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Impact of omega-3 polyunsaturated fatty acids on arrhythmic activity of myocardium and characteristics of cardiac rhythm in patients with unstable angina

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Summary

Objective

To evaluate the impact of omega-3 polyunsaturated fatty acids (PUSFA) on myocardial arrhythmic activity and characteristics of cardiac rhythm variability in patients with unstable angina

Materials and methods

We've conducted an open randomized trial that involved 41 patients aged 45-70 years and diagnosed with coronary heart disease (CHD): unstable angina. All patients underwent standard complex therapy. Patients were subdivided into two groups: omega-3 PUSFA supplement (1g/day) was added to the therapy in the first (main) group, whereas the patients of the second (control) group received standard therapy. Patients underwent 24-h electrocardiogram (ECG) monitoring with estimation of ventricular and supraventricular extrasystolic activity and main characteristics of cardiac rhythm variability on the 3rd and 14th days of treatment.

Results

Estimation of supraventricular activity during 24 hours revealed significant reduction of the number of extrasystoles both in the main and control groups (reduction from 40.5 (21.8-122.5) to 29.5 (6-68.3) in the main group (p<0.01) and reduction from 10 (0-18) to 7.5 (3.8-56.3) in the control group (p<0.05). Differences between groups were

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statistically significant. In the main group the number of ventricular extrasystoles reduced significantly from 7.5 (1.8-31.8) to 1 (0-18.8), p<0.05. Comparison of cardiac rhythm variability parameters revealed significant increase of SDNN (by 38% and 28.7% in main and control groups, respectively, p<0.01) and HF in both groups (p<0.05), pNN50 and VLF in the main group by 41.4% and 21.5%, respectively (p<0.01, p<0.05).

Conclusion

Addition of omega-3 PUSFA (1g/day) supplement to the complex therapy of patients with unstable angina leads to reduction of ventricular arrhythmic activity and increases total reserve of neurohumoral regulation.

Key words

Omega-3 polyunsaturated fatty acids, unstable angina, arrhythmic activity, cardiac rhythm variability.

Introduction

Coronary heart disease (CHD) still keeps the leading position between the causes of morbidity and mortality in the majority of world countries. The risk of fatal arrhythmias development due to electric instability and damage of membranes of cardiomyocytes is one of factors that influence CHD outcomes, and in particular its acute forms. Due to this CHD treatment considers the use of antiarrhythmic therapy restricted to beta-blockers and amiodarone that should not be used for long-term treatment because of adverse effects related to iodine presence [5, 6].

The above-mentioned drawbacks explain the necessity of search for new drugs suitable for careful correction of proarrhythmic activity. Due to this it seems to be promising to use omega-3 polyunsatutated fatty acids (PUSFA) that positive influence on myocardial arrhythmic activity mediated by change of the structure of cardiomyocytal membranes has been proved by numerous studies. Omega-3 PUSFA also has positive effect on cardiac rhythm variability (CRV). CRV impairment precedes the development of fatal arrhythmias, and several CRV parameters can be predictors of sudden cardiac death [3, 7].

The **objective** of this study was to evaluate the impact of omega-3 PUSFA on myocardial arrhythmic activity and characteristics of cardiac rhythm variability in patients with unstable angina.

Materials and methods

We've conducted an open randomized trial that involved 41 patients aged 45-70 years and diagnosed with coronary heart disease (CHD): unstable angina (UA) based on clinical infestationsons and electrocardiography (ECG) results. All patients underwent standard complex therapy that included angiotensin-converting enzyme (ACE) inhibitors (enalapril 5-15 mg/day), beta-blockers (bisoprolol 2.5-10 mg/day), statins (atorvastatin 20-40 mg/day), antianginal drugs (long-acting nitrates: isosorbide-5-mononitrate 20-40 mg/day), anticoagulants (heparin 20000 U/day subcutaneously with consequent dose reduction), double antiplatelet therapy (aspirin 75 mg/day+clopidogrel 75 mg/day).

