Hematological Effects during Clinical Extracorporeal Circulation: A 200 Case Study of the Shiley M-2000 Membrane System

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Abstract

***(J. Extra-Corpor. Technol.* 19[3] p. 312–315 Fall 1987, 6 ref.) The hematological effects of the Shiley M-2000 Membrane Oxygenator System were evaluated during and after cardiopulmonary bypass (CPB) in 200 patients who required coronary artery revascularization. A strict protocol for perfusion management and blood sampling was established and adhered to. Bypass times varied from 1½ hours to 8½ hours ($\bar{x}$ = 2 hrs 48 mins). Hemolysis was observed to be minimal, blood cells were well preserved, and, in particular, platelet counts and platelet function remained stable, even in bypass times in excess of 8 hours.**

It was noted that when CPB was discontinued, and protamine sulphate infusion commenced, platelet function decreased slightly, although the platelet counts remained unchanged. Average postoperative blood loss was 390 mls (210 mls–1,400 mls range), statistically significantly lower than the average blood loss in a previous study at our center, which utilized the same protocol but an alternative membrane (Cobe CML).

In summary the Shiley M-2000 Membrane is a safe and extremely hemocompatible system for use in short- to medium-term perfusions.

Introduction

Unfortunately, cardiopulmonary bypass (CPB) is still associated with postoperative hemorrhage, which is frequently due to a decrease in platelets, caused by the bypass procedure.[1] It is a well established fact that membrane oxygenators are superior at preventing this negative effect.[2,3]

Approximately 12 months ago in the United Kingdom, a new design of Membrane Oxygenator became commercially available, the Shiley M-2000. It is unique in the fact that it uses the time-proven flat-sheet Microporous Polypropylene Membrane, combined with an innovative concept called "Bi-Level" crossflow.

Impressed by experimental data,[5] we agreed to undertake a clinical trial. The function of the trial was to evaluate the system generally and, more specifically, to investigate its level of hemocompatibility, with specific reference to blood trauma.

Materials and Methods

The trial was performed on 200 consenting patients, requiring elective cardiopulmonary bypass, for coronary artery revascularization. Patients with a known history of coagulation disorders were excluded from the study, as were patients taking drugs known to affect hematology. In each operation, the perfusion circuit consisted of a Shiley Hard-Shell Venous Reservoir with integral cardiotomy filtration, Shiley M-2000 Membrane Oxygenator, and Sarns Roller Pump (7000 series). The extracorporeal tubing was polyvinylchloride except for the pump headers which were

Postoperative Blood Loss in 200 Patients Undergoing Cardiopulmonary Bypass

N = 200	*M2000*	*CML*
Range (ml)	210–1,400	310–1,630
$\bar{x}$ (ml)	390	770

Student's t–test ($P<0.05$) showed significant difference between samples.

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silicone. No arterial line filtration was employed, as we believe this to be detrimental to the patient.[4]

The total priming volume of the extracorporeal circuit was 2,000 mls (1,500 mls lactated Ringers, 500 mls dextrose 5%), which was acceptable. Of this 2,000 mls, the oxygenator prime was approximately 700 mls. Also added to the prime was Heparin (50 mg), Sodium Bicarbonate (1mmol/Kg), Magnesium Chloride (5 mmols), and Mannitol (15g). Five minutes before cannulation of the aorta, heparin was administered intravenously at an initial dose of 3mg/kg, subsequently 50 mg heparin was given after each period of 30 mins on bypass. After CPB had been discontinued the heparin was reversed by giving protamine sulphate at a ratio of 1:1.

Bypass was instituted via an aortic cannula (Polystan 6mm), and a 2-stage right atrial pipe (Sarns). Full flow was achieved and cooling to 28°C commenced. At 30°C (esophageal temp), the aorta was cross-clamped, and one liter of crystalloid cardioplegia was infused into the aortic root at 4°C. Subsequent doses of cardioplegia (500 mls) were infused at 30 minute intervals, and sterile slush was placed over the myocardium. Once the last distal anastomosis had been completed, the aortic cross-clamp was released and rewarming commenced. Proximal anastomoses were completed during the rewarming period of bypass.

