COMPARITIVE STUDY BETWEEN INTERMITTENT ANTEGRADE WARM CARDIOPLEGIA AND INTERMITTENT ANTEGRADE COLD CARDIOPLEGIA IN OPEN MITRAL VALVE SURGERY

Thesis

Submitted for Complete Fulfillment of MD Degree in Cardiothoracic Surgery

By

Waleed Adel Abdelmoniem Hussien (M.B.B.Ch.; M.Sc. General Surgery)

Supervisors

Prof. Dr. EHAB MOHAMED EL-SHEHY

Professor of Cardiothoracic Surgery
Faculty of Medicine
Cairo University

Ass. prof. Dr. AMR MOHAMED FATHY ROUSHDY

Assisstant Professor of Cardiothoracic Surgery Faculty of Medicine Cairo University

Ass. prof. Dr. AHMED ABDELRAHMAN MOHAMED

Assisstant Professor of Cardiothoracic Surgery
Faculty of Medicine
Cairo University

Faculty of Medicine
Cairo University
2015

بسم الله الرحمن الرحيم



صدق الله العظيم

سورة طه ایة ۱۱۶

Acknowledgement Acknowledgement

First and foremost, thanks to "ALLAH", the most gracious and most merciful, to whom I relate my success in achieving anything in life.

It's my pleasure to express my profound gratitude, deepest appreciation, and ultimate thanks to my professors:

Prof. Dr. Ehab ElShihy, My mentor, Professor of cardiothoracic surgery, faculty of medicine, Cairo University. For his endless support, continuous encouragement, generous supervision and guidance.

Ass. Prof. Dr. Amr Rouchdy Assistant professor of cardiothoracic surgery, Faculty of Medicine, Cairo University. He gave me much of his time, experience, and endless support that cannot be expressed in words.

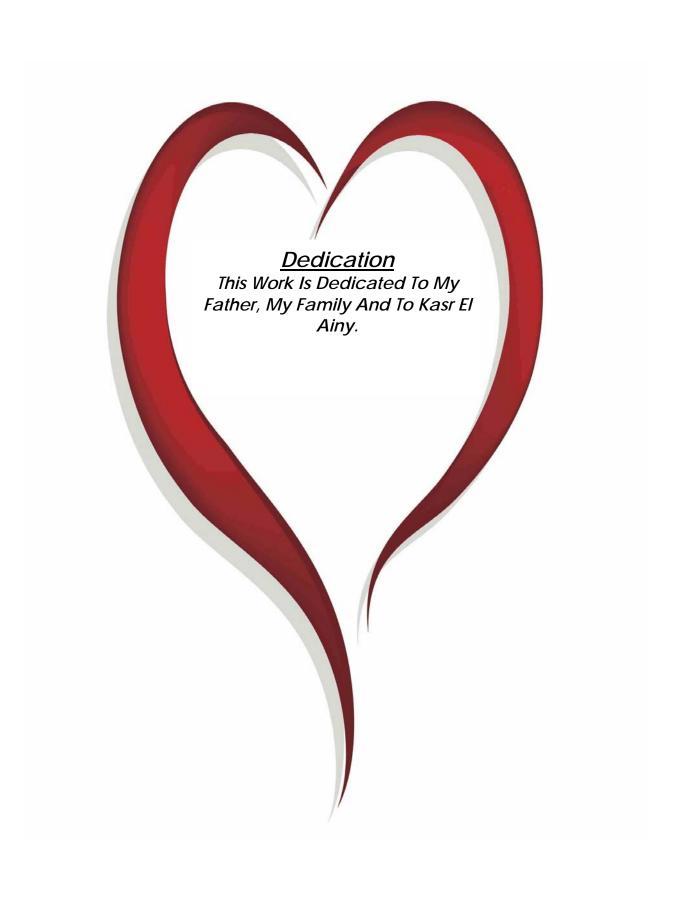
Ass. Prof. Dr. Ahmed Abdelrahman, Assistant professor of cardiothoracic surgery, faculty of medicine, Cairo University. For his valuable help and encouragement during the preparation of this work

For each and every one of you I am greatly indebted

I would also like to express my deep thanks and respect to *Ass. Prof. Dr. Alaa Farouk* Assistant professor of cardiothoracic surgery, faculty of medicine, Cairo University, for his complete support, cooperation and help throughout this study.

With pleasure, I would like to express my appreciation and thanks to *Ihab Omar*, *Khaled Mortada and Hany ElGamal* my colleagues and brothers for helping me throughout this study in the data collection and statistics.

At last, I would like to express my thanks to *every patient* who gave us the chance to learn from him. May God alleviate their sufferings and may all our efforts be just for their own benefit.



ABSTRACT

Background: The optimal temperature of cardioplegia solution in patients undergoing mitral valve surgery is still debatable.

