TITLE: PLATELET PROTECTION DURING CARDIOPULMONARY BYPASS with albumin prime and prostaglandins E_1 infusion

AUTHORS: ELLISON N, ADDONIZIO VP, NIEWIAROWSKI S, MACVAUGH H III, HARKEN AH, COLMAN RW, EDMUNDS LH JR.

AFFILIATION: Departments of Anesthesia, Surgery, and Medicine, University of Pennsylvania, School of Medicine, Philadelphia, Pennsylvania 19104

I. Introduction

Precoating extracorporeal surfaces with albumin or temporary platelet inhibition with prostaglandins E_1 (PGE_1) in an in vitro circuit have prevented the decrease in platelet count and function commonly seen after cardiopulmonary bypass (CPB). Infusion of PGE_1 has been shown to preserve platelet number and function and reduce postoperative bleeding times in rhesus monkeys who had CPB. (1) This study was designed to test the hypothesis that albumin precoating and/or PGE_1 infusion would preserve platelet number and function and decrease postoperative bleeding times in humans during CPB, and to determine the hemodynamic effects of PGE_1. Approval of our institution's Committee on Human Experimentation and informed consent of all patients studied was obtained.

II. Methods

Nineteen patients scheduled for coronary artery surgery were studied and randomly divided into 3 groups: saline prime-bubble oxygenator (SBO), albumin prime-BO (ABO), and albumin prime-BO-PGE_1 infusion (ABO+PGE_1). In addition five other patients were studied using an albumin prime with a membrane oxygenator: two received PGE_1 (AMO+PGE_1) and three did not (AMO). In the saline groups the prime solution consisted of 2000 cc lactated ringers and in the albumin groups the prime consisted of 1000 cc 5% albumin and 1000 cc lactated ringers. In the PGE_1 groups the drug was infused starting 5 minutes before the initiation of and throughout CPB at 0.1 mcg/kg/min.

Platelet counts and aggregation and release of low affinity antiheparin protein (LA-AHP) were measured prior to and 5 and 60 minutes into CPB and 30 minutes after termination of CPB. Template bleeding times were measured preop, post-induction, and 30 minutes after heparin reversal. Twenty-four hour chest bottle drainage loss was measured.

III. Results

There were no statistical differences (unpaired T-test) in any of the parameters of platelet function measured among the 3 groups except for the 60 minute platelet count of the ABO+PGE_1 group being greater nor did platelet aggregation to ADP change appreciably in any group. The 5 patients in whom the membrane oxygenator were used were too few to permit statistical analysis, but showed the same results. PGE_1 is an extremely potent vasodilator (table two). The perfusion pressure was consistently higher in the control group throughout CPB despite the fact the treatment group received 30.6±6.6 mg phenylephrine during CPB and the control group only 0.9±0.2 mg.

IV. Discussion

Transient inhibition of platelet function and preservation of platelet number during CPB were the stated goals of this study. Hemodilution alone cannot explain the drop in platelet count. The additional drop in platelet count presumably reflected platelet interaction with the foreign surface of the heart lung machine. The marked rise in LA-AHP, a sensitive indicator of platelet granular content release, also indicates that platelet function was not inhibited. In monkeys doses up to 0.5 mcg/kg/min PGE_1 were infused to achieve platelet inhibition. The vasoactive properties of PGE_1 precluded the administration of such high doses in humans.

Species variation is unlikely to explain this failure when compared to the monkey studies since the in vitro circuit used human blood. Rather, the role of the cardiac suction device and failure to achieve platelet inhibition with the lower doses used are more likely explanations. We conclude that neither albumin priming nor PGE_1 in the dose range used prevent platelet-surface interaction during CPB in vivo in humans and that the vasoactive properties of PGE_1 preclude safe, effective, transient inhibition of platelets in humans.

V. References

1. Addonizio VP et al: Effects of prostaglandin and albumin on platelet loss during in vitro simulation of extracorporeal circulation. Blood 53:1033-1042, 1979.

Table one. Platelet count and function during CPB

Group	SBO	ABO+ PGE_1	ABO	AMO	ABO+ PGE_1
No. of Patients	5	7	7	3	2
Platelet Count (% of control)					
CPB x 5'	73.6±3.5	79.9±6.0	69.2±5.5	73	65
CPB x 60'	75.6±5.9	88.0±2.3*	67.8±5.2*	76	75
30' after	80.9±2.2	79.6±0.6	73.4±7.5	70	65
LA-AHP (multiple of control in mcg/ml)					
CPB x 5'	1.5	2.2	0.9	0.8	0.7
CPB x 60'	6.3	4.7	3.1	2.6	2.0
Bleeding time (increase in minutes)	1.3±1.5	2.0±1.2	#	#	#
#=postop BT>30 minutes in one or more patients					
24 hour Chest bottle drainage (ml)	421±66	502±87	410±34	363	456

Table two. Mean perfusion pressures during CPB

	5' Before Start		5' After	30'	60'
Control	91.7±2.8	89.3±2.1	65.3±3.2	86.0±2.9	93.8±4.3
PGE_1	90.0±2.9	83.2±2.9	46.7±2.9*	65.6±3.8*	70.0±2.2*

*=difference statistically significant from control value at this time. P<0.001, unpaired T-test