During the perfusion moderate whole body hypothermia (28°C) was carried out, with blood flow rates of 2.4 L/Min per M^2 body surface area (BSA) at normothermia, and 1.7 L/Min per M^2 BSA at hypothermia. BSA was calculated using the Dubois Nomogram. Systemic blood pressure during CPB was maintained in the range 45–80mmHg, using aramine and chlorpromazine as required.

Blood samples for hematological analysis were taken at aortic cannulation, and at 15 minute intervals for the first hour of CPB, then at 30 minute intervals for the next 2 hours, and if the procedure continued beyond 3 hours, samples were taken hourly. Also, samples were taken 24 and 48 hours postoperatively.

The following parameters were measured: plasma hemoglobin, by means of the hemoglobin-cyanide method, and full blood count with the use of a Coulter counter. Platelet function was also measured. Platelet function was assessed as the platelet aggregation, induced by adenosine diphosphate (ADP) in platelet rich plasma. Citrated platelet-rich plasma was stored at room temperature, and was tested 60 minutes after sampling. Platelet aggregation was measured as the maximal optical density loss (MOD_{max}) after ADP-induced platelet aggregation and was calculated as a percentage of the MOD_{max} of platelet-poor plasma. In the first sample different concentrations of ADP were used to induce platelet aggregation, in order to find the concentration which resulted in a 70% change of the max achievable decrease in optical density. This ADP concentration was then used to induce platelet aggregation in all following samples.

Postoperative blood loss was measured through 2 chest drains, which were connected as soon as full heparin reversal had been achieved.

Blood Sampling Protocol

Pre CPB	15 Mins	90 Mins	Hourly Thereafter
	30 Mins	120 Mins	
	45 Mins	150 Mins	
	60 Mins	180 Mins	

Results

Of the 200 patients included in the study, 197 survived the operation and had an uneventful recovery. Three patients died postsurgery, due to left ventricular failure (LVF).

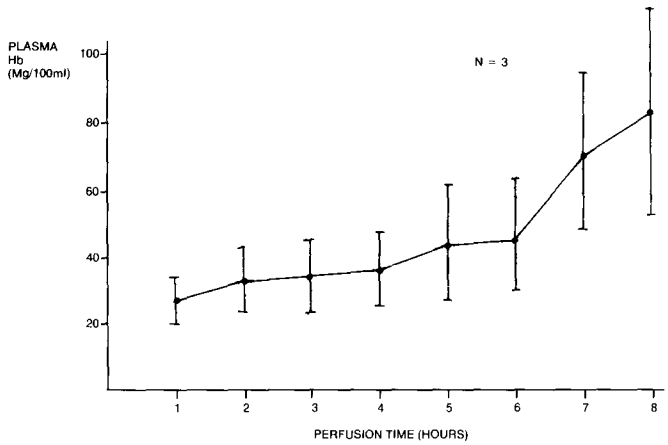
Platelet Numbers. These are expressed as a percentage of their original value before CPB, the drop to approximately 55% of their original value at the onset of CPB is due to hemodilution. Once on bypass, platelet numbers are well preserved throughout the duration of CPB. In the 3 perfusions lasting in excess of 8 hours, there was no depreciation of platelet numbers.

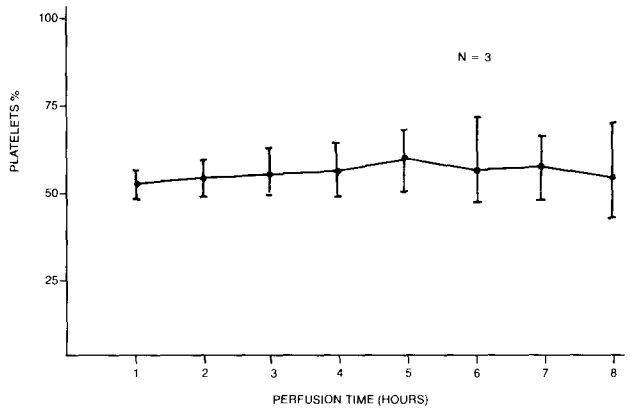
Platelet Function. The initial value of platelet function at aortic cannulation, measured as MOD_{Max} of ADP-induced platelet aggregation, was $61 \pm 16\%$. The results shown are expressed as a percentage of this value. There was no significant change in platelet function during CPB, and platelet function even increased to 112% after 45 minutes of bypass. However, after protamine administration, platelet function fell to 80% of the initial value, although platelet numbers remained constant. Platelet function on days 1 and 2 postoperatively was greater than it was at the time of aortic cannulation (112%).

