The results of the use of thrombolytic therapy in acute myocardial infarction at the prehospital and hospital stage

R. Kattakhanova[1*] and *O.* Umirzakov[1]

[1]Fergana Medical Institute of Public Health, 2A, Yangi Turon Street, Fergana, 150100, Uzbekistan

Abstract. The aim of the study was study of the use of thrombolytic therapy (TLT) in patients with myocardial infarction (MI) with ST segment elevationat the prehospital and hospital stage. The study included 181 patients with ST elevation MI. Depending on the thrombolytic used, the patients were divided into two groups: patients treated with streptokinase were included in the 1st group (n=78); the 2nd group (n=51) included patients with MI with ST segment elevation, who did not undergo TLT due to late seeking medical help or the presence of contraindications. TLT was performed both at the prehospital stage and in a hospital setting. We analyzed the time before TLT, the clinical course of MI, mortality, and complications. The time from the onset of clinical symptoms was 2.70.22 hours. The high efficiency of these thrombolytics was established in 66% of patients. Mortality during TLT was 6.4–7.7%, without TLT - 24%. Carrying out TLT in the first 3 hours from the onset of a heart attack was accompanied by a decrease in mortality to 3.4%. Not a single case of intracranial hemorrhage and allergic reactions was recorded.± TLT with streptokinase in patients with MI with ST segment elevation on the ECG in real clinical practice was characterized by high efficiency, a decrease in hospital mortality, complications, and a low percentage of side effects.

1 Introduction

Reperfusion therapy is the most effective method to reduce the risk of death and other adverse outcomes in patients with acute persistent coronary artery occlusion. The latter leads to the development of acute coronary syndrome with ST segment elevation on the ECG. The modern approach to the treatment of this category of patients is thrombolytic therapy (TLT) and/or percutaneous coronary interventions (PCI). Taking into account the low availability of timely invasive treatment, it is quite obvious that TLT is currently the most commonly used method of myocardial reperfusion for the majority of patients. The advantages of TLT include the possibility of carrying out in the early stages from the onset of myocardial infarction (MI) and the relative ease of execution. According to scientific studies, it has been shown that the use of TLT in the first 5 hours in patients with MI

* Corresponding author: rkattakhanova@inbox.ru

reduces mortality compared to placebo by 26% [1-14]. In view of the foregoing, the study of the effectiveness of TLT remains relevant to this day.

Purpose of the study -to study the clinical results of thrombolytic therapy with the use of thrombolytics - streptokinase in patients with myocardial infarction with ST segment elevation at the prehospital and hospital stage.

2 Methods

The study included 181 patients with ST-segment elevation MI who were admitted on an emergency basis to the Therapeutic Resuscitation Department of the RRCEMMP FF for the period of 2020. Inclusion criteria: anginal pain lasting more than 30 minutes in combination with ST-segment elevation on the ECG by 1 mm or more or acute blockade of the left leg of the bundle of his. The study did not include patients with acute MI with ST segment elevation who had contraindications for TLT: previous hemorrhagic stroke, ischemic stroke within the previous 3 months, signs of bleeding or recent bleeding (in the previous 2–4 weeks) or hemorrhagic diathesis, exacerbation of peptic ulcer disease, major surgery, significant head trauma in the last 3 months, suspected aortic dissection, persistent and poorly controlled arterial hypertension (BP > 180/110 mm Hg at admission). Patients who did not have contraindications for TLT depending on the used thrombolytic were divided into two groups: the 1st group (n=8) consisted of patients using streptokinase at the prehospital stage, and the 2nd group (n=122) consisted of patients using streptokinase at the hospital stage. Both groups were comparable in terms of sex and age. Group 3 (n=51; 42 men and 9 women; mean age 56.1.8 years) was formed from patients with MI with ST segment elevation who did not undergo TLT due to late seeking medical help or the presence of contraindications. The 1st group (n=8) consisted of patients with the use of streptokinase at the prehospital stage, and the 2nd group (n=122) consisted of patients with the use of streptokinase at the hospital stage. Both groups were comparable in terms of sex and age. Group 3 (n=51; 42 men and 9 women; mean age 56.1.8 years) was formed from patients with MI with ST segment elevation who did not undergo TLT due to late seeking medical help or the presence of contraindications. The 1st group (n=8) consisted of patients with the use of streptokinase at the prehospital stage, and the 2nd group (n=122) consisted of patients with the use of streptokinase at the hospital stage. Both groups were comparable in terms of sex and age. Group 3 (n=51; 42 men and 9 women; mean age 56.1.8 years) was formed from patients with MI with ST segment elevation who did not undergo TLT due to late seeking medical help or the presence of contraindications.

