A clinical comparative study between crystalloid and blood-based St Thomas’ hospital cardioplegic solution

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Abstract

Objective: Myocardial protection with blood cardioplegia during cardiac surgery is increasingly preferred, but few studies have compared the protective effects of crystalloid cardioplegia to the same solution with blood as the only variable. This clinical study compared the protective effects of crystalloid or blood-based St. Thomas’ Hospital cardioplegic solution No. 1. Methods: Fifty higher risk patients undergoing elective coronary artery bypass surgery, with an ejection fraction less than 40%, were randomly allocated to receive cold (4°C) intermittent crystalloid St. Thomas’ No. 1 cardioplegia (n = 25), or a similar blood-based solution (n = 25) with a haematocrit of 10–12%. We determined (1) peri-operative and post-operative arrhythmias, (2) left and right ventricular function (24 h) using the thermodilution technique, (3) left ventricular high-energy phosphate content sampled before ischaemia, the end of ischaemia and the end of bypass.

Results: Pre-operative haemodynamic data, aortic cross-clamp and bypass times were similar in both groups of patients; there was no mortality. At the end of ischaemia there were no differences in ATP content between groups but creatine phosphate was maintained at a significantly (P < 0.007) higher level in the blood-based St. Thomas’ cardioplegia group than the crystalloid St. Thomas’ cardioplegia group (20 ± 2 (SE) vs. 13 ± 1 μmol/g dry wt, respectively). Return to spontaneous sinus rhythm was significantly (P = 0.002) increased in the blood-based St. Thomas’ cardioplegia group (96%) compared to the crystalloid St. Thomas’ cardioplegia group (60%). Early post-operative ventricular dysfunction occurred in both groups, but normal LV function (stroke work index) recovered significantly (P = 0.043) more rapidly (by 2 h) in the blood-based St. Thomas’ cardioplegia group of patients. Conclusions: In a higher risk (EF < 40%) group of patients undergoing elective cardiac surgery, addition of blood to an established crystalloid cardioplegic solution significantly enhanced myocardial protection by reducing arrhythmias, improving rate of recovery of function and maintaining myocardial high-energy phosphate content during ischaemia. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Patients; Cardioplegia; Myocardial protection; Function; Arrhythmias; Metabolism

1. Introduction

Since its re-introduction in the 1970’s, cold cardioplegic arrest has been the method of choice for myocardial protection during cardiac surgery, providing 2–3 h of safe ischaemic arrest with maintenance of good myocardial preservation. Despite this, however, increasing hospital mortality (30 day) occurs with longer ischaemic durations. The increasing use of angioplasty, together with other demographic and logistic pressures, has resulted in the majority of cardiac surgical patients being elderly, tending to have more severe and diffuse disease and requiring increasingly more grafts. In addition, the progressive experience in coronary artery surgery has altered the indications for operation to include patients with increasingly impaired left ventricular function with diffuse coronary disease in whom myocardial protection is difficult to achieve. These factors impose more rigorous demands on the myocardial protection.

Myocardial protection was initially achieved using crystalloid cardioplegic solutions [1]; however, after Buckberg et al. [2] introduced the concept of blood as the basis for cardioplegia, there has been an increase in the use of blood-based cardioplegic solutions, particularly in the US [1] but also in Europe and the UK. Over this period, a number of studies, both experimental [3–5] and clinical [6–10], have suggested the superiority of blood cardioplegia over crystal-
loid cardioplegia. In many of these comparative studies, however, the formulation and/or the administration of the crystalloid cardioplegic solutions have been less than optimal, as was highlighted by Tyers, in the discussion section of a paper by Iverson et al. [8]. They had demonstrated a significant advantage with blood over crystalloid cardioplegia but had selected an ‘inappropriate crystalloid solution’ to compare to blood cardioplegia. Thus, crystalloid solutions have been used that contain zero calcium (which could have led to calcium overload problems during reperfusion [7,8,11]), an inappropriate infusion temperature (for example, 27°C [4]) or studies in which too many variables were compared to enable a definite conclusion to be reached. All this makes it hardly surprising that blood cardioplegic solutions have been shown to be more efficacious than crystalloid solutions in most studies, but they fail to provide convincing evidence that blood cardioplegia is significantly more efficacious. There have also been some studies [11–13] suggesting that blood cardioplegic solutions provide no better myocardial preservation than crystalloid cardioplegic solutions. Despite these factors, there is an increasing tendency in cardiac centres to change to blood cardioplegic solutions.

