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Intracoronary Streptokinase for Acute Anterior STEMI with A Superimposed Thrombus a 12 Months Follow Up

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Research Article

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Abstract

Background: Intracoronary fibrinolytic administration immediately after primary PCI improves microvascular perfusion, decreases long-term infarct size, and improves LV function especially in patients with superimposed thrombus. As a consequence intracoronary thrombolytic is considered one of the pharmacological strategies for management of high thrombus burden lesions during PCI.

Objectives: To assess the effect of low dose intracoronary streptokinase (ICSK) during primary PCI in patients presenting with acute anterior wall S-T segment elevation myocardial infarction with a definite thrombus in the left anterior descending artery on clinical, angiographic and echocardiographic outcomes.

Methods: A total of 167 patients at the National Heart Institute, Egypt who had undergone primary PCI following an acute anterior wall STEMI presentation were included in this randomised controlled study (with a thrombus grading > thrombus grade 2) and no history of coronary angioplasty or myocardial infarction of the LADs. Patients were randomized into two groups: a control group (n = 90) receiving no extra therapy, and a study group (n = 77) receiving ICSK during primary PCI. Following PCI, angiographic results and S-T segment resolution were evaluated. A follow-up of MACE and echocardiographic results was subsequently carried out at 6 and 12 months.

Results: Post-PCI indices of perfusion, such as TIMI flow grade 3 (79% vs. 51%), MBG 3 (43% vs. 20%), and cTFC (18.20 ± 4.01 vs. 30.95 ± 3.75), were considerably better in the ICSK group than in the control group. The ICSK group's SWMA index score was substantially lower than that of the control group on the 6- and 12-month follow-ups (1.01 ± 0.02 vs 1.28 ± 0.04, and 1.22 ± 0.11 vs 1.7 ± 0.06, respectively).

Conclusion: The use of low dose ICSK during primary PCI in acute anterior STEMI patients with coronary thrombi enhanced coronary perfusion and LV function, presenting a favorable approach for managing high thrombus burden PCI.

Keywords: Intracoronary Streptokinase; Thrombus Burden; S-T Elevation Myocardial Infarction; Primary PCI; Microvascular Perfusion; Distal Embolisation

Abbreviations: MACE: Major Adverse Cardiac Events; ICSK: Intracoronary Streptokinase; LAD: Left Anterior Descending Artery; RLD: Reference Lumen Diameter; CABG: Coronary Artery Bypass Grafting; STEMI: S-T Elevation Myocardial Infarction; BMS: Bare Metal Stents; DES: Drug Eluting Stents; MBG: Myocardial Blush Grade.

Introduction

Intracoronary heavy thrombus burden during PCI frequently caused management decision difficulties for the interventionist and was a major factor in the reduced post-PCI myocardial blush, distal embolization, and slow or no-reflow phenomenon, all of which increased the risk of myocardial infarction after PCI. As a result, selecting the best course of action for dealing with this issue during primary PCI in acute STEMI patients has frequently proven difficult [1].

Heavy thrombus burden was graded into five grades: G0, G1, G2, G3, G4, and G5 based on its size and angiographic description. Angiographically, it can appear as a cut-off pattern of occlusion in the IRA, presence of a floating thrombus, accumulated thrombus proximal to the occlusion, persistent dye stasis distal to the occlusion, incomplete occlusion with accumulated thrombus greater than three times the reference lumen diameter (RLD), and RLD of the IRA of ≥ 4.0 mm [2].

High thrombus burden lesions were managed using a variety of techniques during PCI: pharmacological treatments included anticoagulants, glycoprotein IIb IIIa inhibitors, vasodilators, and thrombus aspiration; mechanical treatments included embolic protection devices, rheolytic thrombectomy, and ischemic preconditioning [3].

Aim of the Work

This study aims to evaluate the impact of low dose intracoronary streptokinase (ICSK) on clinical, angiographic, and echocardiographic outcomes during primary PCI in patients presenting with acute anterior wall S-T segment elevation myocardial infarction with a definite thrombus in the left anterior descending artery.

Patients and Methods

The ethical committee at our institute gave its approval to this randomized controlled study. All eligible patients gave their written informed permission. 176 patients who had an acute anterior S-T elevation myocardial infarction (STEMI) within 12 hours after the start of chest discomfort were included in the study.

Acute anterior STEMI patients were included in the study if their coronary angiography revealed a left anterior descending artery (LAD) with a thrombus grading > thrombus grade 2 (G2), which is defined by the TIMI thrombus grading score as a definite thrombus with greatest dimensions < ½ the vessel diameter and no history of coronary angioplasty or myocardial infarction.

