

EFFECTS OF CARDIOPLEGIA WITH ADENOSINE : ADVANTAGES ON POSTISCHEMIC RECOVERY AND CARDIAC ARREST

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SUMMARY : *In a comparative study, effects of adenosine cardioplegia have been determined on cardiac arrest and postischemic recovery. Two kinds of cardioplegics were used to arrest the hearts: I. potassium cardioplegia II. adenosine cardioplegia. The hearts, previously being perfused by Krebs - Henseleit solution were arrested by cardioplegic infusion. After 45 minutes of hypothermic ischemia, postischemic recovery of heart rate, ventricular contractility, heart work and postischemic changes of tissue enzymes were compared between the two groups.*

Both cardiac arrest and postischemic recovery were much better in the group of adenosine cardioplegia.

Key Words : *Adenosine, Cardioplegia.*

INTRODUCTION

A comparative study has been performed on isolated guinea pig heart. Effects of adenosine in cardioplegia have been determined on cardiac arrest and postischemic recovery.

Two kinds of cardioplegics were used to arrest the hearts; I. potassium cardioplegia - II. adenosine cardioplegia.

Langendorf's perfusion technique was used as a model of cardiopulmonary bypass. The hearts previously being perfused by Krebs - Henseleit solution were arrested by cardioplegic infusion. After 45 minutes of hypothermic ischemia postischemic recovery of heart rate, ventricular contractility, heart work and postischemic changes of tissue enzymes (LDH, SGOT, SGPT) were compared between the two types of cardioplegic solutions. Also arrest ti-

me and number of arrest beats were recorded and compared between the two groups. Both cardiac arrest and postischemic recovery were much better in the group of adenosine cardioplegia.

In cardiac surgery, the degree of myocardial protection is very important and weaning from cardiopulmonary bypass relies on this procedure. Therefore a lot of research on cardioplegic solutions have been performed (Hearse et al. 1974; Jong et al. 1990; Luiz et al. 1989; Schubert et al. 1989; Sparks and Bardenheuer, 1986).

Adenosine has several theoretical peculiarities that make it attractive as the component of a cardioplegic solution.

Adenosine, by activation of the potassium channels, inhibits the sinus and atrioventricular nodes (Belardinelli and West, 1988; Belardinelli et al.

1988; Jong et al. 1990; Luiz et al. 1989). The nucleosid also indirectly inhibits myocardial contractility, enhances the tolerance of the myocardium to ischemia, arrest and may improve recovery of cardiac contractile force after hypoxia (Dobson, 1983; Ely et al. 1985; Jong et al. 1990; Takeo et al. 1988).

Some authors have shown that (Jong et al. 1990), rapid cardiac arrest with adenosine cardioplegia is possible only with high concentrations of adenosine and they state that adenosine has to be washed out after the induction of cardiac arrest. But some others however, suggest that a lower dose of adenosine can still rapidly cause mechanical arrest of the heart without requiring washout (Jong et al. 1990).

In the present study we used higher doses of adenosine and compared its effects with potassium on cardiac arrest and myocardial recovery in the guinea-pig's isolated heart.

MATERIALS AND METHODS

Animals

Hearts were obtained from male guinea pigs (n=20) weighing 280-370 gr.

The animals were anesthetized by ether and given 200 units of heparin by the femoral vein. The hearts (1.8 - 2.4 gr) were rapidly removed and cannulated via the aorta.

Perfusion techniques and plegic solutions

The hearts were mounted on a Modified Langendorf Perfusion Apparatus and perfused by an aerated (oxygen 95 %, carbondioxide 5 %) Krebs - Henseleit solution at a rate of 2 ml/min at 37°C. The composition of the solution was NaHCO₃ 25 mMol / L, NaCl 118 mMol / L, KH₂PO₄ 1.2 mMol / L, KCL4.8 mMol / L, Mg₂ SO₄ 1.2 mMol / L, CaCl₂ 1.2 mMol / L and glucose 11.1 mMol / L.

