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The Value of Preoperative Administration of Aminophylline as a Cardio Protective Agent During Coronary Artery Bypass Grafting

Submitted for the partial fulfillment of MD degree
In cardiothoracic surgery

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Abstract

Objectives: Despite surgical and pharmacological advances in myocardial preservation during CABG, myocardial Ischemia Reperfusion damage remains the most uncontrolled aspect of cardiac operations. This study aims at evaluating the possibility that aminophylline could serve as a potential myocardial protector against reperfusion injury during coronary artery bypass grafting (CABG).

Methods: It is a prospective, randomized, single blinded, placebo - controlled study including two groups of patients. The sixty patients were randomly assigned by a random number generator to cases group (n=30) or control group (n=30).Aminophylline, 200 mg orally per day for 3 days, with a total dose of 600 mg was given to 30 patients (cases group), and placebo was given to the 30 others (control group).All patients underwent uniform pre/intra/post-operative management. All patients were followed up with Measurement of cardiac markers (Troponin I) and cardiac enzymes (CK-MB). Blood samples were collected before induction of anesthesia (T0), after 30 min of aortic cross clamping (ACC) (T1), and 1, 24, and 48 h postoperatively (T2, T3, T4).Measurement of preoperative concentration of aminophylline in serum.12 lead ECG 48 hours postoperatively for any new Q waves or ST elevation or depression. Echocardiographic examination with full study and measurement of cardiac volume, function, and ventricular geometry at the 6th postoperative day.

Results: there were no hospital mortalities or perioperative MI's in either group. The total ICU stay hours and ventilation hours were significantly higher in the control group 67.20±21.28 and 16.47±8.76 hours respectively while in the case group they were 46.87±14.46 and 12.20±3.56 hours respectively with a p-value <0.05. The need of inotropes in the case group was lower than that in the control group in the immediate post by pass period. The need of inotropes in the case group again was lower than that in the control group in the ICU. Four patients needed the use of IABP equally in both groups. Measured enzyme levels in both groups were significantly higher than preoperative values all through the postoperative study period. These levels were less in the case group than those of the control throughout the entire measurement period. However, TnI and CK-MB levels in both groups were not significantly different with a p-value >0.05.

Conclusions: aminophylline may actually has some beneficial actions like decreasing the ventilation hours. The need of inotropic support and total ICU stay hours. However, the main objective and standard for its evaluation was cardiac enzymes Troponin I and CK-MB which both showed no significant difference between those on aminophylline and other patients not receiving the drug. Also, there was no correlation between aminophylline serum levels and those of cardiac enzymes.

Keywords: Aminophylline, ischemia-reperfusion injury, troponin, cardio pulmonary bypass, CABG.

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To my lovely young daughter Mariam everything was by you and for you, you have been and will always remain my one true love. Sorry for being away so much .love you and adore you, sweetie.

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List of Abbreviations

ACC: Aortic Cross Clamping

ACLS: Advanced Cardiac Life Support

ADP: Adenosine Diphosphate

APAF-1: Apoptosis-Activating Factor 1

ATP: Adenosine Triphosphate

Bad and Bax: Proapoptotic Proteins Bad and Bax

Bcl: B-Cell Cll/Lymphoma

Ca^{2+}: Calcium Ion

CABG: Coronary Artery Bypass Grafting

cAMP: Cyclic Adenosine Monophosphate

CK: Creatine Kinase

CO: Cardiac Output

CPB: Cardiopulmonary Bypass

DNA: Deoxyribonucleic Acid

FITC: Fluoroscein Isothiocyanate

GSH: Reduced Glutathione

GSSG: Oxidized Glutathione

IL-1: Interleukin-1

IL-6: Interleukin-6

I-R: Ischemia Reperfusion

LDH: Lactate Dehydrogenase

MDA: Malondialdehyde

MI: Myocardial Infarction

MPO: Myeloperoxidase

MPTP: Mitochondrial Permeability Transition Pore

NADP: Nicotinamide Adenine Dinucleotide Phosphate

NADPH: Nicotinamide Adenosine Dinucleotide Phosphate

Nfkb: Nuclear Factor Kappa B

NO: Nitric Oxide

NOS: Nitric Oxide Synthase

PARP: Poly (ADP)-Ribosylating

PKA: Protein Kinase A

PKC: Ca^{2}-Dependent Protein Kinase

ROS: Reactive Oxygen Species

ROSC: Return of Spontaneous Circulation

SGOT: Serum Glutamic-Oxaloacetic Transaminase

SIR: Systemic Inflammatory Response

SIRS: Systemic Inflammatory Response Syndrome

SR: Sarcoplasmic Reticulum

TNF: Tumor Necrosis Factor

TnI: Troponin I

TnT: Troponin T

USA: United States of America

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