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Research paper

The skin microcirculatory changes in the normal and hypertensive elderly

M.S. El Nahid *, A. El Ashmaui

Internal Medicine Department, Cairo University, Cairo, Egypt

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ABSTRACT

Introduction: The skin microcirculatory changes mimic the changes in other vascular beds, including the cardiac. Several studies aimed to study the functional and structural changes in the skin microcirculation of the elderly population. Controversies rose from whether the encountered changes were due to ageing or due to associated diseases. We, therefore, aimed at studying the skin microcirculation in a group of elderly subjects away from disease states that are known to affect the microcirculatory status. We also studied a group of elderly hypertensive patients for comparison. Both groups were compared to young healthy adults.

Methods: The study population included 145 subjects, divided into three groups: group A: 50 healthy elderly subjects free from diabetes, hypertension and hypercholesterolemia, group B: 60 elderly patients with long standing essential hypertension and group C: 35 young healthy subjects. The microcirculation was assessed by means of the Laser Doppler Fluxmetry (LDF). The provocative test used was the reactive hyperemia test (RH). Further evaluation of the apparent structural abnormalities in skin microvascular structure was done using the capillaroscope.

Results: Results showed no statistically significant difference in the RH measurements between the normal elderly group and the control group with a statistically significant difference in the capillary density by capillaroscopy. The hypertensive group revealed different results.

Conclusion: The study of the microcirculatory changes in normal elderly subjects revealed the presence of structural abnormalities. These changes are independent of any disease state.

1. Introduction

The skin microvascular function can mirror the state of microcirculation in all other vascular beds. Several disease states seem to alter skin microvascular function and structure; examples include diabetes [1], hypertension [2], hypercholesterolemia [3] and collagen vascular disease [4]. Many of these disease states are frequently encountered in the elderly population. Whether ageing, per se, independent of any disease states, has an effect on the skin microcirculation is a matter of controversy. It is the aim of our study to evaluate the elderly skin microcirculatory changes, away from any disease that might have an effect on the microcirculation. We will use the Laser Doppler Fluxmetry (LDF) to examine the functional changes and the capillaroscope to study the structural changes at the level of the microcirculation.

2. Material and methods

2.1. Clinical and laboratory assessment

This research has gained the approval of the internal medicine review board. An informed consent has been obtained from all participants after a detailed explanation of the study procedure. The study population included 145 subjects; 97 males and 48 females with an age range of 26–82 years old. Normal elderly subjects were recruited from a social club for senior citizens in Cairo. Patients were recruited from the internal medicine out-patient clinics in Cairo University. Subjects and patients were subjected to thorough history taking, clinical examination, laboratory investigations (fasting, post-prandial blood glucose and total cholesterol) and the Ankle-Brachial Index (ABI) measurement.

They were divided into three groups: group A included 50 normal elderly subjects with an age range of 65–75 years old. Those who were non-smokers, with a FBG ≤5.5 mmol/L (<100 mg%), PPBG <10 mmol/L (<140 mg%), SBP <140 mmHg, DBP

* Corresponding author. 15B, Radwan Ibn Tabib St, Giza, Cairo, Egypt. Tel.: +20 012 277 110 27.
E-mail address: dr.migos@yahoo.com (M.S. El Nahid).

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<90 mmHg, cholesterol <5.2 mmol/L (<200 mg%), with a normal ABI were included in the study. Their ECGs were free. They were not on any kind of medications. Group B included 60 elderly subjects with an age range of 66–82 years old, with long standing uncontrolled essential hypertension (7–10 years) with or without diabetes or hypercholesterolemia. These were on irregular antihypertensive treatment; diuretics, ACEI, beta-blockers and calcium channel blockers, single or in combination. Group C, the control group, included 35 young healthy subjects, with an age range of 25–40 years old. Those who were non-smokers, with a FBG ≤5.5 mmol/L (<100 mg%), PPBG <10 mmol/L (<140 mg%), SBP <140 mmHg, DBP <90 mmHg, cholesterol <5.2 mmol/L (<200 mg%), with a normal ABI were included in the study. Their ECGs were all free. They were not on any kind of medications.

2.1.1. Assessment of the macrocirculation

An Ankle-Brachial Index (ABI) measurement was done to exclude macrovascular diseases, before having the microcirculation assessed. The ABI is the ratio between the systolic blood pressure in the ankle to that in the arm. It is normally above 0.96. Values less than that represent peripheral arterial occlusive disease (PAOD). It is universally agreed that a normal ABI ensures a healthy macrovasculature [5].