Streptokinase was administered at a dose of 1.5 million IU over 60 minutes in 2 stages: an intravenous test dose of 150,000 IU, then an infusion of 1,350,000 IU over 60 minutes. TLT was performed in the cardio intensive care unit under the control of the main hemodynamic parameters and ECG. Basic therapy included anticoagulant therapy with unfractionated heparin or low molecular weight heparins, antiplatelet agents, nitrates, β-blockers, ACE inhibitors, statins. To assess the effectiveness of TLT, we studied the dynamics of the ST segment of the electrocardiogram 90 minutes and 24 hours after the start of TLT and during the entire period of inpatient treatment. TLT was considered effective when the regression of ST segment elevation was more than 50% of the initial level after 90 minutes. The study also analyzed the time to TLT, the clinical course of myocardial infarction, death during the hospital period, the development of ischemic or hemorrhagic stroke, the occurrence of bleeding, other cardiac complications, including arrhythmias, recurrent infarction.

Cardiac arrhythmias were assessed using a 24-hour monitoring device on a CEDAN heart monitor.

Clinical and demographic characteristics of patients are presented in Table 1.

The study sample of patients consisted of 105 men and 25 women aged 36 to 71 years (551.7 years). The largest groups were 51–60 and 61–71 years old. Among the studied patients, persons of working age accounted for 60.6%, of which every second was employed. Anterior wall infarction was diagnosed in 61 patients, posterior-inferior wall infarction - in 59, infarction, circularly covering the walls of the left ventricle in 10 patients. Every fourth patient had a history of myocardial infarction. 59 (45%) patients had arterial hypertension, 34 (26%) had diabetes mellitus, 1 patient underwent CABG.

Table 1. Clinical characteristics of the studied patients (n=130).

Indicator	n(%)
Gender male	105 (85)
Female	25 (12)
Age ≤ 40 years	6 (4)
41–50 years old	6 (4)
51–60 years old	62 (48)
61–71 years	44 (34)
MI of the anterior wall of the left ventricle	61 (47)
MI of the posterior wall	59 (45)
MI circular LV	10 (8)
history of myocardial infarction	32 (25)
Arterial hypertension	59 (45)
Diabetes	34(26)
Cardiogenic shock, signs of acute heart failure	39 (30)

MI - myocardial infarction

Table 2. Dynamics of ECG parameters in the compared groups.

Indicator	1 group (n=8)	2 group (n=122)	3 group (n=51)
Initial ST elevation, mm	4.35 ±0.48	4.28 ±0.38	4,5±0,41
ST elevation at 90 min, mm	2.3 ±0.21	2.1 ±0.37	4.1± 0.5
ST elevation at 24 h, mm	1.1 ±0.32	1.26 ±0.33	3.8 ±0.31
Time of formation of a negative T wave, days	4.1 ±0.41	6 ±0.31	6.8 ±0.25

Upon admission to the hospital, all patients were classified as high-risk: every second patient had anginal pain, 4 patients had clinical death at the prehospital stage. 30% of patients were diagnosed with cardiogenic shock, acute heart failure class 2-4 (according to Killip) and a high risk of cardiovascular complications according to the TIMI scale.

The time from the onset of MI symptoms to the start of TLT ranged from 0.5 to 7 hours. During the first "golden hour" TLT was performed in 28 (22%) patients, within 2-3 hours - in 61 (47%), 4 -6 h - in 39 (30%), later than 6 h - in 2 (1.5%). The mean time to the onset of thrombolysis was 2.70.2 hours. In the 1st group, the time to TLT was 1,1±0,6 hours, in the 2nd group — 2,3±0,2 hours, that is, the time savings with prehospital TLT was 48 min ($p<0.05$). In the 1st group, effective thrombolysis took place in 8 patients. In general, in this group, there was a regression of the initial ST segment elevation by 42% after 90 minutes from the start of TLT and by 71% after 24 hours. In group 2, effective thrombolysis was observed in 122 patients, which was accompanied by a decrease in the ST segment from 4.28±0.38 mm to 2.1±0.37 mm after 90 minutes and to 1.26±0.33 mm after 24 hours (Table 2).