Percentage recovery of heart rate =

$\frac{\text{Postischemic heart rate} \times 100}{\text{Preischemic heart rate}}$

Percentage recovery of ventricular contractions =

$\frac{\text{Postischemic cotractions} \times 100}{\text{Preischemic contractions}}$

Percentage recovery of heart work =

$\frac{\text{Postischemic heart rate} \times \text{postischemic contractions} \times 100}{\text{Preischemic heart rate} \times \text{preischemic contractions}}$

Percentage change of tissue enzymes = $\frac{\text{Postischemic enzyme (LDH, SGOT, SGPT) concentrations} \times 100}{\text{Preischemic enzyme concentrations}}$

Two different cardioplegic solutions (10 experiments in each group) were used to arrest the hearts. The composition of these solutions were; group 1 : NaCl 123 mEq / L, KCl 20 mEq / L, MgCl₂ 16 mEq / L, glucose 200 mg / dl, NaHCO₃ 9 mEq / L, pH 7.6; group 2 : NaCl 123 mEq / L, Adenosine 10 mMol / L, MgCl₂ 16 mEq / L, glucose 200 mg / dl, NaHCO₃ 9 mEq / L, pH 7,8

Protocol

After ten minutes the heart had begun to work, we recorded the contractility, heart rate and also collected perfusate samples from the right atrium to determine tissue enzymes. The hearts were arrested by infusion of one of the cardioplegic solutions from the aortic root at a rate of 2 ml / min for 3 minutes at 4°C. Over this 3 minutes of plegic infusion the arrest time and number of beats were assessed. Following cardiac arrest the plegic solution was removed by infusion of 2 ml isotonic saline from the aortic root. During the ischemic period the hearts were kept at 8-10°C by topical cooling with isotonic saline. After 45 minutes of ischemia the reperfusion was begun by the same buffer at 37°C. At the tenth minute of reperfusion again the contractility and heart rate were recorded and perfusate samples were collected.

Calculations

The following calculations were made.

Arrest Time : Time (seconds) from the onset of cardioplegic infusion until the loss of myocardial contractions.

Arrest beats : Number of heart beats during 3 minutes of cardioplegic infusion.

Data analysis

The mechanical data such as contractility and heart rate were recorded by using "UGO BASILE 7004" isometric force displacement transducer and calculated from the recordings. The biochemical parameters (LDH, SGOT, SGPT) were analysed by "Technican RA-1000 autoanalyser using "Chromatest" kits. For statistical work-ups, Student's t. test and one way analysis of variance were done by "Microstat" PC programme.

RESULTS

Effect of adenosine on cardiac arrest

From the beginning of the cardioplegic infusion, the time to cardiac arrest was significantly reduced by adenosine containing solution and also the number of beats during the 3 minutes of cardioplegic infusion were reduced by the same solution.

Cardiac arrest time was diminished from 52.2 ± 15.0 seconds to 5.23 ± 1.8 seconds with adenosine cardioplegia. ($p < 0.01$ for comparisons between the groups) (Fig 1, 2).

The number of arrest beats with potassium cardioplegia infusion were 39.4 ± 8.9 . Where it was 5.9 ± 1.5 with adenosine cardioplegia ($p < 0.01$) (Fig 2).

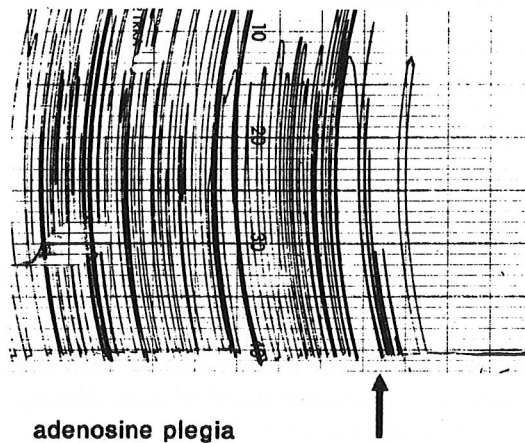
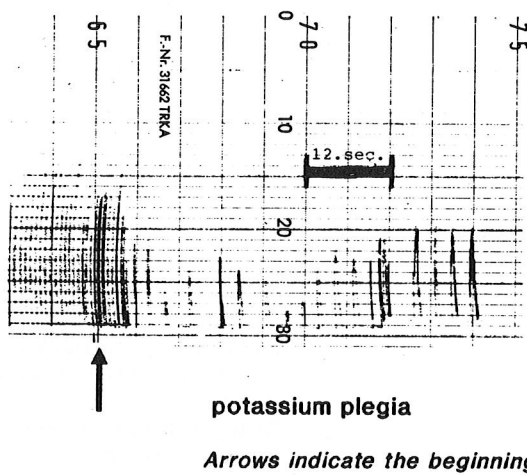


