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TO THE QUESTION OF EFFICACY AND SAFETY OF FORTELYZIN® THERAPY ON ACUTE CORONARY SYNDROME: TWO CLINICAL CASES

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SUMMARY

The article presents two clinical cases of successful reuse thrombolytic drug Fortelyzin® in the total dose of 25-30 mg observed by the authors in patients with acute coronary syndrome with ST-segment elevation, treated in the urgent cardiology department of the State budget institution of Ryazan region «Regional clinical hospital». Patients belonged to different gender and age groups and had various short term forecast on the scale TIMI or GRACE, different duration of ischemic damage of the myocardium until reperfusion. The above observations confirm the high safety and efficiency of Fortelyzin® in acute coronary syndrome.

Key words: *acute coronary syndrome, thrombolytic therapy, fortelyzin*

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INTRODUCTION

To carry out thrombolysis on acute coronary syndrome with ST-elevation the following preparations such as streptokinase, tissue plasminogen activator TPA (alteplase, tenecteplase) and prourokinase have been offered in the National clinical recommendations [1]. However, in Russian cardiology practice, a new thrombolytic (clot-busting drug) Fortelyzin® («SuperGene», Russia) has appeared recently. It has been included into «the Vital and Essential Drugs list» by the Russian Government since 2015 [2]. The above-mentioned clot-busting drug has a sufficient evidence base of efficacy and safety of its therapy on acute coronary syndrome with ST-elevation, although there is comparatively less experience in its implementation [3, 4].

In this regard, the following accumulation of experience and the analysis of clinical monitoring of successful reuse of thrombolytic drug Fortelyzin® is actual because it is a good example of reliability and safety of the preparation.

Clinical case №1. Patient K., 66 years old, male, was firstly hospitalized by the ambulance to the intensive therapy ward of the urgent cardiology department (SBI of Ryazan region «Regional clinical hospital») suffering from typical angina pains. The period of clinical deterioration lasted 7 h. The anamnesis included arterial hypertension (without regular treatment), gout (polyarthritis for 10 years, recrudescence – allopurinol). During the examination: serious condition. There was vesicular breathing, without wheezing. Heart rhythm was regular, arterial normotonia, stable hemodynamics. There was no hypostasis. The body mass index of the patient was 34 kg/m^2.

The ECG showed sinus rhythm, ischemia and myocardial damage of the lower wall the left ventricle: ST-elevation in II, III, AVF (picture 1a). According to the ECG data, the existence of akinesian zones of the low segments of the left ventricle was confirmed. The blood tests revealed the increase of creatinephosphokinase-MB (CPK-MB) level, troponin T level, cholesterol level; APPT (activated partial thromboplastin time) – 23,4 sec.

The patient was diagnosed with ischemic heart disease (IHD): acute coronary syndrome with ST-elevation. Hypertension 3rd stage, III degree, risk 4. Obesity I degree. Chronic heart failure (CHF) I degree. Gout, chronic polyarthritis without exasperation. Risk of death in 2 weeks according to TIMI grade – 4 points (19,9%), high risk of death in hospital according to GRACE grade – 143 points (more 3%) [5, 6].

In obedience with «The order of medical treatment of the patients with cardio-vascular diseases» approved by the Ministry of Health in 2012 [7], the above-mentioned patient was treated with a system thrombolytic therapy Fortelyzin® in 15 mg dose on the scheme of «double bolus» (in 7,5 h from the beginning). The concomitant treatment: clopidogrel 300 mg (in the ambulance), acetylsalicylic acid 250 mg (in the ambulance), unfractionated

heparin (UFH) intravenous bolus 60 IU/kg, infusion 12 IU/kg/h, isosorbide dinitrate intravenous infusion 10 mg.

The control ECG showed that after the above-mentioned thrombolytic therapy, the ST elevation myocardial infarction (STEMI) preserved. In this regard, in 8.5 h from the symptoms development the patient was taken to the cath lab for an angioplasty. During the angioplasty, a multifocal atherosclerosis was found out, with stenosis of the anterior interventricular artery (AIA) – up to 80% (TIMI 3), stenosis of the circumflex artery (CA) – up to 90% (TIMI 3), stenosis of the right coronary artery (RCA) – up to 95% (TIMI 2). Further, the patient was given a balloon angioplasty and arthroplasty of the stenosis zones RCA with a bare metal stent, which finished with the evidence of a "no-reflow" phenomenon (the lack of blood flow in the artery below of the stent, TIMI 0).

