HbA1c as an indicator of preconditioning in patients with a first time Acute Myocardial Infarction

Thesis

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List of Contents

List of Tables

List of Figures

List of Figures (Cont.)

List of Abbreviations

ACC	American College of Cardiology
ACS	Acute coronary syndrome
AHA	American Heart Association
AGE	Advanced glycosylation end products
AT II	Angiotensin II
CABG	Coronary artery bypass graft.
CAD	Coronary artery disease .
CAMS	Cell adhesion molecules
CAN	Cardiac autonomic neuropathy
CETP	Cholesteryl ester transfer protein
CHD	Coronary heart disease
CHF	Congestive heart faliure
CML	N-(carboxymethyl) lysine
COX-2	Cyclooxygenase-2
CRP	C-reactive protien
DAG	Diacyl glycerol
DES	Drug eluting stent
DM	Diabetes mellitus
eAG	Estimated Average glucose
ECG	Electrocardiogram

List of Abbreviations (Cont.)

eNOS.	Endothelial nitric oxide synthase
ERK	Extracellular regulated kinase
ET-1	Endothelin-1
FFA	Free fatty acids
FWOP	First window of protection
GM-CSF	Granulocyte-macrophage colony stimulating Factor
HbA1c	Glycated hemoglobin
HDL	High-density lipoprotein
HMGB1	High-mobility group box-1
HTN	Hypertension.
HS	Heparin sulfate
IP3	Inositol triphosphate
IPC	Ischemic preconditioning
JAK	Janus kinase
K_{ATP}	ATP-sensitive potassium channel
ICAM	Intercellular adhesion molecule
IL-1	Interleukin-1
iNOS	Inducible nitric oxide synthase
IκB	Inhibitor of nuclear factor kappa B

List of Abbreviations (Cont.)

LDL	Low-density lipoprotein
Lp a	Lipoprotein a
LV	Left ventricular.
LVEF	Left ventricular ejection fraction.
MACE	Major adverse cardiac events
MAO	Monoamine oxidase
MAP	Mitogen-activated protein
MEK	Mitogenactivated protein kinase
MI	Myocardial infarction.
MCP-1	Monocyte chemoattractant protein-1
M-CSF	Macrophage-colony stimulating factor
MPTP	Mitochondrial permeability transition pore
MSR	Macrophage scavenger receptor
NFkB	Nuclear factor kappa B
NO	Nitrous oxide
MTHFR	Methylene tetrahydrofolate reductase
PAI-1	Plasminogen activator inhibitor 1
PCI	Percutaneous coronary intervention
PDK	Phosphodiesterase kinase
PG	Prostaglandin

List of Abbreviations (Cont.)

PI3K	Phosphatidylinositol-3-kinase
PKB	Protein kinase B
PKC	Protein kinase C
PLC	Phospholipase C
PLD	Phospholipase D
PTCA	Percutaneous transluminal coronary angioplasty.
RAGE	Receptor for advanced glycosylation end products
ROS	Reactive oxygen species
SMCs	Smooth muscle cells
STAT	Signal transducer and activator of transcription
SWOP	Second window of protection
TF	Tissue factor
TK	Tyrosine kinase
TNF-α	Tumor necrosis factor-alpha
VCAM-1	Vascular cell adhesion molecule-1.
VLDL	Very Low-Density Lipoprotein
VSMC	Vascular smooth muscle cell
vWF	von Willebrand factor
VLA-4	Very late antigen-4

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Ayman Ashmawy Gaballa

Introduction

Heart disease, particularly coronary heart disease (CHD) is a major cause of morbidity and mortality among patients with diabetes mellitus. Compared to nondiabetics, diabetics are more likely to have CHD, to have multivessel disease when it occurs, and to have episodes of silent ischemia. As a result of these and other factors, diabetics with CHD have a worse outcome and poorer long-term survival compared to nondiabetics with CHD ***(Richard W. Nesto, 2009).***

Morbidity, mortality and re-infarction rate are higher following MI in diabetic than non-diabetic subjects, with one-year mortality in this population as high as 50% ***(Ian L. Williams et al., 2003).***

Transient ischemic episodes have cardio protective effects against subsequent ischemia, which is called ischemic preconditioning ***(Murry et al., 1986).***

Angina pectoris occurring shortly before the onset of AMI limits infarct size, maintains left ventricular (LV) function and enhances survival ***(Kloner et al., 1998).***

Kloner et al., reviewing 3,002 patients enrolled in the TIMI-9B study, have reported that the benefits of pre-infarction angina on clinical events were manifest only when the time between onset of angina and infarction was within 24 h and that a history of any angina alone was not associated with a reduced event rate. Thus,

"prodromal angina" was defined as angina occurring within 24 h before the onset of infarction ***(Kloner et al., 1998)***.

Some experimental studies have reported that ischemic preconditioning is lost in the presence of diabetes. It has been suggested that longer duration of diabetes, higher plasma glucose level were associated with the increased vulnerability of diabetic hearts ***(Kersten et al., 2000).***

There are several possible mechanisms that may explain the loss of ischemic preconditioning in diabetic hearts ***(Speechly-Dick et al., 1995).***

Ischemic preconditioning is mediated by activation of the KATP channel. It has been reported that the nature of the KATP channel is altered in diabetic hearts ***(Smith, 1996).***

Also, acute hyperglycemia has been shown to abolish ischemic preconditioning ***(Kersten et al., 1998).***

In addition, oral hypoglycemic drugs inhibit the KATP channel. Several previous studies have reported that oral hypoglycemic drugs prevent ischemic preconditioning and increase mortality after AMI. However, it is still noteworthy that the cardioprotective effects of prodromal angina were lost even in patients with diabetes who had been treated without oral hypoglycemic drugs ***(Garratt et al., 1999).***

Hemoglobin A1c (HbA1c) is a minor component of hemoglobin to which glucose is bound. HbA1c also is referred to as Glycosylated or glucosylated hemoglobin.HbA1c concentration

reflects average blood glucose concentration over 3-4 months and is a sensitive and reliable marker of glucose metabolism. Cross-sectional studies in nondiabetic individuals have shown a relationship between HbA1c and prevalent CAD as well as markers of sub clinical atherosclerosis ***(Kato et al., 2004).***

HbA1c level above 6.2% were associated with an increased risk of macro vascular disease. For each 1% elevation in HbA1c level, CAD increased by 11% ***(Coutinho et al., 1999).***

A strategy of intensive glucose control that lowered the glycated hemoglobin value to 6.5% yielded a 10% relative reduction in the combined outcome of major macro vascular and micro vascular events ***(The ADVANCE Collaborative Group, 2008).***

Aim of the Work

Study the value of HbA1c an indicator of ischemic preconditioning in acute myocardial infarction through:

1. Study the effect of DM on preconditioning in AMI.
2. Study the benefit of controlling DM in preserving preconditioning.