

EFFECT OF POST-MYOCARDIAL INFARCTION STREPTOKINASE (SK) THERAPY, ON MYOCARDIAL VIABILITY - EVALUATION WITH THALLIUM-201 SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY (TL-201 SPECT)

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ABSTRACT

Objective: To evaluate the effect of post-myocardial infarction Streptokinase therapy on myocardial viability, employing Thallium-201 single photon emission computed tomography (TL-201 SPECT).

Design: Retrospective, experimental study.

Place and duration of study: The Nuclear Cardiology Department, Armed Forces Institute of Cardiology / National Institute of Heart Diseases, Rawalpindi, from 1st April 2009 to 31st October 2009.

Patients and Methods: Male patients, who had suffered from acute myocardial infarction (AMI), in an area supplied by the left anterior descending (LAD) artery, had infarct-related electrocardiogram (ECG) changes and received or did not receive Streptokinase therapy, were included. Those with a normal ECG, or history of revascularisation, or non-ST elevation MI, or more than one MIs, were excluded. The patients were divided into groups 1 (who received Streptokinase) and 2 (who did not receive Streptokinase). Each group contained 42 patients and all underwent scintigraphic viability study through intravenous injection of 3.0 mCi (123 MBq) of TL-201, followed by rest-redistribution SPECT imaging on a dual head, dedicated cardiac gamma camera system (Philips Cardio MD ®). Emory's cardiac toolbox ® and AutoQUANT ® were used for data processing and quantitative estimation of viable myocardium. Empirical scores from 0 to 2 were assigned to each of the scans, in the order of increasing viability, and these were compared across the two groups.

Result: Group 1 contained 42 patients (age range = 38 to 80 years, mean = 53.98 ± 11.26 years), in whom empirical viability scoring was done. Score 0 was seen in 2 patients, score 1 was seen in 15 patients and score 2 was seen in 25 patients from this group. Group 2 also contained 42 patients (age range = 38 to 80 years, mean = 56.71 ± 9.05 years), in whom viability score of 0 was seen in 3 patients, score 1 was seen in 11 patients and score 2 was seen in 28 patients from this group. Age difference between the two groups was statistically insignificant ($p = 0.223$). The myocardial viability results analysed by 3 × 2 contingency table applying chi-square (χ^2) test also showed no significant difference between groups 1 and 2 ($p = 0.611$).

Conclusion: This study did not find any significant difference in myocardial viability - post-myocardial infarction - in patients who received or did not receive Streptokinase therapy.

Keywords: Streptokinase therapy, Thallium-201, SPECT, myocardial viability, single photon emission computed tomography.

INTRODUCTION

Use of Streptokinase as a therapeutic tool to dissolve intra-coronary clots in 1959¹ and then its general adoption for intravenous thrombolytic treatment after Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico (GISSI)² study in the mid 80s, revolutionised the management of acute myocardial infarction (AMI). Many studies have documented the efficacy of this treatment

and as it has been proven to improve survival, and limit the extent and severity of myocardial damage / scarring^{3,4}, it has now translated into evidence based guidelines⁵.

As a majority of patients in the present day cardiology practice seek partial or complete revascularisation at some stage of their follow-up and up to 50% of the patients with severely impaired ventricles have hibernating myocardium⁶, it has become immensely important that estimation of myocardial viability be carried out prior to this expensive and invasive undertaking⁷. The modalities available for viability estimation vary from myocardial viability studies employing SPECT

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to contrast-enhanced magnetic resonance imaging (MRI)⁸, stress echocardiography and positron emission tomography (PET)⁹. Of these, scintigraphic viability estimation, specially the techniques employing Thallium-201 have adequate data supporting their efficacy (both in patients with recent or old MI)^{10,11} and are readily available, cost-effective and reliable. With the recent advancement in information technology and computing hardware and software, 'Emory's cardiac toolbox'[®] and associated programmes like 'AutoQUANT'[®] and 'AutoSPECT'[®] have become a necessity for any reputable nuclear cardiology setup. Attenuation correction in SPECT and hybrid systems with multislice computed tomography (CT) and auto-registration have made analyses and complicated quantitative estimations, frequently employed in scintigraphy, much more convenient and the future holds much promise for further improvement¹².

Not many studies have been conducted in Pakistan for evaluation of myocardial viability, after the use of thrombolytic therapy (like Streptokinase) post-myocardial infarction; and perhaps only a few employed an objective, well-substantiated technique, like SPECT scintigraphy. Nitrate augmented Tc-99m MIBI has been used and compared with TL-201¹³ but no study employed the time tested benchmark, TL-201 SPECT, in itself, for viability estimation. In the context of prevalence data on coronary artery disease (CAD) and other studies linking the risk factors and actual disease prevalence South Asia (including Pakistan) is conspicuously absent from many global initiatives¹⁴.

