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IS PROTEIN C REALLY ACTIVATED DURING EXTRACORPOREAL CIRCULATION FOR CARDIAC SURGERY ?

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Haemostasis changes (HC) during extracorporeal circulation (ECC) for cardiac surgery may occasionally increase morbidity and mortality.Although extensively studied,the mechanisms of these HC are still not very well understood. Alongside haemodilution,thrombopenia and thrombopathies,primary fibrinolysis was incriminated in the post ECC HC. The protein C (PC) system is a natural anticoagulant that inactivates factors V and VIII and the tissue type plasminogen activator (tPA) inhibitor thus increasing the activity of tPA activator.Activation of PC, resulting in lower plasma concentration would activate coagulation processes and might explain activation of the coagulation cascade inspite of heparinization.The aim of this study was to investigate if :1. PC is activated during ECC and 2. if its activation is related to perioperative bleeding.

METHODS: After informed consent 13 patients,8 M and 5 F,aged 26-76 yr, undergoing cardiac surgery (CABG N =5 ,valvular replacement N=8) were studied. Anesthesia was induced and maintained with fentanyl,flunitrazepam and pancuronium. Moderate hypothermia (27$\pm$1.1 °C) was induced.Mean ECC time was 119 $\pm$27 min (range 67-147).Heparin doses were 10 000 UI + 9000 UI/ sqm.Blood products were not given to patients during the study.The first 12 hours bleeding was 453 $\pm$ 288 ml (range 125-1090) Protein C activity (PCA), antigen (PCAG),protein S (PS),fibrin degradation products (D-Dimers), Immunoglobulin G (IGG),and RBC were measured before (T0), after (T1) induction of anesthesia,30 minutes after ECC onset (T2),before (T3) and after (T4) protamine administration and 2 hours after arival to ICU (T5).Correction for haemodilution was done by dividing a measured value by the value of the IGG or RBC at the same moment.Results are expressed as mean $\pm$ 1SD.Comparison between groups was done by ANOVA and multiple comparison tests.

RESULTS:Correction for haemodilution showed that during the whole period of the study IGG decreased significantly ($P<0.05$) more than RBC.D-Dimers significantly increased more than 5 times the control value (from 0.2 to O.98 mcg/l) at T3 and up to 2.36 $\pm$ 2 mcg/l at T6 PCA decreased significantly ($P<0.05$) at T2 (83 $\pm$ 7 %) and T3 (79 $\pm$ 13 %) of control (T0) only when correction for hemodilution was done by the RBC.PCAG and PS showed no significant change during the study.No correlation was found between PCA values and perioperative bleeding.

DISCUSSION:Presence of D-Dimers is a proof of activation of the coagulation cascade despite high heparin doses used.Since PCA was significantly lower during ECC (T2) and after reestablishement of the pulmonary circulation (T3) it seems possible that PC may be activated.Unchanged values of PCAG may be due to inactivated PC still present in the circulation. Since changes in the PCA values are significant only when the RBC are used for haemodilution correction,care should be taken in other studies when this correction is employed.

In conclusion, protein C may be activated during ECC for cardiac surgery but this activation does not seem to have clinical implications.

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TITLE: AN ASSESSMENT OF THE DURATION OF CEPHAPIRIN-INDUCED COAGULATION ABNORMALITIES AS MEASURED BY THE THROMBOELASTOGRAPH

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Prophylactic administration of antibiotics is an established practice for cardiothoracic (CT) surgery. About 80% of the antibiotic therapy used by CT surgeons is cephalosporins.[1] The thromboelastograph (TEG) is used to monitor whole blood coagulation, predict risk for postoperative hemorrhage after cardiopulmonary bypass (CPB) and guide transfusion therapy.[2] Cephalosporin antibiotics have been demonstrated to produce coagulation abnormalities after chronic administration.[3] The role of cephalosporin antibiotics on coagulation and the TEG for CPB procedures has not been previously reported. This study evaluates the duration and effects of cephapirin on the TEG.

After institutional review committee approval and written informed consent, 30 pts scheduled for elective coronary artery bypass grafting surgery (CABG) were prospectively evaluated. All pts had normal preoperative coagulation studies and had not received either anticoagulation or platelet medication within 7 days of surgery. Anesthesia was induced and maintained with a potent narcotic and muscle relaxant. Five minutes after induction of anesthesia, whole blood was tested for coagulation function (T_0) using a Hellige TEG (Haemoscope, Morton Grove, IL). After the baseline TEG sample was obtained, 1gm of cephapirin (Cefadyl^R,) was administered. Ten (T_{10}) and 30 (T_{30}) minutes after cephapirin administration, whole blood was sampled for TEG analysis. Specific TEG parameters recorded included reaction time (R), alpha angle and maximum angle(MA). Each pt served as his own control. A two tailed paired and unpaired Student's t-test was used to determine statistical difference between TEG variables. One way ANOVA and multivariant analysis were used to evaluate the modifying effect of antianginal medications, anesthetics, coagulation studies and demographic characteristics on TEG analysis of whole blood coagulation.

Ten minutes after cephapirin administration, significant changes in alpha, MA and R were present ($p<0.05$). Thirty minutes after cephapirin administration there was no statistical difference as compared with the baseline TEG. Cephapirin can cause a significant but transient change in the viscoelastic properties of blood. Coagulation parameters of the TEG should be measured prior to cephapirin administration to prevent errors in establishing baseline values prior to CPB.

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