clinical update

Leukocyte Reduction of Blood Cardioplegia
Summary

The use of leukocyte reduced blood cardioplegia has been clinically demonstrated to significantly reduce myocardial reperfusion morbidity in routine elective CABG (Coronary Artery Bypass Graft), high risk, pediatric and transplant patients during CPB (cardiopulmonary bypass). Clinical trials using leukocyte reduced blood cardioplegia have reported:

- Significant reduction in the incidence of atrial fibrillation.
- Significant reduction in incidence of low cardiac index.
- Significant reduction in ventricular fibrillation.
- Significant reduction in the need for antiarrhythmic drugs.
- Significant reduction in markers of myocardial damage (Troponin I, Troponin T & CPK MB).
- Significant reduction in ultra-structural damage in transplanted hearts.

Clinical Problem

Despite extensive use of blood cardioplegia and improvements in administration and reperfusion techniques, myocardial dysfunction and associated morbidity remain the most frequent complications post CPB. The incidence of atrial fibrillation is reported to occur in approximately 20-30% of CPB patients.

While the etiology of myocardial dysfunction post-bypass is complex, numerous animal and human clinical trials have demonstrated that activated neutrophils play a major role in ischemia-reperfusion injury to the myocardium. A number of studies by Allen, Bolling, Sakamoto and co-workers have demonstrated that modification of the blood reperfusion conditions (including leukocyte reduction) can significantly reduce ischemic-reperfusion injury.

Clinical Solution

Routine CPB Patients

Recently, Yurvati et al demonstrated that the use of leukocyte reduction filters combined with the use of aprotinin significantly reduced the incidence of atrial fibrillation by 72% in routine CABG patients. A follow up study by the same group and additional data from Samankatwet et al suggested that leukocyte reduction of the blood cardioplegia is primarily responsible for the myocardial protective effect.

Palatianos et al have shown that leukocyte filtration of blood cardioplegia significantly reduces myocardial reperfusion morbidity in patients undergoing primary elective, coronary artery bypass.

<table>
<thead>
<tr>
<th>Leukocyte reduced perfusate (n=60)</th>
<th>Control (n=60)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical mortality (30 days)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Myocardial Infarct (peroperative)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Low cardiac index</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>Reperfusion ventricular fibrillation</td>
<td>3</td>
<td>17</td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>0</td>
<td>22</td>
</tr>
<tr>
<td>Pacing required</td>
<td>0</td>
<td>4</td>
</tr>
</tbody>
</table>
Biochemical markers of myocardial injury were also significantly reduced.

<table>
<thead>
<tr>
<th>Post-operative markers (time point)</th>
<th>Leukocyte reduced perfusate</th>
<th>Control</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPK-MB ug/mL (6 hours)</td>
<td>14.2+/−6.1</td>
<td>18.9+/−7.7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>CPK-MB ug/mL (12 hours)</td>
<td>5.7+/−3.0</td>
<td>9.7+/−2.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Troponin I ug/mL (6 hours)</td>
<td>6.8+/−4.1</td>
<td>11.2+/−6.5</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Troponin I ug/mL (12 hours)</td>
<td>6.8+/−2.1</td>
<td>12.0+/−8.3</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Similar reductions in Troponin T and CPK-MB were also reported by Suzuki et al where leukocyte reduced blood cardioplegia was used for elective open heart surgery patients.10

**Troponin - T (p<0.05)**

![Graph showing Troponin T levels](image)

**CPK-MB (p<0.05)**

![Graph showing CPK-MB levels](image)

**Pediatric Patients**

In open heart surgery pediatric patients, Hiyashi et al have reported that leukocyte reduced blood cardioplegia can significantly reduce malondialdehyde, human heart fatty-acid binding protein, creatine kinase-MB release and catecholamine dosage required.7 Reduced reperfusion injury and improved myocardial protection has also been reported by Allen et al when leukocyte reduction is used in pediatric patients.10 Significantly, Allen reported that the introduction of a normoxic bypass strategy, combined with leukoreduced modified reperfusion techniques significantly improved survival in patients undergoing Norwood procedures (retrospective analysis: pre-June 1996, Survival=53%, July 1996-March 2000 post introduction of modified bypass strategy, Survival=78%).10

**High Risk / Emergency Patients**

Roth et al have shown that leukocyte reduction significantly reduced Troponin T release from the coronary sinus in patients with a left ventricular ejection fraction less than 30%, and also significantly reduced the requirement for dopamine post CPB (0.36+/−0.11 vs 0.49+/−0.14 mg/kg/min, P<0.05).8 This work is supported by the findings of Sawal et al who reported that left ventricular hypertrophy patients receiving leukocyte depleted terminal blood cardioplegia had significantly improved recovery of myocyte and endothelial damage than did controls.9 Sawal also reported that the leukocyte reduced patients had significantly fewer neutrophils adhering to endothelial cells at reperfusion, significant reductions of markers of reperfusion injury, higher percentage of spontaneous defibrillation, lower dopamine requirement and lower capillary wedge pressure.9

**Cardioplegia leukoreduction in patients with severe left ventricular dysfunction**

![Graph showing Cardioplegia leukoreduction](image)

Adapted from Roth M et al.9

**Heart Transplantation**

Pearl et al showed that transplanted hearts reperfused with leukocyte reduced blood exhibited less ultra-structural damage than hearts perfused with whole blood.15
A second article by the same authors demonstrated significant reductions in release of CPK-MB and the vasoconstrictor, thromboxane B2 (Tx-B2) when hearts were perfused with leukocyte reduced blood. The authors concluded: "Reperfusion with amino acid enriched leukocyte depleted blood cardioplegia solution followed by leukocyte depleted blood alone is recommended for all transplanted hearts." 

Quote from paper
"Leukocyte depletion may be beneficial at the time of reperfusion, particularly as an adjunct to terminal cardioplegia or during cardiac surgery to attenuate reperfusion injury, especially in adult patients. Removal of leukocytes appears to be useful when serious reperfusion injury is expected to occur during open heart surgery." 

References
For a complete reference list please see latest "Summary of data" available from your PALL representative or distributor.