This study attempts to fill this void employing this non-invasive technique, available in almost all major cities of Pakistan (the gold standard for viability estimation, ¹⁸F fluorodeoxyglucose (¹⁸FDG) PET, being available in only one centre in the country, to date). Similar studies, may help define national guidelines for administering thrombolytic therapy to patients of acute myocardial infarction, will boost clinicians' confidence in the usefulness of this approach in our setup and ultimately, through better management and

better-guided revascularisation decisions, lead to improvement of morbidity and mortality figures in our post-myocardial infarction patients¹⁵.

OBJECTIVE

To evaluate the effect of post-myocardial infarction Streptokinase (SK) therapy on myocardial viability, employing Thallium-201 single photon emission computed tomography (TL-201 SPECT).

PATIENTS AND METHODS

This is a retrospective, comparative study employing convenient sampling, wherein patients, who reported for myocardial viability assessment to the nuclear Cardiology Department of the Armed Forces Institute of Cardiology / National Institute of Heart Diseases (AFIC/NIHD), Rawalpindi, from 1st April 2009 to 31st October 2009, were included.

Inclusion criteria - male patients of ischaemic heart disease, who had suffered from MI in LAD (left anterior descending) artery territory, i.e., anterior, anteroseptal, anteroapical and / or anterolateral MI, in the past and had corresponding ECG changes. Patients who received or who did not receive Streptokinase (SK) therapy, were included.

Exclusion criteria - patients with inferior or lateral MI, patients with a history of two or more MIs including non-ST elevation MI (NSTEMI), patients who had undergone primary percutaneous coronary intervention (PCI), percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass graft (CABG) in the past, and patients who had a normal resting electrocardiogram (ECG), with no evidence of MI.

The subjects were divided into two groups on the basis of their having received thrombolytic therapy with SK, post-MI. Group 1 consisted of patients who received SK therapy within a few hours of the AMI.

Group 2 consisted of patients who were either late for SK or were not given SK due to some other reason.

The study was approved by the Institutional Ethics Committee of AFIC /

NIHD, and prior to the scan, informed consent was obtained from every patient.

Protocol for TL-201 SPECT - All the patients were asked to report for the test, after an overnight fast. On arrival, an injection of 3.0 mCi (123 MBq) of Thallium-201, was given intravenously in the arm, under resting conditions. Rest-redistribution protocol was followed and SPECT imaging was done supine, employing a dual-head, dedicated cardiac SPECT gamma camera system (Philips Cardio MD ®), interfaced with an acquisition computer. The acquisition arc comprised 64 projections from the right anterior oblique (RAO) to the left posterior oblique (LPO) plane and the total acquisition time was 11:12 minutes for the rest and 12:32 minutes for the redistribution images. Step and shoot mode, with a non-circular, clockwise, SPECT orbit and 64 x 64 matrix were used. The pixel size was 6.40 mm. Following rest acquisition, the patients were asked to place 1 or 2 tablets of Glyceryl trinitrate sub-lingually, depending on their resting blood pressure (BP) and the induced fall in BP observed in each case.

Data Analysis was done using a 'Sun Solaris'® processing station through 'Pegasys'® software version 5.0. Raw images transferred from the acquisition station were processed employing filtered back projection, through associated SPECT processing software version 5.0. Final processing was done using 'Emory's cardiac toolbox' ® and 'AutoQUANT'® version 5.1.1 was used for quantitative estimation of viable myocardium. 3-D rendering of the data and 20 segment polar mapping were employed for delineation of viable and non-viable myocardium. For better reproducibility of results and to remove inter-observer variation, software generated maps of myocardium at risk and automatically projected extent of viable and non-viable regions were used.

Viability Estimation in Lad Territory

As the region of interest comprised the LAD territory, counts from the segments of left ventricular myocardium that constitute its area of distribution were analysed through

'AutoQUANT'®, using its automated processing feature. The scores generated were used to report the regions so identified, as viable or non-viable. For subsequent statistical analysis, empirical viability scores from 0 to 2 (derived from the affected segments of the left ventricular myocardium) were assigned to each of the scans, in the order of increasing myocardial viability; and these were compared across the two groups:

Score 0 - 0% to 30% viable myocardium

Score 1 - 31% to 69% viable myocardium.

Score 2 - ≥70% viable myocardium

Statistical Analysis

Statistical analysis of the data was done using SPSS version 15. Descriptive statistics were used to describe the data. Chi-square (χ^2) test was used to compare viable myocardium between both the groups. $p < 0.05$ was considered significant.

RESULTS

Forty two patients in group I have ages ranged from 38 to 80 years (mean age = 53.98 ± 11.26 years). The total aggregate viability score in the group was 65 out of a maximum of 84. Randomly selected 25 of the scans were reported by observer number 1 and 17 were reported by observer number 2.

Forty two patients in group II had ages from 38 to 80 years (mean age = 56.71 ± 9.05 years). The total aggregate viability score in the group was 67 out of a maximum of 84. Identical to group 1, randomly selected 25 of the scans were reported by observer number 1 and the other 17 were reported by observer number 2.

The age difference between groups 1 and 2, was statistically insignificant ($p = 0.223$). On statistical analysis of the viability scores for groups 1 and 2, the scores for both groups were also not found to be significantly different from each other ($p = 0.611$). The results are described in Table.

