

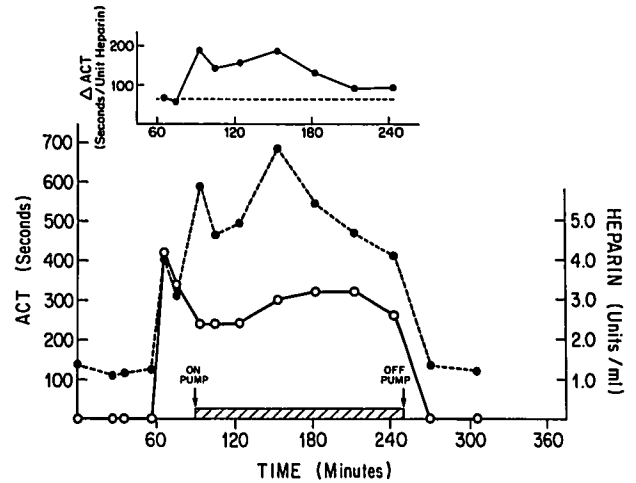
Title: ACTIVATED CLOTTING TIME AND HEPARIN LEVELS DURING HYPOTHERMIC CARDIOPULMONARY BYPASS
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Introduction. Since the activated clotting time (ACT) provides a convenient assessment of heparin effect in whole blood (1) and a linear dose response curve for in-vitro additions to blood (2), it has been recommended for determination of anticoagulation requirements during cardiopulmonary bypass (CPB) and calculation of protamine dosage for heparin neutralization post CPB (3). We evaluated whether the administered heparin - ACT dose response curve prepared before CPB accurately reflected actual heparin levels during or after CPB.

Methods. We used a standard heparin (H) regimen (3 mg/kg pre CPB, 80 mg in the pump prime, and 1 mg/kg at hourly intervals during CPB) in 28 patients (pts) undergoing coronary artery bypass surgery. Following termination of CPB protamine sulfate (PS) 3 mg/kg was given. Additional PS requirements were determined using a serial protamine titration test. A clear prime was used for the oxygenator and systemic hypothermia to 20°C was employed during construction of the distal anastomoses. Blood samples for ACT and H levels were drawn prior to and after initial heparinization, periodically during CPB, and before and after protamine neutralization. We measured ACT with a Hemochron 400 D (International Technidyne) and determined H levels with a standard assay (4). H sensitivity was expressed as the increase in ACT from pre-heparin levels divided by the plasma H concentration. Values are presented as means ± standard error. Statistical analysis is with Student's t-test.

Results. Our combined data is shown in the table. The increase in ACT, the decrease in H level, and the almost doubling of H sensitivity are highly significant statistically (p < .001). The response of one individual pt is shown in the figure. Mean PS dosage was 250±13 mg. This was almost exactly the amount estimated from the pre-protamine H level and a dose response curve relating plasma H response to the initial H injection assuming a 1:1 H:PS ratio (254±16 mg). It was significantly less (p < .05) than the amount projected using the dose response curve relating ACT to injected H (353±27 mg).

	# assays	ACT (sec)	HEP (u/min)	ACT sensitivity (sec/U hep)
Preheparin	70	121±2	-	-
Postheparin				
Pre CPB	37	493±30	4.0±0.2	95±8
During CPB	119	674±25	3.1±0.1	180±7



Closed circle = ACT; Open circle = Heparin levels.

Discussion. Although the ACT response to H varies widely among pts, the basis for using the ACT is a consistent relationship in any specific pt. If this individual response to H varies during CPB then the dose response curve constructed prior to CPB will not accurately determine subsequent H or PS requirements. We observed that the ACT per unit of plasma H was not constant during CPB, and therefore conclude that under the conditions of our study - hypothermic CPB with moderate hemodilution - the ACT does not accurately reflect H levels. We do not know the relative contribution of hypothermia or hemodilution to these findings. Calculation of PS dose from the initial H-ACT dose response curve is misleading and may lead to overestimation of PS needs.

References

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