CORRESPONDENCE

An Evaluation of the Impact of Therapeutic Phlebotomy on Systemic Endothelial Functions in Polycythemic Patients with the Flow-Mediated Vasodilatation Method

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Dear Editor,

Polycythemia is a disease state in which the proportion of blood volume that is occupied by red blood cells increases. Phlebotomy is a procedure that removes blood from the body. It is the process of making an incision in a vein with a needle. Regular phlebotomy treats people with primary or secondary polycythemia [1]. Flow-mediated vasodilation (FMD) is a non-invasive ultrasound method of evaluating endothelial function. With an ultrasound-based method, arterial diameter is measured in response to an increase in shear stress, which causes endothelium-dependent dilatation [2, 3]. In this study, our aim was to evaluate the systemic endothelial functions by FMD method in patients with polycythemia 1 h before and 48 h after phlebotomy.

The present prospective study included 47 male patients with polycythemia [hemoglobin (Hb) ≥ 16.5 g/dl] aged ≥ 18 years at Kayseri Education and Research Hospital were included. In all patients, the following laboratory evaluations were performed: complete blood count (CBC), serum iron indices, and routine biochemical tests. Also, all patients underwent the FMD study before and after phlebotomy at Cardiology Department with Doppler ultrasound. Antecubital veins were used for the phlebotomy in all the patients and 400–450 mL of blood was withdrawn into plastic bag, which was prefilled with

63 mL of citrate–phosphate–dextrose. All patients underwent FMD study 1 h before and 48 h after phlebotomy. At the time of FMD examination, information regarding coronary risk factors was recorded for each patient and included age, gender, body mass index (BMI), smoking status, and comorbidity. Brachial artery FMD was measured with a high-frequency (7.0–13.0 MHz) ultrasound scanning probe to obtain longitudinal images of the brachial artery at a point 5–10 cm proximal to the antecubital fossa (Philips HD11 XE Ultrasound system). Angle correction software was used during Doppler imaging to approximate a 20-degree angle of incidence to bloodflow. Increased shear stress was achieved by producing reactive hyperemia. A pressure cuff placed on the right forearm was inflated up to 50 mmHg higher than systolic blood pressure for 5 min in order to induce ischemia by occluding arterial flow. Arterial diameter measurements were repeated within 60 s of cuff deflation. Arterial diameter was measured from the right arm at the intima-media interface of the clearest echocardiography line. Images were acquired with electrocardiogram gating, with measurements made in end diastole corresponding to the onset of the R wave. Measurements were reported as % change in diameter. The relationship between age, smoking and comorbidities and change of FMD was evaluated with the Pearson correlation analysis. Also, the results before and after phlebotomy were statistically evaluated according to the paired-samples *t* test. A *p* value ≤ 0.05 was considered statistically significant.

Baseline clinical and laboratory characteristics of patients are provided in Table 1. The mean age of the patients was 40.28 ± 16.78 years. A significant decrease in Hb, hematocrit and platelet levels was identified after phlebotomy. The mean FMD levels were found to be significantly higher in the post-phlebotomy period compared

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Table 1 Baseline characteristics of patients (n = 47)

Variables	
Age (years) ^a	40.28 ± 16.78
Male	50
BMI (kg/m ²) ^a	25.3 ± 3.6
Hypertension (%)	19 (40.4)
Diabetes Mellitus (%)	5 (10.6)
COPD (%)	18 (38.3)
Smoking (%)	38 (80.8)
Hemoglobin (g/dl) ^b	18.20 (16.80–21.20)
Hematocrit (%) ^b	53.60 (47.90–64.70)
Serum iron (μmol/l)	98 (32–305)
TIBC (μg/dl) ^b	251 (52–485)
TS (%) ^b	39 (25–267)
Serum ferritin (ng/ml) ^b	52 (21–177)
Total cholesterol (mg/dl) ^b	188.50 (83–254)
Triglyceride (mg/dl) ^b	170 (51–545)
LDL cholesterol (mg/dl) ^b	99.50 (13–182)
HDL cholesterol (mg/dl) ^b	43 (29–76)

BMI body mass index, *COPD* chronic obstructive pulmonary disease, *HDL* high density lipoprotein, *LDL* low density lipoprotein, *TIBC* total iron binding capacity, *TS* transferrin saturation

^a Mean ± SD

^b Median (range)

to pre-phlebotomy period (10.12 ± 3.46 and $7.78 \pm 4.83\%$, respectively, $p < 0.001$).

Our study demonstrate that endothelium-dependent FMD is markedly impaired in patients with polycythemia and therapeutic phlebotomy improved the endothelial function. There is limited information about FMD in patients with polycythemia. Neunteufl et al. [4] showed

that polycythemia vera is associated with endothelial dysfunction in their study. They found that FMD was impaired in polycythemia vera compared the control group (7.6 ± 2.9 vs. $11.6 \pm 5.7\%$, $p = 0.009$). In another study, Yucel et al. [5] investigated whether regular blood donation is associated with improved endothelial function in healthy adults. FMD was improved after blood donation (9.9 ± 3.8 vs. $10.75 \pm 3.9\%$, respectively) ($p = 0.006$). Our data were in accordance with their findings.

In conclusion, with this study, we demonstrated with the FMD method that therapeutic phlebotomy improves endothelial functions in polycythemic individuals. Although not yet recommended for routine clinical use, FMD testing has provided valuable insights into vascular changes associated with polycythemia.

Compliance with Ethical Standards

Conflict of interest All authors declare that they have no conflict of interest.

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