Although experimental evidence has demonstrated better myocardial protection with St. Thomas’ Hospital cardioplegic solution No 2 (Plegisol) [14], commercial cost implications in the UK have meant that St. Thomas’ Hospital cardioplegic solution No 1 (STH1) is used in preference in the majority of centres. In this study, we have investigated the myocardial protective properties of STH1 and compared it to a blood cardioplegic solution that is as similar to STH1 as possible, allowing a true comparison of the protective effect of crystalloid versus blood cardioplegia.

2. Materials and methods

Ethical committee approval for this study was obtained from the West Lambeth Health Authority Ethics Committee. After informed consent, 50 patients undergoing elective coronary artery bypass surgery were randomised to receive either crystalloid cardioplegic solution or a blood-based cardioplegic solution; there were 25 patients in each group and randomisation was achieved using a computer-generated randomisation assignment table. The operative details of the patients are given in Table 1.

2.1. Anaesthetic protocol

All patients were premedicated with papaveratum and hyoscine; intra-arterial monitoring via the right radial artery was established under local anaesthetic prior to the induction of anaesthesia. Anaesthesia was induced with midazolam, fentanyl and pancuronium and maintained with isofluorane, nitrous oxide and etomidate during surgery. Following induction, conventional central venous catheters were inserted. In addition, a Swan-Ganz thermistor-tipped catheter was inserted pre-operatively, and remained in situ for 24 h. At the end of surgery, anaesthesia was reversed, if the haemodynamic and gas-exchange status of the patient was satisfactory, and the patient returned to the high-dependency or intensive therapy unit self-ventilating.

2.2. Cardioplegia

2.2.1. Composition

The crystalloid St. Thomas’ Hospital cardioplegic solution No 1 (STH1) was prepared by addition of an ampoule of STH1 (manufactured by Martindale Pharmaceuticals, Romford, Essex, UK) to a 1 l bag of Ringer’s solution. For the blood cardioplegia, a double strength STH1 was prepared by adding 1 ampoule to 500 ml of Ringer’s solution, which was then mixed in a ratio of 1:1 with blood drawn from the cardiopulmonary bypass machine (haematocrit of approximately 25%) to give a blood cardioplegic solution with a similar composition to STH1, but with a

<p>| Table 1 |
|---|---|
| Clinical and operative details of patients in the two study groups (crystalloid (STH1) or blood-based (BSTH1) cardioplegic solutions) |</p>
<table>
<thead>
<tr>
<th></th>
<th>STH1</th>
<th>Range</th>
<th>BSTH1</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62.4 ± 1.7</td>
<td>46–76</td>
<td>60.5 ± 2.1</td>
<td>31–74</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>21/4</td>
<td>21/4</td>
<td>20/5</td>
<td>20/5</td>
</tr>
<tr>
<td>Pre-op ejection fraction (%)</td>
<td>35.8 ± 0.9</td>
<td>25–40</td>
<td>32.2 ± 1.2</td>
<td>24–40</td>
</tr>
<tr>
<td>Bypass time (min)</td>
<td>75.9 ± 4.6</td>
<td>42–111</td>
<td>83.9 ± 4.2</td>
<td>34–120</td>
</tr>
<tr>
<td>Aortic cross clamp time (min)</td>
<td>37.3 ± 2.0</td>
<td>22–56</td>
<td>42.8 ± 2.2</td>
<td>19–63</td>
</tr>
<tr>
<td>Cardioplegia volume (ml)</td>
<td>1220 ± 51</td>
<td>1360 ± 46</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operation type:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SVGx3</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IMAx1 + SVGx2</td>
<td>3</td>
<td>3</td>
<td></td>
<td></td>
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<tr>
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<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IMAx1 + SVGx4</td>
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<td>IMAx1 + SVGx5</td>
<td>2</td>
<td>3</td>
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<td></td>
</tr>
</tbody>
</table>

SVG, saphenous vein graft; IMA, internal mammary artery.
haematocrit of 10–12% (BSTH1). The composition of the cardioplegic solutions is shown in Table 2.

