Coated versus Noncoated Circuits in Pediatric Cardiopulmonary Bypass

Anjo M Draaisma BS, EKP and Mark G Hazekamp MD, PhD

Department of Cardiothoracic Surgery, University Hospital Leiden, Leiden, the Netherlands

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A systemic inflammatory response after pediatric cardiac surgery is not uncommon. The cardiopulmonary bypass (CPB) circuit is seen as the main activator of the inflammatory response. For that reason, several coatings have been developed to create a more biocompatible CPB circuit. At this moment, several coatings are commercially available: human albumin coating, Duraflo II and Carmeda coatings (both based on heparin), phosphorylcholine PHISIO coating (which mimics the outer cell membrane), polymethoxyethylacrylate coating, and the biopassive surface Trillium coating.

Do these coatings result in less inflammatory response after pediatric cardiac surgery? In reviewing the literature on coating of pediatric CPB circuits, a lot of controversies are found. *In vitro* studies show significantly better biocompatibility of coated circuits than of noncoated circuits [1-3]. The outcomes of *in vivo* or clinical studies are less convincing; many times only a few parameters show improvement [4–7]. Some of the problems found in reviewing studies on coatings are: different methodologies, lack of proper control groups, differences between the patients concerning age and bodyweight, and different prime volumes in different groups. Furthermore, measured parameters are numerous, and sample moments show large variability (table 1).

In the adult population, many more studies on coatings have been published. Here, we find more evidence for beneficial effects of coatings, but it is not clear whether the results of these studies can simply be extrapolated to the practice of pediatric cardiac surgery [13].

Several factors may cause an inflammatory response. The artificial surface of the CPB circuit is an important activator, but other activators are probably as important: ischemia-reperfusion, surgical trauma (especially that of cardiovascular surgery), endotoxemia, and blood–air contact [14]. Patients that have cardiovascular operations without the use of CPB have been reported to show also signs of serious inflammatory response [15–17]. Although CPB is not the only causative factor for an inflammatory response, coating of the CPB circuit is expected to result in improved biocompatibility with less activation of the complement system, the contact system, as well as a reduced activation of leucocytes and platelets.

To what should we thus adhere? *In vitro* studies provide the most reliable information because of their controlled environment and similar outcomes. The most important for
clinical studies is a homogeneous patient group, especially in the pediatric population where a wide spread in age, bodyweight, and diagnosis is commonly encountered.

Table 1. Pediatric In Vivo Studies: Randomized and Prospective

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>N</th>
<th>Measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schreurs et al. [8]</td>
<td>1998</td>
<td>19</td>
<td>Less platelet activation/ complement activation similar</td>
</tr>
<tr>
<td>Jensen et al. [9]</td>
<td>2004</td>
<td>40</td>
<td>Fibrinolysis reduced/ inflammatory parameters not measured</td>
</tr>
<tr>
<td>Grossi et al. [10]</td>
<td>2000</td>
<td>23</td>
<td>Less C3a, IL-8/ similar C5a, IL-6</td>
</tr>
<tr>
<td>Olsson et al. [11]</td>
<td>2000</td>
<td>19</td>
<td>Less C3a, C5b-9, and IL-6</td>
</tr>
<tr>
<td>Ashraf et al. [12]</td>
<td>1997</td>
<td>21</td>
<td>Less C5b-9, elastase, (IL-6)/ similar IL-8</td>
</tr>
<tr>
<td>Horton et al. [4]</td>
<td>1999</td>
<td>200</td>
<td>Similar IL-6, IL-8, and platelets</td>
</tr>
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</table>

Our group recently performed a prospective, randomized, and blinded clinical study in 28 neonates and small infants to compare complement activation and leucocytes stimulation of phosphorylcholine coated and noncoated CPB circuits. Strict inclusion criteria were used: bodyweight between 3 and 6 kg, no syndromal anomalies such as Down syndrome, no severe cyanosis (oxygen saturation < 75%), no circulation arrest, no reoperations, and no premature patients. All patients received the same protocolized way of anesthesia and CPB management; none of the patients received aprotinin or other drugs that might interfere with the inflammatory response. No ultrafiltration, conventional or modified, was used in the study patients. No differences were observed between the two groups for the changes of complement factor C3b/c, elastase HNE, interleukin-6, and C-reactive protein before, during, and after CPB until 6 hours postoperatively. We concluded that phosphorylcholine coating does not result in a reduction of inflammatory response (data not shown).

Summarizing the review of the literature and our study, we conclude that an improved biocompatibility by coating is most reliably demonstrated by in vitro studies, whereas clinical studies in the pediatric population do not show equally convincing beneficial effects. More strictly protocolized randomized prospective clinical studies will be needed to gather evidence for positive effects of CPB circuit coating in pediatric cardiac surgery.
In the meantime, we should realize that coating alone cannot lead to an adequate reduction of inflammatory response. Other agents should be considered for this purpose, such as ultrafiltration during and/or after CPB, corticosteroids and protease inhibitors, and the use of monoclonal antibodies [18]. Efforts to further miniaturize the pediatric CPB-circuit will also be helpful.

References


