A436

TITLE: PREDILUTION AND TITRATED INHIBITION OF PLATELET AGGREGATION: A PRINCIPLE FOR HEMOFILTRATION IN THE IMMEDIATE POSTOPERATIVE PERIOD

AUTHORS: W Hödl MD, A Chiari MD, C Müller MD, K Legat MD, M Zimpfer MD

AFFILIATION: Department of Anesthesiology and General Intensive Care, University of Vienna, 1090 Vienna, Austria

Inhibition of humoral coagulation after surgery with heparin, sufficient to perform continuous, microprocessor-controlled, pump-driven, veno-venous hemofiltration, might be harmful because of an increased risk of hemorrhage. The potent inhibitor of platelet aggregation, prostacyclin, has been shown to cause cardiovascular side-effects and cannot be titrated by using conventional laboratory tests. The goal of the present study was to control the employment of prostacyclin by using a new in vitro test of platelet aggregation and to define overall hemodynamics during inhibition of primary hemostasis.

METHODS: With institutional approval and, if possible, written consent, 25 patients with postoperative, acute renal failure have been studied during 29 periods of predilutional hemofiltration. Predilution offers the advantage of enhanced solute- and volume removal with lower tendency to filter clotting and diminished anticoagulation requirements. Prostacyclin (group 1, n=10), or both heparin (410±186 IU/h) and prostacyclin (group 2, n=19) were administered topically into the extracorporeal system. Blood samples were taken from the patients' radial artery and directly behind the hemofilter. Platelet function was determined by measuring in vitro bleeding times and -volumes, according to the system of Kratzer and Born (1), thus allowing a precise titration of the prostacyclin dosage.

RESULTS AND CONCLUSION: Starting at an infusionrate of 3-4 ng/kg/min, the dosage of prostacyclin was continuously titrated up to a level where full antithrombotic effect was achieved (group 1: 6.2±2.3 ng/kg/min, group 2: 7.0±2.3 ng/kg/min), (Fig.1). No significant changes of heart rate, mean arterial pressure or systemic vascular resistance were observed at any timepoint of measurements. Therefore continuous, microprocessor-controlled, pump-driven, veno-venous hemofiltration in predilutional mode with prostacyclin as an anticoagulant, slowly titrated to it's full antithrombotic effect can be employed routinely in the treatment of postoperative acute renal failure.

REFERENCE: (1) Haemostasis 15: 357-362,1985

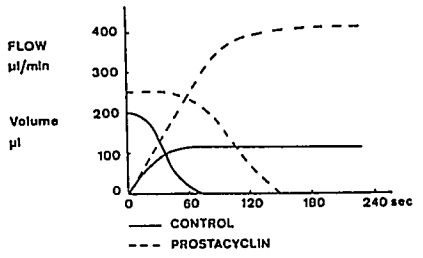

Fig.1 shows characteristic curves of blood flow and bleeding volume under control conditions and then after addition of prostacyclin.

A437

TITLE: THE MANAGEMENT OF ANTI-COAGULATION DURING CARDIOPULMONARY BYPASS (CPB)

AUTHORS: M.K.Urban M.D.Ph.D., M.Gordon M.D., D.T. Farrell C.C.P., and W.B. Shaffer C.C.P.

AFFILIATION: Department of Anesthesiology, Yale University School of Medicine, Yale-New Haven Hospital, New Haven CT 06510

Introduction: The accurate assessment of the adequacy of anticoagulation by heparin is essential for the management of patients undergoing CPB surgery. Since there is considerable variation in patient response to heparin administration, Bull et.al.[1] introduced the concept of measuring the clinical response to heparin therapy by the Activated Clotting Time (ACT). However, since the ACT is not specific for heparin and may not correlate with heparin levels during hypothermic CPB[2], a quantitative analysis of heparin levels may lead to the superior management of anticoagulation during CPB and protamine reversal. Hence, we compared the Hepcon® HMS system which allows automated analysis of heparin concentrations with conventional ACT analysis for the management of anticoagulation in patients for elective CABG surgery.

Methods: After HIC approval, 38 consecutive patients, age 51-85 years (66±10), undergoing CABG-surgery were randomly assigned to our standard ACT protocol or the Hepcon® HMS system. The ACT protocol included: 400 units/kg of heparin prior to CPB; maintenance of the ACT greater than 500 sec during CPB; and heparin reversal with protamine at 1.3mg/100 units of circulating heparin estimated from an ACT-heparin dose curve[1]. ACTs were measured in duplicate using the HemoTec ACT analyzer. The HMS protocol included: an initial dose of heparin determined by a heparin dose-ACT response curve to achieve an ACT of 500 sec.; maintenance of that heparin concentration using a heparin/protamine titration assay; and at CPB completion, protamine administered at 1.3mg/100 units of measured circulating heparin. Chest tube (CT) blood drainage was monitored for the first 3 hours and blood product transfusion was monitored for the first 24 hours post-operatively. One patient in the ACT group was excluded from analysis for surgical bleeding postoperatively. Data were analyzed by Chi-square with continuity correction, $p<0.05$ considered significant.

Results: The initial heparin dose required to achieve an ACT>500 sec. was significantly lower in those patients managed by the HMS system than our usual protocol (Table). However, by the end of CPB patients managed with the HMS system received significantly more heparin than the control group but required significantly less protamine for complete reversal. Post-CPB coagulation parameters and the quantity of CT-drainage was similar in both groups. Both the PT and PTT were elevated post-CPB, but there was no correlation between PT (r=0.67) and PTT (r=0.52) and the quantity of CT drainage over 3 hours. Both groups had similar transfusion requirements.

Discussion: Management of anti-coagulation during CPB with a direct heparin assay, resulted in the need for the administration of significantly more heparin than when dosing was performed on the basis of the ACT alone. This suggests a lack of correlation between ACT and heparin concentrations. However, despite the higher doses of heparin administered during CPB, less protamine was required for reversal since its dosage was based on the circulating heparin concentration and not on an extrapolation curve from the ACT. Management of CPB anti-coagulation using a titration system that allows for quantitative heparin and protamine dosing may be superior to the traditional ACT based methodology.

References:

1. J. Thorac Cardiovasc Surg 69:685-689, 1975.
2. Ann Surg 193:105-111, 1981

	Heparin Dosing	
	Control (n = 17)	HMS (n = 20)
Baseline ACT	139 ± 17	132 ± 12
Initial Heparin (µg/kg)	400	302 ± 82 *
Total Heparin (µg/kg)	497 ±81	606 ± 111 *
Total Protamine (mg/kg)	5.2 ± 1.2	3.5 ± 1.3 *
Post-CPB:		
PT (sec)	13.5 ± 0.9	13.5 ± 4.3
PTT (sec)	45.5 ± 11	45.8 ± 12
Fibrinogen (mg/dL)	203 ± 54	228 ± 75
ACT (sec)	127 ± 17	118 ± 14
CT-drainage (mL)	362 ± 159	317 ± 159

PT = prothrombin time, control < 13 sec.
PTT = partial thromboplastin time, control < 38 sec.
* $p < 0.05$