In the ECG picture, that treatment stage (in 9 h from the beginning) was accompanied by an ST-elevation preservation and an atrio-ventricular blockage (AV- blockage) 2nd-3rd degree appeared (picture 1b).

That clinic diagnostic situation (reoccurrance of occlusion on the blocked branch of the coronary artery after the angioplasty (percutaneous coronary intervention (PCI)) with complications, a negative ECG development), and also the absence of antagonists IIb/IIIa of the glycoprotein platelet receptors caused the necessity of the second 10 mg dosing of thrombolytic drug Fortelyzin® (in 9 h from the symptoms development) with the accompany of continuing infusions UFH and isosorbide dinitrate.

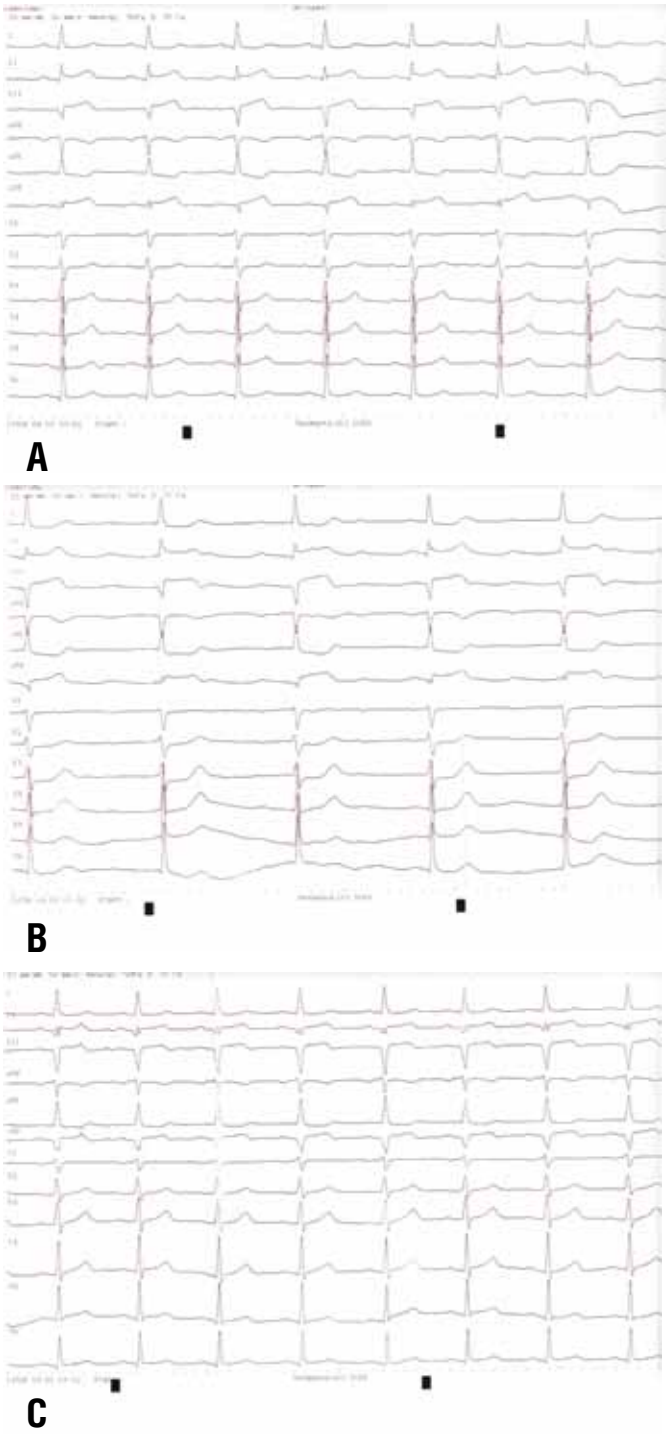
In 90 min after the second dosing of Fortelyzin® in the ECG, there were not any signs of AV- blockage, in 180 min there was a decrease of the ST- elevation by more than 50% (picture 1c).

