6th Perfusionists' Meeting: Cardioplegia in Theory & Practice

Joint meeting of the Society of German Perfusionists (DGfK) and Dr. Franz Köhler Chemie GmbH company, Bensheim, 12 May 2022

Round Table: Q&A, Tips & Tricks for using CUSTODIOL®

Participants

- Dr. Sabrina Martens (pediatric surgeon and deputy physician in Münster)
- Prof. Dr. Nicolas Doll (cardiac surgeon and clinic director in Bad Rothenfelde)
- Dr. Frank Münch (perfusionist and head of the department in Erlangen)
- Dr. Stefan Fritz (chemist and product manager in Bensheim)

Custodiol®, developed by the German physiologist Hans Jürgen Bretschneider at the University of Göttingen in the early 1970s (Histidine-Tryptophan-Ketoglutarate, HTK-solution) has been developed as a crystalloid cardioplegia with an intracellular composition and strong buffering system, offering up to three hours of myocardial protection in conjunction with hypothermia ("single dose"). In May 2022, 60 German perfusionists met for an expert meeting and round table discussion in Bensheim, Germany. The goal of this meeting was to discuss the clinical application of Custodiol®, including administration guidelines, pitfalls, and recommendations by long-time users.

Open access

To watch the recorded webinar scan the QR-Code or visit www.koehler-campus.com/kardiotechniker-fachtagung-2022/

The topics were centered around the following questions:

1. Which cardioplegia is employed in your practice?
2. Do you give a second dose of Custodiol®?
3. How much volume is given at the second dose of Custodiol®?
4. Which sodium levels are relevant and what is your strategy for treating hyponatremia?
5. How do you treat hypervolemia?
6. Retrograde application of cardioplegia

While 4 chairmen discussed the topics, the audience participated in a survey (topics 1 to 5), while topic 6 was also briefly discussed.

1. Which cardioplegia is employed in your practice?

Determining the optimal choice of a cardioplegic solution in the hospital can be tricky. In some cases, the chief surgeon decides, in other cases there are various methods within one department. Some centers follow a strict protocol based on the procedure type, using Calafiore for short operations (CABG, CHD) and employing Custodiol® for more extensive cases (valves, complex surgeries). Whereas in other centers the choice strongly depends on the operating surgeon rather than on the procedure. In most cardiothoracic centers, the expected cross-clamp time determines the choice of cardioplegia.

Custodiol® is the preferred choice in most centers, followed by Calafiore and Buckberg's 4:1 cardioplegia. Some pediatric centers use St. Thomas, while Del Nido cardioplegia is being established in Germany (figure 1).

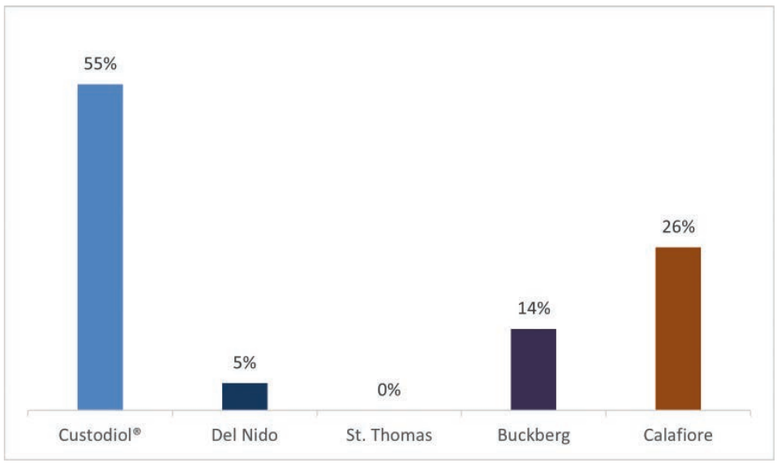

Figure 1: Which cardioplegia do you prefer?

Conclusion: The type of operation respectively expected cross-clamp time determines the choice of myocardial protection with Custodiol® being the preferred cardioplegia for complex surgeries (cross-clamp times over 90 minutes).

2. Do you give a second dose of Custodiol®?

One of the most discussed aspects for "single dose" techniques concerns the timing and necessity of administering a second dose. The survey "Do you give a second dose of Custodiol®?" shows that participants give a second dose after 90 minutes cross-clamp time, in alignment to the Leipzig protocol for cardioplegia. Another large group administers a second dose only in case of cardiac activity (figure 2).