2.2. Administration
Coronary surgery was performed during cold (4°C) cardioplegic arrest. For both crystalloid and blood cardioplegic groups, 1 l of 4°C solution was infused into the aortic root at a pressure of 80 mmHg until arrest, reducing to 50 mmHg after arrest and during subsequent infusions. The typical infusion duration was 1.5 min but this was dependent on the distal run-off from the coronary circulation. Subsequent infusions of 300 ml were used if there was clinical or electrical evidence of myocardial activity, or if the period of cross-clamping exceeded 30 min. The crystalloid cardioplegic solution was given by the anaesthetist using a pressure bag directly into the aortic root. The cold blood cardioplegic solution was infused into the aortic root using the Sorin blood cardioplegia delivery system (Sorin Biomedica CSC14) at a temperature of 4°C.

2.3. Surgical protocol
Non-pulsatile cardiopulmonary bypass was established using a single two-stage right atrial and ascending aortic cannulae, a disposable membrane oxygenator (Bard HP 5707) and arterial line filter (Pall EC3840, 40 μm). The perfusion circuit was primed with 2 l of Hartmann’s electrolyte solution (Ringer’s lactate solution) and the systemic perfusion circuit was primed with 2 l of Hartmann’s electrolyte solution (Ringer’s lactate solution) and the systemic perfusion volume (SV), cardiac output (CO), systemic vascular resistance (SVR), left ventricular stroke work index (LVSWI), right ventricular stroke work index (RVSWI), right ventricular ejection fraction (REF) and cardiac index (CI) and a number of other variables were obtained for all patients. There was, however, a wide variation in values obtained in this randomised sample of patients and so the preoperative baseline value for each patient was normalised to 100% and all other values were expressed as a percentage of this baseline value.

2.4. Electrocardiographic analysis

Patients were assessed for the presence and the severity of arrhythmias during the immediate post-operative period, during the time in the intensive treatment unit (usually 24 h) and on the fifth post-operative day. We identified (1) the incidence of reperfusion-induced ventricular fibrillation, (2) the number of direct-current shocks required to convert to sinus rhythm, (3) the incidence of AV dissociation and (4) the incidence of intraoperative myocardial infarction (as defined by the development of new Q waves).

2.5. Clinical function assessment
Clinical data were recorded before, during and after operation in all patients. Haemodynamic data were obtained using the thermodilution technique (Explorer, Baxter Healthcare Ltd.); this involves the use of a Swan-Ganz catheter inserted into the pulmonary artery and incorporates a fast-response temperature probe. A 10 ml bolus of iced saline solution was injected (within 3 s) into the right atrium and the change in blood temperature is measured over time in the pulmonary artery, and cardiac output and other variables are derived from these data. Measurements were determined in rapid succession, and three values in close agreement were averaged; values judged to be outside the range of close agreement were excluded. Measurements were made during the pre-operative phase (after onset of general anaesthesia), during the operative phase (when the chest had been opened), and at 0.5, 1, 2, 4, 6, 8 and 24 h after ischaemia. Absolute values of mean aortic pressure (MAP), heart rate (HR), stroke volume (SV), cardiac output (CO), systemic vascular resistance (SVR), left ventricular stroke work index (LVSWI), right ventricular stroke work index (RVSWI), right ventricular ejection fraction (REF) and cardiac index (CI) and a number of other variables were obtained for all patients. There was, however, a wide variation in values obtained in this randomised sample of patients and so the preoperative baseline value for each patient was normalised to 100% and all other values were expressed as a percentage of this baseline value.

2.6. High-energy phosphate compounds

Three full thickness left ventricular needle biopsies (1.5 mm TruCut biopsy needle; Baxter Healthcare Ltd., Newbury, Berks, UK) were taken from the apex of the left ventricle (1) immediately before application of the aortic cross-clamp (control), (2) at the end of the ischaemic arrest period (ischaemia) and (3) after 10 min of supportive bypass (reperfusion). Biopsy samples were prepared for high performance liquid chromatography (HPLC) measurement of high-energy phosphate compounds and their metabolites according to the method described by Smolenski et al. [15]. Briefly, this involved immediate washing of the biopsy in an ice-cold isotonic buffer solution before freezing in liquid nitrogen (within 15 s from the time of collection). Samples were stored under liquid nitrogen for later analysis; they were then freeze-dried and tissue was extracted, cen-
trifuged and neutralised and samples were analysed using a Merck-Hitachi LiChrograph HPLC system.

