Can Anti-Streptokinase Antibody Predict Myocardial Infarction Outcomes After Streptokinase Treatment?

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Abstract

Background: The aim of this study was finding the association between anti- Streptokinase (SK) levels based on previous streptococcus infection and the clinical outcome of acute myocardial infarction (AMI) among Iranian patients after SK treatment.

Methods: In this prospective study, 31 consecutive patients presented to the emergency room of a referral university hospital within six hours of the onset of symptoms of AMI were recruited over a 3-year period (2007-2010). Blood samples for the analysis of the effect of neutralizing antibodies to SK assays were obtained immediately on arrival at the hospital. In-hospital and out-hospital clinical outcome defined as including return of typical chest pain after 48 hours, appearance of complex arrhythmia after 24 hours, maximum CPK serum concentration during first three days of admission, Left Venticular Ejection Fraction (EF) on the last day of admission, surgical interventions (CABG, PTCA), re-MI and re-admission due to cardiac problems during the one-year follow-up.

Results: Overall, 31 patients (7 female, 24 male with the mean age of 56.83 ± 2.21 years) were included in this study. The recurrence of typical ischemic chest pain 48 hours after AMI, appearance of complex arrhythmia during the admission to CCU and 24 hours after AMI, maximum CPK serum concentration during the first three days of admission, and left EF on the last day of admission were not significantly different between the two compared groups ($p > 0.05$).

Conclusion: According to this study, previous exposure to streptococcal infections may not reduce the efficacy of a single dose of SK and it does not seem necessary that its titer be measured before SK administration.

Keywords: Streptokinase, Myocardial infarction, Anti-streptokinase antibody (JPMA 62: S-31; 2012).

Introduction

Thrombolytic therapy has been a major advance in the management of acute myocardial infarction (AMI)[1] and can reduce mortality and morbidity rates related to AMI.[2] There are few differences among the major thrombolytic agents[3] and it has been shown that Streptokinase (SK) has minimal side effects and low cost compared with other fibrinolytic agents.[4]

Most patients presented to coronary care units have circulating antibody of anti streptokinase (ASK), though at a low titer which is because of its antigenic nature.[5] ASK are nearly ubiquitous in the population as a consequence of previous streptococcal infection. This may led to failure to respond to SK.[7,8]

The titer of ASK antibodies in the general population and especially in coronary patients at risk of MI is not well-known and their potentially harmful effects are even less known.[9,10]

This study aimed to find the association between anti-SK levels and short and one year clinical outcomes among Iranian patients, who have suffered from AMI and have been treated by SK, after SK according to ASK.

Methods

In this prospective study 80 consecutive patients presented to the emergency room of a referral university hospital within six hours of the onset of the symptoms of AMI were recruited over a 3-year period (2007-2010).

The inclusion criteria was defined as having chest pain for at least 30 minutes which was not relieved by sublingual nitroglycerin. All patients had at least 1 mm of ST elevation in two contiguous pericardial or limb leads, increase in circulating cardiac serum is enzyme of creatin phosokinaz (CK) and did not have any of the standard contraindications to thrombolytic therapy.

Subjects who were older than 75 years or had hypersensitivity to SK or previous treatment with SK, bundle branch block and patients who needed emergent intervention (angiography or CABG) were excluded.

Overall, 31 eligible patents were followed for one year. All subjects were informed of the purposes of the research and invited to participate in the study, after obtaining their oral consent. The Isfahan Cardiovascular Research Center ethics committee approved the protocol of the study and the Declaration of Helsinki was observed.

At arrival to emergency room blood pressure is measured by averaging two blood pressure readings taken during the physical examination. Blood samples for the analysis of the effect of ASK assays were obtained immediately on arrival at the CCU. Immediately before thrombolytic therapy 10 cc of blood was collected from each patient. Half of the blood was allowed to clot with its serum immediately analysed for CPK. The other 5 cc was centrifuged (3000 rounds per minutes) for 10 minutes to remove its serum. Samples of blood were frozen and stored at -70°C until the measurement of ASK concentration titer. SK in a standardized fashion of 1.5 million units in 500 ml normal saline or 5% dextrose water was administered intravenously over a period of 60 minutes.

After administration of SK, patients were transferred to the coronary care unit and monitored for electrical side effects of AMI (arrhythmia) and the return of typical ischemic chest pain after 48 hours. The creatin phosokinase serum (CPK) concentration was measured every eight hours in the first 24 hours of admission and also 48 and 72 hours after admission. Colored doppler echocardiography was carried out on all patients on the last day of admission to evaluate left ventricular ejection fraction and mechanical side effects of MI by one cardiologist. Having been discharged from the hospital, the patients were followed up for re-MI, re-admission due to cardiac problems, death due to cardiac problems and surgical interventions every 3 months by means of telephone calls and were visited every 6 months by just one cardiologist for detection of side effects of MI for one year.

The hospital files of readmitted patients during this one-year period of follow up were evaluated to determine whether the cause of admission was cardiac or not and the film of angiography of the patients who underwent PTCA or CABG was evaluated by just one cardiologist. The cardiologist was unaware of the patients' details. ASK antibody (IgG) was determined, substrate was added, and the optical density (OD) read at 450 and 620 nm on an LP400 plate reader (Diagnostics Pasteur, North Ryde, Australia).[11]

The mean value of the IgG serum concentration of 50 normal people who did not have the positive history of cardiac problems and had not received SK before was used to determine the cutoff point of 0.3 million units according to which the patients were distributed in two groups of high and low IgG concentration. In-hospital and out-hospital clinical outcome was defined as the recurrence of typical ischemic chest pain 48 hours after AMI, appearance of complex arrhythmia 24 hours after AMI, maximum CPK serum concentration during the first three days of admission, Left Ventricular Ejection Fraction (EF) on the last day of admission, surgical interventions (CABG, PTCA), re-MI and re-admission due to cardiac problems during the one-year follow-up.

