Clinical effects of the heparin coated surface in cardiopulmonary bypass

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Abstract

Objective: In a randomised study of 120 patients, undergoing primary operation for coronary heart disease, two groups were investigated as regards to the effects of heparin coated cardiopulmonary bypass on brain function parameters and general clinical outcome. The study group (n = 56) was perfused using an extra-corporeal circuit treated with covalent bonded heparin; the control group (n = 59) used an identical set-up without heparin treatment. Systemic heparin doses were calculated to achieve ACT levels of 250 and 500 s, respectively. Postoperative course was evaluated by examining a set of clinically relevant parameters including a detailed registry of postoperative deviations. Brain function was assessed by the biochemical marker S-100 and tests of memory performance. Results: There were several signs of reduced operative trauma in the study group. Hospital stay was reduced by nearly 1 day (P ≤ 0.05). Time on postoperative ventilatory support was approximately 4 h shorter (P = 0.009). Chest drain blood loss was decreased both at 8 (P = 0.01) and 24 h (P = 0.007) postoperatively. Body temperature was lower after surgery and especially on days 2 (P = 0.03) and 3 (P = 0.01). Perioperative creatinine elevation was significantly reduced (P = 0.03). Neurological deviations were fewer (P = 0.01). Brain function assessment revealed reduced plasma levels of S-100 both at termination of cardiopulmonary bypass (P = 0.008) and 7 h later (P = 0.04). However, no remediation of memory impairment could be demonstrated. Conclusions: Cardiopulmonary bypass with covalent bonded heparin attached to the extra-corporeal circuit in combination with a reduced systemic heparin dose seems to reduce safely and effectively the operative stress to the patient. There were also signs of improved cerebral protection. © 1997 Elsevier Science B.V.

Keywords: Cardiopulmonary bypass; Heparin; Biocompatible materials; Thoracic surgery; Memory; Nerve tissue protein S-100

1. Introduction

Cardiopulmonary bypass (CPB) exposes the blood to foreign surfaces. This contact induces defence mechanisms such as activation of coagulation as well as the fibrinolytic, complement and kallikrein systems [11,12,31]. Intrinsic coagulation, normally blocked by systemic heparin, may also be inhibited by surface bonded heparin [31]. The thromboresistant heparin layer mimics the native endothelium and inhibits the cellular and humoral response to CPB [5,16,31]. Hence, the heparin bonded surface appears to be less traumatic than the usual plastic material used in CPB. However, the significance of the heparin bonded surface on general clinical outcome and brain function parameters is incompletely examined.

The purpose of this study was to evaluate the general clinical influence of a bio-active surface in CPB and especially its effect on brain function parameters. The latter combined monitoring of the biochemical marker S-100 with a brief assessment of memory functions, as well as a clinical registration of neurological deviations from the normal postoperative course.
2. Materials and methods

The clinical effect of heparin coated CPB was investigated in 120 patients undergoing primary aorta-coronary bypass surgery. A population with normal left ventricular function, age less than 75 with no history of thrombolytic therapy, ongoing aprotinin or aspirin medication, coagulation disorder or neurological dysfunction was selected. After obtaining informed consent, patients were by the computer randomly assigned to a study or a control group. Group allocation was blinded to personnel involved in the postoperative course, including those determining neurological deviations, but had to be open to surgeon, anaesthetist and perfusionist. The trial was approved by the Ethics Committee of the University of Umeå.

2.1. Conduct of CPB

Study group patients were perfused with a circuit, in which all parts, including the cardiotomy reservoir were treated with Carmeda BioActive Surface (CBAS), where heparin is covalently bonded to the artificial material [13]; the control group had an identical non-treated set-up. Common to each group was: Maxima membrane oxygenator (Medtronic, Anaheim, CA 92807, USA), a collapsible venous reservoir, a cardiotomy reservoir and polyvinyl tubing. Priming solution combined 2000 ml of Ringer acetate, 100 ml of mannitol and heparin; 7500 I.E. in the control and 2500 I.E. in the study group.

Moderate hypothermic (32.6 ± 0.07°C), non-pulsatile, α-stat CPB was performed using Sarns 9000 roller pump, controlling blood flow to obtain venous oxygen saturation (SvO2) of more than 70% and mean arterial pressure (MAP) higher than 50 mmHg. Central venous pressure (CVP) was kept below 10 mmHg to preserve cerebral perfusion pressure. Blood from the pericardial cavity was retrieved to a cardiotomy reservoir. Possible clot formation and blood stagnation was counteracted by recirculating ≈ 150 ml/min of arterial blood through the reservoir. Re-warming was commenced when performing the last peripheral coronary anastomosis to carry rectal temperature up to 36°C. After termination of CBP, blood was recirculated through an arterio-venous shunt and re-infused until stable hemodynamic conditions were established.