2.7. Statistical analysis

Data are expressed as the mean ± SEM. Univariate analyses were conducted using χ²-analysis or the Fisher’s exact test where appropriate. Between group analysis was conducted with a repeated-measures analysis of variance (incorporating the Bonferroni correction for multiple comparisons) and an unpaired t-test when appropriate. On non-normally distributed continuous data, the Mann–Whitney U-test for non-parametric data was performed. Data were analysed using Abacus Concepts StatView statistical software (Abacus Concepts, Berkeley, CA) on an Apple Macintosh computer. A P value of less than 0.05 was considered significant.

3. Results

3.1. Patient data

Patient data are shown in Table 1. There were no differences between the two groups in terms of age, sex, preoperative ejection fraction, bypass time, aortic clamp time, cardioplegic volume administered or type of operation performed.

3.2. Electrocardiographic results

Electrocardiographic data are shown in Table 3. There was a significant (P = 0.002) increase in the incidence of spontaneous sinus rhythm in the BSTH1 group (24/25: 96%) compared to the STH1 group (16/25: 64%) and this was associated with a significant (P = 0.023) decrease in the incidence of DC shocks required to convert to sinus rhythm in the BSTH1 group compared to the STH1 group; only one DC shock was needed in all patients requiring cardioversion. The incidence of post-ischaemic AV dissociation and of transient pacing were slightly higher in the STH1 group but were not significantly different from the BSTH1 group. There were no significant differences in the incidence of post-operative arrhythmias, either at 1 day or 5 days post-operatively.

Table 3

<table>
<thead>
<tr>
<th>Incidence</th>
<th>STH1</th>
<th>BSTH1</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous sinus rhythm</td>
<td>16 (64%)</td>
<td>24 (96%)</td>
<td>0.002</td>
</tr>
<tr>
<td>DC shocks</td>
<td>9 (36%)</td>
<td>1 (4%)</td>
<td>0.023</td>
</tr>
<tr>
<td>Post-ischaemic dissociation</td>
<td>17 (68%)</td>
<td>11 (44%)</td>
<td>NS</td>
</tr>
<tr>
<td>Transient pacing</td>
<td>15 (60%)</td>
<td>10 (40%)</td>
<td>NS</td>
</tr>
<tr>
<td>Duration of pacing (min)</td>
<td>39.1 ± 8.8</td>
<td>33.0 ± 10.1</td>
<td>NS</td>
</tr>
<tr>
<td>Post-operative arrhythmias</td>
<td>6 (24%)</td>
<td>7 (28%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

3.3. Clinical and haemodynamic results

There was no mortality in either group. Two patients (4%) in each group sustained intra-operative myocardial infarction, diagnosed by the appearance of new Q-waves in 12-lead electrocardiogram. These 4 patients subsequently needed inotropic support for low cardiac output (diagnosed as cardiac index lower than 2 l/min per m²) to support the heart while weaning from CPB; interestingly, however, the two patients in the BSTH1 group required support for 24 h each (although one of these patients also required intra-aortic balloon pump for 24 h), whereas the two in the STH1 group required support for 240 and 144 h. No other patients from either group required inotropic support. Extubation times were divided into early (less than 6 h) or late (longer than 6 h); there were no differences in the incidence (16 vs. 15 patients) or duration of extubation (31.3 ± 10.6 vs. 19.5 ± 2.3 h) between the STH1 and BSTH1 groups, respectively. Mean ITU stay for patients in the STH1 group was 61.0 ± 14.9 h (median 24; range 24–332 h) which was reduced to 28.5 ± 1.8 h (median 24; range 24–48 h) in the BSTH1 group; however, this difference was not significant. The mean hospital stay was 8.2 days (median 7; range 6–18 days) and 7.0 days (median 6; range 5–11 days), respectively.

