Arrhythmia Due to Reperfusion After Thrombolytic Therapy in Patients with Acute Myocardial Infarction

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Objective: **The aim of this study was to determine the relation between the incidence and frequency of ventricular arrhytmias and the time course of ST-segment changes in patients with successful thrombolysis.**
Method: **This study included 46 patients (31 males 53±12 years) with acute myocardial infarction (MI) who were treated with streptokinase (SK Group) and 41 MI patients (27 males 55±12 years) who did not receive any thrombolytic agent (Control Group). Electrocardiograms were obtained 90 minutes 6, 12, 18, 24, 48 and 72 hours after thrombolytic therapy and reduction in ST elevation at 90 minutes was calculated. All patients had wall motion abnormalities.**
Results: **Overall arrhythmias were observed in 67% (n: 31) of patients in SK group compared to 63% (n:26) in control group (p=0.05). In subgroup analysis of SK group ventricular tachycardia (VT) was more frequent (37%) in patients with more than 50% reduction in ST elevation at 90 minutes compared with in other subgroups of patients (p<0.01). Postinfarction angina and systolic dysfunction were more frequent in the control group compared to the SK group (p<0.05).**
Conclusion: **Our results suggest that reperfusion with fibrinolytics or the faster reflow may induce ventricular arrhythmias. However, it can also prevent the impairment in systolic function of the left ventricle.**

Key words*: Myocardial infarction, thrombolysis, reperfusion, arrhythmia*

Myocardial reperfusion by intravenous thrombolytic agents has been used succesfully for myocardial salvage in acute myocardial infarction (1). The benefical effects of thrombolysis are at the expense of an increase in residual myocardial ischemia. Early thrombolytic treatment results in an electrically more stable myocardium. Restoration of coronary flow is often associated with a decrease in ST-segment elevation, marked improvement or resolution of chest pain, but increased incidence of arrhythmias. The arrhythmias include increased numbers of ventricular premature beats, ventricular tachycardia, AV block or accelerated idioventricular rhythm (2,3).

The aim of this study was to investigate the relation between the incidence of arrhythmia and ST-segment changes and to compare clinic and laboratory data in patients with acute myocardial infarction (MI) who received thrombolytic therapy and who did not.

Material and Method

Patients and thrombolytic therapy: A consecutive series of patients receiving intravenous streptokinase (SK) for MI from May 1992 to May 1993 were included in this stuy. Patients younger than 75 years with continious chest pain less than 6 hours in duration, unresponsive to sublingual nitroglycerine were treated.

The electrocardiographic (ECG) diagnosis of anterior MI included ST-segment elevation of 0.2 mV or more in at least 2 precordial leads. Both 0.2 mV of ST-segment elevation in inferior leads and reciprocal ST depression in anterior and lateral leads were required for inclusion of inferior infarction. Patients whose initial electrocardiograms suggesting subendocardial infarction were not treated. All patients treated had the diagnosis of MI confirmed by subsequent elevation of both total creatine kinase (CK) and CK-MB isoenzyme levels. Intravenous streptokinase was administered at a dose of 1.5 million IU in 45-60 minutes. Aspirin therapy with 300 mg/day and nitrates were given following thrombolytic therapy. No other prophylactic therapy was given.

Electrocardiography: Standart 12-lead ECGs were recorded before SK therapy and 90 minutes, and at 6, 12, 18, 24, 48, 72 hours after SK therapy initiation.

Patients with acute myocardial infarction who were

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Table I. Age in the study groups

	SK Group		Control Group		p
Gender	n	Age (years)	n	Age (years)	
Male	31	52±10	27	53±9	0.692
Female	15	63±8	14	59±12	0.297
Total	46	53±10	41	55±12	0.399

Table II. Heart rate and blood pressure (BP) in the study groups

Variables	SK Group (n: 46)	Control Group (n: 41)	p
Heart rate (beats/m)	79±21	76±13	0.432
Systolic BP(mmHg)	118±26	129±27	0.056
Diastolic BP (mmHg)	77±15	83±15	0.066
Mean BP (mmHg)	92±17	98±18	0.432

Table III. Three subgroups of patients with fibrinolysis according to the rate of reduction in ST segment elevation at 90 minutes after thrombolytic therapy

	Control Group		ST<30%		ST 30%-50%		ST>50%	
Arrhythmias	n	%	n	%	n	%	n	%
PVC	14	35%	10	66%	9	60%	10	63%*
VT	1	2%	1	7%	2	13%	6	37%*
APC	10	24%	4	6%	4	26%	5	31%
AV Block	14	35%	7	46%	8	53%	7	44%

APC: atrial premature contraction, PVC: premature ventricular contraction, VT: ventricular tachycardia.