2.2. Surgical technique

Left internal mammary artery was used in the majority of cases. Its preferred destination was the left anterior descending coronary artery. The aorta and the right atrium were cannulated. Peripheral anastomoses were performed after cross clamping the aorta and antegrade administration of hypothermic St Thomas crystalloid cardioplegia solution. Repeated doses of cardioplegia were given at signs of electro-mechanical cardiac activity. Proximal anastomoses were carried out using a side-biting clamp and generally in one session. The quality of the aortic wall was assessed by palpation and visual inspection of the excluded aortic wall inside the side-biting clamp grip. An arbitrary scale from normal, to slight or severe arteriosclerotic changes was used. Thorough de-airing of the excluded aortic segment as well as of the venous grafts was carried out. Weaning from CPB was done gradually, while observing ST-segment changes. Protamin was given after bypass was completed, the arterial cannulae removed and remaining blood in the heart-lung machine transfused through the venous cannulae.

2.3. Management of anti-coagulation

Heparin and protamin requirements were calculated using the Hepcon HMS system [7]. Activated clotting time (ACT) target level was set to 500 s in the control and 250 s in the study group. Adequate anti-coagulation was controlled by repeated ACT measurements using the Hemotec apparatus employing kaolin as activator substance [18]. The effect of heparin was neutralised by giving a protamin dose 1.1 times the remaining heparin quantity at termination of CPB. Residual circulating heparin after protamin administration was determined by a heparinase check procedure [3].

2.4. Anaesthesia and postoperative care

Patients were monitored with arterial and central venous pressures, pulse oximetry and a seven-lead ECG including ST-segment analysis. Pre-medication comprised flunitrazepam 1 mg orally + morphine 10 mg i.m. + scopolamine 0.4 mg i.m. The patient’s normal dose of β-blocker was given orally with the pre-medication. Anaesthesia was induced and maintained by using fentanyl, midazolam and isoflurane, with pancuronium for muscle relaxation. Propofol was usually added during re-warming. Patients were ventilated to normo-capnia with oxygen in air. Postoperative ventilatory support continued until hemodynamic and respiratory conditions were stable. Analgesia and sedation were achieved with a combination of ketobemidone, propofol and midazolam. The use of inotropics, vasodilators and beta blocking agents followed our standard clinical protocol.

2.5. Collection of clinical data

Detailed patient related information is routinely registered in our departmental database. A subset of clinically relevant variables were selected and analysed.
Special interest was focused on postoperative deviations, i.e. conditions deviating from a normal postoperative course [32]. Deviations were divided into 12 main categories. Due to sub-categories, individual patients may have had more than one deviation per category. Deviations were registered by the primary nurse, before the patient was transferred from the intensive care unit (ICU) and at discharge from hospital. Registrations were corroborated by the discharging physician.

While on CPB arterial line micro-bubbles larger than 40 µ were continuously recorded by a Hatteland bubble count detector interfaced to a personal computer. This made it possible to evaluate the incidence of embolic events in the arterial line [6]. MAP during CPB was calculated by performing a computerised integration of the trended arterial blood pressure curve.

2.6. Evaluation of cerebral function

Cerebral injury was assessed by three methods: the biochemical marker S-100, a test of memory function and the occurrence of neurological deviations. S-100 was measured in arterial blood by the method of Sangtec 100® (AB Sangtec medical, Box 20 045, S-161 02 Bromma Sweden). This test employs a two-site immunoradiometric assay (IRMA) with monoclonal antibodies specific to the β-sub-unit of the S-100 protein. The detection limit for S-100 was 0.2 µg/l and the inter-assay coefficient of variation was less than 8% in the working range 0.2–60 µg/l. In this study S-100 was determined at five different time intervals; prior to, at the termination of CPB, 7 h later and in the morning of the first and second postoperative day.

2.7. Assessment of memory

Evaluation of memory function comprised three tasks. Subjects were presented with 40 line drawings depicting common objects or animals [23]. They were asked to memorise the pictures as efficiently as possible. A Macintosh computer, utilising the Superlab tachistoscopic program [1] was used for presentation of the pictures and collection of data. The pictures were presented at a rate of one picture every 2 s. The task was always administered by a specially trained nurse, who was supervised and monitored by an experienced neuropsychologist.