Representative data for cardiac index (CI), left ventricular stroke work index (LVSWI) and right ventricular stroke work index (RVSWI) are shown in Fig. 1, together with the percent change when the pre-operative value was normalised to a baseline value of 100%. CI was relatively low in both groups of patients before and during the operation, but had increased considerably by 0.5 h after ischaemia; however, in the control (STH1) patients, CI was depressed at 1 h post-ischaemia and remained at a lower value until 8 h. In contrast, in the BSTH1 group, there was less of a depression of CI and this recovered more rapidly to a stable level by 4 h (Fig. 1A,B). All post-operative values of CI in both groups of patients were higher than the pre-operative and perioperative values. LVSWI was also depressed at 0.5 h post-operatively in both groups of patients and remained depressed at 1 h, but subsequently gradually recovered in the STH1 group of patients and was back to the pre-operative value by 24 h; in the BSTH1 group of patients, LVSWI had recovered to the pre-operative value by 2 h, was maintained at this level to 6 h, but then further improved to above pre-operative values at 8 and 24 h (Fig. 2A). These changes are shown more clearly in Fig. 2B, where the values were expressed as a percentage of the pre-operative value (normalised to 100%); this indicates that there was a significant (P = 0.043) difference in LVSWI in the BSTH1 group of patients, recovering significantly faster than the STH1 group of patients at 2 h (P = 0.045) and 4 h (P = 0.026) post-ischaemia.

In contrast to these results, RVSWI values were similar in both groups of patients, although there appears to be a trend towards an earlier recovery in the BSTH1 group compared...
to the STH1 group of patients (Fig. 3A). RVSWI reached a plateau by 4 h in the BSTH1 group and by 6 h in the STH1 group; there was no further improvement up to 24 h, with values approximately 90% of the pre-operative values (Fig. 3B).

3.4. Myocardial metabolism

Myocardial adenosine triphosphate (ATP), adenosine diphosphate (ADP), adenosine monophosphate (AMP), creatine phosphate (CP), adenosine, inosine, hypoxanthine, metabolic cofactors (NAD and NADP) and energy charge in biopsies taken before ischaemia, at the end of ischaemia and after reperfusion in both groups of patients are shown in Table 4. Creatine phosphate levels were significantly ($P = 0.0067$) higher at the end of ischaemia in the BSTH1 group compared to the STH1 group of patients; there were no other differences in these compounds between the two groups.

4. Discussion

In this clinical study, we have compared an intermittent cold crystalloid cardioplegic solution (the St. Thomas’ Hospital cardioplegic solution No 1; STH1) to an intermittent cold blood cardioplegic solution which has been formulated to be as similar as possible to the crystalloid formulation but with
the additional blood component (BSTH1). There were slight differences between the 2 formulations and these are detailed in Table 2; the principle differences, however, relate to the haematocrit, which was 10–12% in the blood-based solution, a slightly lower calcium concentration and an increased buffering capacity in BSTH1 which maintained the pH at 7.4. The study demonstrated that BSTH1 significantly improved the incidence of spontaneous sinus rhythm resulting in a significant reduction in the necessity for DC shocks during the immediate reperfusion period. BSTH1 had no significant effects on other arrhythmias.

Recovery of function (represented by CI, LVSWI and RVSWI) was not significantly different by 24 h post-operatively; significant differences were observed, however, in the rate at which recovery occurred, with patients in the BSTH1 group demonstrating significantly more rapid recovery at 2 and 4 h post-operatively than patients in the STH1 group. There were no differences in the two groups between patients requiring inotropic support for intra-operative myocardial infarction (with two patients in each group) but, in the STH1 group, this support was required for considerable durations. No other patients required inotropic support for low cardiac output. Extubation times were not different between the two groups of patients, either in incidence of early or late extubation or in the duration of late extubation. The cross-clamp durations in this series of patients undergoing elective surgery were not different between the two groups of patients and were relatively short; longer periods of ischaemic cross-clamp may have exacerbated any differences observed between the cardioplegia techniques. Mean ITU stay and mean hospital stay were slightly reduced in the BSTH1 group of patients; however, the number of patients in this study are too small to make any conclusive statement regarding these differences.

A comprehensive analysis of myocardial metabolism, comparing high-energy phosphate compounds and their metabolites, together with metabolic co-factors, revealed no significant differences between the two groups except for a significant increase in creatine phosphate at the end of ischaemia in the BSTH1 group of patients. This would suggest improved myocardial protection during ischaemia as creatine phosphate is utilised in preference to ATP during ischaemic myocardium.

