The Role of Activated Coagulation Times in Cardiac Surgery

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Heparin is generally administered during cardiopulmonary bypass (CPB) on an empirical basis without constant monitoring of clotting times. There is a wide variation in the amount of heparin and the frequency of supplemental doses during CPB. Although the half-life of heparin has been shown to be approximately 1.5 hours, we were concerned that factors such as anesthesia, hypothermia, hemodilution, and CPB might affect this life span.

In an effort to determine whether heparin, in fact, could be administered reliably on an empirical basis, we utilized the Activated Coagulation Time (ACT) described by Hattersley on all patients undergoing open-heart surgery since November 1974. This test was chosen because of its reported reliability, reproductability, and ease of performance.

METHODS AND TESTS

Twenty-five consecutive adult patients undergoing CPB were studied. Their ages ranged from 18 to 67 years. The surgical procedures performed are shown in Figure 1.

<table>
<thead>
<tr>
<th>Operative Procedure</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Double coronary artery bypass</td>
<td>8</td>
</tr>
<tr>
<td>Triple coronary artery bypass</td>
<td>4</td>
</tr>
<tr>
<td>Quadruple coronary artery bypass</td>
<td>1</td>
</tr>
<tr>
<td>Open mitral commissurotomy</td>
<td>2</td>
</tr>
<tr>
<td>Open mitral commissurotomy and single coronary</td>
<td>1</td>
</tr>
<tr>
<td>Mitral valve replacement</td>
<td>4</td>
</tr>
<tr>
<td>Aortic valve replacement</td>
<td>2</td>
</tr>
<tr>
<td>Mitral valve replacement and double coronary</td>
<td>1</td>
</tr>
<tr>
<td>Mitral and aortic valve replacement</td>
<td>1</td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
<td>1</td>
</tr>
</tbody>
</table>
mitral valve replacement, and one with a double valve replacement) were undergoing their second cardiac surgical procedure. One patient was returned to the operating room for bleeding.

Platelet counts and fibrinogen levels were determined preoperatively and postoperatively. Plasma hemoglobin levels were determined at the termination of CPB. Arterial blood gases and hematocrits were monitored pre-bypass, at 30 minute intervals during bypass, and post-bypass.

Activated coagulation time (ACT) was measured prior to heparinization, at 30 minute intervals thereafter until the termination of bypass, and 15 minutes after the administration of protamine. When additional protamine was required an ACT was again monitored.

The standard technique for ACT determinations was utilized. Two ml of blood were withdrawn into a plastic syringe from the arterial monitoring line or the sampling port of the oxygenator. This was placed into a prewarmed tube containing 12 mg of diatomaceous earth (Celite). Immediately after introduction of the blood into the tube, a timer was started and the tube was inverted a few times to mix the contents. The tube was then placed into a heating block set at 37°C until one minute had elapsed on the timer. Then, at five-second intervals the tube was removed from the heating block and tilted until the first clot formed. The ACT was determined to the nearest five seconds. All of the above factors were kept constant.

A Galen oxygenator, a Swank cardiotomy filter, and a Pall arterial filter were incorporated into the CPB circuit which was primed with 1500 to 2000 cc Plasmalyte pH 7.40 No. 148, 100 gm albumin, and 2500 USP beef lung heparin \( \dagger/1000 \) cc crystalloid. All subsequent liters of Plasmalyte and each unit of blood added to the circuit contained 2500 USP heparin.

Moderate hypothermia to 30°C and moderate hemodilution to hematocrits of 18% were utilized in all cases. Esophageal and rectal temperatures, urinary output, arterial and central venous pressures were monitored.

PROCEDURES

After induction of anesthesia, an ACT was taken to determine the patient’s baseline normal. The normal ACT described by Hattersley is a value of less than 130 seconds. Our patient’s preheparin ACT ranged from 85 seconds to 155 seconds with a mean of 110 seconds.

Prior to cannulation, 300 USP/Kg of beef lung heparin was injected into the right arterial appendage. No further heparin was administered except when the ACT was 480 seconds or below.

CPB time ranged from 45 minutes to 199 minutes with an average of 107 minutes.

After termination of CPB, the patient was given 1.5 mg protamine sulfate for each 100 USP heparin administered during bypass. If the post-bypass ACT was prolonged, additional protamine sulfate was administered until return to preheparin values.

RESULTS

The first ACT determined after heparinization showed a broad range of an-
ticogulation as displayed in Figure 2. Coagulation times varied from 420 seconds to more than 900 seconds with the patient’s temperature at 30 °C. During hypothermia the ACT generally remained the same or decreased. However, during rewarming, ACTs in eighteen patients decreased, three remained the same, and four prolonged.

Six patients required a single dose reheparinization with 100 USP/Kg to maintain an ACT above 480 seconds. Two patients required reheparinization twice at varying intervals. (Figure 3)

Factors such as moderate hemodilution, acid base balance, and urinary output did not have any direct effect on the ACT. Urinary output ranged from 12 to 730 cc during bypass, with an average of 225 cc. A diuresis did not result in a decreased ACT.

At the termination of CPB, ACT levels varied from 422 seconds to over 900 seconds. ACTs were not necessarily prolonged after protamine administration if they had been over 600 seconds at the completion of bypass. Nine patients received supplemental dosages of protamine due to a prolonged ACT. An increased capillary ooze at the operative site could be correlated with an increased ACT.

Blood loss and hematological data are described in Figure 4. No significant correlation could be made between the ACT and the hematological data as is suggested by Figure 5. However, subjectively, the total blood loss appeared to be decreased when monitoring ACTs to achieve adequate reversal of protamine. This has also been observed by Mattox. 4

<table>
<thead>
<tr>
<th>Variable</th>
<th>Correlation Coefficient</th>
</tr>
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<tbody>
<tr>
<td>Fibrinogen Decrease (%)</td>
<td>-0.0570</td>
</tr>
<tr>
<td>Platelet Decrease (%)</td>
<td>+0.1082</td>
</tr>
<tr>
<td>Plasma Hemoglobin (%)</td>
<td>+0.0416</td>
</tr>
<tr>
<td>Blood Loss/Kg/24 Hours</td>
<td>+0.2940</td>
</tr>
</tbody>
</table>

Figure 5
DISCUSSION

Adequate anticoagulation during CPB is essential to prevent clotting in the extracorporeal circuit and possible death of the patient. Heparin has generally been administered on an empirical basis without regard to any form of coagulation testing. Perhaps problems such as disseminated intravascular coagulopathy, heparin rebound, and excessive postoperative bleeding could be attributed to inadequate heparin and protamine administration.

It cannot be assumed that each patient will react to heparin in a standard fashion. The wide variation in heparin metabolism has been described by others.\(^5\)\(^7\)\(^8\).

It would appear that heparin metabolism varies with temperature. However, hemodilution and increased urinary output have no apparent effect on the circulating heparin levels.

One question still remains: What is an adequate ACT level for CPB when the patient is systemically heparinized? Hill has described 180 to 240 seconds during long-term CPB.\(^1\) Bull believes that this level is too low for CPB in cardiac surgery and should be above 300 seconds and below 600 seconds.

In our study, we preferred an ACT above 480 seconds and did not observe abnormal bleeding tendencies if this level exceeded 600 seconds. However, techniques of reproducing ACT from institution to institution may vary. Therefore, minimum and maximum levels should be determined initially over a broad patient selection, utilizing a standard protocol for each institution.

In conclusion, we felt that the activated coagulation time was an essential test utilized on a routine fashion in cardiopulmonary bypass. Heparin administration should be accompanied by a test to determine the adequacy of anticoagulation.

REFERENCES