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TREATMENT OF ACUTE STEMI WITH THROMBOLYSIS: TENECTEPLASE VS. STREPTOKINASE

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Key words: *STEMI, thrombolysis, tenecteplase, streptokinase.*

Summary

The aim of this study – to compare the efficacy of streptokinase with tenecteplase, while treating patients with ST elevated acute myocardial infarction by thrombolysis. To evaluate, how these agents affect TIMI blood flow, using coronarography. To compare bleeding complications between streptokinase and tenecteplase groups.

The study material and methods. The analysis of 240 patients was performed. 118 patients were treated with tenecteplase vs. 122 with streptokinase during a period of 2005-2008 in various Lithuanian hospitals. Thrombolytic treatment was administered within 6 hours from the onset of myocardial infarction symptoms. Coronarography was carried out within 24 hours from the onset of myocardial infarction symptoms.

Results. Coronarography showed the rate of TIMI-3 blood flow in 88 (74.5%) patients of the tenecteplase group. In the streptokinase group TIMI-3 was established in 39 patients (31.9%). The TIMI-2 blood flow in the tenecteplase group was established in 22 patients (18.6%), and 25 patients (20.5%) in the streptokinase group. TIMI-1 blood flow was found in 5 patients (11.2%) in the tenecteplase group and in 20 patients (16.5%) in the streptokinase group. TIMI-0 was found in 3 patients (2.6%) in the tenecteplase group and in 36 patients (31.1%) in the streptokinase group. There were no marked bleeding registered in either of the groups.

Conclusions. Tenecteplase restores the blood flow in the infarction related coronary artery better than streptokinase.

INTRODUCTION

Morbidity and mortality from cardiovascular causes have a high prevalence in developed countries. Prevalence of cardiovascular morbidity is 28% of all the population in Lithuania and 55,4% die from cardiovascular causes. The incidence of heart attack during past years is increasing in Lithuania , ~ 210 cases/100.000 per year (totaly 7796 myocardial infarction cases). In Lithuania mortality caused by myocardial infarction is ~ 40/100000 (~2,9% of all population) per year [2]. Within past 4 years mortality from MI decreases according to better treatment strategies (from 32 to 29/100.000)[2].

Acute myocardial infarction with ST elevation in ECG (STEMI) is a medical emergency with it‘s life threatening and chronic complications. The generaly received conception of modern STEMI treatment is reperfusion therapy – to open occlusive thrombosis in an epicardial coronary artery. Percutaneous coronary intervention (PCI) is the gold standard for an early STEMI management. Unfortunately, often some difficulties for the immediate PCI arise. Guidelines of the European Society of Cardiology reccomend initial thrombolysis if PCI within 2 hours is not possible [3]. As soon thrombolysis is made, as much lower incidence rate of STEMI complications and mortality are seen. Benefits of prehospital thrombolysis outweigh the risk of complications, associated with bleeding [4]. Many different thrombolytic agents are now available, so we should consider not only economical, but mostly important – farmacological options and comparative studies for the priority of choosing one.

The aim of this study – to compare the efficacy of strep-

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tokinase with tenecteplase, while treating patients with ST elevated acute myocardial infarction, administering thrombolytics. To evaluate, how these agents affect TIMI blood flow, using coronarography. To compare bleeding complications between streptokinase and tenecteplase groups.

STUDY MATERIAL AND METHODS

Retrospective analysis was made using STEMI patients data from various Lithuania's hospitals in a period of 2005-2008. All of the patients received thrombolytic therapy within 6 hours from the onset of myocardial infarction symptoms. Coronarography was carried out within 24 hours from the onset of myocardial infarction symptoms, attempting to evalutate TIMI blood flow.

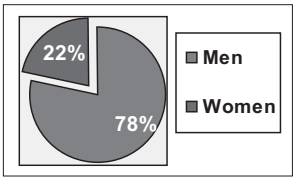
Totaly 240 patients were included and divided into two groups. Investigative group – treated with tenecteplase, control group - streptokinase.

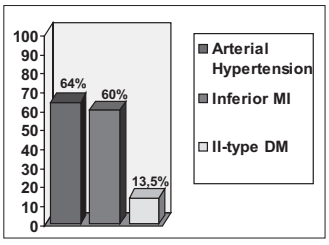
RESULTS

Tenecteplase (TNC) group consisted of 118 patients (78 men [66%]), average age – 57,2 years. Streptokinase (SK) group consisted of 122 patients (83 men [88%]), average age - 55,6 years.