Task one: following a brief interval, where subjects were engaged in counting backwards during 60 s, an implicit memory task was administered. Fragmented pictures, 20, were presented, one at a time. Half of the pictures were fragmented versions of pictures that were presented earlier; half were new. Subjects were asked to identify the pictures. The difference in result between the previously presented pictures and the new ones, was taken as a measure of implicit memory, i.e. perceptual learning [21]. Tasks two and three involved assessment of explicit memory. In the second task, 20 previously studied pictures were shown, one at a time. Ten pictures were reversed 180° along the vertical axis; ten pictures were not transformed. The task was to determine whether the pictures were reversed or not.

The third task comprised a yes–no recognition test. Subjects were presented with 20 pictures. Half were studied before, half were new. For each picture, subjects were asked to indicate if the picture had appeared before or if it was novel. The session lasted for 20–25 min.

Implicit memory was defined as the degree of priming or perceptual learning in the first task comprising identification of fragmented pictures. Explicit memory was defined as the ability to discriminate old from new in the second and third tasks. On the basis of the distribution of hits and false alarms, the discrimination index d prime was calculated [22].

2.8. General clinical performance

General clinical performance was determined as length of stay in ICU and hospital, time on ventilatory support, blood loss, fluid balance and perioperative differences of white cells, creatinine and platelets. Concentration measurements were corrected for dilution as indicated by haematocrit, with the exception of S-100 according to common practice for this particular analysis. The general inflammatory response was reflected by measuring the morning body sublingual temperature for 5 consecutive days. Postoperative blood loss was estimated as chest drainage volume at 8 and 24 h. Auto-transfusion of mediastinal blood was the rule during the first 12 postoperative h. Guidelines for blood transfusions followed a standard protocol.

2.9. Statistical analysis

Data with a normal distribution are presented as means ± S.E. of the means (S.E.M.). Comparisons between groups were performed by analysis of variance (ANOVA). Data not approximate to the normal distribution are given as median values and range. Group differences were analysed using Mann-Whitney U test and Pearson χ² for tabulated data. A P-value less than 0.05 was regarded as statistically significant.

3. Results

Four patients were excluded at admission to the operating theatre, not fulfilling the entry criteria, one patient died during intensive care due to rupture of abdominal aortic aneurysm, leaving 59 (n = 59) patients in the control and 56 (n = 56) in the study group.
Table 1
Patient population and clinical characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (n = 59)</th>
<th>Study (n = 56)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>64.0 ± 0.9</td>
<td>64.0 ± 1.0</td>
<td>0.99</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>172.3 ± 1.1</td>
<td>172.4 ± 1.1</td>
<td>0.96</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>79.6 ± 1.4</td>
<td>78.2 ± 1.5</td>
<td>0.52</td>
</tr>
<tr>
<td>Male/female</td>
<td>49/10</td>
<td>43/13</td>
<td>0.40</td>
</tr>
<tr>
<td>Diabetes (yes–no)</td>
<td>7–52</td>
<td>8–48</td>
<td>0.70</td>
</tr>
<tr>
<td>Previous myocardial infarction (yes–no)</td>
<td>13–46</td>
<td>9–47</td>
<td>0.42</td>
</tr>
<tr>
<td>NYHA classification (I-II-III-IV)</td>
<td>0–10–47–2</td>
<td>1–9–46–0</td>
<td>0.56</td>
</tr>
<tr>
<td>Smoker (yes–no)</td>
<td>7–52</td>
<td>10–46</td>
<td>0.37</td>
</tr>
<tr>
<td>Platelet count (×10^9/l)</td>
<td>248.8 ± 6.8</td>
<td>233.3 ± 7.2</td>
<td>0.13</td>
</tr>
<tr>
<td>White cell count (×10^9/l)</td>
<td>6.6 ± 0.2</td>
<td>6.4 ± 0.2</td>
<td>0.57</td>
</tr>
<tr>
<td>Creatinine (mmol/l)</td>
<td>97.8 ± 1.9</td>
<td>95.9 ± 1.2</td>
<td>0.50</td>
</tr>
<tr>
<td>History of hypertension (yes–no)</td>
<td>28–31</td>
<td>18–38</td>
<td>0.09</td>
</tr>
<tr>
<td>Aortic wall quality (normal–slight–severe)</td>
<td>46–10–3</td>
<td>43–12–1</td>
<td>0.55</td>
</tr>
<tr>
<td>No of anastomosis</td>
<td>3.7 ± 0.1</td>
<td>3.4 ± 0.1</td>
<td>0.24</td>
</tr>
<tr>
<td>Pump time (min)</td>
<td>95.9 ± 3.2</td>
<td>94.4 ± 4.1</td>
<td>0.78</td>
</tr>
<tr>
<td>Aortic clamp time (min)</td>
<td>56.6 ± 2.3</td>
<td>55.4 ± 2.8</td>
<td>0.75</td>
</tr>
<tr>
<td>Mean arterial perfusion pressure CPB (mmHg)</td>
<td>57.2 ± 0.7</td>
<td>59.5 ± 0.8</td>
<td>0.04</td>
</tr>
<tr>
<td>Haematocrit during CPB</td>
<td>33.0 ± 0.5</td>
<td>32.5 ± 0.7</td>
<td>0.43</td>
</tr>
<tr>
<td>Temperature °C</td>
<td>32.5 ± 0.1</td>
<td>32.7 ± 0.1</td>
<td>0.33</td>
</tr>
<tr>
<td>Surgical team (cases/surgeon)</td>
<td>11–3–4–14–21–2–1</td>
<td>9–5–2–6–17–16–1–0</td>
<td>0.83</td>
</tr>
<tr>
<td>Perfusion team (cases/perfusionist)</td>
<td>13–10–17–17–2</td>
<td>18–8–14–10–6</td>
<td>0.28</td>
</tr>
<tr>
<td>Use of nitroglycerine post CPB (yes–no)</td>
<td>10–49</td>
<td>9–47</td>
<td>0.90</td>
</tr>
<tr>
<td>Inotropic support post CPB (yes–no)</td>
<td>12–47</td>
<td>8–48</td>
<td>0.39</td>
</tr>
</tbody>
</table>

