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التوثيق الالكتروني والميكروفيلم

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التوثيق الالكتروني والميكروفيلم

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on The ability of

Influence of different statins on the ability Clopidogrel to inhibit platelet aggregation in patients with unstable angina

thesis submitted for partial fulfillment for Master Degree in Cardiology

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By

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El-Minia University, 2005

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List of Abbreviations

ACC/AHA: .....American College of Cardiology/ American Heart Association

ACE: .....Angiotensin-Converting Enzyme

ACTH..... Adrenocorticotropic Hormone

ADP..... Adenosine Di phosphate

ATP.....Adenosine Tri phosphate

BP .....Blood Pressure

CHD.....Coronary Heart Disease

CK .....Creatin kinase

CO..... carbon monoxide

COX..... cyclooxygenase

CRP .....C-reactive protein

CYP..... cytochrome P 450

ECG.....Electrocardiograph

ER.....Endoplasmic reticulum

GP ..... Platelet glycoprotein Platelet glycoprotein

HDL..... High Density Lipoproteins

hs-CRP..... High-sensitivity CRP

LDL.....Low Density Lipoprotien

LVH.....Left Ventricular Hypertrophy

MMPs..... matrix metalloproteinases

MI..... Myocardial infarction

NO..... Nitric oxide

PAI..... plasminogen activator inhibitor

PPAR..... peroxisome proliferator activated receptor

PSGL.....P-selectin glycoprotein

RXR..... Retinoid X Receptor

SD.....Standard Deviation

SMC..... smooth muscle cells

TG .....Triglycerides

TIA .....Transient Ischaemic Attack

TTP..... thrombotic thrombocytopenic purpura

VLDL..... Very Low Density Lipoproteins

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Introduction

Introduction

The clinical presentations of ischaemic heart disease include stable angina pectoris, silent ischaemia, unstable angina, myocardial infarction, heart failure, and sudden death. For many years, unstable angina has been considered as an" intermediate syndrome" between chronic stable angina and acute myocardial infarction. In recent years, its physiopathology has been clarified and there have been major advances in management. **(Bertrand et al, 2002)**

Pathological, angioscopic and biological observations have demonstrated that unstable angina and myocardial infarction are different clinical presentations that result from a common underlying pathophysiological mechanism, namely, atherosclerotic plaque rupture or erosion, with differing degrees of superimposed thrombosis and distal embolization. **(Bertrand et al, 2002)**

Clopidogrel inhibits platelet aggregation through binding selectively and noncompetitively to platelet ADP receptor in an irreversible manner preventing activation of glycoprotein IIb/IIIa receptor which mediates the final common pathway of platelet aggregation .The dosing is 75mg/d .A single dose starts to have significant antiplatelet effect within 2 hours of ingestion ,with steady-state levels of platelet inhibition after 3 to 7 days ,this effect persists for 7 to 10 days **(Topol et al 2000)**

Clopidogrel is an inactive thienopyridine prodrug that requires in vivo conversion in the liver to an active metabolite that exerts its antiplatelet effect .In rats it has been suggested that clopidogrel is activated by cytochrome P450 1A2,whereas an analogue of clopidogrel ,CS-747,is speculated to be activated by human cytochrome P450 3A4 (CYP3A4).Other investigators have confirmed that clopidogrel is metabolized by human CYP3A4 using genetically engineered human microsomes**(Clarke et al)(WIE et al 2003).**

The CYP450 enzyme system is one of the most important metabolic pathways catalyzing the oxidation of various endogenous and exogenous