Inclusion criteria were the following: left ventricular ejection fraction (estimated with echocardiography) ≥45%, lack of intolerance of prescribed drugs, signed informed consent.

Exclusion criteria were the following: intolerance or adverse effects of a prescribed drug, cardiogenic shock, disseminated intravascular coagulation (DIC) syndrome; chronic renal and hepatic insufficiency, chronic kidney and liver failure, thrombolytic therapy, lack of signed informed consent.

Patients were subdivided into two groups: omega-3 PUSFA supplement (1g/day) was added to the therapy in the first (main) group, whereas the patients of the second (control) group received standard therapy.

Patients underwent 24-h ECG monitoring with estimation of single and paired ventricular (SVE and PVE, respectively) and supraventricular extrasystolic (SSVE and PSVE, respectively) activity on the 3rd and 14th days of treatment. We estimated the main characteristics of CRV: standard deviation of the NN interval (SDNN), a representative of parasympathetic and sympathetic regulation (pNN50), low frequency (LF) – a representative of sympathetic influences, high frequency (HF) – a representative of parasympathetic influences, very low frequency (VLF) – a representative of humoral influences. Since statistical analysis of data in both groups revealed non-normal distribution of arrhythmic episodes (according with Kolmogorov-Smirnov criterion, d_{max}<0.2), we used the methods of non-parametric statistics (sign test (ST), Mann-Whitney test). CRV parameters had normal distribution (Kolmogorov-Smirnov criterion d_{max}>0.25), and statistical analysis of results was performed using parametric methods (Student's test) ans Statistica 6.0 software.

Table 1. **Arrhythmic activity of myocardium in patients with UA estimated on the 3rd and 14th days of treatment**

Group	Day of monitoring	Characteristics	Median	25th percentile	75th percentile	Used statistical test and significance
Main group (n=24)	3rd	SSVE	40.5	21.8	122.3	-
		PSVE	3	0	3	-
		SVE	7.5	1.8	31.8	-
		PSVE	0.5	0	2	-
	14th	SSVE	29.5	6	68.3	ST, p<0.01
		PSVE	0	0	0.25	ST, p<0.05
		SVE	1	0	18.8	ST, p<0.05
		PSVE	0	0	0	ST, p<0.05
Control group (n=17)	3rd	SSVE	10	3.8	56.3	-
		PSVE	0	0	1	-
		SVE	1	0	1.25	-
		PSVE	0	0	0	-
	14th	SSVE	7.5	0	18	ST, p<0.05
		PSVE	0	0	0	Non significant
		SVE	1	0	78	Non significant
		PSVE	0	0	0	Non significant

Results

Patients of the main and control groups had initially high level of arrhythmic activity that had been reduced with higher or lower significance by the 14th day of treatment (Table 1).

Estimation of supraventricular extrasystolic activity within 24h revealed significant decrease of the number of extrasystoles in both main and control groups, but the statistical significance of the results was higher in the main group (reduction from 40.4 (21.8-122.5) to 29.5 (6-68.3) in the main group, p<0.01; reduction from 10 (3.8-56.3) to 7.5 (0-18) in the control group, p<0.05). The differences between the groups were statistically significant (p<0.05). The number of ventricular extrasystoles reduced significantly only in the main group (from 7.5 (1.8-31.8) to 1 (0-18.8) p<0.05.

The main parameters of CRV in patients with UA within 24 h are present in the Table 2.

Comparison of CRV parameters measured within 24 h in main and control groups reveals significant increase of SDNN (by 38 and 28.7% in the main and control groups, respectively, p<0.01). HF increased significantly (p<0.05) in both groups, and pNN50 and VLF increased by 41.4% and 21.5%, respectively, in the main group (figure 1, p<0.01, p<0.05, respectively).