In 50 h, the patient was replaced from the intensive therapy ward to an ordinary ward of the urgent cardiology department.

During the following 14 days, the patient was treated with a double antiaggregant therapy including clopidogrel, acetylsalicylic acid in standard doses, atorvastatin 20 mg/day, enalapril 20 mg/day, from the third day – metoprolol 50 mg/day. There were not any angina pains equal to myocardial ischemia. In the blood tests, an objective development of increase occurred during the first 12-24 h, which was followed by an increasing CPK-MB level, the above-normal troponin T concentration had been preserving for 9 days. During the 2nd day, an increase of APPT up to 98-44,7 sec (at 2-3 times) occurred on the UFH infusion background. The control ECG showed dynamic signs of transformation from an acute phase to a subacute phase of Q-wave MI of the lower wall the left ventricle. The Holter monitoring on the 7th day showed rare single ESV and ESSV. Any ischemic changes ST-T did not occur.

During the treatment time, the patient did not have any clinic-lab signs of interior or exterior bleeding.

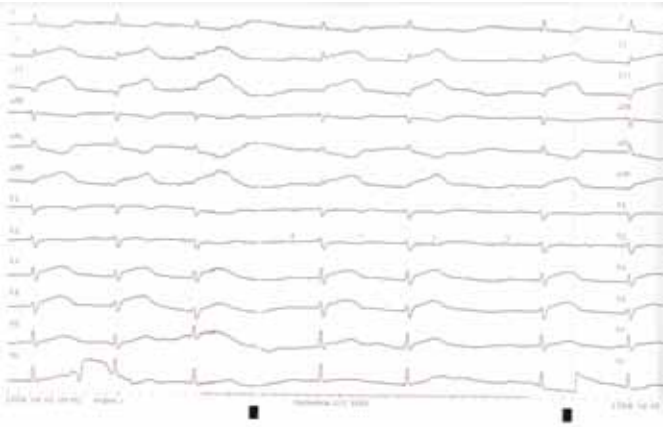
Clinical case №2. Patient H., 81 years old, female, was firstly hospitalized by the ambulance to the intensive therapy ward of the urgent cardiology department (SBI of Ryazan region «Regional clinical hospital») with the diagnosis - acute coronary syndrome with ST-elevation in 2 h after the disease beginning. At entry, there were complaints about angina pains in the region of the heart, general weakness. The anamnesis included arterial hypertension (for about 15-20 years, treated with enalapril, bisoprolol, acetylsalicylic acid), arthropathy deformans of big joints. During the examination: serious condition. There was vesicular breathing, without wheezing. Irregular rate of heart contractions (46-55 /min), arterial normotonia, stable hemodynamics. Pitting edema of knees and feet. The body mass index of the patient was 24 kg/m^2.



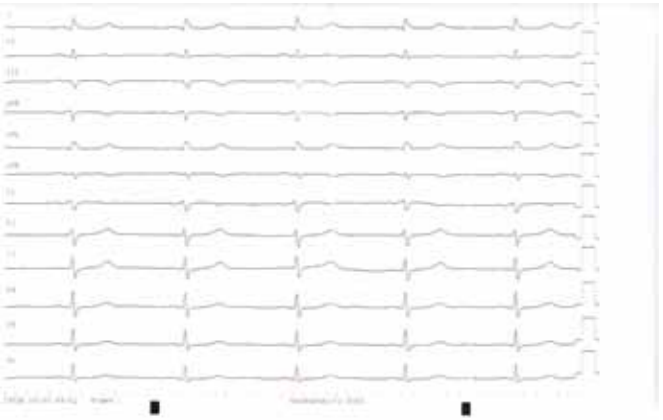
Picture 1. The ECG picture of patient K. a) before Fortelyzin® dosing; b) after the percutaneous coronary intervention; c) after the second dosing of Fortelyzin®

The ECG showed an AV-blockage 2nd degree 1st type, an ischemia and a myocardial injury of the lower wall the left ventricle: ST-elevation in II, III, AVF, V3-V5 (picture 2a). In the blood tests there were normal levels of CPK-MB and troponin T, normal cholesteremia, APPT – 22,9 sec, hemoglobin 100 g/l, hematocrit 30,2%.

