

Failure of Streptokinase Therapy in Diabetic and Non-Diabetic Patients Presenting with ST Elevation Myocardial Infarction

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ABSTRACT

Aim: To compare the frequency of failure of streptokinase therapy in diabetic versus non-diabetic patients presenting with ST elevation myocardial infarction.

Methods: It was a cohort study of 100 cases. Non probability purposive sampling method was used. Patients between 30-70 years of either sex diagnosed with STEMI presented within 12 hours of chest pain were divided into Group A having diabetes and Group B: having no diabetes. Streptokinase was given to each patient within 1 hour of presentation. The sum of ST-segment elevation was measured by hand held caliper at 80ms (two small squares) beyond "J" point in leads 1, aVL, V₁ to V₆ for lateral, leads II, III, aVF for inferior and leads V₁ to V₄ for anteroseptal infarction. Reperfusion was considered as failure if ST resolution was <30% after 90 minutes of SK infusion.

Results: In diabetic patients mean ST resolution was 35.01±18.29% with minimum and maximum of 6.25% and 77.30% respectively while in non diabetics mean ST resolution was 60.33%±27.31%. with minimum and maximum of 3.60% and 100% respectively. In diabetic patients, reperfusion was unsuccessful in 21(42%) and in 29(58%) it was successful. In non-diabetic patients, it was unsuccessful in 6 (12%) while it was successful in 44(88%).

Conclusion: A significant proportion of diabetic patients did not achieve complete reperfusion within 90 min of starting thrombolytic therapy.

Keywords: Myocardial infarction, diabetes, streptokinase, reperfusion therapy.

INTRODUCTION

Myocardial infarction (MI) is the rapid development of myocardial necrosis caused by a critical imbalance between oxygen supply and demand of myocardium¹. Acute coronary syndrome includes unstable angina, ST segment elevation (STEMI) and non-ST segment elevation myocardial infarction (NSTEMI). Diabetes mellitus is one of the six primary risk factors for myocardial infarction². In Pakistan prevalence of Myocardial Infarction is 6.8%³. Moreover prevalence of diabetes in MI patients is 7.05%⁵. Indeed, 75-80% of adult diabetic patients' die of coronary artery, cerebrovascular, peripheral vascular diseases or combination of these^{5,6}. Streptokinase was the first thrombolytic drug to be introduced in the treatment of myocardial infarction upto 12 hours after the onset of the chest pain⁷. The outcome of acute myocardial infarction treated with fibrinolytic therapy can be evaluated by the measurement of ST segment resolution at 90 min after streptokinase infusion, in 12 lead electrocardiogram⁸. Although successful recanalization of the epicardial vessel is a necessary condition, it is the micro-vascular flow that most strongly correlates with outcome. ST-segment

changes reflect myocardial rather than epicardial flow and hence yield prognostic information beyond that provided by coronary angiogram alone^{9,10}. ST segment resolution within 90 min is a simple measure of assessing reperfusion in patients receiving fibrinolytics¹¹. Standard 12 lead ECG does not include posterior leads for posterobasal valve of left ventricular and is non sensitive indicator of right ventricular damage¹¹. A study conducted by Choudary ANR, et al (2008) in Bangladesh showed that reperfusion was unsuccessful in a significant proportion of diabetic patients with STEMI. It was 67.2% while in non-diabetics its frequency was only 19.8%¹². The purpose of study is to assess the thrombolytic effect of streptokinase in diabetic and non-diabetic myocardial infarction patients by using 12-lead ECG.

PATIENTS & MEHTODS

It was cohort study performed in department of Medicine, Mayo Hospital, Lahore for 6 months. Non-probability, purposive sampling method was used. 100 cases; 50 in each group was calculated with 80% power of test, 1% margin of error and taking expected percentage of failure of reperfusion therapy i.e. 67.2% in diabetic patients and 19.8% in non-diabetic patients presenting with STEMI. Patients of 30-70 years of either sex. with STEMI presented

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within 12 hours of chest pain were included. Patients having Impaired glucose tolerance(IGT), previous myocardial infarction, hemophilia, SLE, deranged clotting profile i.e. PT>18 sec, APTT>35 sec were excluded. After taking consent and details like name, age and gender, streptokinase was given to each patient at a dose of 1.5 million units, diluted in 100ml of normal saline, within 1 hour of presentation. The sum of ST-segment elevation was measured by hand held caliper at 80ms (two small squares) beyond 'J' point in leads I, aVL, V₁ to V₆ for lateral, leads II, III, aVF for inferior and leads V₁ to V₄ for anteroseptal infarction. Reperfusion was considered as failure if ST resolution was < 30% after 90 minutes. All data was entered into SPSS version 14 and was analyzed using same software. All quantitative data like age, ST resolution was presented in form of Mean \pm S.D. Qualitative data like gender, failure of reperfusion therapy was presented in form of frequency and percentage. Chi-square test was used to compare the failure of reperfusion in both groups.