4.1. Myocardial arrhythmias

Few studies have examined the effect of crystalloids or blood cardioplegic solutions on the incidence of post-operative arrhythmias. Mullen et al. [16] demonstrated that blood cardioplegia was associated with a lower incidence of post-operative supraventricular arrhythmias than a crystalloid cardioplegia, whereas there were no differences in post-operative ventricular arrhythmias. However, the crystalloid cardioplegic solution had low-sodium (27 mmol/l) and zero-calcium concentrations; this was potentially less protective than the blood cardioplegia and could account for the higher incidence of arrhythmias. A significantly lower incidence of conduction disturbances has previously been demonstrated by Rousou et al. [17] in patients arrested with blood cardioplegia than in patients arrested with a crystalloid solution. In contrast, Gundry et al. [18] observed the reverse, with a significantly higher incidence of conduction disturbances with blood cardioplegia than with crystalloid cardioplegia; however, potassium concentrations were higher (30–35 mmol/l) in the crystalloid solution than the blood solution (18 mmol/l).

One of the components of STH1 is procaine, included at a concentration of 1 mmol/l, which is thought to have mem-

Fig. 3. Right ventricular stroke work index (RVSWI) at various times throughout the operative and post-operative periods. (A) Shows the abso- lute data and (B) shows the percentage change when the pre-operative value has been normalised to a baseline value of 100%. Data are shown as mean ± SEM. STH1, St. Thomas’ Hospital cardioplegic solution No. 1. BSTH1, blood-based St. Thomas’ Hospital cardioplegic solution No. 1.
brane stabilising effects. Recently, Sellevold et al. [19] investigated the effect of adding 1 mmol/l procaine to the St. Thomas’ Hospital cardioplegic solution No. 2 (Plegisol; Abbott) and demonstrated a significant reduction in reperfusion-induced ventricular fibrillation (VF) requiring DC cardioversion together with a reduced level of myocardial enzyme release on the first post-operative day. In a previous study [20], we demonstrated a relatively high incidence of VF in patients arrested with STH1 that was significantly attenuated when 10 mmol/l creatine phosphate was used as an additive. In the present study, the incidence of VF was lower than in this earlier study but was further significantly reduced when BSTH1 was used, supporting the conclusions of Mullen and Roussou’s groups [16,17].

4.2. Myocardial function

Crystallloid potassium-based cardioplegia was introduced into clinical practice in the mid-70’s [21], and the concept of cold intermittent blood cardioplegia followed soon after [2]. Blood cardioplegia has subsequently become the most widely used solution in the US [1] and is being used increasingly in both Europe and the UK.

There have been many experimental and clinical studies comparing the efficacy of crystallloid and blood cardioplegic solutions. Most experimental studies have demonstrated superiority of blood over crystallloid cardioplegia, but the majority of these studies have tended to use conditions and/or formulations that favoured blood cardioplegia. Thus, comparisons were made between blood and crystallloid cardioplegia during ischaemia at 27°C in studies by Bing et al. [3] and by Feindel et al. [4], with hearts protected by blood cardioplegia showing improved protection or reduced necrosis, respectively. It is well known that crystallloid cardioplegia should be used at lower temperatures than the moderate hypothermia (27°C) used in the above studies. This was demonstrated by Magovern et al. [12] who showed that a similar degree of protection was achieved when dog hearts were infused with either crystallloid or blood cardioplegia at 4 and 20°C, respectively; however, reduced recovery was observed with blood cardioplegia at 4°C or crystallloid cardioplegia at 20°C. Axford-Gatley et al. [22] observed no differences in terms of necrosis between dog hearts protected at 4°C with crystallloid cardioplegia, and blood cardioplegia at either 4 or 27°C. All hearts were successfully weaned from bypass suggesting no differences in the protective properties of these solutions at the different temperatures; interestingly, the effect of crystallloid cardioplegia at 27°C was not examined. In the present study, both crystallloid and blood solutions were infused at 4°C, with the hearts being maintained during ischaemia at around 15°C.

In a similar way, the presence of calcium, and oxygenation of the cardioplegic solutions, were shown to be important. Calcium was absent from the crystallloid cardioplegic solutions in the studies of Bing [3] and Feindel [4], and Heitmiller [11] subsequently demonstrated the importance of calcium as a component of crystallloid solutions. Oxygenation of the cardioplegic solution has also been shown to exert a significant additional protection [5,23], such that oxygenated crystallloid cardioplegic solutions were as efficacious as blood cardioplegia.