Exclusion criteria included a history of coronary artery bypass grafting (CABG), a history of coronary angioplasty or LAD infarction, patients with a history of recent stroke or gastrointestinal bleeding that precludes the use of streptokinase, patients with coagulopathy, renal impairment, dye allergy, or cardiogenic shock, as well as patients with suspected mechanical complications.

All patients received 300 mg of aspirin, 600 mg of clopidogrel, and 100 I.U./kg of unfractionated heparin after completing the history taking, clinical examination, 12-lead ECG, admission, and peak CK-MB.

Following this, they underwent coronary angiography via percutaneous access into the femoral or radial arteries using the Seldinger technique. Only patients with thrombus grading > grade 2 (G2) were included after the coronary angiography. Following primary PCI, patients were randomly assigned to one of two groups: the study group (n = 77) received low dose (250 KU) intracoronary streptokinase (ICSK) during primary intervention (250 000 IU of streptokinase diluted in 15 ml of normal saline, with two thirds (2/3) of the dose infused); the control group (n = 90) underwent conventional primary intervention without receiving intracoronary thrombolytic.

In certain circumstances, the operator may decide to employ additional techniques, such as an aspiration device or glycoprotein IIb/IIIa inhibitors, to finish the treatment since the patients' angiographic findings were not adequate.

Following primary PCI, the quality of reperfusion and the efficacy of revascularization were evaluated electrocardiographically using the S-T elevation resolution score, angiographically using the TIMI flow grading method, myocardial blush grade (MBG), and corrected TIMI frame count (cTFC).

The patients had echocardiography and serial evaluation of serum biomarkers while they were in the hospital. Six and twelve-month follow-up appointments comprised clinical examination and repeat echocardiogram to measure segmental wall motion abnormalities (SWMA), left ventricular ejection fraction (LVEF), and SWMA index score. Transthoracic echocardiography was used to calculate the SWMA index score. Each myocardial segment is given a score between 1 and 4, with 1 denoting normokinetic, 2 hypokinetic, 3 akinetic, or 4 dyskinetic. Then, the total of the previously indicated segmental values is divided by 16 (the number of myocardial segments) to obtain the wall motion score index; hence, a SWMA index score of 1.0 (16/16) is regarded as normokinetic.

Statistics

SPSS (statistical package version sixteen) was used for the collection, verification, revision, and statistical analysis of the data. While continuous variables were displayed as mean values ± standard deviation (SD), categorical variables were portrayed as absolute and relative frequencies (%). The chi-square test and Pearson correlation coefficient were used for categorical variables, while the t-test was used for continuous data when comparing the two groups. A P value of less than 0.05 indicated statistical significance, while a P value less than 0.01 indicated extremely significant differences.

Results

The study population consisted of 167 patients who had undergone primary PCI to LAD after having anterior STEMI. Patients were divided into 2 groups:

Group A (Study Group)

This comprised 77 patients who underwent primary PCI and were administered intracoronary streptokinase (of which two thirds were administered immediately following the achievement of at least TIMI 1 flow, following the guiding wire's passage and the injection of 200 µg of nitroglycerin to prepare the microvasculature, and the remaining third after the stent was deployed).

Group B (Control Group)

It included 90 patients who underwent conventional primary PCI without receiving intracoronary thrombolytic.

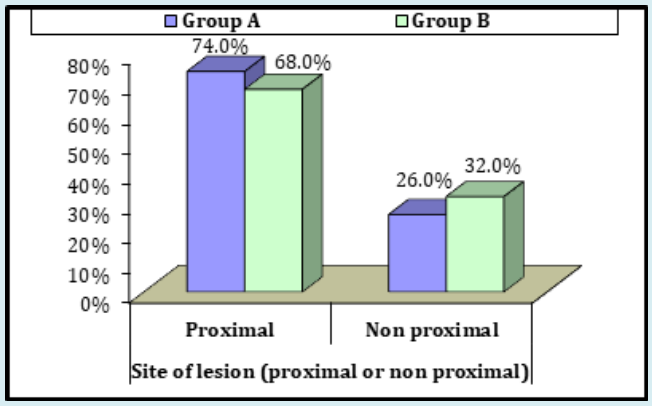

Figure 1: Diagrammatic comparison of patients undergoing primary PCI who were given intracoronary streptokinase. (Group A) patients who underwent conventional primary PCI (group B) as regards site of the lesion; whether proximal lesion or non-proximal lesions (i.e: mid or distal segments lesions).

