WARM BLOOD OR COLD CRYSTALLOIDS CARDIOPLEGIA SUPERIORITY OF EITHER TECHNIQUE IN MYOCARDIAL PROTECTION IN MITRAL VALVE REPLACEMENT SURGERY

Thesis

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ACT	: Activated clotting time
ADP	: Adenosine diphosphate
ATP	: Adenosine triphosphate
CCC	: Cold Crystalloid Cardioplegia.
Ca+2	: Calcium
CK	: Creatine kinase
CK-MB	: Creatine kinase-myocardial band
CO2	: Carbon dioxide
CPB	: Cardiopulmonary Bypass
ICU	: Intensive care unit
IAWBC	: Intermittent ante grade warm blood cardioplegia.
KCL	: Potassium chloride
MAP	: Mean arterial blood pressure
Mg	: Magnesium
MVR	: Mitral Valve Replacement Surgery.
Na+2	: Sodium
NO	: Nitric oxide
NADH	: Nicolinamide Adenine Dinucleoide Hydrogenase.
NYHA	: New York Health Association classification
O2	: Oxygen
PCO2	: Partial pressure of carbon dioxide
PO2	: Partial pressure of oxygen
ROS	: Reactive oxygen species
TV	: Tricuspid Valve

ABSTRACT

Background and objectives: Several advantages can theoretically favor the use of normothermic perfusion, including the shortened duration of CPB, and simplification of the CPB management, it has been proposed as a more physiologic technique than hypothermic bypass for the maintenance of the body during cardiac surgery; we design a Prospective Randomized study to compare both approaches in terms of early myocardial protection.

Methodology: Fifty patients who had mitral valve surgery in our institute were prospectively divided into two groups: **Group I** (n=25) received intermittent antegrade cold crystalloid cardioplegia with systemic hypothermia, and **Group II** (n=25) received intermittent antegrade warm blood cardioplegia. Clinical and metabolic studies have been carried to evaluate the efficacy of myocardial protection in both groups.

Results: No differences were found between the two groups as regards the mortality, intubation time, total ICU stay time and the duration of inotropic support post operatively. However, the hypothermic group needed more defibrillation in the reperfusion period, more inotropic support to wean off bypass, and had more chest tube drainage. There was no difference in the postoperative level of CK and CK-MB between the two groups; however troponin I release was higher in the cold group. There was also no difference in the ventricular performance at follow up.

Conclusion: Intermittent antegrade warm blood cardioplegia results in less myocardial cell damage than cold crystalloid cardioplegia, as assessed by the release of cardiac-specific markers. Better right ventricular preservation is possible but does not result in less need for inotropic support and consider a safe alternative to the standard intermittent antegrade cold blood cardioplegia.

Key Wards:
Cardioplegia, Myocardial Protection,
Mitral valve surgery. Cardiac enzymes.

INTRODUCTION AND AIM OF THE WORK

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INTRODUCTION:

Several advantages can theoretically favor the use of normothermic perfusion, including the shortened duration of CPB, the reduced need for hemodilution with the subsequent avoidance of ultrafiltration requirement, and simplification of the CPB management, Indeed, intracellular pH changes induced by hypothermia no longer exist, and the acid–base balance is not affected. The hemoglobin dissociation curve is maintained within the normal range and allows better tissue oxygen delivery.

Myocardial protection during cardiac surgery *aims* to preserve myocardial function while providing a bloodless and motionless operating field to make surgery easier, Myocardial protection, since the original reports of Bigelow has been obtained by decreasing myocardial oxygen demand as a consequence of hypothermia. **(1)**

Moreover, Melrose described the use of electromechanical cardiac arrest induced by potassium infusion, permitting cardiac surgery to be performed on a non-beating flaccid heart. **(2)**

The combination of both of these techniques has been the ‘cornerstone’ in myocardial protection during surgery until now, allowing surgery with excellent clinical outcome. **(3)**

The *term* Myocardial Protection refers to strategies and methodologies used either to attenuate or to prevent post ischemic myocardial dysfunction that occurs during and after heart surgery, Post ischemic myocardial dysfunction is attributable, in part, to a phenomenon known as *ischemia-reperfusion-induced injury*. **(4)**

Clinically, it manifests by low cardiac output and hypotension and may be subdivided into two subgroups: reversible injury and irreversible injury, the two typically are differentiated by the presence of electrocardiographic abnormalities, elevations in the levels of specific plasma enzymes or proteins such as creatine kinase and troponin I or T, and/or the presence of regional or global echocardiographic wall motion abnormalities.

Within a short time, many cardiac surgeons shifted from using potassium-induced arrest to normothermic cardiac ischemia (normothermic heart surgery performed with the aorta occluded while the patient was on cardiopulmonary bypass), intermittent aortic occlusion, or coronary artery perfusion. Experimental and clinical evidence showed, however, that normothermic cardiac ischemia was associated with metabolic acidosis, hypotension, and low cardiac output **(5)**.