Table IV. The localization of infarction in study group

	SK Group		Control Group		p
Localization	n	%	n	%	
Inferior	14	30	12	29	0.891
Anterior	26	55	26	63	0.879
Posterior	4	9	1	3	0.470
Miscellaneous	2	6	2	5	0.689

Table V. Risk factors for coronary artery disease in study groups

	SK Group		Control Group		p
Variables	n	%	n	%	
Male	31	71	26	64	0.06
Hypertension	10	22	14	35	0.01
Hyperlipidemia	14	30	2	5	0.03
Smoking	31	74	22	55	0.14
Obesity	27	59	22	55	0.03
Family history	12	26	4	10	0.01
Diabetes	5	11	2	5	0.01
Reinfarction	7	15	4	10	0.01

Table VI. Echocardiographic results in study groups

	Control Group % (n)	SK Group % (n)	p
Wall-motion abnormality	92 (38)	81 (35)	0.13
Systolic abnormality	35 (14)	30 (14)	0.01
Diastolic abnormality	78 (32)	59 (27)	0.05
Mitral regurgitation	80 (33)	60 (28)	0.06
Tricuspit regurgitation	27 (11)	30 (14)	0.01
Aortic regurgitation	27 (11)	20 (10)	0.01
LV dilatation	45 (18)	32 (15)	0.01

Table VII. Complication rates in study groups

	Control Group, % (n)	SK Group, % (n)	p
Bleeding	0 (0)	4 (2)	0.05
Cardiojenic shock	7 (3)	2 (1)	0.04
Arrhythmia	63 (26)	67 (31)	0.05
Heart failure	14 (6)	11 (5)	0.05
Postinfarction angina	19 (8)	4 (2)	0.01
In-hospital mortality	7 (3)	6 (3)	0.08

admitted to coronary care unit more than 6 hours of onset of pain were excluded from study. Patients with previous SK therapy and contraindication of SK therapy were also excluded (3).

Statistical analysis: Values are given as mean ± standard deviation. Percentages were compared with chi-square test. Paired values were compared with student t-test.

Results

Eighty seven patients with acute MI were included in this study. Mean age was 53±12 years for placebo (Table I). Mean time interval from the onset of pain to thrombolysis was 3.5±0.2 hours. There were no significant changes between heart rate and blood pressure in both groups as presented in Table II. We showed that wall motion abnormality was 100% for both SK and control groups while ejection fractions used as an indicator of systolic dysfunction was 30% in the SK group and 35% in the control group. Diastolic function abnormality was seen in 90% of the SK group and 78% in the control group assessed by Doppler echocardiography.

An ECG was taken at 90 minutes after the initiation of thrombolytic therapy for detection of ST segment changes. Ventricular tachycardia was more frequent in patients with ST segment decreases more than 50% compared to the other groups (Table III, Figure 1). There were no significant changes regarding atrial premature contractions, atrioventricular block and premature ventricular contraction between the groups. Majority of patients in both groups had anterior MI but without significant changes.

Risk factors profile for Coronary Artery Disease (CAD) in these study groups are presented in Table IV. Hyperlipidemia, diabetes mellitus and reinfarction were higher in SK therapy group while hypertension was not. In-hospital mortality was not significantly different in either of the groups. Over all arrhytmia was more frequent in the SK therapy group compared to the control group (Table VI).

In-hospital ischemic events or complications and fibrinolysis-induced hemorrhagic complications were shown in Table VII. Cardiogenic shock and postinfarction angina were more less in SK group compared to control group (each $p<0.005$). Other complications also tended to be lower in SK group.

Discussion

The main finding of this study is that the ratio of ST-segment decrease is related to the frequency of premature ventricular contractions and ventricular tachycardia. When the rate of ST-segment decrease is related to the rate of reperfusion, our results suggest that faster reflow is more arrhythmogenic. Several noninvasive markers can be used in the assessment of reperfusion to a reasonable degree of accuracy after thrombolytic therapy. Reperfusion is recognized clinically by the abrupt cessation of pain, ventricular arrhytmias (most characteristically accelerated idioventricular rhythm), rapid evalution of the ECG to Q waves and an early peak of CK (by 12 hours); however, all of these signs may be misleading. Approximately 50 years ago, noninvasive markers such as resolution of ST-segment shifts on electrocardiography or the devolepment

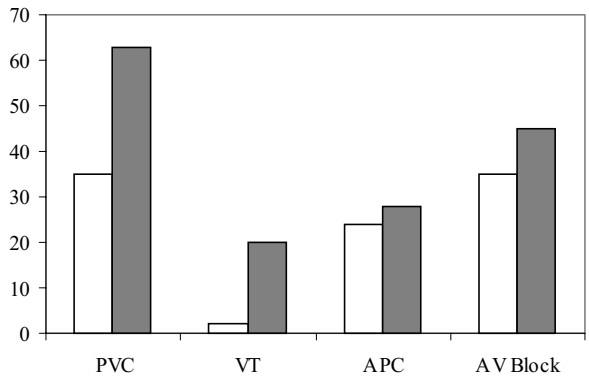

Figure 1. Arrhythmia profiles in patients with SK therapy (grey bars) or without SK therapy (white bars) (*: p<0.05).

of an accelerated idioventricular rhythm were observed in experimental animals (4). These markers are observed in humans as well, and are still reported in the current litearature as signs of reperfusion. The percent reduction in ST-segment elevation was used to predict reperfusion potency. When ST-segment elevation fall by less than 25% of the baseline value, persistent coronary occlusion was likely, with a predictive accuracy of 86% (4,5). The complete resolution of ST and T wave changes were associated with a 96% patency rate at the 90 minutes coronary angiograms obtained after thrombolytic therapy (6).