Patient population and clinical characteristics are presented in Table 1. Group data are statistically comparable except for the perfusion pressure, which was slightly lower in the control group (P = 0.04).

The total number of detected micro bubbles in the arterial line were 24 (0–384) in the control, compared with 26 (0–1670) in the study group (P = 0.87). The bubble count was low in nearly all patients, except for a few in the study group. High bubble counts were related to air entrainment in the venous line.

3.1. Management of anti-coagulation

The administered doses of heparin and protamin in relation to ACT response are presented in Table 2. After protamin administration ACT decreased to a level significantly lower than corresponding prebypass ACT. No thrombus formation in any parts of the extra-corporeal circuit was evident at inspection post bypass.

3.2. S-100 response to CPB

Preoperative analysis of S-100 revealed no detectable levels. At termination of CPB, S-100 concentrations increased in both groups, though significantly more in the control group 1.3 ± 0.16 µg/l versus 0.95 ± 0.12 µg/l in the study group (P = 0.009). After 7 h, concentrations of S-100 dropped, but were still higher (P = 0.04) in the control group. The values on the first and second postoperative day did not differ between the groups (Fig. 1).

3.3. Memory performance

The priming effect reflecting implicit memory performance is presented in Table 3. No differences were observed between groups.

Explicit memory performance is presented in Table 4. There were no statistically significant effects for the second task, involving recognition of orientation. Regardless of group allocation, memory performance deteriorated post CPB in the third, yes–no recognition task (P < 0.05).

3.4. Postoperative deviations

Of the patients in the study group, 41% deviated in some respect from a totally uncomplicated postoperative course, compared with 56% in the control group (P = 0.11). The amount of deviations are presented in Table 5. The number of patients with neurological deviations was significantly lower in the study group (P = 0.01); one patient compared with nine in the control group. Altogether, 16 neurological deviations were observed: one in the study group versus 15 in the control group. Types of deviations were confusion, dysphasia, pareses, impaired vision and balance.
3.5. General clinical performance