2.1.2. Assessment of the microcirculation

2.1.2.1. The Laser Doppler Fluxmetry. Assessment of the skin blood flow was made using the LDF Periflux 4001 master/4002 Satellite Perimed, Sweden. Measurements were taken after complete physical and mental rest for at least 20 minutes. The study took place in room temperature maintained at 24 °C, the probe was held on the dorsum of foot by a double-sided adhesive tape supplied by the manufacturer. Special care was taken to support the fiber optic cable and to keep the body stationary. Apparatus calibration was done according to guidelines by the manufacturer.

First, a registration of baseline flow (2 minutes) was performed, recording the *basal flux*. Then arterial occlusion was performed with a supra-systolic pressure using a pneumatic cuff of a sphygmomanometer for 3 min at the ankle level, thus recording *flow after occlusion* (the *biological zero* [BZ]). Following the release of pressure, the highest flux value measured was recorded, the *peak flux*. Because the output could not easily be translated into absolute values of blood flow, the magnitude of the changes in skin perfusion was calculated as the ratio between peak and mean baseline perfusions. Thus the ratio between the peak flux and the basal flux was calculated by the *apparatus* as the *percent change* [6].

The reactive hyperemia is defined as a temporary increase in blood flow after the release of temporary occlusion of arterial inflow. The post-ischemic phase of the reactive hyperemia test is recorded by the LDF as increase in the signal to a peak (maximum flow after occlusion) and then returns to the resting value. This response to a provocative test is determined by the microvascular neural, myogenic and endothelial activity. Consequently, the reactive hyperemia was considered a good estimate of microvascular function or dysfunction [7].

2.1.2.2. The nail-fold capillaroscope. The capillaroscope was used for direct visualization of the nail-fold capillaries. Two fingers were tested in each subject, the middle and ring fingers of the hand. The nail-fold was lubricated with paraffin oil and the area was examined thoroughly under the microscope. Four sequential microscopy fields were recorded (whilst the focusing level is systematically adjusted) and the capillaries counted and examined whilst playing back the video. Several parameters can be examined in the nail-fold capillaries. In our study, we examined the capillary density and the presence or absence of abnormal capillary forms. Capillary density was calculated as the average density in the two fingers. Density was measured as the number of capillary loops in 3 mm [8]. Abnormal capillary forms included enlarged or giant capillaries, the presence of capillary hemorrhage and abnormalities in the organization of the normal capillary array [9]. The microscope used was the Dynamic Capillaroscopy (KK Technology, England).

2.2. Statistical analysis

Data were statistically described in terms of mean ± standard deviation (±S.D.), median and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using one-way analysis of variance (ANOVA) with Bonferroni post-hoc multiple pair wise comparisons. Adjustment for all significant factors was done using analysis of covariance (ANCOVA) through general linear model analysis. Correlation between various variables was done using Pearson moment correlation equation for linear relation in normally distributed variables and Spearman rank correlation equation for non-normal variables *P*-values less than 0.05 was considered statistically significant. All statistical calculations were done using computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

3. Results

3.1. The description of the clinical, laboratory and LDF data

A total of 145 patients with 97 males and 48 females were included in the study. Table 1 describes the clinical, laboratory and LDF values in each of the three studied groups.

As shown in the table, the minimum and maximum values, in the healthy elderly group, for age, SBP, DBP, FBG, PPBG and cholesterol were all within acceptable normal limits. This ensures strict adherence to the selection criteria.

3.2. The analysis of the LDF data

3.2.1. In the healthy elderly group

After adjustment for baseline criteria, there was no statistically significant difference in the LDF measurements; the basal flux, the peak flux, the BZ and the percent change between the healthy elderly group and the young group (*P*-value: 0.648) (Table 2A).

3.2.2. In the elderly hypertensive group

After adjustment for baseline criteria, there was a statistically significant difference in the basal flux, the peak flux and the percent change between the hypertensive elderly and the young healthy groups (*P*-value: <0.035, <0.001, <0.001) (Table 2B).

After adjustment for baseline criteria, there was a statistically significant difference in the basal flux, the peak flux, the BZ and the percent change between the healthy elderly group and the hypertensive elderly group (*P*-value: <0.001, <0.001, 0.001, <0.001) (Table 2C).

These results show that there is a statistically significant difference in the reactive hyperemia test as measured by the LDF between the hypertensive group and the young group and as well the healthy elderly group. There was no statistically significant difference between the healthy elderly group and the young group. This finding points out that ageing, per se, is not associated by any functional microcirculatory dysfunction. Moreover, the abnormalities in the hypertensive group, such as high blood pressure and abnormal lipid profile, may be responsible for a statistically significant difference in the LDF measurements between the hypertensive elderly group and the two other groups.