RESULTS

Mean age of all patients was 50.02 \pm 8.16 years having minimum age of 32 and maximum of 70 years. Mean age of diabetic patients was 51.10 \pm 7.91 while that of non diabetics was 48.94 \pm 8.34 years. Among diabetic patients minimum age was 32 while maximum was 65 years. Minimum and maximum age among non diabetic patients was 35 and 70 years. There were 72(72%) males while only 28(28%) were females. In diabetic patients there were 35 males and 15 females while in non-diabetics there were 37 males and 13 females. Mean ST resolution at 90 minute after application of SK was 47.67 \pm 26.39%. Minimum and maximum ST resolution in all patients was observed as 3.60% and 100% respectively. In diabetic patients mean ST resolution at 90 minutes after SK was 35.01 \pm 18.29%. Minimum and maximum ST resolution was 6.25% and 77.30% among diabetic patients. Patients who were non-diabetic their mean ST resolution was 60.33 \pm 27.31%. Minimum and maximum ST resolution among non-diabetic patients was 3.60% and 100%. In diabetics reperfusion was not successful in 21(42%) and successful in 29(58%). In non-diabetic patients, reperfusion was not successful in 6(12%) and successful in 44(88%). Higher rate of failure of reperfusion was observed among diabetic patients as compared to non-diabetic patients (p value=0.001).

DISCUSSION

Diabetes Mellitus is a dyslipidemic disease and increases the rate of atherosclerotic progression of

vascular occlusion. Among patients with an acute myocardial infarction, 10-25% had diabetes mellitus. Even when promptly receiving thrombolytics, outcome in diabetics is still worse than non-diabetics, manifesting impaired post-thrombolysis, left ventricular function and prognosis¹². The outcome of acute myocardial infarction treated with fibrinolytic therapy can be evaluated either by coronary angiographic measurement of TIMI(Thrombolysis in Myocardial Infarction) blood flow or by measurement of ST segment resolution at 90 min after streptokinase infusion, in 12 lead electrocardiogram¹³. Mean age in all was 50.02 \pm 8.16 years. Mean age of diabetic patients was 51.10 \pm 7.91 years. In another study, mean age was 60.5 \pm 10 years (range 28-76). Among diabetes mean age was 59.10.3 years and among non-diabetics it was 64.2 \pm 8.2 years¹³. Several studies have reported similar angiographic success in both type 2 diabetic and non-diabetic subjects, while others have shown that the diabetics have less complete resolution of ST elevation than the non-diabetics¹³⁻¹⁵. It has been hypothesized that type 2 diabetes might interfere with intravenous thrombolysis effectiveness, as estimated by angiographic or ECG. Descriptive statistics for ST resolution at 90 minute after infusion of SK calculated as: mean ST resolution was 47.67 \pm 26.39%. In diabetic patients mean ST resolution at 90 minutes after SK was 35.01 \pm 18.29%. In non-diabetics, mean ST resolution was 60.33 \pm 27.31%. In a recent comparative study of ST-segment resolution by thrombolytic versus primary coronary intervention (PCI), failure of resolution of ST-segment by thrombolytic was observed in 21.5% acute myocardial infarction patients after 90 min of initiation of fibrinolytic therapy¹⁶. By using the same resolution criteria, in our study we observed similar results in non-diabetic myocardial infarction 12% showed failed resolution and in 88%, reperfusion therapy did not fail. But in case of diabetic myocardial infarction, 42% showed failed resolution and in remaining 58% reperfusion therapy did not fail. In our study, ST-resolution failure in non-diabetic patient was less whereas type 2 diabetic subjects were presented with significantly higher incidence of failed ST-resolution than non-diabetic. There is significant association between failure of reperfusion therapy with respect to the diabetic status of the patient. Higher rate of failure of reperfusion therapy was observed among diabetic patients as compared to non diabetic patients. This significant change in ST-resolution between non-diabetic and diabetic was similar with the study by Zairis, et al., who showed significant difference between diabetic and non-diabetic patient in relation to incomplete (65.9%vs31.8%;p<0.001) resolution¹³. In our study it was proved that reperfusion failed in a

significant proportion of diabetic patient with STEMI in comparison with non-diabetic persons (42.0% vs.12.0%) These finding reinforces the need for increased efforts to discover newer pharmacological agents to reduce failed reperfusion after streptokinase therapy in diabetic patients with myocardial infarction. To further improve outcome after myocardial infarction and thrombolysis among patients with diabetes, newer strategies such as peri-infarction metabolic control and primary angioplasty should be investigated.

