ACTA MEDICA LITUANICA. 2005. VOLUME 12 No. 4. P. 77–81

The influence of trimetazidine on ventricular late potentials in patients after myocardial infarction

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Background. Myocardial infarction can disturb generation and extension of electrical activity in the heart. Trimetazidine exerts a cytoprotective influence on the heart cells.

Materials and methods. This study involved 47 people. The examined group consisted of 31 people and the control group of 16 people. The examined group was divided into two groups: with and without the presence of ventricular late potentials. All patients underwent ultrasonocardiography, stress test, and high resolution signal-averaged ECG was performed before and after the administration of a single dose of trimetazidine.

Results. Trimetazidine exerts an influence on RMS_{40} in patients after myocardial infarction. Statistically significant ($p < 0.05$) increase of RMS_{40} (from 50.1 to 53.4 uV) occurred after a single 60 mg dose of trimetazidine. The difference was greater in the subgroup without the presence of ventricular late potentials ($p < 0.001$).

Conclusion. Administration of 60 mg trimetazidine to patients after myocardial infarction does not influence the occurrence of new late potentials or the disappearance of the existing ones.

Key words: myocardial infarction, trimetazidine, ventricular late potantials

INTRODUCTION

In many cases, myocardial infarction can cause limited heart muscle necrosis. Cardiac muscular tissue which outlasted ischemia may be in subepicardial, subendocardial or intramural regions of the heart (1–3).

The elements of connective tissue create barriers which increase the separation between muscular bundles, change their parallel orientation, elongate the electric excitability and disturb ventricular activation (4–10).

Ventricular late potentials are a manifestation of fragmented and delayed activation of the myocardium. They may be recorded non-invasively from the body surface by the high resolution and signal-averaged ECG or directly from the heart (2, 11–16).

Trimetazidine (chemical name 1-(2,3,4-trimetaxybenzyl)-piperazine dihydrochloride) has been used in the treatment of ischemic heart disease for over 30 years (17–20). Trimetazidine has an antianginal effect due to preservation of electrical excitability and also decreases cell degradation in anoxic condition (19, 21–26). It improves the efficiency of oxygen consumption, as well as protects cardiac cells against the decreasing intracellular level of ATP and accumulation of H^+. It also limits accumulation of Na^+ and Ca^{2+} inside cardiac cells and restricts free oxygen radical production (18, 19, 27–29).

Considering triametazidine's cytoprotective action and mechanisms developing ventricular late potentials it seems justifiable to consider also the influence of the drug on the parameters of high resolution and signal-averaged ECG.

MATERIALS AND METHODS

Our research was carried out on a group of 47 people, of them sixteen, aged from 24 to 56 years (mean, 29.688 ± 7.552) formed the control group with no cardiovascular history data.

A group of 31 people, aged 37 to 72 years (mean, 57.16 ± 9.8) after myocardial infarction was examined: 25 men aged from 37 to 72 years (mean, 56.96 ± 9.67) and 6 women aged from 45 to 72 years (mean, 60.5 ± 10.34). In the examined group,

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patients with recorded ECG sinus rhythm, without bundle branch block and without episodes of ventricular tachycardia (VT) were included. None of them had clinical symptoms of VT. Patients with inferior wall infarction or a combination of inferior wall and other infarction site were predominant in the examined group (24 people, 77.4%). The period after acute myocardial infarction ranged from 2 month to 19 years (mean, 57.6 ± 59.1 months). Stable angina pectoris was diagnosed in all of the patients. Before inclusion into the study all those patients had their cardiovascular anamnesis taken and underwent physical examination twice in a 24-hour period. Standard 12-lead ECG and high resolution signal-averaged ECG (SAECG) was recorded twice in a 24-hour period with the use of a standard computer system (MEDEA Gliwice, Poland). The signals were obtained from orthogonal leads, amplified, averaged and combined into a vector magnitude – filtered QRS complex. Filter frequencies of 40 to 250 Hz were used (30–32).