For most of the Minimal Invasive Cardiac Surgery (MICS) procedures the cross-clamp time lies below 90 minutes. Certain operations can take up to several hours. In such cases the perfusionist communicates both the 90 minutes mark and any occurrence of cardiac activity appearing over 90 minutes cross-clamp time to the operating surgeon. Then a second dose of Custodiol® might be given.

Early cardiac activity occurring after 20 minutes of cross-clamp time has been described for various cardioplegic methods. This early activity usually lasts for a short duration (1-5 minutes) before subsiding. This is not related to a change in cardiac enzyme activities (CK-MB). Temperature shifts or incomplete equilibration could be the reasons, but it remains unclear.

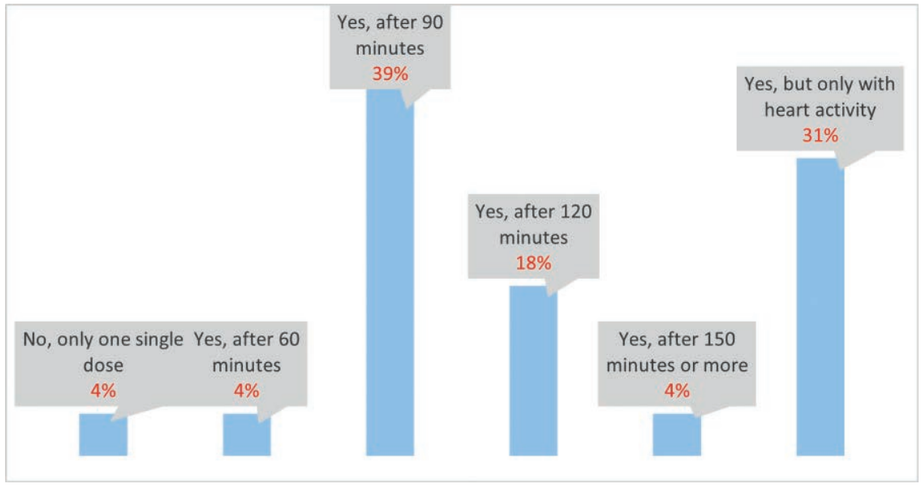

Figure 2: Do you give a second dose of Custodiol®?

Conclusion: In most of all cardiothoracic procedures, a second dose of Custodiol® is not needed, only when cardiac activity has been monitored, indicating the end of cardiac arrest. Nevertheless, some centers standardly give a second dose after 90 minutes of cross-clamp time.

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3. How much volume is given at the second dose of Custodiol®?

During cardioplegia the heart only receives small amounts of oxygen. Under these ischemic conditions, anaerobic glycolysis generates acidic metabolites causing damage to the cellular membranes. A second dose of cardioplegia aims to “flush out” the heart. Therefore, there is no need for using high amounts of cardioplegic solution. Only a few Milliliters of 200-400 ml (sometimes 700-800 ml) of Custodiol® are needed to flush out the acidic metabolites. This helps the heart to start beating when the cross-clamp is opened for reperfusion with blood.

In pediatric cardiac surgery, a first dose is administered over a period of 5 minutes, in order to establish the equilibration. For a second dose, 15 ml/kg are given, which is approximately half of the first dose.

Conclusion: In adult cardiac surgery 200-400 ml (sometimes 700-800 ml) of Custodiol® are given as a second dose. In pediatric cardiac surgery, half of the first dose is given.

4. Which sodium levels are relevant and what is your strategy for treating hyponatremia?

Custodiol® is an intracellular solution, reflected in its electrolyte composition. Bretschneider’s concept is based on a low sodium (15 mM) solution. This low sodium content protects the myocardial cells from the formation of edema. The extracellular sodium concentration is about 10 times higher. Since Custodiol® can enter the patient’s system via the two-stage cannula, the question of hyponatremia arises: Which sodium concentrations are critical, and who is responsible for managing the patient’s sodium content? In addition to the perfusionist and cardiac surgeon, the anesthetist and intensive care physicians are also involved in this issue.

