Role Of New Antiplatelets In Acute Coronary Syndromes

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LIST OF ABBREVIATIONS

ACS : Acute coronary syndrome

ACC : American collegue of cardiology

ADP :Adenosine diphosphate

AHA : American health association

ASA : Acetyl salicylic acid

ATP : Adenosine triphosphate

BMS : Bare-metal stent

CABG : Coronary artery bypass graft

CAD : Coronary artery disease

CI : Confidence interval

COX : Cyclo-oxygenase

CV : Cardiovascular

CYP٤٥٠ : Cytochrome P٤٥٠

DES : Drug eluting stent

FDA : Food and drug administration

GP : Glycoprotein

HPR : High platelet reactivity

HR : Hazard ratio

LMWH : Low molecular weight heparin

LTA : Light transmittance aggregometry

MACE : Major adverse cardiac events

MDR١ : Multi-drug resistance protein ١

MEA : Multiple electrode aggregometry

MI : Myocardial infarction

NPR : Normal platelet reactivity

NSAIDs : Non steroidal anti-inflammatory drugs

NSTEMI : Non –ST-elevation myocardial infarction

OR : Odds ratio

PARs : Protease activated receptors

PCI : Percutaneous coronary intervention

PFA : Platelet function analyser

PG : Prostaglandin

PPI : Proton pump inhibitor

PRP : Platelet rich plasma

PTCA : Percutaneous transluminal coronary angioplasty

RPA : Residual platelet aggregation

RR : Relative risk

STEMI : ST-elevation myocardial infarction

TEG : thromboelastogram

TNF-α : Tumour necrosis factor alpha

TVR : Target vessel revascularization

TxA٢ : Thromboxane A٢

UA : Unstable angina

VASP : Vasodilator-stimulated phosphoprotein

VWF : von Willebrand factor

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Introduction

Coronary heart disease is a common cardiovascular disease, affecting millions of patients allover the world, and continues to be the leading cause of death in industrialized countries. Atherothrombosis is the main pathophysiologic mechanism leading to acute coronary syndromes (ACS). Platelet activation is one of the essential mechanisms in the genesis and onset of atherothrombotic complication so antiplatelet therapy is a cornerstone of the management of ACS ***(Lloyd-Jones et al.,*** ***).***

There is a growing body of evidence that there is variability in response to antiplatelet treatments and this represents a potentially important clinical problem. Understanding the mechanisms underlying this phenomenon is important in improving patient care, but due to the diversity of factors involved, a clear predictive model for responsiveness to antiplatelet therapy is still missing. Attempts have been made to characterize the efficacy of antiplatelet therapy using platelet function testing but based on current information, its routine use is not recommended particularly as costs and cost effectiveness have not been established and agreement between laboratory methods is lacking ***(Lordkipanidze et al.,*** ***).***

Dual antiplatelet therapy with aspirin and clopidogrel has provided a foundation for dramatic improvement in outcomes of patients with ACS, however emerging antiplatelet therapy provides more potent and swift platelet inhibition than clopidogrel, as well as the promise of improved clinical outcomes. The ultimate goal remains increased efficacy, without an accompanying increase in bleeding. Indeed defining a therapeutic window that maximizes platelet inhibition while minimizing bleeding remains an elusive goal for individual patients (***Wiviott et al.,*** ***).***

Aim of The Work

This essay discusses the advantages of recent antiplatelet agents in the treatment of acute coronary syndromes, compared to current antiplatelet therapy.

Chapter ١
Pathophysiology of acute coronary syndromes

Acute coronary syndrome (ACS) refers to a spectrum of conditions that develop from blood flow that is insufficient to meet the metabolic needs of the myocardium, it describes any condition characterized by signs and symptoms of sudden myocardial ischemia-a sudden reduction in blood flow to the heart.

ACS includes a set of clinical presentations with a similar underlying pathophysiology. This description encompasses unstable angina (UA), non-ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI). In each case, the underlying problem is due to disruption of an atherosclerotic plaque and subsequent thrombus formation. This results in a reduction or cessation of blood flow to the myocardium. The ultimate presentation depends on a number of factors, including the extent of thrombus formation, the degree to which blood flow is diminished, the acuity with which the process has developed and the extent of collateral blood flow present within the coronary circulation ***(Lloyd-Jones et al., d).***

STEMI results from a fully occluded coronary artery which needs urgent thrombolysis, whereas UA and NSTEMI normally result from a partially or intermittently occluded coronary artery, they are traditionally grouped together due to overlap in terms of symptoms, electrocardiogram (ECG) findings, and treatment. The distinction between these two entities can be subtle, but, by and large, depends on demonstrating the presence (NSTEMI) or absence (UA) of myocardial necrosis ***(Lloyd-Jones et al.,*** ***).***

Non modifiable factors that influence risk for coronary artery disease include age, sex, family history and ethnicity or race. Men have a higher risk than women. Men older than age ٤٥, women older than age ٥٥, and anyone with a first-degree male or female relative who developed coronary artery disease before age ٥٥ or ٦٥, respectively, are also at increased risk. Modifiable risk factors include elevated levels of serum cholesterol, low-density lipoprotein cholesterol, and triglycerides; lower levels of high-density lipoprotein cholesterol; and the presence of type ٢ diabetes, cigarette smoking, obesity, a sedentary lifestyle, hypertension and stress ***(Burke et al., ٢٠٠٧).***

The understanding of the pathophysiological mechanisms of atherosclerosis and of ACS has progressed

significantly in recent years. This has allowed for the opportunity for the more precise identification of ACS, development and implementation of more specific therapeutic interventions, in addition to the improved potential for primary intervention ***(Bhatt and Topol,).***

Virtually all regional acute myocardial infarcts are caused by thrombosis developing on a culprit coronary atherosclerotic plaque. The very rare exceptions to this are spontaneous coronary artery dissection, coronary arteritis, coronary emboli, coronary spasm, and compression by myocardial bridges. Thrombosis is also the major initiating factor in unstable angina, particularly when rest pain is recent and increasing in severity. Necropsy studies suggest that a new thrombotic coronary event underlies ٥٠–٧٠٪ of sudden deaths caused by ischaemic heart disease ***(Stary et al.,).***

Pathophysiology of atherosclerotic plaque

Complex plaques of mature atherosclerosis are the end result of a long pathophysiologic process, which typically begins in early adulthood. Endothelial dysfunction appears to play an initial role in atherosclerosis. Injury to the endothelium results in establishment of the cycle of