Analysis of the filtered QRS complex included:

• U-QRS – the total filtered QRS duration

• RMS_{40} – the root-mean square voltage of the terminal 40 ms of the filtered QRS

• LAS_{40} – the duration of low-voltage oscillation remained below 40 uV of the filtered QRS complex (33).

The onset and offset of QRS complex were determined by computer algorithm as a midpoint of a 5 ms segment in which the average signal exceeded the mean noise level plus 3 standard deviations and could be verified visually (34–36).

The evidence of late potentials was based on ACC Expert Consensus Document, January 1996 (15, 37).

A minimum of 401 QRS complexes were recorded. The time of registration was from 5 to 9 minutes depending on the patient's heart rate.

All patients underwent ultrasonocardiography with an estimation of systolic (ESD) and diastolic (EDD) left ventricular dimension, intraventricular septum (IVS), posterior wall (PW), and ejection fraction (EF%) (38). They also had a cycloergometer test to obtain the submaximal heart rate limit according to the standard protocol or till the appearance of symptoms which prevented carrying out the test. The duration of the effort, workload, systolic (SBP) and diastolic (DBP) blood pressure, heart rate (HR) at peak of exercise and rate pressure product (RPP) were estimated (39–42).

Table 1. **Value of ejection fraction (EF%) in the group with and without ventricular late potentials (VLP) before and after trimetazidine administration**

EF [%]	Examined group						Control group	
	Total		Subgroup with VLP		Subgroup without VLP			
	Before TMZ	After TMZ	Before TMZ	After TMZ	Before TMZ	After TMZ	Before TMZ	After TMZ
> 50	4 (12.9%)	6 (19.35%)	1 (11.11%)	1 (11.11%)	3 (13.64%)	5 (33.72%)	16 (100%)	16 (100%)
50–40	22 (70.97%)	20 (64.52%)	7 (77.78%)	7 (77.78%)	15 (68.186%)	13 (59.1%)		
39–20	5 (16.13%)	5 (16.13%)	1 (11,11%)	1 (11.11%)	4 (18.18%)	4 (18.18%)		
	N = 31	N = 31	N = 9	N = 9	N = 22	N = 22	N = 16	N = 16
Statistical difference	< 0.001		> 0.05		< 0.001		> 0.05	
	> 0.05							

Table 2. **Duration of ORS complex in the examined and control groups**

T-QRS [ms]	Examined group						Control group	
	Total		Subgroup with VLP		Subgroup without VLP			
	Before TMZ	After TMZ	Before TMZ	After TMZ	Before TMZ	After TMZ	Before TMZ	After TMZ
Middle	84.67	84.419	88.444	88.333	83.136	82.818	76.563	76.125
SD	7.799	8.131	8.048	8.093	7.324	7.762	6.366	6.206
SEM	1.401	1.460	2.683	2.698	1.562	1.655	1.592	1.552
N	31	31	9	9	22	22	16	16
Statistical difference	> 0.05		> 0.05		> 0.05		> 0.05	

Table 3. **U-QRS value (total filtered ORS duration) in the examined and control groups**

U-QRS [ms]	Examined group						Control group	
	Total		Subgroup with VLP		Subgroup without VLP			
	Before TMZ	After TMZ	Before TMZ	After TMZ	Before TMZ	After TMZ	Before TMZ	After TMZ
Middle	116.484	116.419	123.778	124.333	113.500	113.182	105.625	105.438
SD	10.914	11.230	8.628	9.513	10.473	10.386	7.588	7.257
SEM	1.96	2.217	2.876	3.171	2.233	2.214	1.897	1.814
N	31	31	9	9	22	22	16	16
Statistical difference	>0.05		>0.05		>0.05		>0.05	

Table 4. **RMS40 value (Root-mean square voltage of filtered ORS) in the examined and control groups**