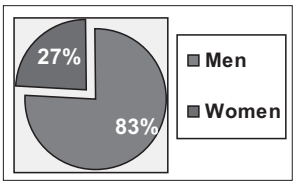
In TNC group 71 patient (60%) had inferior STEMI, SK group – 77 patients (63%).

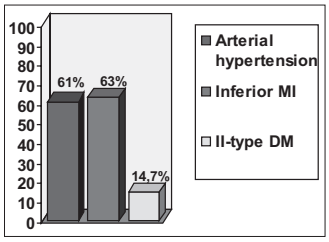
In TNC group arterial hypertension had 76 patients (64%), SK group – 72 (61%). Type-II Diabetes Mellitus had





Streptokinase group:





16 patients in TNC group (13.5%), SK group – 18 (14,7%).

Characteristics of the groups is summarized at the charts:

Tenecteplase group:

After coronarography, TIMI-3 blood flow in TNC group had 88 patients (74,5%), SK group – 39 patients (31,9%). TIMI-2 blood flow in TNC group had 22 patients (18,6%), SK group – 25 patients (20,5%). TIMI-1 blood flow in TNC group had 5 patients (11,2%), SK group – 20 patients (16,5%). TIMI-0 blood flow in TNC group had 3 patients (2,6%), SK group – 38 patients (31,1%).

TIMI blood flow	Tenecteplase group	Streptokinase group
TIMI-3	74.5% (88)	31.9% (39)
TIMI-2	18.6% (22)	20.5% (25)
TIMI-1	11.2% (5)	16.5% (20)
TIMI-0	2.6% (3)	31.1% (38)

There were no major bleeding registered in either of the groups.

TIMI blood flow data systematized at the 1-st table:

1-st table: TIMI blood flow in tenecteplase and streptokinase groups

According to the results, patients treated with tenecteplase had a better TIMI blood flow on coronarography. Better TIMI blood flow directly shows better reperfusional tenecteplase options, compared to streptokinase.

DISCUSSION

In most of all cases of STEMI, the main cause is intracoronary thrombosis, leading to distal coronary artery blood flow block. In 1880 it was firstly postulated by Carl Weigert, William Osler [5]. Until 1950 STEMI management was mostly palliative. Nowadays modern treatmet of STEMI is understood as immediate coronary blood flow restore. The break of management is made with first agent – streptokinase.

Associate Professor of Medicine William Smith Tillett invented Streptokinase in 1933. He observed that streptococci agglutinated in test tubes that contained human plasma but not in those that contained human serum. While most people would have dismissed this as trivial, Tillett considered it significant. He inferred that the agglutination of streptococci is caused by a component of plasma that is deficient in serum. This led him to conclude that the streptococci had synthesized a fibrinolytic agent that was responsible for dissolving the clots. Later, the direct agent – enzyme called streptokinase, was invented [6]. Streptokinase works as a catalyst. Unique blood coagulation system has it's own endogenous fibrinolytic systems. Plasmin is one of the most important endogenous fibrinolytics. Plasmin is an important enzyme present in blood that degrades many blood plasma proteins, most notably, fibrin clots. Plasmin is a serine protease that is released as plasminogen from the liver into the circulation and activated by various catalysts, such as tissue plasminogen activator, streptokinase [7].

Streptokinase was used as an agent for several conditions (mostly for pleural diseases). In 1960, after many preclinical trials, US doctors Boucek and Murphy were

first, who used streptokinase to treat STEMI in human patients [8]. After leading several smaller studies, in 1979, trial with 2388 patients demonstrated great superiority of streptokinase co-treatment (comparing with standart heparin infusion), reducing 6 months mortality after STEMI [9]. In 1976 E. I. Chazov demonstrated some evidence that intracoronary thrombolysis using streptokinase is better than systemic [10]. After next several studies, no distinction for fibrinolytic administration way was found to be better [11]. Unfortunatelly, there is no general agreement on fibrinolytics administration in patients with STEMI.

In 1985 GISSI study with more than 11.000 patients finally showed advantages of intravenous thrombolysis, reducing 12 months mortality after STEMI:

17,2% in steptokinase and 19% in control group [12]. As streptokinase is administered within 12 hours from the onset of heart attack, TIMI-3 blood flow on coronarography is registered in 33% patients [13].

Thrombolytics, especially streptokinase, have several side effects and limitations. A higher rate of stroke and intracerebral hemorrhaging is seen [14]. Streptokinase is associated with allergic reactions, within 4 days antibodys are found. At least one year break should be made between two prescribtions. Contraindications are: recent internal bleeding, haemorrhagic cerebral diseases, ischemic stroke past 6 months, pregnancy, uncontrolled hypertension, major surgery, recent trauma with resuscitation [7].