Hyponatremia caused by cardioplegia can be prevented. Scavenging the right atrial effluent helps mitigating serum sodium level changes. Another technique would be using hemofiltration limiting hyponatremia to a short time range of 20-30 minutes before returning to normal sodium levels. The majority of perfusionists add sodium bicarbonate to the system of the extracorporeal circuit while cardioplegia is running. 50-100 ml $NaHCO_3$ (8.4%) are given per 2 liters of cardioplegia. Using these methods prevents the development of seizures.

A moderate hyponatremia begins at 130 mM and becomes severe at 125 mM sodium (figure 3).

Figure 3: Which sodium concentration defines hyponatremia?

Patients with a value below 120 mM should be constantly monitored. It should be noted that some patients are already hospitalized with a low sodium level. Patients with renal insufficiency can develop chronic hyponatremia, requiring careful and moderate sodium treatment, see discussion below:

This type of isotonic hyponatremia does not negatively affect the clinical outcome per se. Hyponatremia only becomes deleterious when osmolarity becomes hypoosmolar. Such a combination of unphysiologically low sodium and low osmolarity can cause cerebral swelling by shifting water from the extracellular to the intracellular space. Given that the Custodiol® solution’s osmolarity is physiologic (290-310 mOsmol/L), such water shifts do not occur.

It is important to slowly substitute low doses of saline chloride or sodium bicarbonate. Sometimes $NaHCO_3$ is given as a buffer. This additional sodium should also be accounted for or might suffice to prevent hyponatremia. Guidelines recommend substituting 1 mMol/L per hour (guidelines by US nephrologists). Distribution of sodium over the interstitium is rather slow compared to other electrolytes which is the reason why it must be administered slowly until it reaches homeostasis. The hematocrit can be used as a parameter to indicate the state of homeostasis.

If sodium is administered too fast or in excessive amounts, it can overshoot the physiological level and lead to the development of a hypernatremia. Therefore, it is critical to avoid overtreatment of sodium. Excessive administration of intravenous saline or sodium bicarbonate can result in hypernatremia with severe elevations, seizures, and comas.

Conclusion: Hyponatremia can be prevented by adding 50-100 ml $NaHCO_3$ (8.4%) are given per 2 liters of cardioplegia into the extracorporeal circuit at the beginning of the cross-clamp time. This can be repeated later during the surgery.

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5. How do you treat hypervolemia?

Perfusionist and anesthetists work close together managing the patient's systemic volume.

Despite notable advances in extracorporeal circulation during the last decade, cardiac surgery with cardiopulmonary bypass (CPB) is still associated with an increased risk of blood transfusions. The primary setup of the CPB circuit demands a priming volume of approximately 1500 mL of crystalloid solution, which leads to a relevant hemodilution. Hemodilution resulting in low hematocrit levels during CPB is known to be responsible for impaired hemostasis, detrimental effects on end-organ function and on cognitive outcome. In consequence, nearly 50% of all cardiac surgery patients receive a transfusion of red blood cells. Blood transfusions have been associated with several serious complications, like transfusion related acute lung injury, modulation of the immune system and increased post-operative infection risk. Furthermore, blood transfusions are an independent risk factor for morbidity and mortality after cardiac surgery and responsible for considerable healthcare costs.

As mentioned earlier (see topic 4.), a high volume of cardioplegia can enter the circuit of the heart-lung-machine due to perforations in the two-stage-cannula which is located near the coronary sinus. This additional volume relates to a decrease of systemic sodium. Only a minority of cardiac surgeons are scavenging the cardioplegia from the right atrium. Most of the perfusionists are using ultrafiltration (hemofiltration) (figure 4) to reduce the total volume to normal values.

Retrograde autologous priming (RAP) is a method that reduces hemodilution during cardiopulmonary bypass (CPB), the reduction of blood transfusions by increasing the hematocrit intraoperatively, especially in patients who have risk factors as anemia, small body surface area, and refuses to receive blood products. This method uses the patient's own blood during of the pump system setting up. The modern RAP procedure minimizes hemodilution by displacing the crystalloid priming volume of arterial and venous lines via passive exsanguination of native blood prior to CPB initiation. RAP leaves enough space for a follow-up with 1000 ml cardioplegia without the need for ultrafiltration in the case of a non-high-risk patient. Noradrenalin can be used to adjust the pressure. Older and more frail patients must be treated carefully and moderately. Hemoglobin (Hb) is an important parameter which must be monitored with regards to the priming procedure. Normal Hb values are 14 – 18 g/dl (men) and 12 – 16 g/dl (women).

