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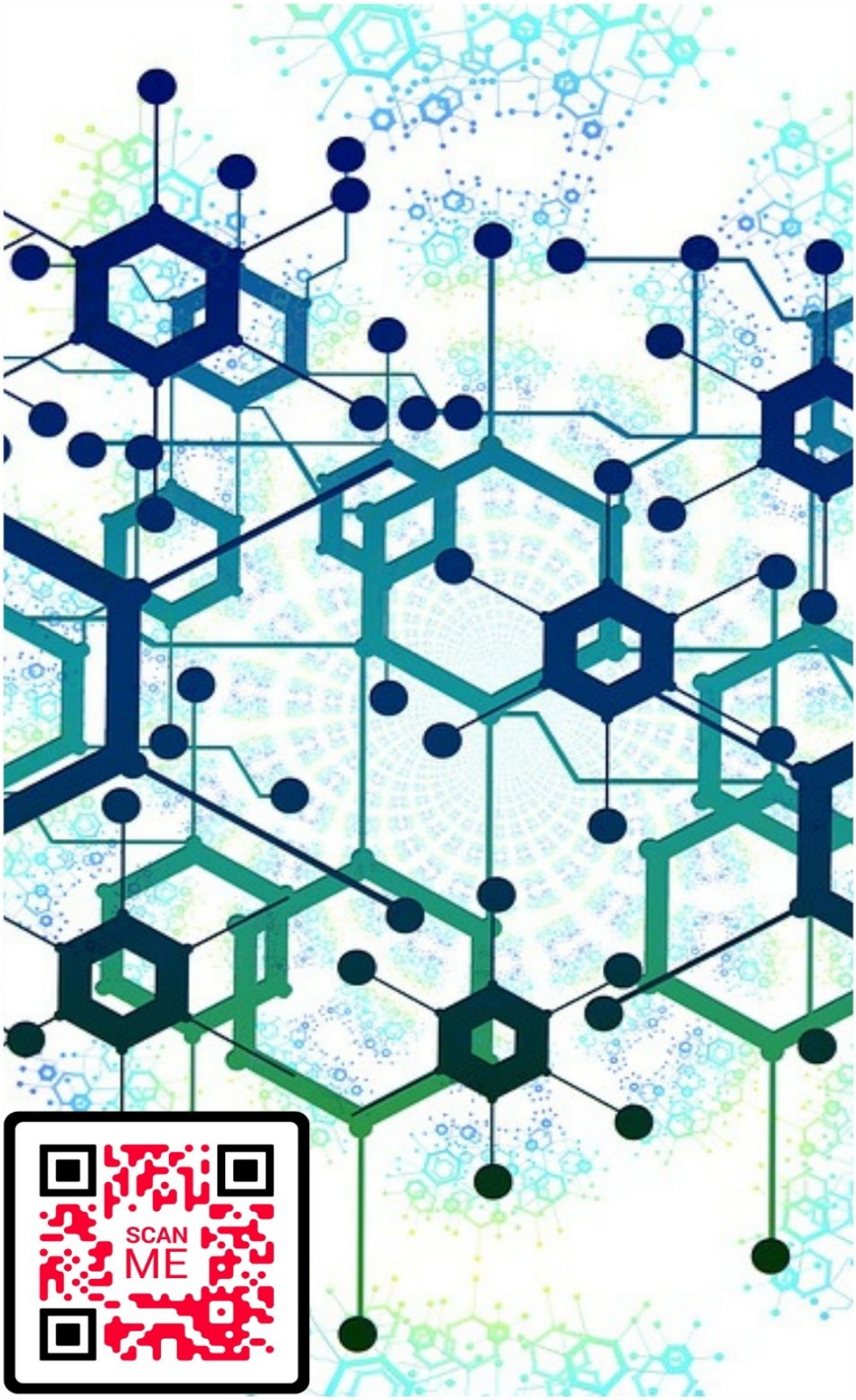

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Optimizing Cardioplegic Solutions: A Focus on Pharmaco-Cold Strategies