As a consequence, there was a renewed interest in discovering ways to arrest the heart. In 1975, Braimbridge et al introduced the St. Thomas solution [crystalloid solution based on Ringer's solution with

its normal concentrations of sodium and calcium, with the addition of potassium chloride (16 mmol/L) and 16 mmol/L of magnesium chloride to arrest the heart instantly] into clinical practice at St. Thomas Hospital **(6)**

Coincident to this controversy, another variant of cardioplegia was introduced, that of using potassium-enriched blood cardioplegia. The theory was that blood would be a superior delivery vehicle based on its oxygenating and buffering capacity **(7)**, in the 1980s, blood-based potassium solutions were advocated to further improve myocardial protection and to reduce myocardial enzymes release, however, recent changing trends in the population at risk have resulted in increasing number of high-risk patients presenting for cardiac surgery, with a consequent rise in intraoperative and postoperative morbidity. **(8)**

Despite of the improvement in myocardial protection accomplished in past years, there is a room for further improvement, in particular in high risk patients, in the hope of preventing postoperative ventricular dysfunction and improving overall outcome. The available literature allows us to summarize the following current trends and the future perspectives in myocardial protection in cardiac surgery.

1. CURRENT TRENDS IN MYOCARDIAL PROTECTION

1.1. Warm heart surgery

The use of normothermia myocardial protection has increased and routinely achieved with excellent results by retrograde continuous warm blood cardioplegia **(9)** or by intermittent cardioplegia with antegrade warm blood **(10)**.

Although cold crystalloid cardioplegia is associated with an excellent clinical outcome in elective surgery, blood cardioplegia techniques seem to offer superior cardio protection in high risk situations, such as advanced left ventricular dysfunction **(11)**, acutely ischemic myocardium **(12)**, heart transplantation **(13)**, hypertrophied myocardium **(14)**.

1.2. Novel techniques of cardioplegic delivery

The use of normothermic cardioplegia necessitated the development of novel methods of cardioplegic delivery to permit near-continuous perfusion. The introduction of retrograde perfusion in coronary sinus has been demonstrated to decrease the need of cardioplegic interruptions, allowing distribution of cardioplegia to regions supplied by stenosed vessels and improving subendocardial cardioplegic delivery.

1.3. Optimal cardioplegic temperature

The controversy about the optimal temperature to perform the operation and for the delivery of cardioplegic solutions is probably

obsolete since there is increasing evidence that the best physiological compromise for the heart and the brain can be obtained performing the operation at a temperature of 32–33 C **(15,109)**.

2. NEW PERSPECTIVES IN MYOCARDIAL PROTECTION

Despite the advances reported above, current cardioplegic techniques have shown suboptimal protection in high risk patients. Recent perspectives likely involve the use of cardioplegic additives or appropriate new formulations of cardioplegic solutions to further improve protective effects.

2.1. Beta-blockade addition in myocardial protection:

It is known that b-adrenergic antagonists attenuate the extent of myocardial injury during ischemia and reperfusion, reducing myocardial oxygen consumption and sympathetic tone and stabilizing cell membranes **(16)**.

The use of esmolol as a cardioplegic agent may be a beneficial alternative to standard techniques, even if the inability to deliver esmolol in blood cardioplegia because of inactivation requires further investigations for the determination of surgical relevance and applicability.

2.2. Glucose–insulin cardioplegia

Glucose–insulin–potassium solutions have been commonly used to treat ischemic myocardium in a variety of medical and surgical situations. Despite encouraging results obtained by smaller non-

randomized studies **(17)** or by randomized trial in elective coronary artery surgery **(18)**, the recent Insulin Cardioplegia Trial **(110)** failed to demonstrate a significant benefit of insulin–cardioplegic solution in the setting of high-risk patients undergoing isolated myocardial revascularization.

2.3. **Strategies to limit reperfusion injury**:

Additional strategies to limit reperfusion injury and to control inflammatory response increasingly, cardioplegic solutions have been designed to include antioxidants for the inactivation of free radicals generated during ischemia and for the provision of scavengers to the intravascular and interstitial compartments during initial reperfusion **(19)**.

2.4. Myocardial preconditioning

Ischemic preconditioning is a powerful protective endogenous adaptive response of the myocardium against a prolonged ischemia **(20)**. However, the application of ischemic preconditioning requires a temporary stop of the blood supply, which can be difficult to perform in many clinical situations.

2.5. Na^/H^ exchange inhibition and myocardial protection

Protons accumulating during ischemia are extruded at the time of reperfusion in exchange for sodium ions. The resulting sodium overload cannot be adequately handled by the sodium/potassium pump because it is inefficient due to ischemia-induced shortage of

energy. This excess of intracellular sodium is then extruded from cells through the sodium/calcium exchanger, which functions in a reverse mode.

2.6. Nitric oxide/L-arginine supplemented cardioplegia

Nitric oxide, an endogenously produced labile gas, has been demonstrated to reduce myocardial ischemia–reperfusion damage in experimental animal models; moreover, it seems to exert a myocite protective role as antiapoptotic factor and as mediator in ischemic preconditioning **(21)**.

AIM OF THE WORK:

The objective of this study is to evaluate the safety and effectiveness of intermittent antegrade warm blood cardioplegia (IAWBC) with normothermia CPB, regarding myocardial protection in Mitral Valve Replacement Surgery (MVR) as compared to the intermittent antegrade perfusion of cold crystalloid cardioplegia (CCC) with hypothermic CPB.