Objective: To compare between warm and cold cardioplegia in patients undergoing mitral valve surgery.

Patient and Methods: A prospective comparative study on 100 patients undergoing mitral valve replacment surgery. Patients were divided into two groups; (warm group, used antegrade warm blood cardioplegia n = 50) and (cold group, used antegrade cold blood cardioplegia n = 50). Biomarkers of cardiac injuery, operative and clinical data were collected.

Results: The need for DC shock, initial dose and duration of inotropes, total drainage and the serum troponin, LDH levels were lower in the warm group by highly significant statistically values (*p* value<0.01).

The serum level of CK and CK-MB were less in the warm group by statistically significant values (*p* value<0.05).

The serum creatinine level, total bypass time, time to regain consciousness, time for extubation and incidence of wound infection were less in the warm group by insignificant statistically values (p value>0.05).

The aortic cross clamp time was less in the cold group by statistically insignificant values.

Conclusion: Intermittent antegrade warm blood cardioplegia shows better myocardial protection than Intermittent antegrade cold cardioplegia in mitral valve replacement surgery.

Key Words: Hypothermia , warm cardioplegia, myocardial protection , mitral.

CONTENTS

Content	Page
List of Abbreviations.	
List of Figures	
List of Tables.	
Introduction and Aim of the Work	1
Review of Literature:	3
Chapter (1): Historical Overview	3
Chapter (2): Reperfusion injury	7 15
Chapter (3): Basic Principles of myocardial protection	18
Chapter (4) Types of cardioplegic solutions	23 36
Chapter (5) Cardioplegia Temperature And Its Physiological Effects	50
Chapter (6) Biomarkers of cardiac injury in cardiac surgery	
Patients and Methods.	47
Results	54
Discussion.	68
Conclusions and Recommendations.	81
Summary	83
References.	85
Arabic Summary	

List of Abbreviations

ATP	: Adenosine triphosphate
°C	: degree celesius
Ca+2	: Calcium
CK	: Creatine kinase
CK-MB	: Creatine kinase-myocardial band
dl	: deciliter
ECG	: Electrocardiogram
H	: Hydrogen
h	: hour
ICU	: Intensive care unit
IPC	: Ischemic preconditioning
KCL	: Potassium chloride
K	: Potassium
L	: Litre
LDH	: lactate dehydrogenase
MAP	: Mean arterial blood pressure
Mg	: Magnesium
MI	: Myocardial infarction
min	: minutes
ml	: milliliter
mM	; millimole
mosm	: milliosmole
mV	: millivolt
Na+2	: Sodium
ng	: nanogram
NO	: Nitric oxide
O2	: Oxygen
ROS	: Reactive oxygen species
St. Thomas	: Saint Thomas

List of Figures

Figur e No	Title	Page No
1	Mean age distribution among warm and cold groups.	50
2	Sex distribution among the two groups.	55
3	Difference in bypass time between both groups.	56
4	Difference between mean aortic cross clamp time between the two groups.	57
5	Difference between warm and cold groups regarding need for DC shock.	58
6	Mean joules needed to regain sinus rhythm in both groups.	59
7	Initial dose of inotropic support in both groups.	60
8	Duration of inotropic support in both groups.	60
9	Mean total postoperative drainage in both groups.	61
10	Time needed for recovery of consciousness in both groups.	62
11	Mean time needed for extubation in both groups.	62
12	Mean value of serum creatinine level in both groups.	63
13	Mean value of CK level postoperative in both groups.	64
14	Mean postoperative serum CK-MB values in both groups.	64
15	Mean postoperative serum LDH values in both groups.	65
16	Mean postoperative serum Troponin values in both groups.	66
17	Incidence of occurrence of wound infection in the cold group.	66
18	Incidence of occurrence of wound infection in the warm group.	67

List of Tables

Table No	Title	Page No
1	Antegrade delivery protocol for cardioplegia.	22
2	Summary of significance of mean values of cardiac biomarkers between the two groups.	67

INTRODUCTION AND AIM OF THE WORK

The remarkable advances in cardiac surgery over the last 40 years have led to the concept of "routine" open heart surgery. Although advances in cardiac surgical technique, cardiac anesthesia, and critical care have all contributed to reducing the morbidity and the mortality of cardiac operations, the evolution of intraoperative myocardial protection has been equally critical.⁽¹⁾

The debate on the optimal temperature of cardioplegia still unsolved. Despite that hypothermia offers decrease in the oxygen demands, on the other hand oxygen availability in blood cardioplegia is influenced by temperature because of the leftward shift in the oxyhemoglobin saturation curve in response to hypothermia. (2)

There are additional drawbacks to hypothermia including membrane destabilization, Na-K adenosine triphosphatase inhibition and resultant edema, calcium sequestration, and the need of a longer period of reperfusion to rewarm the heart. (3)

AIM OF THE WORK:

The objective of this study is to evaluate the safety and effectiveness of intermittent antegrade warm myocardial protection as compared to the standard intermittent antegrade cold blood cardioplegia in patients undergoing open mitral valve surgery.