Today we have several generations of more modern fibrinolytics. Handling gene engineering, recombinant tissue plasminogen activators (t-PA): alteplase, reteplase, tenecteplase are synthesized. Those new generation agents have lower antigenity, much higher specificity for fibrin degradation. Alteplase has a short half-life and is administered only by intravenous infusion. Reteplase because of it‘s longer half life can be administered with a bolus therapy in patiens with STEMI [7].

Tenecteplase – improved t-PA agent. Using some gene engineering changes, agent is made more specific for fibrin. Tenecteplase has a higher resistance for it‘s endogenous t-PA inhibitor PAI-1. Agent can be administered by bolus within 5-10 sec., optimal dose vary from 30 to 50 mg. [15, 16].

Many trials valued t-PA efficacy, comparing to streptokinase. GUSTO trial found that 30 days mortality after STEMI in t-PA and streptokinase groups didn‘t differ; still one-year mortality significantly decreased in t-PA group. [17] GISSI-2 and ISIS-3 trials, found no difference in mortality as copmared streptokinase and t-PA groups. However t-PA were found more effective in patients who were at a younger age, anterior MI or have had previous treatment with streptokinase [18,19].

ASSENT-2 trial, including 17.000 patients, compared alteplase and tenecteplase efficacy. One year mortality didn‘t differ (9,1% in alteplase and 9,2% in tenecteplase groups). Tenecteplase group had less frequent bleedings. [20] According to TIMI 10A and TIMI 10B trials: within 90 min. from the onset of STEMI treated with tenecteplase, TIMI-3 blood flow was found in 65,8% patients, alteplase group – 62,7% [21].

It is proven that better TIMI blood flow reflects efficacy of thrombolysis and allows to prognose mortality. It established that (STEMI patients treated with streptokinase) 12 years survival in TIMI-3 group have 72% patients, TIMI-2 – 67%, TIMI-1-0 groups – 54% patients [22]. Tenecteplase should be administered in STEMI, even if PCI is delayed > 30 min. – significantly more often is found TMI2-3 blood flow, than PCI alone [23].

Our study presents that patients, treated with tenecteplase have a better coronary blood flow than those treated with streptokinase.

CONCLUSIONS

Tenecteplase restores the blood flow in the infarction related coronary artery better than streptokinase.

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ŪMAUS MIOKARDO INFARKTO SU ST BANGOS PAKILIMU TROMBOLIZINIS GYDYMAS: TENEKTEPLAZĖ AR STREPTOKINAZĖ

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Santrauka

Raktažodžiai: ūmus miokardo infarktas su ST bangos pakilimu, trombolizė, tenekteplazė, streptokinazė.

Tyrimo tikslas. Palyginti tenekteplazės ir streptokinazės poveikio efektyvumą, trombolizės būdu gydant pacientus sergančius ūmiu ST bangos pakilimo miokardo infarktu. Po trombolizinės terapijos atlikti koronarografiją ir palyginti kaip šie medikamentai daro įtaką TIMI kraujotakos atsistatymui pažeistoje kraujagyslėje. Palyginti kraujavimo komplikacijų dažnį tenekteplaze ir streptokinaze gydytų pacientų grupėse.

Tyrimo medžiaga ir metodai. Išanalizuoti 240 pacientų, 2005-2008 metais gydytų įvairiose Lietuvos ligoninėse, ligos atvejai. 118 pacientų buvo gydyti tenekteplaze, 122 – streptokinaze. Trombolizinė terapija buvo taikoma praėjus ne daugiau kaip 6 valandoms nuo miokardo infarkto simptomų pasireiškimo. Koronarografija buvo atlikta per 24 valandas nuo miokardo infarkto simptomų pasireiškimo.

Rezultatai. Koronarografijų duomenimis, TIMI-3 kraujotakos atsistatymas registruotas 88 (74,5%) pacientams gydytiems tenekteplaze ir 39 (31,9%) pacientams gydytiems streptokinaze. TIMI-2 kraujotaka atsistatė 22 (18,6%) pacientams gydytiems tenekteplaze ir 25 (20,5%) pacientams gydytiems streptokinaze. TIMI-1 kraujotaka registruota 5 (11,2%) pacientams tenekteplazės grupėje ir 20 (16,5%) pacientų streptokinazės grupėje. TIMI-0 kraujotaka registruota 3 (2,6%) pacientams tenekteplazės grupėje ir 36 (31,1%) pacientams streptokinazės grupėje.

Išvados. Sergant ūmiu miokardo infarktu tenekteplazė atstato kraujotaką pažeistoje kraujagyslėje geriau nei streptokinazė.

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