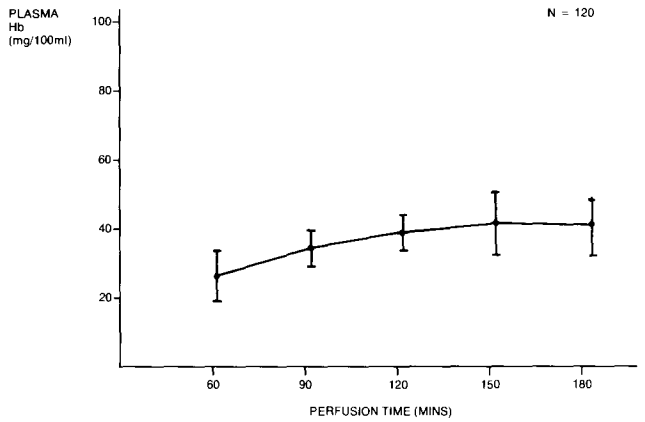
Free Plasma Hemoglobin. Free plasma hemoglobin was found in our samples, although the concentrations were very low with a mean of 31mg/100mls after 90 minutes of perfusion (N = 200). Also, in our cases which lasted in excess of 8 hours, peak free plasma hemoglobin was 110mg/100mls.

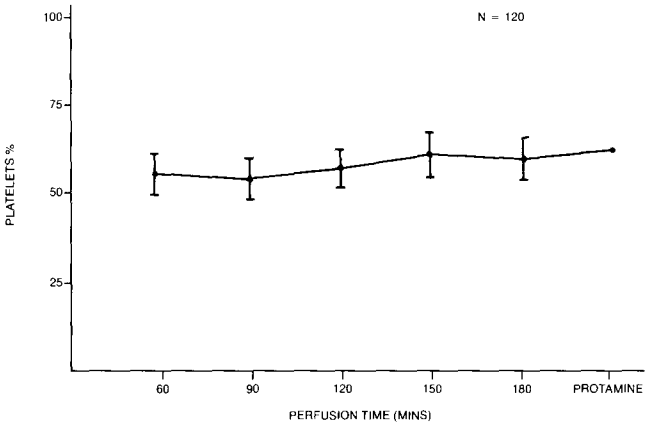
Postoperative Blood Loss. Postoperative blood loss ranged from 210mls to 1,400mls ($\bar{x}$ = 390mls). There was no correlation between blood loss and length of perfusion. Blood loss postoperatively was replaced using whole blood.

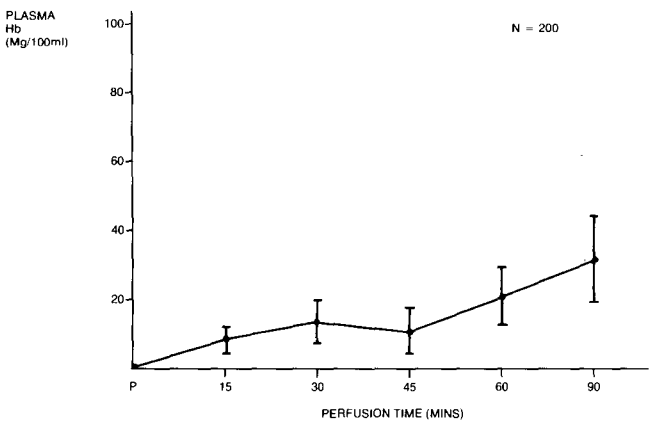
The average postoperative blood loss of 390mls was statistically significantly lower than the average blood loss measured in a previous study at our center, which utilized the same protocol, but an alternative membrane (Cobe CML).