CHAPTER (1) HISTORICAL OVERVIEW

Background and Definitions:

When open heart surgery took off after the development of heart-lung machines, the needs of the surgeon include rapid induction, maintenance and easy reversal of cardiac arrest, because a relaxed heart allows for mobilization and traction, a preferably bloodless and unobscured field, and sufficient time for adequate correction of cardiac or coronary defects also prevent air embolism when the left side of the heart was opened. Myocardial demands, on the other hand, require that the cell machinery remains intact with rapid restoration of metabolism and function after cardiac arrest. (4)

Early techniques that were widely used to arrest and/or protect the heart were based on single or combined modalities such as:

Hypothermia

Hypothermia protects the ischemic myocardium by decreasing heart rate, slows the rate of high energy phosphate degradation. (5) and decreases myocardial oxygen consumption. (6)

Fibrillatory Arrest

Review of Literature

Electrically induced ventricular fibrillation with coronary perfusion was introduced by Glenn and Sewell⁽⁷⁾, and Senning as a means of avoiding air embolism.⁽⁸⁾

However, Buckberg and Hottenrott demonstrated subendocardial ischemia and necrosis with this technique, particularly in the hypertrophied ventricle. (9)

Continuous Coronary Perfusion

In an attempt to mimic the physiologic state, continuous coronary perfusion with a beating heart at normothermia or mild hypothermia at 32°C to prevent the onset of ventricular fibrillation became the preferred technique of myocardial preservation in the late 1960s and 1970s. (10)

However, in reality, continuous perfusion became intermittent as coronary perfusion was often discontinued to achieve better visualization of the operative field during critical portions of the procedure. In addition, problems with the coronary cannula, such as poor fixation, leaking associated with calcified ostia and damage to the coronary artery such as dissection and late stenosis, continued to occur.⁽¹¹⁾

Chemical cardioplegia

Whereas these modalities alone or combined have survived till 1970s they were mostly supplemented with or replaced by arresting the heart by "cardioplegia" based on chemical means. In general terms cardioplegia can be defined as a technique involving single or repeated injections into the aortic root or into the coronary vasculature of a hypo- or normothermic solution (primarily) designed to arrest the heart (stricter sense) and

Review of Literature

(secondarily) also to protect the myocardium (wider sense) during aortic cross-clamping with global ischemia. (4)

Birth and Burial:

Melrose and associates investigated the cardioplegic properties of potassium. After gaining experience in dogs they applied aortic root injections of potassium citrate for arrest of the human heart. The injection provided immediate cardiac arrest and conditions for short-lasting anatomic repair. Accordingly, Melrose's report in 1955 led to international recognition and adoption of his technique. (12)

In 1959 it was reported that myocardial necrosis could always be found in dog hearts after potassium citrate arrest. This then led to the abandonment of chemically induced cardioplegia. (13)

Survival and Success:

Ho"lscher observed the arresting and protective properties of magnesium and the local anesthetic procaine and proposed that the toxicity of the Melrose solution was due to citrate chelation of endogenous magnesium and calcium. (14)

International Reawakening:

Review of Literature

During the 1970s the international interest in chemical arrest of the heart reawakened, and by the end of the decade the procedure of cold chemical cardioplegia had gained close to universal acclaim as the most useful approach to an adequate surgical and metabolic handling of the heart. In USA Gay⁽¹⁵⁾, Levitsky⁽¹⁶⁾, Roe⁽¹⁷⁾, Tyers⁽¹⁸⁾ and Buckberg⁽¹⁹⁾ reassessed the use of potassium below 40 mM for inducing cardiac arrest.

Whereas Buckberg initially advocated crystalloid solutions, he soon changed to blood as the vehicle for potassium induced cardioplegia and advocated intermittent perfusion with cold cardioplegic blood plus systemic hypothermia during aortic occlusion. Also the Buckberg group assessed quantitatively noncoronary collateral flow in the washout of cardioplegic solutions and confirmed the necessity of repeated administration or multi-dose cardioplegia. (19)

However, the main forward drive in cardioplegia research was the group headed by Hearse and Braimbridge at St. Thomas' Hospital in London. The group emphasized pragmatically the importance of a careful approach to the formulation of coronary infusates. Thus they should preferably deviate as little as possible from the extracellular fluid they were to replace and they should be based on a close dose-response characterization of main ionic constituents like potassium and magnesium and of potential additives. (20)