Assessment Of The Effect Of Myocardial Post Conditioning

On MBG In STEMI Patients

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Masters degree in cardiology

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Reem El-Shalakany

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List of abbreviations:

Abbreviations	
AAR	Area at risk
AMI	Acute myocardial infarction
ANP	Atrial natriuretic peptide
Atm	Atmosphere
ATP	Adenosine triphosphate
AUC	Area under the curve
AVC	Aortic valve closure
CCFC	Coronary clearance frame count
CCS	Canadian cardiology society
CHD	Coronary heart disease
CK	Creatinine kinase
C-TFC	Corrected thrombolysis in frame count
D-BMBG	Door to best myocardial blush grade
DD	Diastolic dysfunction
DTB	Door to balloon
EA	Effort angina
ECG	Electrocardiography
E-NO	Endogenous nitric oxide
GIK	Glucose insulin potassium therapy
GP IIbIIIa	Glycoprotein IIb IIa
Hs-CRP	High sensitive CRP
IL-6	Interleukin-6
IS	Infarct size
LGE	Late gadolinium enhancement

LVEF	Left ventricular ejection fraction
MBG	Myocardial blush grade
mKATP	Mitochondrial potassium ATP
mPTP	Mitochondrial permeability transition pore
MRI	Myocardial resonance imaging
NR	No reflow
PKC	Protein kinase C
PPCI	Primary percutaneous coronary intervention
PTD	Pain to door
RI	Reperfusion injury
RIC	Remote ischaemic conditioning
ROS	Reactive oxygen species
SPECT	Single positron emission topograghy
STEMI	ST-segment elevation myocardial infarction
STR	ST segment resolution
Tc	Technicium
TIMI	Thrombolysis in Myocardial infarction
Tn I	Troponin I

Introduction

ST-elevation myocardial infarction is a leading cause of mortality and morbidity. Infarct size is an important determinant of outcome. Hence reduction of myocardial injury is a therapeutic mainstay, best achieved by early reperfusion through primary percutaneous coronary intervention**.** ***(Anderson et al, 2003)***

Patients receiving such treatment will achieve infarct-related vessel patency and reperfusion, but risk sustaining clinically significant myocardial infarction, even when the procedure is done soon after symptom onset**.** ***(Kaltoft et al, 2009)***

Reperfusion contributes to lethal injury following prolonged periods of ischaemia. The idea of reperfusion injury was first introduced by Jennings et al as significant morphological alterations appearing after the onset of reperfusion, including cardiomyocyte swelling, mitochondrial clarification, and amorphous/flocculent densities representing calcium phosphate deposits, hypercontracture, and loss of sarcomere organization.

Attempts to improve outcomes with adjuvant mechanical treatments such as thrombectomy and distal protection devices show inconsistent benefit**.**

(Kaltoft et al, 2006) & (Sardella et al, 2009)

Zhao et al.were the first to report in 2003 the application of postconditioning to limit lethal reperfusion injury in experimental AMI. Later studies by Zhao et al. and others ***(Halkos et al , 2004)*** revealed that postconditioning also reduced cardiomyocyte apoptosis and contracture, coronary endothelial dysfunction, microvascular injury, tissue oedema, and organelle dysfunction.

Remote ischaemic preconditioning induced by repeated brief periods of limb ischaemia before index ischaemia**,** ***(Kharbanda et al,2002)*** reduces myocardial injury in patients exposed to predictable ischaemia**.** ***(Cheung et al, 2006)& (Hausenloy et al, 2007)*** Furthermore, remote ischaemic postconditioning, applied in the early reperfusion phase after prolonged ischaemia, seems to be more effective than local postconditioning in experimental myocardial infarction**.** ***(Gritsopoulos et al, 2009)*.**

Encouraged by this data, we thought of studying whether brief episodes of ischemia-reperfusion of upper limb

performed immediately before coronary reperfusion can limit infarct size.

Aim of the work :

Evaluation of the Myocardial postconditioning on Myocardial Blush Grade through induction of upper limb ischaemia

Methodology:

Study design:

The study is designed as a prospective, single center, randomized, open-label study including 110 patients presenting to the cardiac catheterization laboratory at the Ain Shams University Hospital and the Ain Shams University Specialized Hospital to undergo primary PCI. Patients will be randomized to either have upper limb induced ischaemia before Primary PCI or not through repeated cuff inflations above systolic arterial blood pressure for 3 cuff inflations, each lasting for 3 minutes and separated by 5 minutes apart using a mercury sphygmomanometer.

