ANAESTHESIA

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Anaesthesia Elective Essay

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Different Techniques/Mechanisms of Cardioplegia

Cardioplegia means stopping the heart temporarily. This technique is developed to provide the surgeon a still and bloodless field. Cardioplegia can also commonly refer to the solution that is used to stop the heart. The aim of cardioplegia technique is to stop the heart during the operation and at the same time protecting the myocardium from damage during the period of ischaemia. To achieve this, the patient is placed on cardiopulmonary bypass machine to take over the function of the heart and lungs. Circulation of the heart is isolated from the body using cross clamps techniqueand cardioplegia solution is used in combination with hypothermia to arrest the heart, at the same time reducing the metabolic rate.

As a result of extensive research done since more than 40 years ago, several techniques/mechanisms of achieving cardioplegia has been developed. Each has their own pro and cons which until now, there is no single technique that is 100% superior to any other technique. The aim of this article is to cover briefly some of the techniques that are available right now.

Depolarized arrest

This is the most common method to induce rapid diastolic arrest during cardiac surgery. It is achieved by moderately elevating the extracellular K^+ concentration usually within 15-40mmol/L. Increasing extracellular K^+ concentration causes the resting membrane potential, E_m to progressively depolarized[(1)]. When the resting E_m depolarizes to approximately -65mV (at K^+ concentration of about 10mmol/L), this inactivates the voltage dependent fast sodium channel[(2)], thus preventing the rapid Na^+ induced spike of the action potential. This reaction will cause the heart to stop in diastole. Increasing the extracellular K^+ concentration further more will further depolarize resting E_m. At a resting E_m of about -40mV (extracellular K^+ concentration of 30mmol/L or further), the slow calcium (Ca^{2+}) channel will be activated[(2)] promoting Ca^{2+} overload. Thus, this method is restricted to a relatively narrow concentration window of about 10-30 mmol/L. The St Thomas' Hospital cardioplegic solution has an optimal extracellular concentration between 15-20 mmol/L [(3)], thus the depolarized E_m falls approximately in the middle of the protective E_m window. However, at these levels of depolarization, other ionic currents remain active. It is thought that the voltage dependent activation and inactivation gates of the Na^+ channel operate at a different rates and lead to Na^+ windowcurrent [(4)] this result from an activating current that will tend to increase the intracellular Na^+

concentration, and thus will increase the Ca^{2+} window current[5]. This will cause the heart to contract even in arrested position, leading to Ca^{2+} overload and reperfusion injury. Energy dependent transmembrane pumps remain active in this process, hence they will deplete the critical energy supply in order to correct these ionic imbalance [6,7]. Achieving arrest using extracellular K^+ concentration has been shown to be associated with decreased myocardial ATP levels compared with arrest using magnesium [8]. Other problems that may be associated with depolarized arrest are maintained metabolism, K^+ induced endothelial injury [9,10], and arrhythmias [10].

Polarized arrest

This method achieves cardiac arrest by maintaining polarization of the E_m close to the resting E_m. polarized arrest have a number of advantages which include reduced ionic movement particularly Na^+ and Ca^{2+}, because the threshold potential for activation of the ion channel will not be reached and window current will not be activated. The reduction in ionic imbalance should reduce myocardial energy utilization to correct ionic imbalances. Polarized arrest can be achieved in a number of ways.

Sodium channel blockade

Sodium channel blockade can cause the heart to stop by preventing the rapid Na^+ induced depolarization of the action potential [11]. Local anaesthetic agents such as procaine and lignocaine have been widely used, either as cardioplegic agents or in combination with other agent [3]. Procaine (1 mmol/L) is one of the ingredients of St Thomas' Hospital solution no 1 for membrane stabilization and has been shown to control post-operative rhythm disturbances [12]. However, there is a small risk of toxicity and seizures with these agents [13,14].

Tetrodotoxin

Tetrodotoxin (TTX) is a highly toxic substance but potent and rapidly reversible Na^+ channel blocker. It is an effective cardioplegic and protective agent [15] and has been shownto reduce myocardial oxygen consumption in comparison with hyperkalaemic arrest.Chambers et.al.[16]used TTX at a concentration of 22 µmol/L to arrest rat hearts before long term hypothermic storage preservation. The research demonstrated significantly improved protection compared with hyperkalaemic buffer solution (16 mmol/L). Measurement of E_m during storage showed that TTX maintained the E_m at around -70 mV (polarized arrest) compared with -50mV in the hyperkalaemic solution. Furthermore, high energy phosphate levels (ATP and phosphocreatinine) at the end of the storage were significantly higher in the TTX arrested hearts.

Adenosine

Adenosine induce arrest through a hyperpolarization effect particularly on myocardial conductive tissue [17]. It was also shown to provide good myocardial protection when used alone (10mmol/L) as a cardioplegic agent [18,19] or as an additive (1 mmol/L) to K^+ cardioplegia solution [20]. It was shown to reduce the time to arrest and to be at least as effective as hyperkalaemic arrest. Furthermore, adenosine (1 mmol/L) has been shown to reduce K^+ induced Ca^{2+} overload in isolated myocytes[21]. More recently, the additive beneficial effect of adenosine to K^+ based cardioplegia has been tested clinically and shown to be safe and to reduce post-operative complications[22] although this remain controversial [23]. Another research has shown that a combination of adenosine and lignocaine (polarized arrest) was shown to be an effective protective combination over ischaemic period up to 4 hours [24].

