which is available in almost all centers and enables to measure IMT and arterial compliance indicators (CSC, CSD and EM) more easily (11-12).

There are some studies in which arterial stiffness was measured by a special device based on the changes in wave contour (13). A metaanalysis study demonstrated that predictive ability of aortic stiffness in cardiovascular events was powerful (14). In the study by Ratchford (Elizabeth) et al., short term (30 days) atorvastatin treatment was shown to significantly improve carotid artery elasticity (15). In the randomized study by Vlachopoulos C et al., flow-mediated dilatation method was used on brachial artery and it was demonstrated that 4 days atorvastatin treatment showed preventive effects on endothelial function and inflammation (16). In a study based on endothelial based vasodilatation and carotid artery distensibility in a group of patients with ischemic heart disease and hyperlipidemia (17), 10 and 20 mg atorvastatin were found to have similar effects, while another study conducted on a group of patients with heterozygote familial hypercholesterolemia (18) showed that 20 mg atorvastatin had no effect and 80 mg atorvastatin was found to improve endothelial function by using flow-mediated dilatation measurement. In the study by Junhong Wang et al. which was based on brachial-ankle pulse wave velocity (baPWV) measurement in old hypertensive patients, 20 mg atorvastatin treatment given for 6 months was found to improve arterial stiffness probably by means of its anti oxidative effects (19). Our study was different from other studies in that IMT and arterial compliance measurements were performed on both FA and CCA and our study population was a relatively homogeneous group (premenopausal female patients with dyslipidemia).

Our study also has some limitations. Firstly, the number of the patients included in the study group was relatively low. Secondly, treatment period was 8 weeks and long-term effects of the treatment could not be evaluated. Thirdly, a standard atorvastatin dose was used in the treatment, comparison of the effectiveness of different doses could not be made and the study lacks a control group.

CONCLUSION

Determination of intima-media thickness and arterial compliance by high resolution US in patients with dyslipidemia provides quantitative data for non-invasive monitorization of atorvastatin treatment response. These data may also help in monitorization of overall cardiovascular risk. Further large-scale studies are required to determine the effects of measurement methods on treatment algorithm, morbidity and mortality.

Conflict of interest

There is no conflict of interest in connection with any commercial associations, and all authors have nothing to disclose.

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