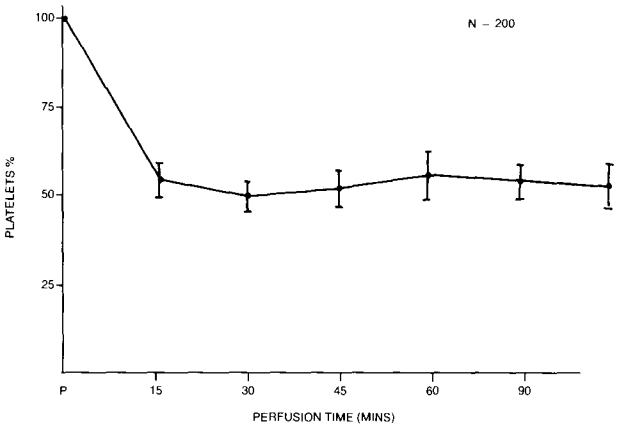

PLASMA
Hb
(Mg/100ml)
N = 3
PERFUSION TIME (HOURS)

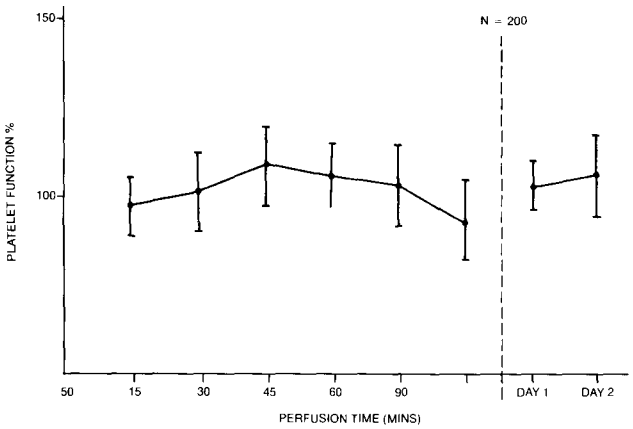

PLATELETS %
N = 3
PERFUSION TIME (HOURS)


PLASMA
Hb
(mg/100ml)
N = 120
PERFUSION TIME (MINS)


PLATELETS %
N = 120
PROTAMINE
PERFUSION TIME (MINS)


PLASMA
Hb
(Mg/100ml)
N = 200
PERFUSION TIME (MINS)


PLATELETS %
N = 200
PERFUSION TIME (MINS)


PLATELET FUNCTION %
N = 200
DAY 1
DAY 2
PERFUSION TIME (MINS)

Discussion

All patients need intensive care treatment after cardiopulmonary bypass, and especially after longer periods of extracorporeal circulation. Hemorrhagic problems, poor peripheral circulation, and organ dysfunction still all too frequently occur. We should all realize that these disturbances are not caused by the operation itself, but by the consequences of the extracorporeal circulation of blood.[6] One of the main factors influencing this is blood trauma, and, more specifically, platelet damage.

The preservation of platelet numbers and function, found during this study, is really quite remarkable. In particular, there was no initial decrease at the start of bypass, caused by the first blood-material contact. We were concerned at the onset of the study as to whether the bi-level cross-flow design may in fact cause problems, but those fears were totally unfounded.

In conclusion, the Shiley M-2000 Membrane proved to be very hemocompatible, resulting in the low levels of blood loss seen postoperatively. As we feel the M-2000 to be very hemocompatible, our attention should be focused on eliminating other factors which damage blood, like cardiotomy suction and protamine administration.

Standard Prime Used for M2000 Membrane System

1,500 ml	Ringers Lactate
500 ml	Dextrose 5%
50 mg	Heparin
1 mmol/Kg	Sodium Bicarbonate
5 mmol	Magnesium Chloride
15 g	Mannitol

References

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Question from the Audience

Question: Joel Davis, South Bend, IN: What platelet function study did you use?
Response: ADP-induced aggregation study.