Study endpoints:

Assessing the MBG where there will be a comparison between two groups: (MBG 0-1 vs. MBG 2-3) in STEMI patients exposed to upper limb Ischaemia prior to Primary PCI

Patient selection criteria:

Inclusion Criteria:

Patients presenting with First Acute STEMI and treated by primary PCI

Exclusion criteria:

- Previous history of Acute myocardial infarction
- Killip class II-IV
- Patients with Dilated cardiomyopathy
- Coarctation of the Aorta
- Peripheral vascular disease that prevents the post conditioning procedure
- Chronic total occlusions
- Bypass graft interventions

Study plan:

All patients will be subjected to the following:

1. Thorough History taking focusing on :smoking ,History of Diabetes Mellitus , Hypertension , Pain to door (PTD) , Door to Balloon (BTB) , Pain to the best MBG
2. Physical examination: Full clinical examination including general and local cardiological examination
3. Repeated cuff inflations : applied on the Brachial artery, 3 inflations, each inflation lasts for 3 minutes separated by 5 minutes interval
4. Primary PCI:

   Primary PCI will be performed according to usual standards of care.

5. By the End of The primary PCI; Myocardial Blush grading (MBG) The angiography is performed in 30 frames per second. The number of frames required for contrast material to reach a distal coronary landmark from the second it first appears in the ostium of the infarct-related artery is counted and recorded. The LAD and circumflex arteries will be assessed best in either the right or left anterior oblique views with caudal angulation, and the

RCA will best assessed best in the left anterior oblique projection with steep cranial angulation***(Gibson CM ,et.al)***

Statistical Analysis:

Data will be analyzed with a commercial statistical package with the appropriate tests.

Introduction

ST-elevation myocardial infarction is a leading cause of mortality and morbidity. Infarct size is an important determinant of outcome. Hence reduction of myocardial injury is a therapeutic mainstay, best achieved by early reperfusion through primary percutaneous coronary intervention**.** [1]

Patients receiving such treatment will achieve infarct-related vessel patency and reperfusion, but risk sustaining clinically significant myocardial infarction, even when the procedure is done soon after symptom onset**.** [8]

Reperfusion contributes to lethal injury following prolonged periods of ischaemia. The idea of reperfusion injury was first introduced by Jennings et al as significant morphological alterations appearing after the onset of reperfusion, including cardiomyocyte swelling, mitochondrial clarification, and amorphous/flocculent densities representing calcium phosphate deposits, hypercontracture, and loss of sarcomere organization.

Attempts to improve outcomes with adjuvant mechanical treatments such as thrombectomy and distal protection devices show inconsistent benefit**.** [8,10]

Zhao et al.were the first to report in 2003 the application of postconditioning to limit lethal reperfusion injury in experimental AMI. Later studies by Zhao et al.[11]and others [6]revealed that postconditioning also reduced cardiomyocyte apoptosis and contracture, coronary endothelial dysfunction, microvascular injury, tissue oedema, and organelle dysfunction.

Remote ischaemic preconditioning induced by repeated brief periods of limb ischaemia before index ischaemia**,**[9] reduces myocardial injury in patients exposed to predictable ischaemia**.**[2,7]

Furthermore, remote ischaemic postconditioning, applied in the early reperfusion phase after prolonged ischaemia, seems to be more effective than local postconditioning in experimental myocardial infarction**.** [5]

Encouraged by this data, we thought of studying whether brief episodes of ischemia-reperfusion of upper limb performed immediately before coronary reperfusion can limit infarct size.

Introduction

Coronary heart disease (CHD) is the leading cause of death world-wide. Its major pathophysiological manifestation is acute myocardial ischaemia-reperfusion injury. Innovative treatment strategies for protecting the myocardium against the detrimental effects of this form of injury are required in order to improve clinical outcomes in patients with CHD. [12]

'Conditioning' the heart to tolerate the effects of acute ischaemia-reperfusion injury can be initiated through the application of several different mechanical and pharmacological strategies. Inducing brief non-lethal episodes of ischaemia and reperfusion to the heart either prior to, during, or even after an episode of sustained lethal myocardial ischaemia has the capacity to dramatically reduce myocardial injury a phenomenon termed ischaemic preconditioning (IPC), preconditioning or postconditioning, respectively.[12]

Intriguingly, similar levels of cardioprotection can be achieved by applying the brief episodes of non-lethal ischaemia and reperfusion to an organ or tissue remote from the heart, thereby obviating the need to 'condition' the heart directly. This phenomenon has been termed remote ischaemic 'conditioning', and it can offer widespread systemic protection

to other organs which are susceptible to acute ischaemia-reperfusion injury such as the brain, liver, intestine or kidney. Furthermore, the identification of the signalling pathways which underlie the effects of 'conditioning', has provided novel targets for pharmacological agents allowing one to recapitulate the benefits of these cardioprotective phenomena--so-termed pharmacological preconditioning and postconditioning. [12]

Initial clinical studies, reporting beneficial effects of 'conditioning' the heart to tolerate acute ischaemia-reperfusion injury, have been encouraging. Larger multi-centred randomised studies are now required to determine whether these 'conditioning' strategies are able to impact on clinical outcomes.[12]

Rapid restoration of coronary blood flow through primary percutaneous intervention (PPCI) remains the gold standard management of acute ST-elevation myocardial infarction (STEMI). As the availability of primary interventional facilities has improved, door to balloon times have fallen and this has been rewarded with concomitant reductions in mortality and morbidity.[13]

Rapid recanalization/reperfusion of an occluded epicardial artery is a paradoxical phenomenon due to its