The intraoperative blood loss was similar in both groups. However, the postoperative chest drain volume was lower in the study group both at 8 (P = 0.01) and 24 h (P = 0.007) (Fig. 2). Of study group patients, 42% needed blood transfusions, compared with 47% in the control group (P = 0.62), corresponding to 858.4 ± 147 versus 991.3 ± 148 ml of transfused blood (P = 0.53). Platelet count reduction was somewhat lower postoperatively in the control group −16.1 ± 5.8 × 10⁹/l versus −10.7 ± 4.6 × 10⁹/l in the study group (P = 0.46). The volume of fluids added during CPB was higher (p = 0.01) in the study group, accompanied by an increased urine output (P = 0.02), rendering comparable fluid balance. The morning body temperature during the first 5 postoperative days is shown in Fig. 3. Temperature rise was found in all patients, but was on days 2 (P = 0.03) and 3 (P = 0.01) significantly less pronounced in the study group. White cell count elevation followed a similar pattern and increased +9.0 ± 0.6 × 10⁹/l versus +10.1 ± 0.5 × 10⁹/l (P = 0.13) in the control group. Post CPB serum creatinine increase was less in the study group; +13.0 ± 2.2 μmol/l versus +19.9 ± 2.1 μmol/l in the control group (P = 0.03). Time on postoperative ventilatory support was significantly reduced from 12.4 ± 1.6 h in control group compared with 9.2 ± 0.84 h in the study group (P = 0.009). The patients in the study group had a 2 h shorter stay in ICU (P = 0.53) and were discharged from hospital nearly one day (9.1 ± 0.41 versus 8.3 ± 0.28) before patients in the control group (P ≤ 0.05).

4. Discussion

Cellular and humoral reactions [5,31] to CPB with related organ damage are well documented [12]. Reducing blood trauma during CPB by covering all surfaces exposed to blood with heparin is theoretically possible [13]. We know from earlier studies that heparin bonded surfaces decrease such adverse reactions [4]. Our results indicate that general clinical outcome may be improved and that cerebral injury as measured by S-100 activity is less pronounced.

Observation of a large data set have enabled a multi-faceted evaluation. Most data and deviations were retrieved from the departmental database. Time on ventilatory support and hospital stay showed important differences, whereas the difference in ICU stay did not. However, this could be due to departmental routines. ICU patients are as a rule dismissed to the ward only once a day. We therefore conclude that the important time parameters show a consistent difference, which could lead to significant cost reductions.

Activation of the complement cascade in CPB and the magnitude of systemic inflammatory response (SIR) may to a certain extent be limited by the use of heparin coating [28]. The clinical manifestation of SIR is not specific. Body temperature, as a crude index of SIR, was significantly higher in the control group, accompanied with a rise of the white cell count. The mean difference of less than 0.5°C may be regarded as small and clinically insignificant. Nevertheless, this difference could partly explain the longer stay in hospital.

Reductions of blood loss and transfusion requirements are of prime concern. This may be accomplished by combining a reduced systemic heparin dose with the use of a heparin treated surface. Conflicting reports exist regarding the necessity of lowering the heparin dose. Borowiec and colleges [4] used a 50% reduction, whereas others obtain similar blood saving effects by giving the normal dose [20]. In our case, heparin titra-

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**Table 2**

Management of anti-coagulation

<table>
<thead>
<tr>
<th>Group</th>
<th>Pre bypass ACT (s)</th>
<th>Initial heparin dose (I.U./kg)</th>
<th>Total heparin dose (I.U.)</th>
<th>ACT response (s)</th>
<th>Protamin dose (mg/kg)</th>
<th>Post bypass ACT (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>144 ± 2.2</td>
<td>370 ± 10</td>
<td>39 900 ± 1053</td>
<td>579 ± 15</td>
<td>3.2 ± 0.1</td>
<td>134 ± 2.7</td>
</tr>
<tr>
<td>Study</td>
<td>141 ± 1.9</td>
<td>120 ± 5</td>
<td>13 900 ± 529</td>
<td>276 ± 6.7</td>
<td>1.3 ± 0.1</td>
<td>135 ± 2.6</td>
</tr>
</tbody>
</table>

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**Table 3**

Performance with respect to the task tapping implicit memory

<table>
<thead>
<tr>
<th></th>
<th>Pre CPB</th>
<th>Post CPB</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0.32 ± 0.03</td>
<td>0.32 ± 0.03</td>
<td>NS</td>
</tr>
<tr>
<td>Study</td>
<td>0.35 ± 0.03</td>
<td>0.33 ± 0.03</td>
<td>NS</td>
</tr>
</tbody>
</table>

Results denote magnitude of the priming effect.

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**Fig. 1.** S-100 response to CPB.
tion assay made it possible to compute the individual dose required to achieve an ACT level of 250 s. On average, one third of a normal dose was given (120–370 IE/kg). The lower dose regime was chosen in order to preserve a functional active heparin surface, not compromising its anti-thrombin III binding capacity [14]. Postoperative blood loss was in our material significantly reduced by about 250 ml/patient. Transfusion requirements were however not affected, possibly due to unwanted variations in clinical practice.

