Aprotinin Use In Patients Undergoing Thoracoabdominal Aneurysmectomy
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Citation

Abstract
Aprotinin is a serine proteinase inhibitor able to preserve adhesive glycoproteins in the platelet membranes. In addition, it inhibits fibrinolysis and inflammatory cascades that might be in part responsible for the high incidence of complications accompanying aortic cross-clamping (1). Aprotinin has shown to be very effective in reducing blood loss in patients undergoing aortic surgery (2,3). However, it has the potential to damage the renal system. This effect seems to be dose-dependent. The use of aprotinin in aortic surgery is therefore still controversial. No study has yet analyzed the costs-benef its of aprotinin in patients undergoing TAAA repair. Our goal was to evaluate the economic consequences and efficacy and to establish the renal safety of low-dose aprotinin in this high-risk patient population.

INTRODUCTION
Aprotinin has been shown to be very effective in reducing blood loss in patients undergoing thoracoabdominal aortic aneurysm (TAAA) surgery using cardiopulmonary bypass (2) and to be cost-effective in cardiac surgery (4,5). The effect of aprotinin on reducing blood and blood product requirements is greater than that of the lysine based analogues. This may be due to the effects of aprotinin on inhibition of plasminogen and to a direct effect on platelet function. Aprotinin has been shown to correct defects in platelet adhesion induced by cardiopulmonary bypass. However, patients undergoing thoracoabdominal aortic aneurysm repair are at high risk for postoperative renal failure and it is known that aprotinin accumulates within the proximal tubular epithelial cells of the kidney. It has therefore the potential to damage the renal system. This effect seems to be dose-dependant. The incidence ranges from 25 to 50 % (6). Cross-clamping of the thoracoabdominal aorta is associated with severe (approx. 90%) decrease of renal blood flow, glomerular filtration rate, and urine output (7). The development of postoperative renal failure is among the most common causes of postoperative mortality. The use of aprotinin in aortic surgery is therefore still controversial. Low-dose aprotinin in patients undergoing thoracic aortic operations using profound hypothermic circulatory arrest did not show deleterious effects on renal function (2). The renal effects of aprotinin in aortic surgery without cardiopulmonary bypass or hypothermic circulatory arrest have not yet been investigated. In addition, no study has yet analyzed the costs-benefits of aprotinin in patients undergoing TAAA repair. Our goal was to evaluate the economic consequences and efficacy and to establish the renal safety of low-dose aprotinin in this high-risk patient population.

METHODS
Our study consisted of a randomized, double blinded, IRB approved cohort of twenty patients. Ten patients were randomized to receive the study drug (aprotinin), and ten control patients received placebo (saline). The study group received a 10,000 U test dose of aprotinin followed by a loading dose of 1 million units given over twenty minutes. An infusion of 500,000 U / hr of aprotinin was continued for the duration of the case or a total dose of 3 million units was reached.

All patients were scheduled to undergo elective repair of TAAA (thoracoabdominal aneurysm) utilizing single lung ventilation, and distal aortic perfusion via a left atrial to femoral centrifugal pump. Prior to aortic cross clamp patients were cooled to 34 degrees C. Upon completion of repair, the patients were re-warmed to 37 degrees C, then
transported to the CVICU.

Figure 1
Figure 1: Thoracoabdominal aortic aneurysm prior to repair

Figure 2
Figure 2: Thoracoabdominal aortic aneurysm after replacement with Dacron graft

Blood product transfusion (except platelet administration) was accomplished using the Haemonetics rapid infusion system. This provided us with an accurate assessment of blood components transfused, as well as ensuring that the temperature of product infusion was uniform.

Analysis of costs (blood product transfusions, length of ICU and hospital stay) and comparison of overall hospital costs of drug and placebo group were used to determine the impact on economics.

The impact on renal function was determined by measurement of dye clearance time and assessment of pre and post operative creatinine values. The dye clearance time is the time in minutes from re-establishing renal blood flow until the detection of dye (indigocarmine) in the urine.

RESULTS

Figure 3
Table 1: Costs Blood Products

<table>
<thead>
<tr>
<th>Drug</th>
<th>Total</th>
<th>OR</th>
<th>ICU</th>
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</thead>
<tbody>
<tr>
<td>Total Drug RBC Cost</td>
<td>$6,739.18</td>
<td>$3,005.31</td>
<td>$3,460.66</td>
</tr>
<tr>
<td>Total Placebo RBC Cost</td>
<td>$7,285.60</td>
<td>$2,923.17</td>
<td>$4,362.43</td>
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<tr>
<td>Total Drug PLT Cost</td>
<td>$6,832.75</td>
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<tr>
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<td>$3,458.00</td>
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<tr>
<td>Total Drug FFP Cost</td>
<td>$8,371.25</td>
<td>$2,624.50</td>
<td>$5,746.75</td>
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<tr>
<td>Total Placebo FFP Cost</td>
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<td>$3,077.00</td>
<td>$5,644.50</td>
</tr>
<tr>
<td>Total Drug Cryo Cost</td>
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<td>$0.00</td>
<td>$1,150.50</td>
</tr>
<tr>
<td>Total Placebo Cryo Cost</td>
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<td>$360.50</td>
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</table>

Figure 4
Table 2: Descriptive Statistics

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<th>H</th>
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<th>SD</th>
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<tr>
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<td>4.6</td>
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<tr>
<td>Placebo</td>
<td>10</td>
<td>3.0</td>
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<tr>
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<td>8.3</td>
<td>8.8</td>
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<td>6.2</td>
<td>6.2</td>
</tr>
<tr>
<td>Total Drug</td>
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<td>7.0</td>
<td>6.3</td>
</tr>
<tr>
<td>Placebo</td>
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<td>5.5</td>
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<tr>
<td>Total Drug</td>
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<tr>
<td>Placebo</td>
<td>10</td>
<td>4.8</td>
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</tr>
</tbody>
</table>

Figure 5
Table 3: Summary Statistics of Costs

Cost analysis revealed a trend towards lower costs in the aprotinin group compared to the placebo group with respect to blood bank, ICU, and overall hospital costs.

Figure 6
Table 4: Total aortic clamp times

Total aortic clamp times were not significantly different.
Aprotinin seems to positively influence the overall hospital costs of patients undergoing TAAA repair. The decreased length in ICU and hospital stay may indicate better organ protection (inhibition of inflammatory cascades by aprotinin) during and after aortic cross-clamping or be a result of decreased transfusion requirements (especially platelets). Our data suggest that the use of low-dose aprotinin has a potential for positive economic impact in this high-risk population.

Concerns have been raised about the use of aprotinin in patients at high risk for renal insufficiency. Our results demonstrate that the use of aprotinin is safe has no adverse impact on renal function in patients undergoing thoracoabdominal aortic aneurysm repair without cardiopulmonary bypass or hypothermic circulatory arrest. Low-dose aprotinin is therefore well tolerated in this patient population.

ACKNOWLEDGMENT

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References

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