Use of Terahertz Electromagnetic Radiation for Correction of Blood Rheology Parameters in Patients with Unstable Angina under Conditions of Treatment with Isoket, an NO Donor

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The effect of terahertz electromagnetic radiation at the emission and absorption frequencies of NO molecular spectrum on blood rheology were studied *in vitro* in patients with unstable angina treated with isoket (NO donor). Irradiated NO donor isoket produced better normalizing effect on blood viscosity and erythrocyte deformability in patients with unstable angina.

Key Words: *nitrogen oxide; electromagnetic radiation; unstable angina*

The interest to NO is explained primarily by its involvement into the regulation of many functions, including the vascular tone, myocardial contractility, platelet aggregation, neurotransmission, ATP and protein synthesis, and immune defense [10]. However, the effect of NO can be damaging, depending on the molecular target and NO-target interactions [6].

Hemodynamic disorders and vascular wall tension can disorder the mechanisms of NO formation in the vascular endothelium. For example, blood flow reduction as a result of coronary artery stenosis in cardiac insufficiency appreciably decreases the production of endothelial NO synthase in cardiomyocytes [13]. This attests to an important role of blood rheology for normal synthesis of endothelial NO synthase, the more so because this effect is completely abolished after blood flow resumption [11,12].

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Terahertz therapy (THT therapy) is a new perspective treatment modality for many diseases; it promotes normalization of blood rheology, activation of natural autoregulatory mechanisms, and improvement of the compensatory potential [2,3,7].

We studied changes in blood rheology in patients with unstable angina receiving electromagnetic radiation (EMR) exposure in the THT mode at a frequency 240 GHz corresponding emission and absorption frequencies of NO molecular spectrum during treatment with isoket, an NO donor.

MATERIALS AND METHODS

Whole blood of patients with unstable angina was analyzed.

The groups of patients with unstable angina (*n*=60, men 42 and women 18, 53.9 and 46.1%, respectively) and healthy controls (*n*=150) were age- and sex-matched. Mean age of patients was 60.4±0.98, of controls 59.9±1.02 years. This age group was selected for evaluating the effects of electromagnetic THT radiation on blood rheology in pa-

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tients with unstable angina of adult and elderly ages (associated with the highest risk of thromboembolic complications of the underlying disease).

Exclusion criteria during the formation of groups for the study were early postinfarction angina, new angina, recent (less than 6 months) history of stroke, body weight below 40 or more than 110 kg, left bundle branch block (except initially stable blocking), *ST* elevation above 1 mm in two neighboring ECG leads, implanted pacemaker, renal failure (creatinine >200 μmol/liter), thrombocytopenia (below 1.50×10^{11}/liter), hepatic insufficiency, septic endocarditis, uncontrollable arterial hypertension (diastolic blood pressure above 105 mm Hg after 15-min rest), congenital or acquired hemostatic disease, other severe concomitant diseases in a decompensated stage.

Studies of the effects of THT field at the radiation and absorption frequency of NO molecular spectrum (RAMS, 240 GHz) on whole blood *in vitro* were carried out on a quasioptic determined noise EHF generator [4]. Experimental blood speci-

TABLE 1. Changes in Whole Blood Viscosity (in mPa×sec) and Functional Characteristics of Erythrocytes in Patients with Unstable Angina under the Effects of *In Vitro* Treatment with Isoket *per se* and Isoket Irradiated for 15 min at NO RAMS Frequency (240 GHz)