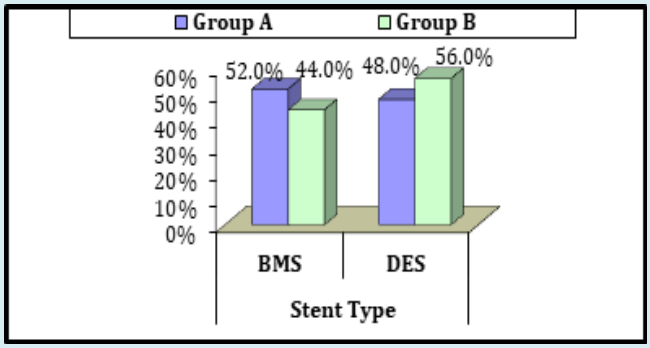

Figure 2: Diagrammatic comparison between patients who received intracoronary streptokinase during primary PCI (group A) and patients who underwent conventional primary PCI (group B) as regards stent type; whether bare metal stents (BMS) or drug eluting stents (DES).

Then, both groups were compared as regards the primary end points (angiographically: post procedural TIMI flow, post procedural MBG and corrected TIMI frame count and electrocardiographically: S-T segment resolution score) as shown in Table 4, and represented diagrammatically in Figures 3-5.

Both post procedural TIMI 3 flow and MBG 3 were statistically significant higher among patients of group A (P-values = 0.026 and 0.001 respectively), mean corrected TIMI frame count was statistically significant lower among patients of group A (P-value= 0.000), while S-T segment resolution score > 70% was yet higher among patients of group A, but not statistically significant (P-value=0.22).

Group A showed statistically higher incidence of TIMI flow 3 and MBG 3, together with statistically significant lower mean cTFC. ST segment resolution was yet numerically better in group A, but still not statistically significant.

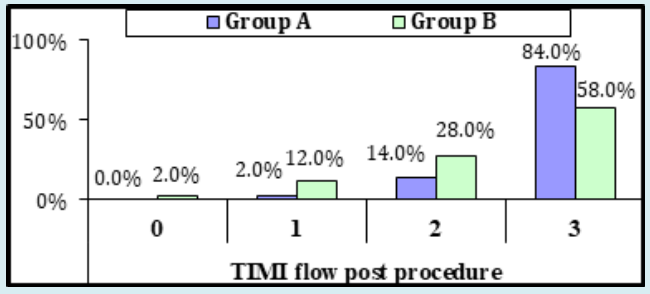

Figure 3: Diagrammatic comparison between patients who received intracoronary streptokinase during primary PCI (group A) and patients who underwent conventional primary PCI (group B) as regards post procedural TIMI flow (whether TIMI 0, TIMI 1, TIMI 2 or TIMI 3).

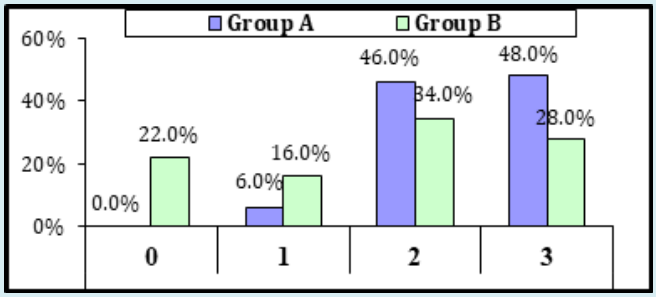

Figure 4: Diagrammatic comparison between patients who received intracoronary streptokinase during primary PCI (group A) and patients who underwent conventional primary PCI (group B) as regards post procedural MBG (whether MBG 0, MBG 1, MBG 2 or MBG 3).

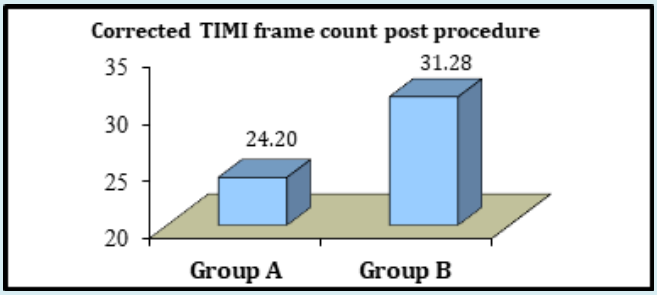

Figure 5: Diagrammatic comparison between patients who received intracoronary streptokinase during primary PCI (group A) and patients who underwent conventional primary PCI (group B) as regards corrected TIMI frame count post procedure.

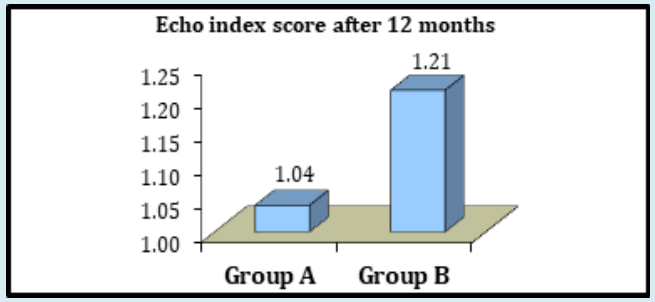

Figure 6: Diagrammatic comparison between patients who received intracoronary streptokinase during primary PCI (group A) and patients who underwent conventional primary PCI (group B) as regards echocardiographic follow up of the SWMA index score after 12 months.