The patient was diagnosed with IHD: acute coronary syndrome with ST-elevation. Hypertension 3rd stage, III degree, risk 4. CHF 2a degree. AV- blockage 2nd degree 1st type. Slight anemia. Arthropathy deformans. Risk of death in 14 days according to TIMI grade – 3 points (13,2%), high risk of death in hospital according to GRACE grade – 183 points (more 3%) [5, 6].

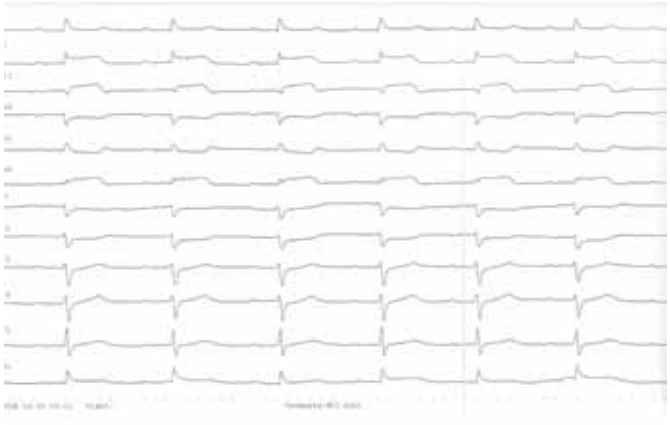


A



B

Picture 2. The ECG of the patient X. a) before Fortelyzin® dosing; b) after the first Fortelyzin® dosing



A

B

Picture 3. The ECG of the patient H. a) before the second dosing of Fortelyzin®; b) after the second dosing of Fortelyzin®

The beginning of the treatment: system thrombolytic therapy with Fortelyzin® in 15 mg dose on the scheme of «double bolus» (in 3 h from the beginning), clopidogrel 75 mg/day, acetylsalicylic acid 250 mg once, and then 100 mg a day; UFH intravenous bolus 60 IU/kg, with further infusion 12 IU/kg/hour during 48 h, isosorbide dinitrate intravenous infusion 10 mg.

In 60-90-180 min after the above-mentioned thrombolysis the control ECG showed stable sinus rhythm, dynamic of the acute stage of the low segments of the left ventricle (decreasing of ST-elevation by 50-70%), in 24 h – segment ST was on the isoline, T-wave inversion in III, AVF (picture 2b).

The control ECG in 12 h from the beginning showed the existence of akinesian zones of the low segments of the left ventricle. The blood tests in 12-24 h revealed the rise of CPK-MB level, troponin T level, APPT –74 sec, hemoglobin 92 gm/l, hematocrit 28,2%. In addition to the above-mentioned treatment, atorvastatin 20 mg/day, lizinopril 10 mg/day, omeprazol 20 mg/day were perfomed

During the following two days the patient's condition was stable, angina pains did not occur. In 60 days from the beginning, a relapse of ischemic pain in the chest cavity took place. According to the ECG: AV-blockage 1st degree, a reoccurrence of ST-elevation in II, III, AVF (picture 3a).

Due to the clinical and ECG sings of a myocardial infarction reoccurrence, the patient was given the second 15 mg dosing of thrombolytic therapy Fortelyzin® on the scheme of «double bolus» (in 20 min from the beginning). Besides that the following treatment plan was performed: UFH intravenous bolus 60 IU/kg with further infusion 12 IU/kg/hour during 48 h, isosorbide dinitrate intravenous infusion 10 mg, morphine 10 mg intravenously, a further antiaggregant therapy in the former dosage.

In 90-180 min after the above-mentioned thrombolytic therapy the patient's ECG results showed a stable sinus rhythm, signs of the recovery of myocardial perfusion of the low segments of the left ventricle – segment ST was on the isoline (picture 3b).

