Prevention of Platelet Adhesion to Extracorporeal Surfaces

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Abstract

Both exsanguination and thrombogenic complications pose threats to the life processes of post-operative patients who have undergone cardiopulmonary bypass. Platelet extraction by extracorporeal tubing contributes significantly to these risks.

This study demonstrates platelet adhesion to polyvinyl chloride and silicone rubber. Experiments were carried out by preparing extracorporeal circuits for three dogs. Polyvinyl chloride and silicone rubber were chosen because of their widespread use in open heart surgery. Subsequent spectrophotometric analysis revealed protein adsorption in albuminized and nonalbuminized circuits. Pre-bypass recirculation of an albuminized prime for at least thirty minutes effectively reduces platelet adhesion to tubing surfaces during bypass.

Introduction

Since polyvinyl chloride and silicone rubber contain chloromethyl and ether groups respectively, the contact surfaces of these polymers are negatively charged. Naturally, positively charged proteins become bound by electrostatic interactions with the surface molecules of the polymer to form a protein monolayer. It can be demonstrated that if these polymeric surfaces are “pre-coated” with albumin prior to blood contact, then further adhesion of other plasma proteins is effectively inhibited. Albumin adsorption proceeds linearly indicating simple first order bimolecular cation exchange. The rate is limited by amphoteric orientation of aqueous proteins. The saturation point is limited by the adsorption strength as defined by the acidity of the hydrated polymer surface.

Non-albuminized tubing allows globulins, glycoproteins, lipoproteins and albumin to adsorb to the surface. Platelet membrane enzymes adhere to plasma proteins containing six oligosaccharide chains, which are not found in albumin. Thus, platelet collisions with other adsorbed plasma proteins precipitate platelet extraction, the events comprising local thrombogenesis and distinct embolization which are major concerns of post-operative morbidity. The mechanisms of protein adsorption and platelet adhesion are shown in Figures 1 and 2.

Methods

For in vitro study, a typical bypass circuit was prepared for recirculation. One quarter inch I.D. silicone rubber tubing was connected to the arterial outlet port of a pediatric oxygenator and carried through a roller pumphead, distal to which ¼” I.D. polyvinyl chloride tubing was attached to complete a recirculation loop to the venous inlet port of the oxygenator. The ¼” tubing was interrupted by ten pairs of “Y” connectors to provide time sequential tubing samples for adsorption.

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analysis. The circuit was primed and debubbled with 800 cc of 25% Ringer's Lactate in 0.9% saline. Additions of 40 cc 20% mannitol (2 cc/kg) and 20 mEq sodium bicarbonate (1 mEq/kg) were added to represent similar additions in the following in vivo study. Next, 160 cc 25% bovine albumin was added to provide a 5% dilution in the primed circuit. Recirculation at 37°C continued for 200 minutes at 1 L/min flow. Tubing samples were clamped and removed every 20 minutes. Adsorbed protein was removed by placing the measured samples in a solution of 1% alkylanyl polyether alcohol in 0.9% saline in a 25°C water bath for 48 hours. Subsequent spectrophotometric analysis was carried out to determine albumin adsorption.

Similar circuits without the "Y" connectors were prepared for three dogs (20 kg ± 1.0), using 90 cm of ½" I.D. silicone rubber tubing, and 200 cm of ⅜" in I.D. polyvinyl chloride tubing. One circuit was albuminized and recirculated for 40 minutes. A dog, heparinized at 300 u/kg, was cannulated and subjected to bypass for 60 minutes at 37°C. Platelet counts were measured before and after bypass. Another circuit was albuminized and recirculated for 5 minutes. A second heparinized dog was subjected to bypass, and platelet counts were done identically. For a bypass on a third dog, another circuit was prepared with crystalloid solutions only and platelet counts were also measured.

**Results**

The results of the in vitro test describe albumin adsorption in ug/cm² with time, for polyvinyl chloride and silicone rubber tubing as shown in Figure 3. Silicone rubber is saturated more quickly and heavily than polyvinyl chloride.

Results in the in vivo test are in Figure 4. For all three dogs, pre-bypass platelet counts were found to be $250 \times 10^3$/mm³. Post-bypass platelet counts were found to be 210, 130 and $122 \times 10^3$/ml, respectively, for the three dogs as in Figure 4, showing platelet extraction of 16%, 48%, and 51%, respectively. The coated circuit recirculated for 40 minutes showed the least platelet extraction.

**Discussion**

Galactosyl transferase, glycosyl transferase, sialy transferase, and N-acetyl neuramic acid transferase are platelet membrane bound enzymes which selectively catalyze reactions with oligosaccharides found in plasma proteins other than albumin, causing platelet adhesion to globulins, glycoproteins, and lipoproteins. Also, coagulation factor XII readily adsorbs to polymeric surfaces. Preliminary coating of extracorporeal surfaces with albumin effectively reduces post-bypass platelet depletion. Further studies should measure post-bypass platelet function as well.

Obviously, the smallest patients, relative to standardized tubing and oxygenator sizes, are at the greatest risk from polymer platelet extraction. Average pediatric circuits present 0.5 m² of surface area to the perfusate; adult circuits are about 1.0 m². These estimates represent only arterial and
FIGURE 3. Recirculation of an albuminized prime.

FIGURE 4. Platelet loss in circuits primed with albuminized (coated) and crystalloid (non-coated) solutions.
venous lines and an oxygenator. Use of other blood return, transfer and delivery lines, and devices (filters, bubble traps, reservoirs and heat exchangers) will increase blood contact area.

In this experiment, pre-bypass recirculation of a 5% albuminized prime for at least 30 minutes limits post-bypass platelet loss from a control of 50% to nearly 16%. Thrombogenic response at the polymer surface will be similar. Even though this conclusion relies on the study of one 0.5 m² dog in a test circuit of 0.5 m² contact area at 37°C for a 60 minute bypass, there should be minimal error in extrapolating the results to human patients. In fact, demonstrably predictable platelet loss can be prevented by pre-coating contact surfaces with 5% albumin solution (Fig. 5).

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References