Then, both groups were compared regarding the secondary end points:

Major adverse cardiac events at follow-up: Group A showed a case of re-infarction and another with cerebrovascular stroke, while group B showed a case of re-infarction and another case of cardiac death. (P value= 0.572).

Bleeding complications as a safety end point: Group A showed two cases of local minimal bleeding and a third case with local small haematoma, while group B had two cases of local small easily controlled haematomas (P value= 0.483).

Discussion

Over the past several decades, the prognosis for patients with acute STEMI has significantly improved because to PCI's restoration of epicardial coronary blood flow. However, intra-coronary thrombus, which frequently results in microvascular dysfunction due to distal embolization after mechanical reperfusion, may impede the effectiveness of PCI [4].

Selecting the best course of action for acute STEMI patients' large thrombus load lesions during initial PCI has always been difficult. Thus, to address this issue, pharmacological approaches such as glycoprotein IIb IIIa inhibitors, vasodilators, thrombus aspiration, embolic protection devices, rheolytic thrombectomy, and ischemic preconditioning, or mechanical approaches such as anticoagulants, were employed [5].

In this work, we aimed to do a randomized controlled trial evaluating the advantages and disadvantages of intracoronary (IC) thrombolytic as a main PCI adjunctive therapy in anterior STEMI patients.

Our study was conducted on 176 patients who had undergone primary PCI to LAD after presenting with anterior STEMI. Patients were divided into a study group (n=77) who received intracoronary streptokinase during primary PCI and a control group (n=90) who underwent conventional primary PCI.

The results of our study indicated that patients in the study group had significantly higher post procedural TIMI 3 flow and MBG 3 (P-values = 0.026 and 0.001, respectively), significantly lower mean corrected TIMI frame count (P-value = 0.000), and significantly higher S-T segment resolution score > 70% (P-value = 0.22), though not statistically significant.

These results are consistent with a research conducted in Istanbul in 2007 as a pilot study including 41 patients receiving primary PCI by Sezer M, et al. [5] and his colleagues. Patients were randomized to receive either no further treatment or intracoronary streptokinase at a dosage comparable to that of our research (250 kU). All microvascular function

measurements, including corrected TIMI frame count, were considerably lower in the streptokinase group two days after PCI, which was consistent with our study's findings [6].

Additionally, these results are consistent with the 2015 study conducted by Bainey and associates. They compared the advantages and disadvantages of IC thrombolytic as an adjuvant medication during primary PCI in STEMI patients in a meta-analysis. There were 131 patients from three randomized trials (71 IC thrombolytic and 60 IC placebo). Comparing IC thrombolytic to placebo, TIMI flow 2 and flow 3 were more frequently seen (P-value=0.004), which was consistent with our study's findings (P-value= 0.026) [7].

A 12-month echocardiographic follow-up in our investigation showed that the study group's SWMA index score was considerably lower than the control group's (1.21±0.30 vs. 1.04±0.08, P value= 0.000). This result was at odds with Sezer M, et al. [5] initial pilot study, which found no evidence of a difference in left ventricular (LV) size or function between the two study groups. This implied that IC administration of SK did not improve left ventricular size or function over the long term. Since Sezer M, et al. [5] study was a pilot, its small study sample (n=41) may have contributed to this discrepancy and rendered its findings less definitive [6].

On the other hand, the final results of Sezer M, et al. [5] main study demonstrated significantly smaller LV volumes and higher echocardiographic LV ejection fraction in the ICSK group over the long term (57.2% vs. 51.8%, p = 0.018), which was similar to the findings of this study (as opposed to the first pilot study).

Apart from the results of the echocardiographic follow-up, Sezer M, et al. [5] study also demonstrated that the ICSK group's infarct size was substantially less than that of the control group, as indicated by the SPECT imaging results (22.7% vs. 32.9%, p=0.003) [8].

In terms of secondary study objectives, there was no significant difference between the two groups for major adverse cardiac events (MACE); re-infarction and cerebrovascular stroke were reported in the study group, while cardiac death and re-infarction were reported in the control group (P value = 0.572).

However, Sezer M, et al. [5] trial produced nearly identical findings: two patients in the control group and one in the ICSK group required surgical revascularization, and one patient in the ICSK group experienced a reinfarction after a month. During the follow-up period, there were three cardiac fatalities in the control group and two in the ICSK group. Furthermore, Bainey's study found no difference in mortality between study group and control group [9].

Conclusion

Administration of low dose ICSK during primary PCI in acute anterior STEMI patients with definite coronary thrombi improved coronary perfusion and caused improvement of LV function during follow-up.

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