Taking into consideration the myocardial infarction reoccurrence, in 1 day the patient was performed with cardio angiography, which revealed the AIA with stenosis up to 50% (TIMI 3), the CA with uneven limits (TIMI 3), the RCA with stenosis up to 98% (NIMI 0-1). The patient was given a balloon angioplasty and arthroplasty of the stenosis zones RCA with a bare metal stent.

In 93 h, the patient was replaced from the intensive therapy ward to an ordinary ward of the urgent cardiology department. During further 15 days the patient had a stable condition. The blood tests showed the normalization of myocardial necrosis markers, APPT – 41 sec. The Holter monitoring on the 15th day did not reveal any ischemic changes of segment ST-T. But a frequent ESV (1650 per day) made it necessary to prescribe cordaron 600 mg/day with further decreasing dosage up to «supporting». Any other medication treatment was not performed.

During the treatment time, the patient did not have any clinic-lab signs of interior or exterior bleeding. Control blood tests: hemoglobin 101 g/l, hematocrit 30,4%.

CONCLUSION

Both above-mentioned cases of the successful second dosing of thrombolytic (decreasing of ST-elevation level in 180 min after the thrombolytic therapy and an infarction artery permeability

according to the cardio angiography data). Medication safety is also illustrated by the absence of any hemorrhagic complications or allergic reactions, taking into consideration that all the patients were of different gender, age, with different co-morbid diseases, had a short-time prognosis period of TIMI and GRACE grades, and time-periods of ischemic injures of myocardium to the reperfusion moment.

All these facts confirm the appropriateness of Fortelyzin® usage in every-day routine work. The scientific interest to this preparation is rising and it is worth further studying and using.

BIBLIOGRAPHY

1. *Clinical guidelines. Diagnosis and management of ST-segment elevation myocardial infarction. Kardiologicheskij Vestnik. 2014; 4: 5-60 [in Russian].*
2. *The Vital and Essential Drugs list for 2016: the decree of the Government of the Russian Federation from 26.12.2015 № 2724-p. Sobraniye zakonodatelstva Rossiyskoj Federacii. 2016; 2: 413 [in Russian].*
3. *Markin S.S., Semenov A.M., Markov V.A. et al. The trial of new made in Russia Thrombolytic Fortelyzin® in patients with acute myocardial infarction. Sibirskij Medicinskij Zurnal. 2012; 27 (1): 27-32 [in Russian].*
4. *Markov V.A., Duplyakov D.V., Konstantinov S.L. et al. Fortelyzin® versus Metalyse® in ST-segment elevation myocardial infarction: results of multicenter randomized trial FRIDOM 1. Kardiologicheskij Vestnik. 2017; 3: 52-59 [in Russian].*
5. *Raposeiras-Roubin S., Abu-Assi E., Cabanas-Grandio P., et al. Walking beyond the GRACE (Global Registry of Acute Coronary Events) model in the death risk stratification during hospitalization in patients with acute coronary syndrome: what do the AR-G (ACTION [Acute Coronary Treatment and Intervention Outcomes Network] Registry and GWTG [Get With the Guidelines] Database), NCDR (National Cardiovascular Data Registry), and EuroHeart Risk Scores Provide? JACC Cardiovasc Interv. 2012; 5 (11): 1117-1125.*
6. *Brilakis, E.S., Mavrogiorgos N.C., Kopecky S.L., et al. Validation of the TIMI risk score for ST-elevation acute myocardial infarction in a community-based coronary care unit registry. Circulation. 2001; 104 (suppl. II): 380.*
7. *The order of rendering of medical aid to patients with cardiovascular disease: order of Ministry of health of Russia 15.11.2012 № 918н [Electronic resource] // URL: https://www.rosminzdrav.ru/documents/9130-prikaz-ministerstva-zdravoohraneniya-rossiyskoy-federatsii-ot-15-noyabrya-2012-g-918n-ob-utverzhdenii-poryadka-okazaniya-meditsinskoy-pomoschi-bolnym-s-serdechno-sosudistymi-zabolevaniyami (Date of access 11.12.2017) [in Russian].*