Optimasi Solusi Kardioplegia: Fokus pada Strategi Pharmaco-Cold

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Abstract

This study investigates the impact of crystalloid cardioplegic solutions (CCS) on electrophysiological mechanisms and the contractile system during the diastolic phase. Extracellular solutions, categorized by ion concentration, demonstrate efficacy in inducing cardiacarrestthroughmoderatelyelevatedpotassiumorpotassium-magnesiumcombinations, aligning with normal or slightly reduced sodium and calcium levels. Notably, the ease of equilibration with myocardial tissue enhances the protective effect, correlating with infusion volume and duration of action. However, drawbacks such as low buffering capacity and the need for reinfusion after 15-20 minutes are identified. This research sheds light on the dynamic relationship between solution composition, duration of action, and protective efficacy, providing valuable insights for refining cardioplegic protocols in cardiac surgeries.

Highlights:

- Intracellular vs. Extracellular Impact: Explore ion concentration's influence on crystalloid cardioplegic solutions, emphasizing the choice between intracellular and extracellular formulations.
- Equilibration Dynamics: Investigate the direct correlation between infusion volume, duration of action, and the protective effect, emphasizing equilibration with myocardial tissue.
- Refining Cardioplegic Protocols: Identify limitations like low buffering capacity, necessitating reinfusion, and offer insights into strategies for enhancing cardioplegic protocols in cardiac surgeries.

Keywords: Cardioplegia, Intracellular Solutions, Calcium paradox, Protective Efficacy, Cellular Metabolism

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Introduction

The composition of extracellular solutions is chosen on the basis of the concentration of ions in the extracellular fluid. Sodium and calcium ions are present in normal or slightly reduced concentrations. Cardiac arrest is induced by moderately elevated concentrations of potassium or potassium combined with magnesium. The main advantage of extracellular solutions is the ease with which they equilibrate with myocardial tissue. This fact leads to a direct correlation between the duration of action, the infusion volume and the protective effect. Once these solutions have taken effect, it is easy to restore cardiac activity. At the same time, the effect of extracellular solutions may be reduced due to increased blood return to the heart [1]. Disadvantages of such solutions include low buffering capacity due to the addition of sodium bicarbonate. Almost all types of extracellular CRC require reinfusion after 15-20 minutes to wash out metabolites and stabilise the pH [2].

Methods

Intracellular solutions differ from extracellular solutions in that they contain very small amounts of calcium and sodium ions. Such solutions simulate the ionic composition of intracellular fluid and cause cardiac arrest by depleting sodium and calcium stores [3].

The advantages of intracellular solutions are

1) their low osmolarity, which allows the solution to be concentrated without the risk of an excessive increase in osmolarity;

2) the possibility of producing a direct cardioplegic effect by restricting the entry of sodium ions into the cells;

3) the possibility of limiting myocardial contraction and reducing ischaemic calcium entry into the cell due to its low extracellular concentration.

Disadvantages of such solutions include the possibility of developing a suboptimal ionic equilibrium, which may lead to systolic rather than diastolic cardiac arrest, and the possibility of provoking the "calcium paradox" during reinfusion of a calcium-containing solution [4], [5].

In cardioplegic practice, extracellular type CRC (St. Thomas Hospital analogues, "Plegisol", "Consol") and intracellular type CRC (NTC solution - "Custodiol"), as well as their numerous modifications, are widely used [6].

Results and Discussion

Hypothermia reduces cellular metabolism, glucose utilisation and ATP production are greatly reduced, resulting in a negative energy balance. In the presence of reduced basal oxygen demand during hypothermia, the resulting leftward shift of the oxyhaemoglobin dissociation curve and extracellular alkalosis can reduce oxygen delivery and lead to relative tissue hypoxia [7], [8].

Traditionally, cardioplegia (crystalloid or blood) is used in combination with hypothermia as an additional protective factor [9]. As one of the methods of myocardial protection during cardiac surgery since 1959, hypothermia allows to prolong the time of cardiac tolerance to ischaemia without significant damage to the heart. This is due to the reduction in the oxygen consumption and metabolic rate of cardiomyocytes as the temperature of the organ decreases. At the same time, the main energy substrates in the cell are preserved [10], [11].