Discussion

Estimation of myocardial arrhythmic activity in patients with UA reveals reduction of PVE and SVE, SSVE and PSVE in the main group, whereas in the control group just the number of SSVE decreased significantly. Our results go along with the results of other studies that demonstrated antiarrhythmic effect of

Table 2. **CRV parameters in the groups of patients with UA**

Parameters	Main group		Control group	
	3rd day	14th day	3rd day	14th day
SDNN	100.9±9.9	139.2±21.2**	104.1±12.1	134.0±9.5**
pNN50	3.44±2.09	6.61±1.77*	4.14±0.69	5.36±1.34
LF	493.3±86.1	482.5±81.2	497.2±50.0	501.0±77.1
HF	209.8±55.8	296.6±62.0*	278.1±51.5	343.1±98.4*
VLF	1582.5±152.0	1922.9±171.3**	1685.7±112.7	1887.2±141.5*

*- significant differences, p<0.05 ** - significant differences, p<0.01

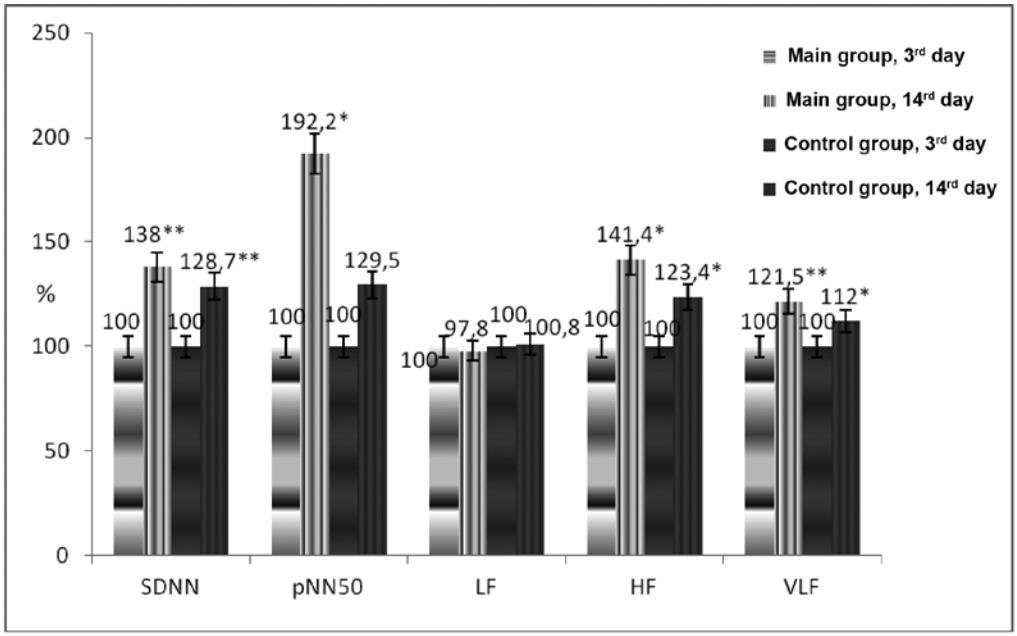

Figure 1. CRV parameters in the studied groups (* - p<0.05, ** - p<0.01)

omega-3 PUSFA in patients with CHD that resulted in reduced ectopic arrhythmic activity. Described mechanisms include as the stabilization of the membrane of cardiomyocytes as the influence on fast sodium and slow calcium channels [4]. Particular efficacy of this supplementary in patients with UA may be explained by susceptibility of cardiomyocytes to the therapy with omega-3 PUSFA, since there are no big necrotic areas in the myocardium in case of UA, unlike acute myocardial infarction. Patients that received omega-3 PUSFA demonstrated significant improvement of temporal CRV parameter pNN50, and frequency parameters HF and VLF increased significantly in both groups. These changes have high prognostic value, since increased values of CRV play an important role in the reduction of fatal arrhythmias risk [1, 2].

Conclusions

1. Addition of omega-3 PUSFA (1g/day) supplement to the complex therapy of patients with unstable angina leads to reduction of ventricular arrhythmic activity.
2. Omega-3 PUSFA increase total reserve of neurohumoral regulation and increase pNN50 values that is important for future prevention of fatal arrhythmic complications.

Conflict of interest: None declared.

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