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Title : HYPOTHERMIA CAN CAUSE ERRORS IN ACTIVATED COAGULATION TIME

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Introduction. The clinical value of Activated Coagulation Time (ACT) as a monitor of heparin therapy during cardiopulmonary bypass (CPB) depends upon the accuracy of the determination. Temperature affects coagulation and it is possible that significant errors in ACT could result from the marked changes in blood sample temperature which occur during hypothermic CPB. This study was performed to 1) Evaluate the effect of blood temperature upon ACT in man. 2) Evaluate the accuracy of a "temperature-controlled" non-automated method for ACT determination during hypothermia.

Methods. To evaluate in vivo changes in ACT occurring with changes in blood temperature, two ml blood samples for ACT were obtained at 24°C and at 28°C, 32°C, 36°C and 37°C blood temperature upon rewarming from hypothermic CPB in 33 consenting patients (avg. rewarm. time 11 mins.). To assure a stable heparin level in all samples, at least 45 minutes were allowed between the last heparin administration and sample drawing. No heparin was administered during the perfusate warming time, and no blood or antithrombin III-containing blood products were administered. Blood samples were injected immediately into Becton-Dickinson ACT tubes which had been prewarmed in a Thermolyne^{R} Dri-Bath calibrated to 37°. After allowing one minute for blood temperature equilibration to 37°, the stopwatch was activated. The sample was examined every 10 seconds over a heated view box. Elapsed time required for formation of the first visible clot was recorded as the ACT. Since in vivo metabolism of heparin during the perfusate rewarming period could cause changes in ACT, an in-vitro study was done to isolate blood temperature effect. Six blood samples for ACT were drawn simultaneously from 24° perfusate in each of 10 patients during CBP. All 6 samples from a given patient had the same heparin concentration. Two samples from each patient were placed in a 24°C waterbath, two in a 32°C waterbath and two in a 37°C waterbath. Previous studies have shown that a 24°C blood sample in a 3 cc plastic syringe will equilibrate to water bath temperature in 10 minutes. Following a 10 minute temperature equilibration period, one sample from each waterbath was injected into a temperature equilibrated ACT tube which was kept in its respective water bath while ACT was measured. The matched sample from each waterbath was transferred to a preheated ACT tube in the Thermolyne^{R} 37°C Dri-Bath. ACT was determined using the Dri-Bath according to standard clinical protocol. The heat transfer efficiency of the Thermolyne^{R} Dri-Bath system was evaluated by placing 24°C blood in a Becton Dickinson ACT tube. Heparin 5 units (0.05 ml) was added to prevent clotting. The rate of temperature increase of the blood sample was recorded using a temperature probe. All studies were Human Committee approved.

Results. Table I shows the changes in ACT recorded during rapid rewarming of hypothermic blood in 33 patients. ACT values were determined using the Dri-Bath. All ACT values were significantly different from the 37°C ACT value ($p<0.05$).

Table I.

Blood Sample Temp. (°C)	Mean Act (seconds) + S.E.M.	Blood Sample Temp. °C	Mean Act (seconds) + S.E.M.
24°	561 ± 18*	36°	467 ± 16.1*
28°	525 ± 18*	37°	441 ± 13.3
32°	503 ± 15*		

* = $p< 0.05$

The effect of initial blood sample temperature upon ACT performed by two different methods is illustrated in Table II. ACT values in the water bath column are the mean ACT for samples equilibrated at each temperature with subsequent determination of ACT at the same temperature. Values in the Dri-Bath column are for samples equilibrated at each temperature and subsequently transferred to the 37°C Dri-Bath for ACT determination.

Table II.

Blood Sample Temp. °C	Water Bath ACT in Sec. Mean ± S.E.M.	DRI-BATH ACT in Sec. Mean ± S.E.M.
24°	2613 ± 346	678 ± 34*
32°	769 ± 36	594 ± 28*
37°	490 ± 22	503 ± 23

* = $p< 0.05$ (paired t)

Heat transfer efficiency studies of the Dri-Bath revealed that 24°C blood samples placed in the bath warmed to only 28°C after one minute. After 15 mins. warming to 37°C was still not accomplished.

Discussion. Examination of the "waterbath" column of Table 2 shows the striking effect of blood temperature upon ACT. The mean value at 24°C was 410% greater than the 37°C value. Matched samples transferred to the Dri-Bath system had much lower ACT values for each initial equilibration temperature, reflecting blood sample warming performed by the Dri-Bath. However, if the Dri-Bath had warmed all samples to 37°C, all mean ACTs in the "Dri-Bath" column would have been identical. The prolonged mean ACT for the 24°C samples (678 seconds) and for the 32°C samples (594 seconds) indicates that the Dri-Bath only partially warmed samples. Our heat transfer studies of the glass tube Dri-Bath system confirm this finding.

Conclusions. 1) Blood hypothermia significantly prolongs ACT independent of heparin level. 2) The "temperature-controlled" Thermolyne^{R} Dri-Bath system may produce significant inaccuracies in ACT during hypothermic bypass due to incomplete sample warming 3) Proper warming of blood samples to 37°C prior to ACT determination is mandatory if ACT values are to adequately reflect heparin levels during hypothermic CPB.