As can be seen from Table 2, the regression of ST segment elevation after 90 minutes in the 1st and 2nd groups was significantly more pronounced compared to the 3rd group. The period of formation of a negative T wave was significantly shorter in the 1st group. In 8 (100%) patients of group 1 and 122 (100%) patients of group 2, TLT in combination with

complex therapy contributed to the rapid relief of pain and stabilization of cardiac hemodynamics, which also indicated the achievement of reperfusion. Of the 130 patients included in the study, 9 (6.9%) people (7 men and 2 women) died during inpatient treatment with Q-MI, predominantly of the anterior wall of the left ventricle (in 5 patients, the current MI was repeated). The average age of the deceased was 58,1±1,3 years. In the 1st group, there were no lethal outcomes, in 2 - 9 (7.3%), at the same time, mortality rates in these groups differed significantly. In group 3 out of 51 patients 12 (24%) died.

The immediate cause of death in patients who received TLT was cardiogenic shock and pulmonary edema (n=8), myocardial rupture with the development of pericardial hemotamponade (n=1). An analysis of mortality, taking into account the time before the start of TLT, showed that out of 89 patients who underwent thrombolysis in the first 3 hours from the onset of MI, 3 (3.4%) patients died. With TLT performed at a later date, 6 (14.6%) of 41 patients died. When analyzing TLT complications, it turned out that bleeding was registered in 5 (3.8%) patients: in group 1 - in 0 (0%) patients, in group 2 - in 5 (3.8%) patients. “Small” bleeding prevailed (from puncture sites, gums, microhematuria), only in one case was bleeding, for the correction of which blood transfusion was required. During TLT, the development of stroke, hypotension and allergic reactions were not observed. During TLT, ventricular fibrillation (VF) was detected in 9 (7%) patients, including 0 (0%) in group 1, 9 (7.3%) patients in group 2. Five patients were diagnosed with the so-called primary VF, not associated with recurrence of MI and heart failure, easily eliminated by electropulse therapy. In four cases, there wasric VF, which led to a lethal outcome. Among other arrhythmias, we detected transient AV blockade of I–III degree in two patients, paroxysms of atrial fibrillation in four patients, accelerated idioventricular rhythm in 5, and ventricular extrasystole in 27.

In order to prevent early and late rethrombosis, we used unfractionated heparin, low molecular weight heparins, and combinations of antiplatelet drugs. Recurrent MI was diagnosed by us in 8 (6.1%) patients, including 0 (0%) patients of the 1st group and 8 (6.1%) patients of the 2nd group. Clinically, MI relapses were manifested by anginal attacks, arrhythmia, aggravation of heart failure, and shock phenomena, which significantly aggravated the course of MI and increased the duration of hospital treatment. Relapses of MI occurred within 7 to 11 days from the onset of myocardial infarction. In group 3 (patients with MI without TLT), the recurrence rate did not differ significantly and amounted to 15%.

The absence of Q wave formation on the ECG, detected in 15 patients, suggests that TLT contributed to the limitation of the necrosis zone. Such myocardial infarction, referred to in the literature as “interrupted infarction”, was noted in 2 (25%) patients of the 1st group and in 13 (10.6%) - 2. The course of myocardial infarction was characterized by the absence of complications, rapid regression of the ST segment, early formation of a negative T wave. The shortening of the time period to TLT in group 1 compared to group 2 by 48 minutes was accompanied by a 2-fold increase in the number of interrupted MIs. In the remaining 6 patients of group 1 and 113 patients of group 2, despite the early terms of admission to the hospital, the formation of a pathological Q wave (QS) on the ECG was noted.

EchoCG data analysis showed that in all surviving patients who received TLT, EF was above 40% (53,9±0,7). Clinically, this corresponded to CHF 1–2 FC. Violation of the geometry of the left ventricle, due to the formation of post-infarction aneurysm, was noted in 11 (8.5%) patients. In group 3 patients, EF ranged from 29% to 60% and averaged 41±1,2.

3 Results and discussion

The most numerous in our study were groups aged 51–60 and 61–71 years. According to the literature, it has been shown that in this age range there is a high incidence of myocardial infarction. It is known that the value of the saved myocardium directly depends on the time elapsed from the moment of occurrence of occlusion to its resolution. Numerous scientific studies have shown that the optimal time before the start of TLT is 0-6 hours. Even in this time interval, the effect of reperfusion manifests itself non-linearly, being maximum during the so-called "golden hour", when 65 lives can be saved out of every 1000 patients, received similar treatment.

