Impact of Intracoronary Vasodilators injection Post-Myocardial Infarction on Incidence of Arrhythmic Events.

Thesis
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Introduction:

Primary percutaneous coronary intervention (PCI) significantly improves the survival of patients with ST-segment elevation myocardial infarction (STEMI) (1).

Presently, timely and effective reperfusion with primary percutaneous coronary intervention (PPCI) for ST-elevation myocardial infarction (STEMI) remains the most effective treatment strategy for reducing myocardial infarct (MI) size, preserving left ventricular ejection fraction (LVEF) and preventing the onset of heart failure. (2,3,4,5)

However, despite the introduction of PPCI, and other advances such as the introduction of antiplatelet therapies, resulting in a reduction in mortality of ~50% at 30 days, substantial mortality and morbidity rates still persist. (6,7)

One of the main determinants of prognosis after AMI is the size of the infarct, (8,9,10) and importantly increased infarct size is associated with an increased incidence of heart failure and arrhythmias. (11,12,13) Thus, there is a clear need for identification of additional strategies that might decrease infarct size and improve outcome.

In the setting of STEMI the immediate reopening of acutely occluded coronary arteries via PPCI is the treatment of choice to salvage the ischaemic myocardium. However, the sudden

reinitiation of blood flow leads to a local acute inflammatory response with further endothelial and myocardial damage. This phenomenon, described as 'reperfusion injury'(14) may explain why, despite optimum myocardial reperfusion, the short-term mortality after AMI approaches 7% and the incidence of heart failure approaches 15–20%.

Experimental in vivo models suggest that while 50% of the final infarct size is because of the ischaemic insult the remaining 50% is because of reperfusion injury.(15) Although, the process of myocardial reperfusion continues to be optimised with recent advances in PPCI technology (thrombus aspiration, novel stents),(16) antiplatelet (prasugrel, ticagrelor) (17) and antithrombotic therapy (bivalirudin), (18) there is currently no effective therapy for reducing myocardial ischaemia-reperfusion (I/R) injury per se.

Post-procedural microvascular obstruction, despite the presence of normal epicardial flow, remains an important limitation of the procedure, which substantially reduces the beneficial effects of PCI (19,20)

The role of vasodilators in prevention of MVO has been studied in several randomized clinical trials. Intracoronary verapamil administered following primary PCI and followed by oral treatment improved myocardial perfusion and regional left ventricular wall motion in treated patients when compared to a control group (21). Intracoronary adenosine and verapamil administered following primary PCI achieved equivalent

improvement of myocardial perfusion, which was superior to placebo (22)

Although the mechanisms underlying post-infarction re-entry arrhythmias are not completely understood, wave breaks at the boundary of an anatomic block and focal activity including early and delayed afterdepolarizations arising from the infarct border zone are the characteristic electrophysiological features of arrhythmogenesis after infarction.(23)

An optimal standard treatment for no-reflow (NR) has not yet been established. Based on the multifactorial pathogenesis of NR during STEMI, a combination of mechanical and pharmacological approaches appears to offer an enhanced solution for achieving the desired microvascular reperfusion.

Importantly, the administration of current anti-platelet therapies during reperfusion therapy for STEMI has not eliminated the NR phenomenon (24). Nitroprusside (NTP) is an alternative drug that is, at present, being used for the reversal of the NR phenomenon. A study investigating the use of this agent in the treatment of the NR phenomenon revealed some promising preliminary results (25).

The causes of NR are complex and multifactorial. The most likely causes include platelet aggregation, distal embolization, spasm of the microcirculation, neutrophilic plugging, tissue edema or a combination of these factors (26). Prevention comprises strategies adopted prior to complete vessel re-

opening, in order to prepare the microcirculation for reperfusion.

Prevention strategies may be targeted to the different mechanisms of NR. Manual aspiration thrombectomy is reasonable for patients undergoing primary PCI. However, infarct size was not reduced by manual aspiration thrombectomy in the INFUSE-AMI trial of patients with large anterior STEMI (27). This may be due to the complex nature of NR, in which remote thromboembolism plays only a partial role.

However, of the several mechanisms that have been proposed to explain the NR phenomenon, vasoconstriction is considered one of the most important and potentially reversible, as suggested by the numerous positive reports of therapeutic vasodilatation in this context.

Aim of the work:

To study the effect of intracoronary vasodilators injection during primary PCI after myocardial infarction on the incidence of arrhythmia occurance throughout hospital stay, and comparing these data with a control group whom will not receive intracoronary vasodilators injection.

Patients and Methods:

This is a prospective study which will enrol a total number of 60 patients with the first attack of acute anterior STEMI occurring within 12 h of the onset of symptoms who underwent emergency PCI. The patients will be divided into three groups, the first one of them will undergo intracoronary injection of Adenosine at the time of primary PCI, and the second one will undergo intracoronary injection ofVerapamil, and the last group will be a control group and receive NaCl. The vasodilators will be injected intracoronary immediately before initial balloon inflation and after crossing the obstruction of the infarct-related coronary artery with a guide wire, and after thrombus aspiration in case of a thrombus containing lesion.

Inclusion Criteria:

1. Sinus rhythm.
2. Patients with first attack of acute myocardial infarction.
3. Anterior STEMI diagnosed on the basis of i) typical chest pain lasting >30 min; ii) ST-elevation of ≥2 mm in the precordial leads; iii)presumed new left bundle branch block; iv) thrombolysis in myocardial infarction (TIMI) flow ≤2 at baseline angiography.

Exclusion Criteria:

1. Age > 70 years.
2. Myocardial infarction not anterior.

3. Cardiogenic shock (defined as a systolic blood pressure of <90 mmHg for >30 min or the requirement for intravenous pressors or intra-aortic balloon counter pulsation)
4. Previous CABG
5. Patient with cardiac Pacemaker
6. A history of bleeding diathesis
7. Contraindication to anticoagulants.

Patients who will meet the selection criteria and who consented to participate in the study will be subjected toarrhythmia monitoring and analysis immediately on admission to the hospital with acute anterior myocardial infarction, during primary PCI and throughout hospital stay, using:

1. Thorough history taking.
2. Baseline 12-lead EKG.
3. Daily CCU Monitoring.
4. Echocardiography.
5. 48-hr Holter monitoring at the 3rdday following primary PCI of acute myocardial infarction.

- **Primary end point:**

  Significant reduction and improvement of any form of tachy- or bradyarrhythmias occurring immediately following acute myocardial infarction and throughout hospital stay.

- **Secondary end point:**

Prevention of the no-reflow phenomenon which may occur during primary PCI of an acutely infarcted coronary artery in the setting of acute myocardial infarction.

STATISTICS:

All results will be subjected to adequate statistical analysis including mean and standard deviations, tabulated and will be discussed .

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