Comparison between the Effect of Intracoronary Sodium Nitroprusside versus Verapamil on the Prevention of the No/Slow Reflow Phenomenon in patients with acute ST Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Intervention

Thesis

Submitted for partial fulfillment of M.D. degree
in Cardiology

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2014

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

"وَقُلِ اعْمَلُواْ فَسَيَرَى اللّهُ عَمَلَكُمْ
وَرَسُولُهُ وَالْمُؤْمِنُونَ وَسَتُرَدُّونَ إِلَى
عَالِمِ الْغَيْبِ وَالشَّهَادَةِ فَيُنَبِّئُكُم
بِمَا كُنتُمْ تَعْمَلُونَ"

صدق الله العظيم

التوبة – آية ١٠٥

Acknowledgment

It is a great thing to feel success and have the pride of achieving all what is always aspired. Nevertheless, one must not forget all those who usually help and push him onto the most righteous way that inevitably ends with fulfillment and perfection.

When the instant comes to appreciate all those kind-hearted people, I soon mention ***Prof. Saed Abd-Elhafiz Khaled,*** *Professor of Cardiology, Ain Shams University, the person who gave me the honor to be his student. He really helped me by his precious opinions and contributive comments that served much in the construction of this work.*

Great thanks are also due to ***Prof. Tarek Khairy Abd-Eldayem,*** *Professor of Cardiology, Ain Shams University. He was always there to care, support, encourage and provide constructive pieces of advice in every possible way.*

I would like to express my deepest thanks to ***Prof. Sameh Saleh Thabet,*** *Assistant Professor of Cardiology, Ain Shams University, for his uninterrupted care and advice, his meticulous supervision precious remarks and continuous encouragement.*

Thanks also to ***Prof. Wael Mahmoud Elkelany,*** *Assistant professor of cardiology, Ain Shams University, who was been the real brother, whom fruitful thinking and continuous advise was behind the progress of this work.*

I cannot forget the help of ***Dr. Tarek Rashid Mohamed,*** *Lecturer of Cardiology department for his cooperation in the practical part of this work.*

I would also like to record my thanks and sincere gratitude to my family for their great help and support throughout the work.

Hesham Mohamed Kamal Abd-el Aziz

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List of Abbreviations

ACC : American College of Cardiology
ADP : Adenosine diphosphate
AHA : American Heart Association
AMI : Acute myocardial infarction
BMS : Bare-metal stents
BNP : Brain natriuretic peptide
CABG : Coronary artery bypass grafting
CBC : Complete blood picture
CTFC : Corrected TIMI frame count
DAPT : Dual antiplatelet therapy
DES : Drug eluting stent
EMS : Emergency Medical System
EPO : Erythropoietin
ER : Emergency room
ESC : European Society of Cardiology
FBS : Fasting blood sugar
FMC : First medical contact
FPP : First-pass perfusion
GP : Glycoprotein
HR : Heart rate
hs-CRP : High sensitivity C-reactive protein
IABP : Intra-aortic balloon pumping
IC : Intracoronary
INR : International normalization ratio
IRA : Infarct related artery
LBBB : Left bundle branch block
LDL : Low-density lipoprotein

List of Abbreviations *(Cont...)*

MACE : Major adverse cardiac events
MBG : Myocardial blush grade
MCE : Myocardial contrast echocardiography
MI : Myocardial infarction
MR : Mitral regurgitation
MVO : Microvascular obstruction
NCEP-ATP III : National cholesterol education program-adult treatment panel III
NRMI : National Registry of Myocardial Infarction
NT-pro BNP : N-terminal fragment of pro-brain natriuretic peptide
PCI : Percutaneous coronary intervention
PT : Prothrombin time
PTCA : Percutaneous transluminal coronary angioplasty
PTT : Partial thromboplastin time
RT-MCE : The real-time myocardial contrast echocardiography
SD : Standard deviation
SWMSI : Segmental wall motion score index
TC : Total cholesterol
TG : Triglycerides
TNF : Tumor necrosis factor
TVR : Target Vessel Revascularization
URL : Upper reference limit
VAPOR : Vasodilator Prevention of No-Reflow
VSR : Ventricular septal rupture

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Introduction

Acute myocardial infarction (AMI) remains a public health problem of epidemic proportions. Recent data from the American Heart Association (AHA) reveal a prevalence of myocardial infarction (MI) of 1.9-5.2%, which varies by age, sex, and ethnicity ***(American Heart Association, 2003).***

Interestingly, in the last decade the National Registry of Myocardial Infarction (NRMI) have recorded a decrease in the percentage of patients with myocardial infarction who present with ST segment elevation (from 36% to 27%, $p \leq< 0.001$), while the percentage presenting without ST segment elevation has increased (from 45% to 63%, $p \leq<0.001$).

