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Endothelial dysfunction in postmenopausal women with type 2 diabetes

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The epidemic of diabetes mellitus is constantly growing. Severe and expensive diabetic complications are disturbances in the macro-microcirculation. Moreover these functional disturbances starts early after the onset of diabetes and determines the progression of other diabetic complications. Endothelial dysfunction is an indicator of the blood circulatory disturbances and depends from the several factors. As, the low blood estrogen level in postmenopausal women with diabetes can deteriorate endothelial dysfunction. However, role of clinical and biochemical factors in development of endothelial dysfunction in postmenopausal women with diabetes remains unclear. The presents of endothelial dysfunction as consider constitutes an independent predictor of cardiovascular events. Besides, endothelial dysfunction can play important role in the progression of diabetic chronic foot ulceration that leads to amputation in 10-15% of the diabetic patients. These functional disturbances need in early detection for prevention the development of cardiovascular disease and chronic diabetic complications. Thus noninvasive and easily techniques are required for the discover endothelial dysfunction. Because endothelial dysfunction presents in all vessels, the assessment of peripheral vascular endothelial function are considered as adequate screening methods. Doppler ultrasound highfrequency study is a noninvasive and adequate technique of measuring microvascular circulation, endothelialdependent and endothelialindependent vessel responsiveness. The assessment of digital blood flow changes during reactive hyperemia by this technique allows to discover endothelial dysfunction.

Methods

In a study, we examined the endothelial-dependent vessel responses in postmenopausal women with diabetes mellitus. There were 27 women with mean age of 53 years (range 50 to 55) entered into this study. We excluded patients with clinical evidence of cardiovascular disease, peripheral vascular disease, uncontrolled arterial hypertension, severe renal, hepatic, respiratory, ophthalmologic or hematological conditions, or diabetic ulceration. Total cholesterol, triglycerides, HDL-cholesterol and none-HDL-cholesterol in blood were estimated. Besides estradiol, total testosterone, follicle-stimulating hormone, luteinizing hormone were also measured by specific immunoenzymoassay.

For wrist and foot digital skin microvascular vessels basal blood flow and endothelialdependent responsiveness were assessed by Doppler ultrasound highfrequency technique. Measuring reactive hyperemia perfusion changes assessed vascular responsiveness.

Blood pressure cuffs were placed on forearm and leg. The baseline vessels flow was measured on one wrist and foot digital. After a 10-min equilibration period the forearm blood pressure cuff was inflated to 200 mm Hg for 5 min. Then the cuff was deflated and changes of microvascular blood flow were assessed on 1, 3 and 5 min. After that same probe was performed in leg. Peripheral blood flow was excluded via leg cuff (250 mm Hg). The magnitude of reactive hyperemia flow was also measured on 1, 3 and 5 min. The measure of reactive hyperemia was calculated as the ratio of the magnitude vessel blood flow after cuff defloration to baseline blood flow.

Results are expressed as mean ± SEM. Data were compared by Student's test. The null hypothesis was rejected at $P<0.05$.

Results

Estradiol level in blood was significantly lower and follicle-stimulating hormone, luteinizing hormone levels were higher then in female of childrearing potential. There was no difference in testosterone

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TABLE 1 - BASELINE CHARACTERISTICS OF SUBJECTS WITH NORMAL (N=19) AND LOW (N=8) WRIST PERFUSION.

Baseline characteristics	*n=19*	*n=8*
Age, y	52.4±1.8	53.1±2.0
BMI, kg/m^2	28.4±2.6	29.0±1.2
HbA1c, %	7.2±0.3	7.1±0.2
Systolic BP, mm Hg	135±5	138±3
Diastolic BP, mm Hg	87±5	85±6
Total cholesterol, mmol/l	6.5±0.32	6.4±0.48
Tryglycerides mmol/l	2.0±0.42	2.1±0.46
HDL-cholesterol, mmol/l	1.5±0.1	1.4±0.2
None-HDL-cholesterol, mmol/l	5.4±0.31	5.36±0.2
Baseline wrist blood flow (sm/sec)	6.8±0.8	2.4±0.6

TABLE 2 - CHARACTERISTICS OF SUBJECTS WITH LOW INCREASING (N=19) AND ABNORMAL DECREASING (N=8) OF REACTIVE HYPEREMIA FLOW IN WRIST.

Characteristics	*n=9*	*n=18*
Age, y	51.4±1.6	52.8±1.8
BMI, kg/m^2	26.8±1.5	28.5±1.8*
HbA1c, %	6.9±0.8	7.2±0.4
Total cholesterol, mmol/l	5.8±0.8	6.4±0.2
Triglycerides, mmol/l	1.1±0.2	2.2±0.5*
HDL-cholesterol, mmol/l	1.9±0.2	1.5±0.2*
None-HDL-cholesterol, mmol/l	5.2±0.4	5.4±0.3
Baseline wrist blood flow (sm/sec)	5.8±0.7	6.2±0.5
Reactive hyperemia vessel reaction in wrist (%)	+38±12.6	-26±10.4*
Baseline foot blood flow (sm/sec)	1.8±0.7	2.4±0.6
Reactive hyperemia vessel reaction in foot (%)	0	0

*p < 0.05 vs. subjects with low increasing of reactive hyperemia flow in wrist.

level in both groups.

Baseline characteristics are shown in a table. In 70.5% cases the skin basal blood flow of wrist was normal. But all subjects showed a very low level of foot perfusion. There were no differences between the patients with basal normal flow and basal low flow with respect to age, body mass index, systolic and diastolic blood pressure, plasma concentrations of cholesterol, triglycerides, HDL-cholesterol and none-HDL-cholesterol, or HbA1c level (Table 1).

The impaired vascular endothelialdependent response in wrist and foot digitals was observed in all subjects. Abnormal decreasing of reactive hyperemia blood flow in finger was obtained in 33% women. Low vasodilator a response was observes in other subjects (increasing of reactive hyperemia blood flow less than 50%). Moreover magnitude of reactive hyperemia reaction independed on baseline blood flow characteristics. It was estimated that obesity, high triglyceride or low HDL-cholesterol levels associate with the abnormal vasoconstrictor endotheliumdependent reaction of wrist vessels (Table 2). Moreover there were no reactive hyperemia foot vessels responses in all subjects.

Conclusions

It is known that microcirculation disturbances, especially endothelial dysfunction, can lead to diabetic ulceration development. Besides endothelial dysfunction is independent predictor of cardiovascular events. This study shows that endothelial dysfunction presents in all postmenopausal women with diabetes and without diabetic ulceration and clinical of coronary disease. Abnormal decreasing of reactive hyperemia blood flow in wrist is discovered in women with obesity and high triglyceride level or low HDL-cholesterol level. In this group of patients the foot microcirculatory disturbances is more severe than in wrist. Additional studies are required to establish the influence of difference clinical and biochemical factors on endothelial dysfunction development in postmenopausal women with diabetes.