DISCUSSION

Thrombolytic therapy with SK has a special place in the current management of a

patient of AMI. In skilled hands, the infusion is started en route to a tertiary cardiac care facility, to limit the extent and severity of myocardial damage and to improve survival.

This study compared, through the recommended scintigraphic technique of TL-201 SPECT, myocardial viability in subjects who, post-MI, were administered SK and those who were not administered this therapy. The use of this technique of viability assessment was preferred over others, due to the physiological uptake and redistribution of the tracer and the documented objectivity, reproducibility, cost effectiveness and non-invasiveness of the technique; which can be favourably compared with PET, the gold standard in myocardial viability assessment, both in terms of concordance rates of upto 88%¹⁶ and outcome of management, guided by either of the two modalities¹⁷.

The reasons for choosing patients who had an MI in the area of distribution of the LAD artery was this vessel's supply to a large area of the left ventricular myocardium and higher incidence of MI in its distribution. Thus an infarct in its territory is, at times, much more extensive than an infarct in other vascular territories. Additionally, patients with relatively proximal LAD disease are commonly referred for scintigraphic viability assessment and may be offered CABG, if viable myocardium exists in its vascular distribution – thereby gaining subsequent survival benefit through a left internal mammary artery (LIMA) graft¹⁸ – or other forms of partial or complete revascularisation, as the situation and circumstances merit¹⁹. Other reasons have their origin in the possibility of misreporting due to artefacts encountered in scintigraphic imaging. Using TL-201 SPECT for estimation of myocardial viability, diaphragmatic attenuation artefact may obscure the inferior wall and breast attenuation in females may obscure parts of the anterior, anterolateral or anteroseptal left ventricular wall. Conversely, in almost all cases, no artefacts obscure the myocardial regions supplied by the LAD artery in male patients with average build; and this helps in definitely establishing the presence, or

otherwise, of viable myocardium in these regions.

This study adds to the previous research on the impact of thrombolytic therapy with SK on myocardial viability, post-MI. The findings are not in agreement with the majority of similar studies on the subject, in that the study has found no significant difference in the groups of patients who received or did not receive thrombolytic therapy. Many studies have questioned the efficacy of thrombolytic therapy and have highlighted the presence of many patients who do not benefit from SK for various reasons. In a recent study from Pakistan²⁰, on ECG analysis, 60 minutes post-SK, 64% patients showed ST segment resolution but 36% patients showed no ST resolution. Similar outcome was observed in by Bhatia *et al*, when failed reperfusion post-MI was seen in 47% of the patients, employing the criterion of serial ECG evaluation²¹. There are others, who do not seem to get the benefit of reduced infarct size or improved left ventricular function²². Another documented observation is the reocclusion of coronary arteries after successful reperfusion therapy in up to 12.4% of the cases, with 58% of such patients being symptomatic²³.

The reasons for these results may vary and a whole spectrum of possibilities may need to be followed up. Inadequacies may need to be explored in the study design and data collection; like relatively small number of patients recruited for the study, lack of patient awareness about thrombolytic therapy (leading to an error in recording history and subsequent group allocation), inconsistencies in documentation of thrombolytic therapy administered and non-availability of previous patient documents for verification of the patients' statements / physicians' entries over time. Another contributory factor may be the relatively younger age of some of the subjects (which may lead to bigger infarct size due to poorly developed collateral circulation). It is pertinent to mention that the mean ages for groups 1 and 2 in this study were 53.98 ± 11.26 years and 56.71 ± 9.05 years, respectively, which are younger than the ages in advanced countries like the USA, where the mean age in

the COURAGE trial was 62 ± 5 years²⁴. An age difference of 10 years in the mean age of Pakistani patients with AMI was noted in another recent study by Jafary et al²⁵.

Other issues, that may need to be closely examined, relate to thrombolytic therapy itself; like delayed administration of the injection, sub-standard preparation (which may include lack of proper storage, unsatisfactory quality checks during manufacture, non-standard preparation and administration), non-adherence to standard guidelines and protocols for SK therapy, documented functional differences in plasminogen activation in allelic variants of SK²⁶ and finally ineffective thrombolysis in our population, due to the presence of antibodies to SK or cross reactivity with some other antibodies²⁷ and / or a possible difference in clot or plaque composition leading to failure of the thrombolytic agent (SK) in lysing / dissolving it.

The results of this study warrant a larger, randomised trial, including more patients from AFIC / NIHD and other centres of excellence in cardiology, in the country, and pursuing the fore mentioned and other possible clues that may adequately explain the findings of this study.

CONCLUSION

This study found no significant difference in myocardial viability, in patients who received or did not receive Streptokinase therapy, post-myocardial infarction.

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Table – Statistical analysis by 3 × 2 contingency table applying Chi-squared (χ^2) test

Categories (SK ⁺ or SK ⁻)	Myocardial Viability Scores		
	0	1	2
Group 1 (SK given)	2	11	28
Group 2 (SK not given)	3	15	25

$p = 0.611$