RMS40 [μV]	Examined group						Control group	
	Total		Subgroup with VLP		Subgroup without VLP			
	Before TMZ	After TMZ	Before TMZ	After TMZ	Before TMZ	After TMZ	Before TMZ	After TMZ
Middle	50.140	53.411	22.232	22.039	61.557	66.245	72.793	71.518
SD	36.435	38.475	7.559	5.715	37.474	38.832	31.669	30.052
SEM	6.544	6.910	2.520	1.905	7.989	8.279	7.917	7.513
N	31	31	9	9	22	22	16	16
Statistical difference	<0.05		>0.05		<0.001		>0.05	

Table 5. **LAS40 value (duration of low voltage oscillation remained below 40 uV of the filtered ORS complex) in the examined and control groups**

LAS40 [ms]	Examined group						Control group	
	Total		Subgroup with VLP		Subgroup without VLP			
	Before TMZ	After TMZ	Before TMZ	After TMZ	Before TMZ	After TMZ	Before TMZ	After TMZ
Middle	28.258	27.194	41.667	42.000	22.773	21.136	25.063	24.500
SD	11.936	12.478	8.000	6.727	8.400	8.532	8.062	7.285
SEM	2.144	2.241	2.667	2.242	1.791	1.819	2.015	1.821
N	31	31	9	9	22	22	16	16
Statistical difference	>0.05		>0.05		>0.05		>0.05	

Two patients did not undergo the cycloergometer test due to some contraindications: thrombus in the left ventricle lumen with a severe left ventricular dysfunction and in the second case owing to mitral valve stenosis (40).

All patients were given a single dose of 60 mg trimetazidine twenty-four hours after the first examination. Two hours after trimetazidine had been given, the same protocol study as the previous day was repeated.

Two subgroups were appointed: patients with (present, p) and without (absent, a) ventricular late potentials in SAECG (pVLP and aVLP).

The homogenity of the examined group and its subgroups was determined by a chi-square test. Student's test for connected variables was used.

RESULTS

Table 1 illustrates the value of ejection fraction in the examined and control groups. Patients from the examined group were divided into three subgroups on the basis of EF values: 39–20%, 50–40%, over 50%. The EF value was over 50% in controls.

Table 2 shows the duration of QRS, Table 3 the total filtered QRS duration (U-QRS) and Table 5 the duration of low voltage oscillation (LAS 40). No statistical differences among the analyzed parameters before and after the administration of TMZ were found.

Table 4 depicts changes of the RMS40 value. A significant statistical increase of the RMS40 value af-

ter the administration of TMZ in the subgroup without VLP was observed.

DISCUSSION

Trimetazidine exerts an influence on RMS_{40} in patients after myocardial infarction. A statistically significant ($p < 0.05$) increase of the RMS_{40} (from 50.1 to 53.4 uV) occurred after a single 60 mg dose of trimetazidine. The difference was greater in the subgroup without ventricular late potentials ($p < 0.001$). In this study, no difference was noted between the signal-averaged ECG's parameters before and after the administration of trimetazidine in the subgroup with late potentials present. A statistically significant improvement of the left ventricular ejection fraction was observed after the administration of trimetazidine (3, 41, 42) only in the subgroup without late potentials.

However, comparing ejection fraction between both subgroups (with and without ventricular late potentials) no statistically significant difference was found. Nevertheless, a low EF% (below 50%) was noted in 86.36% of the subgroup without VLP and in 88.8% of the subgroup with VLP. The difference was greater after administration of TMZ (respectively 77.28% and 88.8% of the patients with EF below 50%).

No statistical differences were found in the cycloergometer test of the whole group and subgroups before and after the administration of 60 mg TMZ.

The results obtained in our study are not similar to the ones described in other studies. It maybe due to different kinds of patients' illnesses: our survey group consisted of patients after myocardial infarction compared to patients with stable angina in other references.

CONCLUSION

Administration of a single dose of 60 mg trimetazidine to patients after myocardial infarction does not influence the occurrence of new late potentials or the disappearance of already existing ones.

Received 17 June 2005
Accepted 2 November 2005

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