Thus, the time from the onset of symptoms to TLT is an important factor in determg the effectiveness of thrombolysis and the achievement of myocardial reperfusion. In the 1st group, the time to TLT was 1.4±0.6 h, in the 2nd group — 2.3±0.2 h, that is, the time savings with prehospital TLT was 48 min. Thus, in 2/3 of the patients, thrombolysis was carried out within the first 3 hours from the onset of pain, which corresponds to the concept of early thrombolysis. Identified delays in carrying out CLT were associated with untimely decision to call an ambulance. The preparation time for the introduction of thrombolytics was minimized due to the well-organized work of cardiologists both at the prehospital stage and in the hospital. Clarification of the time of occurrence of MI, verification of the diagnosis, identification of contraindications to thrombolysis was no more than 10-15 minutes, after which TLT began immediately. The simplest and most sensitive of the indirect methods that determine the effectiveness of TLT and restoration of myocardial perfusion is the dynamics of the QRST complex. With adequate restoration of coronary blood flow, there is a rapid regression of ST segment elevation in leads and the formation of negative “coronary” T waves. It is known that reperfusion is considered effective when the ST segment elevation regresses more than 50% of the initial one after 90–180 minutes. We found that in the 1st group effective thrombolysis took place in 8 (100%) patients, in the 2nd group in 113 (92.6%) patients. after which TLT began immediately. The simplest and most sensitive of the indirect methods that determine the effectiveness of TLT and restoration of myocardial perfusion is the dynamics of the QRST complex. With adequate restoration of coronary blood flow, there is a rapid regression of ST segment elevation in leads and the formation of negative “coronary” T waves. It is known that reperfusion is considered effective when the ST segment elevation regresses more than 50% of the initial one after 90–180 minutes. We found that in the 1st group effective thrombolysis took place in 8 (100%) patients, in the 2nd group in 113 (92.6%) patients. after which TLT began immediately. The simplest and most sensitive of the indirect methods that determine the effectiveness of TLT and restoration of myocardial perfusion is the dynamics of the QRST complex. With adequate restoration of coronary blood flow, there is a rapid regression of ST segment elevation in leads and the formation of negative “coronary” T waves. It is known that reperfusion is considered effective when the ST segment elevation regresses more than 50% of the initial one after 90–180 minutes. We found that in the 1st group effective thrombolysis took place in 8 (100%) patients, in the 2nd group in 113 (92.6%) patients. With adequate restoration of coronary blood flow, there is a rapid regression of ST segment elevation in leads and the formation of negative “coronary” T waves. It is known that reperfusion is considered effective when the ST segment elevation regresses more than 50% of the initial one after 90–180 minutes. We found that in the 1st group effective thrombolysis took place in 8 (100%) patients, in the 2nd group in 113 (92.6%) patients. With adequate restoration of coronary blood flow, there is a rapid regression of ST segment elevation in leads and the formation of negative “coronary” T waves. It is known that reperfusion is considered effective when the ST segment elevation regresses more than 50% of the initial one after 90–180 minutes. We found that in the 1st group effective thrombolysis took place in 8 (100%) patients, in the 2nd group in 113 (92.6%) patients.

Our data on the level of mortality in groups confirm the known fact that the effectiveness of TLT directly depends on the time elapsed from the onset of an anginal attack to the start of reperfusion therapy. It is known that bleeding is the most frequent and dangerous complication of TLT. When analyzing the results of thrombolysis, it turned out that bleeding was registered in 5 patients (3.8%). We noted a low incidence of hemorrhagic complications during TLT.

These data confirm the results of experimental studies on the high specificity of these thrombolytics to thrombus fibrin. No drug intolerance was noted, which confirms their lack of immunogenicity and antigenicity. The appearance of cardiac arrhythmias during TLT indicates in most cases coronary artery recanalization and the effectiveness of thrombolysis. However, it must be recognized that it is rather difficult to distinguish arrhythmias directly related to myocardial reperfusion from arrhythmias resulting from myocardial ischemia. The development of reperfusion arrhythmias is based on complex mechanisms: the formation of oxygen free radicals in ischemic tissue (oxygen paradox), excessive intake of calcium ions from the extracellular space into cardiomyocytes ("calcium paradox"), etc. All this gives the myocardium electrical instability, leading to the development of arrhythmias. Often, reperfusion arrhythmias present neither a therapeutic nor a diagnostic problem, but in some cases they can be life-threatening. During TLT, VF was detected in 9 (7%) patients, which resulted in death in four cases (secondary VF). According to the literature, the effectiveness of electrical cardioversion in secondary ventricular fibrillation is low, and 30-day mortality can reach 40–50%.