The comparison of the two groups of patients with high IgG serum concentration and low IgG serum concentration was performed by chi-square, Fisher's exact, and t tests via SPSS[11] software (SPSS Inc., Chicago, IL). A value of $p < 0.05$ was considered significant.

Results

Overall, 31 patients (7 female, 24 male with the mean age 56.83 ± 2.21 years) were included in this study of which 14 had high IgG serum concentration and 17 had low IgG serum concentration. All of the patients were alive at the end of our study 9 of whom were undergoing angiography (5 PTCA, 4 CABG). Eight patients were re-admitted due to cardiac

Table-1: Characteristics of patients at the commencement of study according to the IgG serum concentration.

	High serum IgG concentration (mean± SD)	Low serum IgG concentration (mean± SD)	P value
Age(years)	52.57 ± 12.06	60.56 ± 10.63	0.07
SBP at the admission (mmhg)	123.89 ± 16.35	141.43 ± 31.40	0.09
Time from onset of symptoms to thrombolysis(h)	2.35 ± 2.14	3.54 ± 2.18	0.16
	(Frequency %)	**(Frequency %)**	
Sex			
Female	21.4	23.5	0.62
Male	78.6	76.5	
DM	21.4	23.5	0.62

Table-2: Differences in short and long term clinical outcome with IgG serum concentration.

	High serum IgG concentration (mean± SD)	Low serum IgG concentration (mean± SD)	P value
Return of typical ischemic chest pain after 48 hour of AMI	28.6	11.8	0.37
appearance of complex arrhythmia during admission in ccu after 24 hour of AMI	7.1	23.5	0.34
CABG or PTCA	35.7	25.0	0.69
re-MI	14.3	6.7	0.60
re-admission due to cardiac problems	35.7	18.8	0.42
	(Mean ± SD)	**(Mean ± SD)**	
maximum CPK serum concentration during first three days of admission	1562.71 ± 800.33	1538.75 ±753.13	0.93
LVEF on the last day of admission	48.50 ± 12.95	43.75 ±11.53	0.29

problems during the study.

Table-1 shows characteristics of patients at the commencement of the study according to the IgG serum concentration. There are no significant differences in age, sex distribution, diabetes mellitus and systolic blood pressure in both groups.

The short term and long term clinical outcomes of both groups were compared in Table-2. Return of typical ischemic chest pain 48 hours after AMI, appearance of complex arrhythmia during admission in CCU and 24 hours after AMI, maximum CPK serum concentration during the first three days of admission, and left ventricular ejection fraction on the last day of admission were not significantly different between the two compared groups ($p > 0.05$). Moreover, there were no significant differences in surgical interventions (CABG or PTCA), re-MI and re-admission due to cardiac problems observed during the one-year follow up of patients between the two groups ($p > 0.05$).

Discussion

As ASK antibody showed previous exposure to streptococcal infraction, and its filter can have some effects on the response to SK in AMI, our results demonstrated that there were no statistically significant differences between titer of ASK antibody and the in-hospital and out-hospital clinical outcome. It is well documented that thrombolytic therapy as a standard treatment for acute myocardial infarction preserves left ventricular function and increases the survival rate.[10,11] ASK level may be different in different populations, reflecting differing incidences of streptococcal infections.[11-13]

Recent studies in India and Iran have shown that the pretreatment level of ASK antibodies was found to be more than twice than the reported level in Europe and USA.[12] In addition, Abuosa et al. demonstrated that streptococcal infections are common in developing countries therefore giving SK as thrombolytic agent in these countries may possibly be less effective. Therefore, the standard dose of 1.5 million units of streptokinase was chosen to overcome the SK antibodies.[13]

Gemmil et al. demonstrated that the influence of pretreatment by SK on the efficacy of the streptokinase was evaluated angiographically at 90 minutes and 24 hours of AMI.[14] Another study showed that variations in pretreatment circulating levels of ASK do not influence angiographically defined early coronary artery patency rates when standard dose of SK are given to patients who have not had SK treatment before.[15]

Fears et al. also showed that the pretreatment ASK antibody level was not a risk factor for poor outcome in response to SK.[14] Another angiographic study has not revealed any relation between the pretreatment concentrations of ASK and SK efficacy as assessed by the reperfusion rate or time of reperfusion with streptokinase.[22,23]

Even in areas endemic for streptococcal infection although patients with myocardial infarction have high levels of preexisting ASK antibodies these antibodies do not appear to interfere with the efficacy of reperfusion with streptokinase.[24]

Another study in Pakistan demonstrated that there is no association between the anti-SK antibody titer and response to the standard dose of SK treatment.[16] In addition, Abuosa et al. showed that the presence of a previous streptococcal infection may not necessarily reduce the effect of SK on the patency of the infarct related artery evaluated angiographically and/or clinical outcome.[13] Thus, the different methods of measuring endpoints for coronary reperfusion seem not to be the key to whether or not any association can be found between pretreatment levels of SK antibodies and reperfusion.

Conclusion

According to this study previous exposure to streptococcal infections may not reduce the efficacy of a single dose of SK and it does not seem necessary that the ASK titer be measured before SK administration.

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Conflict of Interests:

The authors have no conflict of interests.

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