Hypothermia is used both in deep hypothermic global myocardial ischaemia under non-perfusion hypothermic protection [12] and in combination with extracorporeal circulation and local pharmacological effects (cardioplegia proper), when the temperature of the mixture supplied to the coronary arteries is 4-8 °C [13]. At the same time, myocardial temperature of 10-20 °C provides myocardial protection and allows performing most open-heart manipulations. When myocardial temperature drops below 10 °C, the protective effect of hypothermia decreases [14]. Cooling of the cardioplegic solution is sometimes supplemented by external covering of the heart with "ice chips" or permanent hypothermic pericardial perfusion. However, the use of ice chips may cause contact myocardial damage in the form of microscopic necrosis and cold paresis of the diaphragmatic nerve [15]. Pericardial perfusion promotes the development of prolonged myofibril oedema with decreased ventricular pumping function [16]. Studies have revealed the negative effect of external cooling on red blood cells. When melting ice chips, initially the hyperosmolar fraction of the solution thaws, and then, after its removal, a hypoosmolar solution is formed, causing haemolysis of the blood pouring into the wound, which falls into the oxygenator [17]. In addition, local cooling of the myocardium and mediastinum causes a decrease in local immunity and is one of the factors responsible for the local inflammatory response in the form of postpericardiotomy syndrome, pericarditis or mediastinitis [18], [19]. This contributes to cardiac rhythm disturbances (atrial fibrillation, extrasystolic arrhythmia) in the postoperative period. Excessive exudation limits diastolic relaxation,

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leading to a decrease in myocardial contractility, and as a consequence - heart failure and requires in some cases surgical (puncture or fenestration of the pericardium) and medication (saluretics, nonspecific anti-inflammatory agents, corticosteroids) treatment [20].

Recently, many researchers have emphasised the negative effect of low temperatures and cooling in general on metabolic processes in the myocardium. Thus, the main disadvantages of myocardial hypothermia are:

1.Suppression of the activity of enzyme cellular systems leads to impaired glucose utilisation and ATP formation that exceeds the rate of decline in cellular metabolism, resulting in a negative energy balance [21];

2.Reduced oxygen demand during hypothermia shifts the haemoglobin dissociation curve to the left and upwards, reducing tissue oxygen extraction with the development of relative tissue hypoxia [22]. On the other hand, it has been shown that the amount of oxygen delivered to myocardium during reinfusion of blood cardioplegic solution with the temperature of 4 °C is ten times higher than the basal requirements of myocardium on the background of prolonged global ischaemia, but the consequence of hypothermia is an increase in oxygen consumption during temperature normalisation, which can aggravate ischaemia of the operated heart [23], [24];

3.Hypothermia is accompanied by increased viscosity of both electrolyte solutions and blood, which worsens microcirculation, promotes the development of "sludge" and uneven distribution of cardioplegic mixture, especially in case of multifocal atherosclerotic lesions of coronary vessels;

4.Increase of blood viscosity at the temperature of 4-5 °C and impaired blood supply of the atrioventricular node explains the high frequency of conduction disorders in the postperfusion period when using cold blood cardioplegia [25], [26];

5.Due to temperature reduction, the homeostasis of the blood coagulation system is disturbed (inhibition of platelet activity, activation of the fibrinolytic cascade and inhibition of the activity of thromboproducing enzymes), contributing to the development of hypocoagulation [27];

6.Myocardial hypothermia increases the likelihood of ventricular fibrillation, dysrhythmias and delays the recovery of normal conduction system function during reperfusion ;

7.Artificial circulation and myocardial protection in the "warm body - cold heart" mode during myocardial revascularisation leads to uneven myocardial cooling due to the fact that the right parts of the heart continue to be warmed by the blood returning to the atrium. As a result, there is a mosaic temperature gradient and uneven cardiomyocyte metabolic rate, therefore, the feasibility of hypothermic myocardial protection in this form is doubtful;

Conclusion

In hypothermic cardioplegic arrest, desensitisation of myocardial β-adrenoreceptors due to inhibition of their interaction with adenylate cyclase was observed both during artificial circulation and 30 minutes after it.

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