It is known that, despite thrombolytic therapy, there is a high risk of rethrombosis and reocclusion, the frequency of the latter often reaches 10-12%. In order to prevent early and late rethrombosis, antithrombotic therapy is prescribed. In 107 patients, despite the early terms of admission to the hospital, the formation of a pathological Q wave (QS) on the ECG was noted. It can be assumed that the time elapsed from the onset of a pain attack to TLT in these patients was actually slightly longer than what they reported. It is known that timely reperfusion of the myocardium also prevents postinfarction remodeling of the left ventricle, improves the prognosis of patients' lives.

4 Conclusion

There fore, thrombolytic therapy at the prehospital and hospital stage with streptokinase in patients with myocardial infarction with ST segment elevation on the ECG in real clinical practice was characterized by high efficiency, a decrease in hospital mortality, complications and a small percentage of side effects.

Because the use of primary angioplasty is still limited by the real availability of specialized cardiac surgical care for most patients, especially in the coming hours of myocardial infarction, TLT remains the leading method of myocardial reperfusion. Therefore, the use of thrombolytics, provided that they are used as early as possible, plays an important role in the prevention of left ventricular remodeling and in improving the immediate and long-term prognosis of patients with MI.

References

1. Demidova M.M., Tikhonenko V.M., Burova N.N. Assessment of the state of a patient with acute coronary syndrome during thrombolytic therapy with the use of multichannel ECG-monitoring. Cardiology 2009; 49(7–8):25–31
2. Dolzhenko M.N., Dovganich N.V. Reperfusion arrhythmias: a new look at an old problem. Emergency Medicine 2008; 3 (16): 43–47).

3. Dovgalevskiy P.Ya., Furman N.V., Dovgalevkiy Ya.P. The efficacy and safety of thrombolytic therapy of myocardial infarction with ST-segment elevation by tenecteplase in actual clinical practice. Emergency 2009; (3): 43–49.
4. Furman N.V., DovgalevskiĭIa P., Shchetinkina I.N. Early reperfusion and aborted myocardial infarction. Cardiology 2009; 49(11):89–92.
5. Shpektor A.V., Vasil'eva E.Iu., Artamonov V.G. et al. Combined reperfusion in patients with acute myocardial infarction. Cardiology 2007; 47(6):27–30
6. Ioseliani D.G., El'kis I.S., Solov'ev O.P. et al. Combination of prehospital systemic thrombolytic therapy with endovascular procedures in the treatment of patients with acute myocardial infarction Cardiology 2005;45(3):4–9.
7. Iavelov I.S. The use of tenecteplase in acute myocardial infarction. Kardiologiia 2007;47(1):37–46. Russian (Yavelov I.S. The use of tenecteplase in acute myocardial infarction. Cardiology 2007; 47(1): 37–46).
8. Panchenko E.P. Thrombolytic agents in the treatment of patients with acute myocardial infarction. atmosphere. Cardiology 2001; (1): 16–20.
9. Poponina T.M., Poponina Yu.S., Vasil'ev A.G. The risks and benefits of reperfusion strategies in the treatment of patients with acute myocardial infarction with ST segment elevation. Russian journal of cardiology 2010; (5): 103–113.
10. Shostak N.A., Konstantinova E.V. Alteplase administration in patients with ST-segment elevation acute myocardial infarction in typical clinical practice. Cardiology. 2005;45(9):26–28.
11. The Global Use of Strategies to Open Occluded Coronary Arteries (Gusto III) Investigators. A comparison of reteplase with alteplase for acute myocardial infarction. N Engl J Med 1997; 337:1118–1123.
12. The TIMI Research Group. The thrombolysis in myocardial infarction (TIMI) trial. Phase I Findings. N Eng J Med 1985; 312:932–936.
13. Verstraete M., Bernard R., Bory M. et al. Randomized trial of intravenous recombinant tissue-type plasminogen activator versus intravenous streptokinase in acute myocardial infarction. Report from the European Cooperative Studi Group for Recombinant Tissue-type Plasminogen Activator. Lancet 1985; 13:842-848.
14. Yavelov I.S. Thrombolytic therapy in myocardial infarction: what the practitioner needs to know. Difficult patient 2011; 9 (1): 7–13).