Use of cardiotomy suction exposes blood to air, shear stresses and stagnation, whereby coagulation is strongly activated [20]. Full systemic heparinisation is therefore normally indicated. Reducing the heparin dose with use of a heparin coated cardiotomy reservoir is a delicate clinical situation. The potential risk of clot formation is difficult to assess, but several reports confirm the technique to be safe [15,30]. Øvrum and colleges used a similar CPB technique in more than 100 patients, without any complications related to clotting or other aspects of perfusion safety [15]. Our experience confirms these findings.

The use of heparin coated surfaces seems not to have any beneficial effect on memory impairment. Memory performance was assessed through validating explicit and implicit memory function. Explicit memory denotes conscious remembering. Implicit memory denotes performance that may be influenced by previous experiences in an unconscious manner. Typically, patients who suffer from amnesia exhibit deficits regarding explicit memory. Implicit memory may be preserved in amnesia [26]. It has repeatedly been shown that performance in explicit memory tasks is dependent upon the integrity of structures in the medial temporal lobe [24] and the prefrontal association cortex [25]. In contrast, a recent report of selective impairment with regard to implicit memory, highlighted the involvement of a posterior cortical region involving occipital-parietal structures [8]. Keeping these findings in mind, it is tempting to speculate about an involvement of medial temporal structures and perhaps prefrontal associations areas,
following heart surgery. The protective effect of heparin coated surfaces on the inflammatory response may not be related to these cortical areas. Since the use of heparin coated surfaces in our material reduced the incidence of ischemic stroke and because ischemic stroke frequently does not engage medial temporal and prefrontal association areas and most often does not produce memory dysfunction, we take our findings to imply that other sources of neural injury are related to memory impairment. Such causes may include hypoxia, micro aggregates or emboli partly due to a deranged coagulation and eventually located to target areas of the brain. With the aid of robust assessment protocols which can detect memory impairment under clinical conditions and which can be administered by nurses or other members of the staff as part of the routine management of patients with heart conditions, the possibility opens up for a systematic exploration of causes to brain injury following heart surgery.

In this investigation, we deliberately concentrated our efforts to the study of memory functions. There are several reasons why we did so. First, memory problems may be particularly common following CPB. Second, memory assessment is often a sensitive marker of damage to the brain. Third, we wanted to assess a large number of patients, using semi-automated, computerised procedures. Unfortunately, conventional neuropsychological assessment techniques require a large amount of time and resources that would have made the inclusion of 120 patients impossible. While we emphasised the putative amelioration of memory impairment following CPB, at the same time the present study does not rule out the possibility that the use of heparin coated surfaces may protect against other, presumably less frequent cognitive changes that may take place following CPB. In the future, researchers may wish to consider the protective role of heparin coated surfaces on other cognitive domains than memory.

The biochemical parameter, S-100, has been presented as a suitable brain cell injury marker in conjunction with CPB [10]. The protein S-100 is a homo or hetero-dimer consisting of two sub-units, α and β. The isomeric form S-100 (ββ) is present in high concentrations in glial and Schwann cells and S-100 (αβ) is found in glial cells [9]. S-100 is a calcium binding protein with a molecular weight of about 21 000 D. It is eliminated through the kidneys and the estimated half-life is about 2 h [27]. The biological function of the protein is still uncertain. Earlier studies have shown a release of S-100 to cerebro-spinal fluid and serum after head injuries, stroke, subarachnoid haemorrhages [17], also during CPB [19] and to serum during deep hypothermic circulatory arrest [2]. Enhanced biocompatibility in CPB would theoretically be advantageous, both with respect to formation of micro aggregates and the inflammatory response. This in turn may lead to a lower embolic load to the brain, which could be reflected by a lower release of S-100.

In spite of an obviously multi-factorial situation, we were able to find, in this low-risk group of patients signs of improved cerebral protection. The number of neurological deviations were significantly fewer in the study group (1.5% versus 15.2%). On the other hand, the incidence of 15.2% in the control group is unexpectedly high. Furthermore, the cause of neurological deviations are not confined to micro-emboli, but may be due to macro-emboli from the operative site, underlying neuropathology, drug side effects etc. Thus, the exact patho-physiological mechanisms remain unclear. The possibility of prophylaxis against neurological complications is however clinically important.

5. Conclusion

Reduced blood trauma obtained by the use of heparin bonded surfaces brings about a more favourable general clinical outcome and may contribute to preservation of the integrity of the central nervous system.

Acknowledgements

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References