CONCLUSION

Despite the established benefit of fibrinolytic therapy in acute myocardial infarction, a significant proportion of diabetic patients do not achieve complete reperfusion within 90 min of starting thrombolytic therapy. So, due attention is required for the better management of diabetic myocardial infarction patients.

REFERENCES

1. Fenton DE. Myocardial infarction. (Online). 2009. <http://emedicine.medscape.com/article/75-overview>.
2. Ting P, Chua TS, Wong A, Sim LL, Tan VW, Koh TH. Trends in mortality from acute myocardial infarction in the coronary care unit. *Ann Acad Med Singapore* 2007;36:974-9.
3. Khabir A, Fahim J, Imtiaz J, Juanita H, Khan AQ, Nish C. Prevalence and predictors of smoking in Pakistan: results of the national health survey of Pakistan. *Eur J Cardiovasc Prev Rehab* 2005;12(3):203-8.
4. Antman EM, Braunwald E. Diabetes mellitus. In: Longo DL, Kasper DL, Jameson JL, Fauci AS, Hauser SL, Loscalzo J. *Principles of Harrison's internal medicine*. 17th edition. American textbook of internal medicine: McGraw-Hill; 2008:pp.1533.
5. Hermantin P, Cuesta-Linker T, Weisse J, Heinz Schmidt K, Knorst M, Scheld M, et al. Comparative analysis of the activity and content of different streptokinase preparations. *Eur Heart J* 2005;26:933-40.
6. Silva-Orrango P, Colombo P, Bigi R, Gregori D, Delgado A, Salvade P, et al. Thrombus aspiration before primary angioplasty improve myocardial reperfusion in acute myocardial infarction the DEAR-MI (Dethrombosis to enhance acute reperfusion in myocardial infarction) study. *J Am Coll Cardiol* 2006;48(8):1552-9.
7. Svilaas T, Vlaar PJ, van der Horst IC, Diercks FHD, de Semt BJGL, van den Heuvel AFM, et al. Thrombus aspiration during primary percutaneous coronary intervention. *N Engl J Med* 2008;358:557-67.
8. Prasad A, Stone GW, Stuckey TD, Costantini CO, Zimetbaum PJ, Mclaughlin M, et al. Impact of diabetes mellitus on myocardial infarction. *J Am Coll Cardiol* 2005;45:508-14
9. Smith SW. ST Segment evaluation differs depending on the method of measurement. *Soc Acad Emerg Med* 2008;13(4):406-12.
10. Bassand JP, Danchin N, Filippatos G, Gitt A, Hamm C, Silber S, et al. Implantation of reperfusion therapy in acute myocardial infarction: A policy statement from the European society of cardiology. *Eur Heart J* 2005;26:2733-41.
11. Chowdhruy MAR, Hossain AKMM, Dey SR, Akhtaruzzaman AKM, Islam NAF. A comparative study on the effect of streptokinase between diabetic and non-diabetic myocardial infarction patients. *Hangladesh J Pharmacol* 2008;3:1-7.
12. Zairis MN, Makrygiannis SS, Papadaki OA, Lyras AG, Kouzanidis JP, Ampartzidou OS, et al. Diabetes and ST elevation myocardial infarction *Diabetes Care* 2002;25:1890-91.
13. Zairis MN, Lyras AG, Makryginnis SS, Psarogianni PK, Adamopoulou EN, Handanis SM, et al. Type 2 diabetes and intravenous thrombolysis outcome in the setting of ST elevation myocardial infarction. *Diabetes Care* 2004;27:967-71.
14. Angeja BG, De Lemos J, Murphy SA, Marble SJ, Antman EM, Cannon CP, et al. Thrombolysis in myocardial infarction: impact of diabetes mellitus on epicardial and microvascular flow after fibrinolytic therapy. *Am Heart J* 2002;144:649-56.
15. Ishihara M, sato H, Kawagoue T, Shimatani Y, Kurisu S, Nishioka K, et al. Impact of diabetes mellitus on long-term survival after acute myocardial infarction in patients with single vessel disease. *Heart* 2001;86:133-38.
16. Thiele H, Engelmann L, Elsner K, Kappl MJ, Storch WH, Rahimi K, et al. Comparison of pre-hospital combination-fibrinolysis plus conventional care with pre-hospital combination-fibrinolysis plus facilitated percutaneous coronary intervention in acute myocardial infarction. *Eur Heart J* 2005;26:1956-63.