Both perfusionists and anesthetists share responsibility for the overall volume management. Perfusionists have improved their volume management over the last years immensely, while protocols have been standardized between the cardiothoracic centers. In contrast to this, the volume management regime of the anesthetists varies from hospital to hospital and can lead to up to 2.5 liters of additional volume. 5 different clinics can have 5 different techniques meaning that they are adding volumes in the range of 200 ml up to 2500 ml water.

Scavenging the volume from the right atrium would be the optimal technique to prevent hypervolemia. This is the standard procedure for pediatric cardiac surgery. Bicaval cannulation (total bypass), opening of the right atrium and suction of the cardioplegia are technically feasible and no disadvantage for the patient. In adult cardiac surgery, some cardiac surgeons believe that opening of the right atrium is technically not possible for mitral valve procedures. However, this seems to be a misconception. Combined reconstructions of the tricuspid and mitral valves can be performed in combination with suction of the cardioplegia from the right atrium. In summary, for aortic valve procedures, an experienced team should use bicaval cannulation and open the right atrium to suck off the cardioplegia, while the inexperienced team should use ultrafiltration.

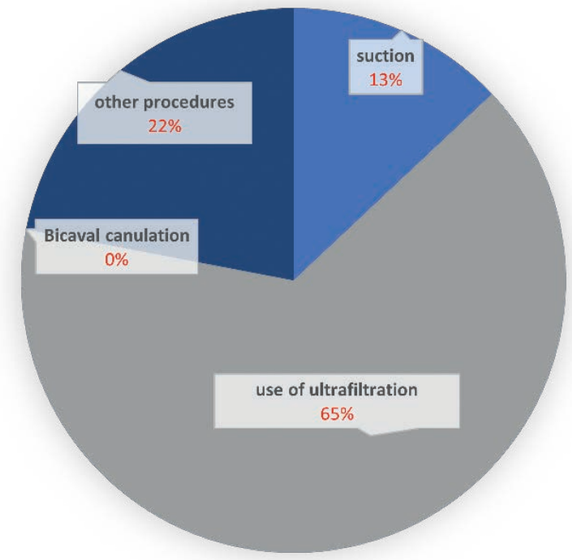

Figure 4: How do you treat hypervolemia?

Conclusion: Hypervolemia can be counteracted by a) sucking out the excessive cardioplegic volume from the right atrium or b) adding ultrafiltration to the system. In pediatric surgery it is mandatory to use a).

Retrograde application of cardioplegia

Some clinics use retrograde application for pediatric surgery such as arterial switch operation (ASO) to correct dextro-transposition of the great arteries (d-TGA). A patient with an aortic stenosis and LAD (left anterior descending coronary artery) closure would warrant the use of a combined retrograde/anterograde application of cardioplegia, ensuring the cardioplegia reaches all parts of the heart.

The retrograde application of any cardioplegic solution requires one additional pressure line. This can be accomplished by using the already installed three-way valve. Despite its simple technique, only 70-75% of the blood drains into the coronary sinus. As a result, the right ventricle is not fully protected in contrast to the antegrade approach, and exclusive reliance on retrograde application should not be the goal. Since the coronary sinus is sensitive to treatment, administration pressure should be lowered (20-30 mmHg for Custodiol®).

Consequently, the cardioplegic method should be thoroughly discussed and optimized for each case and patient.

Conclusion: Retrograde application of Custodiol® is possible, but the pressure should be lowered to 20-30 mmHg.

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Summary

- Within the German cardiac surgery community Bretschneider's cardioplegia is the most often used technique, followed by the methods of Calafiore, Buckberg, and Del Nido
- Most centers give 1.5 liters for the first dose and 200-400 ml for a second dose after 90 minutes of cross-clamp time
- Hyponatremia can be avoided by slowly adding 50-100 ml $NaHCO_3$ (8.4%) to the extracorporeal. Overtreatment of sodium must be avoided to prevent the formation of seizures of the brain
- Several methods can help impeding hemodilution: Retrograde autologous priming (RAP), bicaval canulation, ultrafiltration, and scavenging from the right atrium

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