Recent reports focus on electrocardiographic signs of reperfusion, either by frequently recorded 12-lead electrocardiograms or by continuous ST-segment shift monitoring and analysis.

Early peaking of the total CK level and the CK-MB isoenzyme have identified patients with successful reperfusion after streptokinase therapy (4,7,8). We found that peak CK level reached in twelve hours and CK-MB level were shifted in six hours.

Echocardiography is useful in evaluating regional wall motion abnormalities after thrombolytic treatment. A previous study (10) noted that wall motion abnormalities in all patients before the administiration of thrombolytic therapy and found that 80% showed improvement in the IRA (infarct related artery) subserved segments three days later. In our study, we did not have echocardiographic examination before SK therapy but after three days of SK therapy and placebo group. We saw wall motion abnormalities at 81% in patients with SK therapy compared to 92% in controls. Systolic and diastolic functions were better in patients with SK therapy (59% vs 78% and 60% vs 80%, respectively). Left ventricular dilatation was seen 32% of patients with SK therapy. Mitral tricuspit and aort regurgitations were higher in frequency in controls than SK group. These findings could be related to abnormality of systolic and diastolic function in left ventricule (Table VI).

Serious bleeding complications occur in 0.5-5% of patients (8). We saw GIS bleeding in 2 (4%) patients (Table VII). This finding was comparable to a previous study (8).

Some authors have found reperfusion arrhythmias to be a marker for infarct related artery patency, while other investigators have not found it to be as reliable. In 386 patients treated with tissue plasminogen activator (TPA) for acute MI in the TAMI-1 trial, ventricular tachycardia, ventricular fibrillation, second-and-third degree AV block, and sinus bradycardia were all documented with similar frequencies following thrombolytic administiration. None of the arrhytmias recorded, however could be associated with the rates of reperfusion (7,9).

We found that there was no statisticaly significant relationship between the rate of ST segment decrease and atrial premature contraction and AV-block. However, there was a significant correlation between the reperfusion rate and ventricular tachycardia. These findings might be explained by a more potential toxic effect of faster reflow leading to more severe injury by metabolities such as free radicals and subsequent calcium overload. Therefore, ventricular arrhytmias could be used as clinical markers of reperfusion injury.

References

1. Mickley H, Pless P, Nielsen JR, Berning J, Moller M: Thorombolysis significantly reduces transient myocardial ischemia following first acute myocardial infarction. Eur Heart J 13: 484-490, 1992.
2. Goldberg S, Greenspoon AJ, Urban PL: Reperfusion arrhytmia: A marker of restoration of antegrade flow during intracoronary thrombolysis for acute myocardial infarction. Am Heart J 105: 26, 1983.
3. Braunwald E. SK therapy contrindication: Heart Disease 4 th. ed. Philadelphia WB. Saunders Company 1992, pp:1235
4. Arnold AZ, Topol EJ: Assessment of reperfusion after thrombolytic therapy for myocardial infarction. Am Heart J 4: 441-446, 1992.
5. Saran RK, Been M, Furniss SS: Reduction in ST segment elevation after thrombolysis predicts either coronary reperfusion, or preservetion of left ventricular function. Br Heart J 64: 113-117, 1990.
6. Califf RM, O'neil W, Stack RS, Aronson L and TAMI study group: Failure of simple clinical measurements to predict perfusion status after intravenous thrombolysis. Ann Intern Med 108: 658-662, 1988.
7. Tavlı T, Korkut B, Gök H, Avşar A: Akut myokard infarktüsünden sonra uygulanan trombolitik tedavinin klinik ve laboratuvar bulgularına etkisinin plasebo ile karşılaştırılması. S.Ü. Tıp Fakültesi Dergisi 2: 191-196, 1993.
8. Lee KL, Sigmon K, George BS, Candela RJ, Kereiakes DJ and TAMI Study Group: Early and complete reperfusion a key predictor of survival after thrombolytic therapy (abstr.) Circulation 78: II-501; 1988.
9. Schroeder SA, Krupp MA, Tierney LM, Mc Phee SJ: Medical Diagnosis Treatment. A Lange Medical book. Middle East Edition 268-269, 1991.

10. Broderick TM, Bourdillon PDV, Ryan T: Comparison of regional and global left ventricular function by serial echocardiograms after reperfusion in acute myocardial infarction. J Am Soc Echocardiogr 2: 315-23, 1989.

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