Shear rate, sec^{-1}	Initial (n=150)	Addition of non-irradiated isoket (n=15)	Addition of irradiated isoket (n=15)
300	3.71 (3.4; 4.0)	3.29 (3.1; 3.5) P_1=0.000064 Z_1=3.99	2.77 (2.7; 2.9) P_2=0.000001; Z_2=6.19 P_3=0.000003; Z_3=4.66
200	3.71 (3.4; 4.0)	3.29 (3.1; 3.5) P_1=0.000064 Z_1=3.99	2.77 (2.7; 2.9) P_2=0.000001; Z_2=6.19 P_3=0.000003; Z_3=4.66
150	3.71 (3.4; 4.0)	3.29 (3.1; 3.5) P_1=0.000064 Z_1=3.99	2.8 (2.7; 2.9) P_2=0.000001; Z_2=6.16 P_3=0.000003; Z_3=4.66
100	3.81 (3.5; 4.1)	3.39 (3.2; 3.6) P_1=0.000064 Z_1=3.99	2.96 (2.8; 3.1) P_2=0.000001; Z_2=6.01 P_3=0.000034; Z_3=4.14
50	4.18 (3.8; 4.5)	3.74 (3.5; 4.0) P_1=0.000203 Z_1=3.71	3.29 (3; 3.5) P_2=0.000001; Z_2=5.56 P_3=0.001215; Z_3=3.23
20	4.92 (4.6; 5.2)	4.34 (4.1; 4.6) P_1=0.000005 Z_1=4.56	3.86 (3.6; 3.2) P_2=0.000001; Z_2=5.75 P_3=0.002001; Z_3=3.09
10	5.75 (5.4; 6.1)	5.25 (5.0; 5.4) P_1=0.000090 Z_1=3.91	4.5 (4.1; 5) P_2=0.000001; Z_2=5.93 P_3=0.000125; Z_3=3.83
5	6.86 (6.5; 7.2)	6.4 (6.1; 6.7) P_1=0.000501 Z_1=3.48	5.24 (4.7; 5.7) P_2=0.000001; Z_2=6.26 P_3=0.000003; Z_3=4.66
Erythrocyte deformability index, arb. units	1.027 (1.025; 1.029)	1.03 (1.028; 1.032) P_4=0.000064; Z_4=3.99	1.067 (1.037; 1.1) P_5=0.000001; Z_5=6.28
Erythrocyte aggregation index, arb. units	1.29 (1.27; 1.31)	1.28 (1.27; 1.29) P_4=0.093390; Z_4=1.67	1.3 (1.25; 1.36) P_5=0.450927; Z_5=0.75

Note. Here and in Tables 2, 3: the median is presented, with the lower and upper quartiles in parentheses (%). P_1, Z_1: significance of differences between blood viscosity values after addition of non-irradiated isoket and initial blood viscosity of patients with unstable angina. P_2, Z_2: significance of differences between blood viscosity values after addition of irradiated isoket and initial blood viscosity of patients with unstable angina. P_3, Z_3: significance of differences between blood viscosity values after addition of non-irradiated and irradiated isoket. P_4, Z_4: significant differences in erythrocyte deformability and aggregation indexes in patients with unstable angina after addition of non-irradiated isoket and initial values. P_5, Z_5: significant differences in erythrocyte deformability and aggregation indexes in patients with unstable angina after addition of irradiated isoket and initial values.

men was irradiated at a frequency of NO RAMS (240 GHz; EH_{11} wave type, P=1 mW/cm^2) for 15 min. Control specimen was not exposed.

In order to clear out the role of NO in the realization of the effect of terahertz EMR at a frequency of NO RAMS (240 GHz), the NO donor isoket was exposed for 15 min (EH_{11} wave type, P=1 mW/cm^2).

Blood rheology was evaluated on admission of patients to hospital before therapy. As blood is a non-Newton fluid, its rheological characteristics were studied by rotation viscosimetry [5]. The study was carried out on a Russian rotation viscosimeter with an AKR-2 free floating cylinder.

The data were processed using Mann—Whitney U test (Statistica 6.0 software).

RESULTS

In vitro addition of isoket and the preparation exposed to NO RAMS EMR to the whole blood from patients with unstable angina significantly decreased blood viscosity at all the studied shear rates in comparison with the initial data (Table 1).

Addition of irradiated isoket to the blood led to a more marked reduction of blood viscosity than after addition of non-irradiated preparation: the difference was 15.6% at high shear rates (300, 200, and 150 sec^{-1}) and 14.4% at low shear rates and was statistically significant.

Addition of non-irradiated isoket to blood samples from patients with unstable angina caused no shifts in erythrocyte aggregation and increased their deformability (Table 1).

Addition of non-irradiated and irradiated (240 GHz THT EMR) isoket to the whole blood of patients with unstable angina resulted in statistically significant increase in erythrocyte deformability, but caused no changes in erythrocyte aggregation (Table 1).

The effects of irradiated and non-irradiated isoket on erythrocyte aggregation were similar (the difference being statistically negligible). On the other hand, isoket exposed to THT EMR at 240

TABLE 2. Changes in Blood Rheology (in mPa×sec) in Patients with Unstable Angina under Conditions of a Natural Electromagnetic Field, Exposed to 15-min Irradiation at NO RAMS Frequency of 240 GHz, under the Effect of Isoket