Clinical studies have not generally been as conclusive as the experimental studies described above, and few have attempted to compare the composition of the solutions and examine the effect of the blood component alone in a well-established crystallloid solution (as in the present study). A comparison of Plegisol to a blood cardioplegic solution [9], showed fewer patients in the blood cardioplegia group requiring inotropic support to maintain a satisfactory cardiac index (greater than 2 l/min per m²), and a reduced CK-MB leakage, suggesting better myocardial protection. Fremes et al. [7] comparing crystallloid to blood cardioplegia in a clinical study observed similar recovery profiles of CI and LVSWI to those in the present study over the first 24 h post-operatively; there was a depression in CI in both groups which recovered more rapidly in the blood cardio-

<table>
<thead>
<tr>
<th>Compound (μmol/g dry wt.)</th>
<th>StH1</th>
<th>El</th>
<th>R</th>
<th>StBH1</th>
<th>El</th>
<th>R</th>
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<tr>
<td>ATP</td>
<td>23.85±1.65</td>
<td>23.36±1.28</td>
<td>19.66±1.37</td>
<td>22.32±1.62</td>
<td>23.75±1.37</td>
<td>20.40±1.35</td>
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<tr>
<td>ADP</td>
<td>8.85±0.45</td>
<td>8.82±0.35</td>
<td>8.36±0.50</td>
<td>8.24±0.57</td>
<td>8.32±0.65</td>
<td>8.23±0.45</td>
</tr>
<tr>
<td>AMP</td>
<td>1.99±0.14</td>
<td>1.75±0.15</td>
<td>2.09±0.17</td>
<td>1.88±0.31</td>
<td>1.70±0.12</td>
<td>2.00±0.19</td>
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<tr>
<td>CP</td>
<td>17.68±2.12</td>
<td>13.71±1.13</td>
<td>17.47±1.36</td>
<td>19.91±2.10</td>
<td>19.95±1.89*</td>
<td>22.31±2.59*</td>
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<tr>
<td>Adenosine</td>
<td>0.18±0.03</td>
<td>1.03±0.10</td>
<td>0.36±0.10</td>
<td>0.54±0.26</td>
<td>0.87±0.11</td>
<td>0.54±0.07</td>
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<td>Hypoxanthine</td>
<td>0.02±0.01</td>
<td>0.21±0.04</td>
<td>0.14±0.03</td>
<td>0.11±0.09</td>
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<td>0.11±0.02</td>
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<td>NAD</td>
<td>3.07±0.16</td>
<td>2.77±0.09</td>
<td>2.67±0.16</td>
<td>3.04±0.16</td>
<td>2.98±0.13</td>
<td>2.78±0.15</td>
</tr>
<tr>
<td>NADP</td>
<td>0.19±0.01</td>
<td>0.20±0.02</td>
<td>0.22±0.01</td>
<td>0.20±0.04</td>
<td>0.24±0.03</td>
<td>0.20±0.01</td>
</tr>
<tr>
<td>Energy Charge</td>
<td>0.81</td>
<td>0.82</td>
<td>0.79</td>
<td>0.82</td>
<td>0.83</td>
<td>0.80</td>
</tr>
</tbody>
</table>

*P < 0.0067 compared to the corresponding StH1 value. ATP, adenosine triphosphate; ADP, adenosine diphosphate; AMP, adenosine monophosphate; CP, creatine phosphate; NAP, nicotinamide adenine dinucleotide; NADP, nicotinamide adenine dinucleotide phosphate.
These results are in general agreement with the limited ischaemia in the blood cardioplegia group of patients. Differences between the two groups except for a significantly higher in both groups although the blood cardioplegia group was significantly higher than the crystalloid cardioplegia group; creatine phosphate declined in both groups during ischaemia but remained higher throughout ischaemia in the blood cardioplegia group. The study by Frenes [7] also demonstrated that creatine phosphate was significantly higher in the blood cardioplegic group of patients at the end of ischaemia and after 30 min of reperfusion than in the crystalloid cardioplegic group.

5. Conclusions

We have demonstrated that a blood cardioplegic solution, formulated to be as similar as possible to a clinically well-established crystalloid cardioplegic solution, significantly improves that rate of recovery of higher risk patients (with ejection fraction less than 40%). This enhanced rate of recovery suggests an improvement in myocardial protection by the blood cardioplegic solution, and is likely to have an important role in alleviating post-operative problems in this potentially compromised group of patients.

References