Calcium mechanism in achieving arrest

Hypocalcaemia

The absence of Ca^{2+} in the extracellular space induces cardiac arrest by inhibiting excitation-contraction coupling. This mechanism was used in early cardioplegic solution. However, hypocalcaemia increased the risk of 'calcium paradox' [25] although traces of contaminant Ca^2 , hypothermia and low Na^+, or high Mg^{2+} counteracted this risk. It is though that the relationship between low Ca^{2+}, los Na^+ and high Mg^{2+} are highly complex [3].

Calcium antagonist

Calcium antagonist in high concentration prevents Ca^{2+}-induced Ca^{2+}release and cause arrest by inhibiting excitation-contraction coupling. Calcium antagonist have been suggested to be potentially comparable to hyperkalaemic arrest, but the delayed reversal of these drugs may result in slow recovery. Ca^{2+}antagonist have also been used as additives to K^+cardioplegic solution but their effects are temperature dependent, with little effect during hypothermia [26]. Hence, although calcium antagonist have positive properties, the benefits appear to be outweighed by its negative properties relating to their dose dependent, temperature dependent, and time related effects.

Hypermagnesemia

Increased concentration of Mg^{2+} can arrest the heart, possibly by displacing Ca^{2+} from the rapidly exchangeable binding sites involved in excitation-contraction coupling [27]. However, it is less effective than hyperkalaemia technique and requires higher concentrations. Mg^{2+} is more usually used as an additive protective agent[28] where it is a standard component of the St Thomas' Hospital cardioplegic solution.

Esmolol

Esmolol is an ultra-short acting β-blocker with half-life of about 10 minutes. It has been recently used in cardiac surgery to induce minimal myocardial contraction while maintaining continuous normothermic perfusion to avoid ischaemia. It has been shown to give cardioprotectionequivalent to cardioplegia [29]. At high concentration (approximately 1 mmol/L), esmolol induces cardiac arrest and Chambers [30,31] have shown that multidose infusions of 1.0 mmol/L esmolol solution can completely protect isolated crystalloid-perfused rat hearts for period up to 90 minutes. They also have preliminary unpublished data suggesting that esmolol acts by inducing Ca^{2+} desensitization. This property was not demonstrated by equal concentrations of atenolol.

Hypothermia

This is the other key components in the cardioplegia technique. Hypothermia is used during cardiopulmonary bypass in order to reduce the oxygen requirement of tissues. The Vant Hoff equation allows us to calculate that oxygen consumption will drop about 50% for every 10°C reduction in temperature. This effect in combination with chemical arrest can reduce myocardial oxygen consumption by 97% [32]. The associated decrease in tissue oxygen consumption may then allow the utilization of lower flow rates if necessary[33]. The use of lower flow rates may facilitate surgery and decrease the blood cells damage from the bypass machine.

Cold crystalloid cardioplegia vs Blood cardioplegia

Cold crystalloid cardioplegia is clinically used since the mid-1960s. In principle, this method protects the myocardium by hypothermia and electromechanical arrest. It reduces the myocardial metabolic demands thus prolonging the tolerance to ischaemia. The two types of cold crystalloid cardioplegia are intracellular and extracellular solution. Intracellular type crystalloid solutions contain no or low concentrations of sodium and calcium, whereas extracellular type solutions contain higher concentrations of sodium, calcium, and magnesium. Both contain potassium between 10-20 mmol/L and have other additives such as local anaesthetic and buffer solution.

Blood cardioplegia works with the same basic concept of cardioplegia which in this case, blood is used to deliver the potassium. Using blood as a vehicle to deliver the ingredients of cardioplegia has its own benefits. Blood provides a closer approximation to normal physiology which the most important feature is its oxygen carrying ability. The ability to carry oxygen will make it easier to

resuscitate the heart at the end of the operation and can also prevent ischaemic injury. The electrolyte composition and pH of the blood are physiologic where it can function as a natural buffer of the cardioplegia solution.

After reading from a few sources, it is really difficult to compare which method is more superior. Different research paper about each method claimed that their method is more superior than the other based on the research and analysis that they have conducted. The researcher from each method also claimed that their method is the most widely used in the world. The controversy is not limited whether to use blood or crystalloid, it also involves different ingredients and additives to produce an 'ideal' solution in order to achieve maximum cardioprotection and to reduce mortality and morbidity. Although many randomised trials have tried to prove which method is the best, a clear clinical benefit in terms of decreased mortality and morbidity was not consistently demonstrated in the comparison between blood and crystalloid cardioplegia. Therefore, institutional and the individual surgeon's experience remain the most important determinants of myocardial protection strategy at this moment.

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