Shear rate, sec^{-1}	Initial value under the effect of 15-min irradiation (n=20)	Irradiation (15 min)+non-irradiated isoket (n=15)	Irradiation (15 min)+irradiated isoket (n=15)
300	3.47 (3.25; 3.7)	3.03 (3;3.1)	2.72 (2.6; 2.8)
		P_1=0.000004	P_2=0.000001; Z_2=5
		Z_1=4.6	P_3=0.000006; Z_3=4.54185
200	3.47 (3.25; 3.7)	3.03 (3;3.1)	2.72 (2.6; 2.8)
		P_1=0.000004	P_2=0.000001; Z_2=5
		Z_1=4.6	P_3=0.000006; Z_3=4.54185
150	3.47 (3.25; 3.7)	3.06 (3;3.1)	2.74 (2.6; 2.9)
		P_1=0.000017	P_2=0.000001; Z_2=5
		Z_1=4.3	P_3=0.000012; Z_3=4.37594
100	3.57 (3.35; 3.8)	3.18 (3.1;3.2)	2.85 (2.7; 3)
		P_1=0.000041	P_2=0.000001; Z_2=5
		Z_1=4.1	P_3=0.000015; Z_3=4.33446
50	3.89 (3.65;4.05)	3.58 (3.5; 3.7)	3.07 (2.9; 3.3)
		P_1=0.001224	P_2=0.000001; Z_2=4.95
		Z_1=3.23	P_3=0.000015; Z_3=4.33446
20	4.51 (4.2; 4.7)	4 (3.9; 4.1)	3.64 (3.5; 3.8)
		P_1=0.000025	P_2=0.000002; Z_2=4.76
		Z_1=4.21	P_3=0.000976; Z_3=3.29751
10	5.32 (5.15; 5.45)	4.92 (4.7; 5.2)	4.28 (4.1; 4.6)
		P_1=0.002047	P_2=0.000001; Z_2=4.93
		Z_1=3.08	P_3=0.000262; Z_3=3.65007
5	6.16 (6; 6.4)	5.91 (5.7; 6.2)	5.05 (4.8; 5.6)
		P_1=0.027808	P_2=0.000003; Z_2=4.68
		Z_1=2.2	P_3=0.000018; Z_3=3.94042

TABLE 3. Changes in Functional Characteristics of Erythrocytes from Patients with Unstable Angina Pre-Exposed to THT EMR at NO RAMS Frequency (240 GHz) under the Effects of Isoket *per se* and Irradiated Isoket *In Vitro*

Parameter	Control (n=20)	Isoket *per se* (n=15)	Irradiated isoket (n=15)
Deformability index, arb. units	1.028 (1.02; 1.03)	1.048 (1.032; 1.066) P=0.000001; Z=5	1.046 (1.035; 1.038) P=0.000001; Z=5
Aggregation index, arb. units	1.26 (1.24; 1.27)	1.26 (1.24; 1.28) P=0.802588; Z=0.25	1.27 (1.22; 1.33) P=0.161514; Z=1.4

GHz more effectively increased erythrocyte deformability in the blood of patients with unstable angina (1.067 arb. units) than non-irradiated one (1.03 arb. units; p=0.000003).

Hence, non-irradiated isoket and the preparation exposed to THT EMR at 240 GHz for 15 min caused different changes in blood rheology of patients with unstable angina: irradiated isoket more markedly reduced blood viscosity and caused a greater increase in erythrocyte deformability than non-irradiated preparation.

Addition of non-irradiated and irradiated isoket to the whole blood of patients with unstable angina pre-exposed *in vitro* to EMR at 240 GHz also led to a statistically significant reduction of blood viscosity at all the studied shear rates in comparison with the values in patients whose blood specimens were exposed at the same frequency for 15 min (p<0.001; Table 2).

However, irradiated isoket led to a more pronounced statistically significant reduction of blood viscosity at all shear rates (p<0.001) in comparison with non-irradiated isoket.

Study of erythrocyte deformability and aggregation in patients with unstable angina after a 15-min exposure to THT EMR and under the effect of non-irradiated and irradiated isoket showed just an increase of erythrocyte deformability (Table 3).

Hence, the *in vitro* effects of non-irradiated and irradiated NO donor isoket on whole blood of patients with unstable angina differ by the degree of reduction of whole blood viscosity. Isoket exposed at NO RAMS frequency (240 GHz) for 15 min more markedly reduced blood viscosity than intact isoket. Erythrocyte aggregation did not change under the effect of non-irradiated and irradiated isoket, while erythrocyte deformability changed greater under the effect of irradiated *vs.* non-irradiated isoket.

The effects of irradiated and non-irradiated isoket on whole blood of patients with unstable angina pre-exposed at NO RAMS frequency of 240 GHz for 15 min were different: irradiated isoket caused a more pronounced reduction of blood viscosity. The effects of non-irradiated and irradiated isoket on erythrocyte deformability were the same. Hence, irradiated NO donor isoket exhibited a more pronounced normalizing effect on blood viscosity and erythrocyte deformability in patients with unstable angina, which can be due to increased formation of NO molecules from isoket under the effect of THT EMR at NO RAMS frequency of 240 GHz.

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