Coronary atherosclerotic disease is the underlying substrate in nearly all patients with acute MI. The initiating event is a crack or fissure in the diseased arterial wall, which occurs as a result of loss of integrity of the plaque cap (Plaque disruption). The fissure or even frank plaque rupture leads to exposure of subendothelial matrix elements such as collagen, stimulating platelet activation and thrombus formation. Furthermore, tissue factor is released with the arterial injury, which directly activates the extrinsic coagulation cascade and promotes the formation of fibrin. If an occlusive thrombus forms, patients may develop an acute ST-segment elevation MI unless the subtended myocardium is richly collateralized.

Primary percutaneous coronary intervention (PCI) in patients with acute myocardial infarction (AMI) has been shown to be preferable to thrombolytic therapy in terms of patient survival, higher rates of patency in the infarcted arteries, and lower rates of reinfarction and stroke ***(Weaver et al., 1998)***. Thus, PCI has become the standard therapy for AMI. However, in some patients, after the epicardial coronary occlusion has been resolved, the blood flow may cease or slow down dramatically. This phenomenon is called no reflow or slow reflows.

The no-reflow phenomenon was originally observed in experimental models of acute myocardial infarction (MI) and was described as a failure to restore normal myocardial blood flow despite removal of the coronary obstruction ***(Kloner et al., 1975)*** Since that time, no-reflow has been shown to complicate thrombolytic therapy and percutaneous revascularization with PTCA and other devices ***(Kitazume et al., 1988).*** The occurrence of no-reflow phenomenon after recanalization of the infarct related artery in acute myocardial infarction is described in up to 40% of cases ***(Amit et al., 2006)***.

Defined angiographically, no-reflow manifests as an acute reduction in coronary flow (TIMI grade 0-1) in the absence of dissection, thrombus, spasm, or high-grade residual stenosis at the original target lesion. Lesser degrees of flow impairment (TIMI grade 2) are generally referred to as "slow-flow." However, studies of acute MI patients have reported that scintigraphic evidence for no-reflow may occur in the absence of angiographic slow-flow, suggesting that microvascular injury may be angiographically inapparent in some patients ***(Kondo et al., 1998).***

No/slow reflow is a serious complication of PCI performed for AMI that increases mortality and decreases left ventricular functional recovery. Furthermore, this phenomenon is also linked to ventricular arrhythmias, early congestive heart failure, ventricular remodeling and even cardiac rupture ***(Morishima et al., 2000).*** For these reasons, it is very important to prevent no reflow or slow reflow during PCI for AMI.

The exact mechanisms that underlie the no reflow or slow reflow phenomena are not known. The main pathogenetic mechanisms causing these phenomena were thought to be distal embolization and ischemia-reperfusion injury. However, there is considerable evidence suggesting that these phenomena are mainly due to dysfunction of the microcirculation and the presence of vasospasm at the level of the resistance arterioles ***(Piana et al., 1998)***. Therefore, it is thought that improving the microcirculation would be a very useful strategy for dealing with these phenomena.

Both Nitroprusside and verapamil have been shown to be effective for managing the slow reflow phenomenon once it occurs during coronary intervention ***(Ronenet al., 2008).***

However, it remains unclear what is the optimal treatment to prevent the no/slow reflow phenomena. Since it occurs in a variety of clinical settings and is likely to have more than one mechanism, it is unlikely that a single definitive treatment will be appropriate for all cases.

Aim of the Work

To compare between the effect of intracoronary sodium nitroprusside versus verapamil on the prevention of the no/slow reflow phenomenon in patients with acute ST segment elevation myocardial infarction undergoing primary percutaneous intervention