Fig. 1 : Arrest effect of plegic solutions

Effect of adenosine on myocardial recovery

Mechanical parameters

There were no significant difference between the two groups, for final recovery of the heart rate. The percentage change of the heart rate was, 105.1

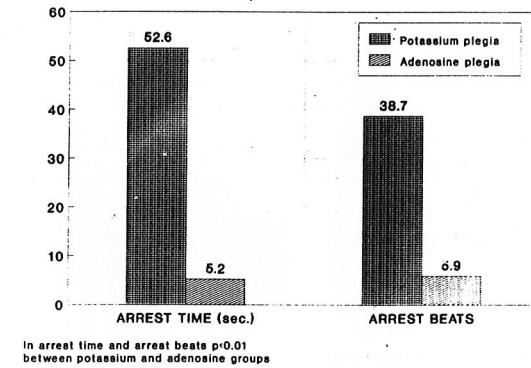
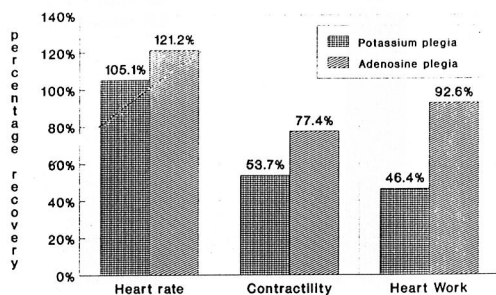


Fig. 2 : Effects of different plegic solutions on cardiac arrest.

± 10.5 % in potassium group where it was 121.2 ± 11.9 % in adenosine group.

Postischemic recovery of the left ventricular contractility was significantly better in adenosine group 77.5 ± 4.2 % when compared with the potassium group 53.7 ± 5.0 % ($p < 0.01$).

Postischemic recovery of cardiac work as a percent of the preischemic calculation was expressively better in adenosine group 92.6 ± 12.8 % then the potassium 46.4 ± 5.8 % ($p < 0.01$) (Fig 3).



p<0.01 between potassium and adenosine groups on contractility and heart work.

Fig. 3 : Effects of different plegic solutions on postischemic recovery of mechanical cardiac functions.

Biochemical parameters

Postischemic percentage changes of SGPT concentrations were significantly higher in potassium group when compared with adenosine group ($p < 0.05$). There was no significant difference among the two groups for SGOT and LDH concentrations.

DISCUSSION

Prior investigations state that classic potassium cardioplegia is very effective on myocardial protection (Engelman et al. 1980; Landymore et al. 1986; Schubert et al. 1989).

Recently some other agents were started to be administered either as a preparation to or in combination with the cardioplegic solutions previously used (Jong et al. 1990; Schubert et al. 1989).

Adenosine is one of the agents that many authors are interested in. Its effects on the heart were extensively investigated in recent years. Although it is mostly known as a coronary vasodilator, adenosine also increases the potassium permeability and leads to hyperpolarization of the cell membranes in the atrial tissue and sinus node (Schrader et al. 1975; Schubert et al. 1989; Stafford, 1966); reduces calcium influx to cause a negative inotropic effect (Drury and Szent Gyorgyi, 1930; Schrader et al. 1975; Schubert et al. 1989; Stafford, 1966), attenuates the stimulatory actions of catecholamines primarily on ventricular myocardium, depresses ventricular automaticity, inhibits the release of norepinephrine induced by adrenergic nerve stimulation,

reduces the degradation of ATP during ischemia, improves replacement of ATP during reperfusion and inhibits platelet aggregation (Belardinelli and West, 1988; Belardinelli et al. 1988).

Because of these effects it can lead to rapid cardiac arrest when used in cardioplegic solutions.

In our study we used adenosine as a preparatory agent for cardioplegia, and compared it with potassium. We found that adenosine is more effective on rapid cardiac arrest and postischemic myocardial recovery. The indicators were arrest time, arrest beats, cardiac work, heart rate, and biochemical parameters (LDH, SGOT, SGPT). Except biochemical parameters, all other indicators showed the beneficial effectivity of adenosine cardioplegia. In biochemical parameters, LDH and SGOT values revealed no difference between the two groups but SGPT values did. Although all of the samples were collected from the isolated myocardial tissue of animals, SGPT is not direct indicator of the myocardial damage. That's why results of biochemical parameters may be a laboratory error.

We assume that adenosine cardioplegia may be an alternative solution in cardiac surgery and we believe that further researches investigating the effects of adenosine on a model mimicking the human physiology will yield more detailed information about this agent.

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