
Hemofiltration as an Adjunct to Cardiopulmonary Bypass for Total Oxygenator Volume Control

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Abstract

A comprehensive literature review of hemofiltration (HFT) and subsequent application to cardiopulmonary bypass is discussed. Any existing hypervolemic situation is an indication for HFT. No contraindications for HFT are known when used in conjunction with bypass. A detailed methodology as well as practical guidelines are presented. Specific details associated with HFT have been addressed including choice of diafilter, ultrafiltrate composition, hemoconcentration, hemolysis and other blood damage, acid-base effects, heparin clearance, loss of proteins and amino acids, acidemia, and rebound hyperkalemia.

Introduction

It is the intent of this publication to introduce the concept of hemofiltration (HFT) to cardiopulmonary bypass (CPB) by literature review. The theory behind and clinical application of HFT during bypass as well as specific indications and contraindications and guidelines for use will be discussed.

Hemofiltration was clinically introduced as an adjunct to hemodialysis for severe fluid overload.^{1,2} Circulation of blood through a diafilter (a modified dialyzer) with vacuum applied to the dialysate side to create a high transmembrane pressure (TMP) was found to remove remarkable amounts of fluid.³ However, during this process of fluid removal, solutes small enough to pass through the membrane pores are also removed, the driving force being the pressure gradient rather than a concentration gradient. This technique allows control in removal of both low molecular weight plasma solutes as well as fluid.

The application of HFT to CPB has much the same

indications as in fluid overload from chronic renal failure. Oxygenator volume can be controlled with HFT especially in conditions of excessive hemodilution. Large amounts of cardioplegia, high circulating blood volumes, pre or peri-pump oliguria or anuria, or inadvertent acquisition of disposable fluids all lead to excessive oxygenator levels which may be easily removed with HFT.

Post-bypass hemoconcentration of red cells and clotting factors by the recirculation of the remaining oxygenator blood through a diafilter is possible. The final product of this concentration process may be more physiological than that offered by centrifugal blood processing devices.

Materials and Methods

Hemofiltration during CPB is a simple process if the proper preparations are made in advance. An option is presented here where one can either pump the HFT blood or not. In either case, the perfusionist should be familiar with the hemofilter. The Cordis units are packed in a glycerin compound to maintain fiber moisture during storage. This glycerin *must* be rinsed and discarded with at least 500 cc of normal saline prior to use. Failure to do so may result in severe hemolysis with secondary acute renal failure.⁴

If the perfusionist elects to pump the HFT blood, the HFT subcircuit must then be pre-measured, assembled, and sterilized. During the set-up of the CPB circuit, a sterile capped six-inch piece of 1/4" I.D. PVC tubing should be attached to the coronary perfusion port of the oxygenator allowing easy access for the HFT subcircuit. When priming the CPB circuit, this six-inch line should be carefully de-bubbled and clamped with a screw clamp. Using a tubing clamp should be avoided as it can be accidentally dislodged resulting in a rapid draining of the blood volume in the arterial reservoir. Once the decision has been made to use HFT, the pre-assembled circuit is easily connected to the CPB circuit. (Figure 1).

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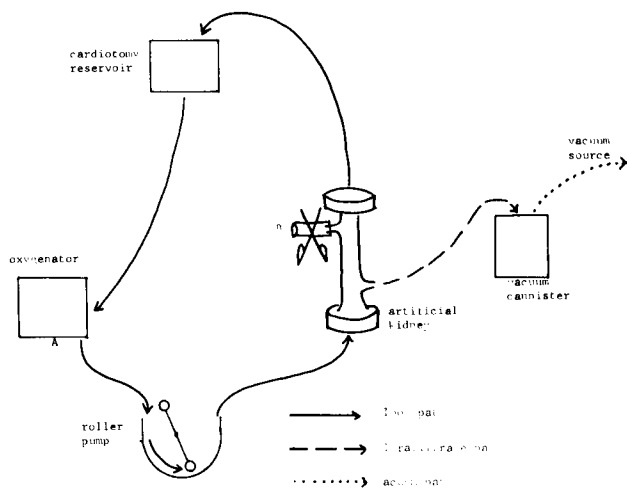


FIGURE 1. This is a block diagram of a circuit used to pump blood for hemofiltration during cardiopulmonary bypass. Blood is pumped from the coronary outlet (A) of the oxygenator via the pump head to the artificial kidney. The upper dialysate port is sealed with a piece of clamped $\frac{1}{2}$ " tubing (B) and the lower dialysate port is connected to a vacuum cannister where the ultrafiltrate is measured. The hemoconcentrated blood leaves the diafilter and then is either emptied into a cardiotomy reservoir or directly into the oxygenator.

Blood is pumped from the coronary port via a roller head to the diafilter^a and emptied into the cardiotomy reservoir. The upper dialysate port is sealed and the lower dialysate port is connected to vacuum.

The HFT circuit requires no special priming techniques. Care should be taken to ensure that the direction of blood flow is away from the oxygenator, avoiding accidental air embolism to the patient. The blood flow rate should be kept constant at about 200 cc/min and the TMP maintained at about 500 mmHg. Ultrafiltrate is then measured in the vacuum cannister.

The alternative to pumping the HFT blood is not pumping it, which leads to a somewhat simpler circuit design (Figure 2). In this case, the diafilter is connected to the CPB circuit by the use of large bore monitoring lines (for example Cobe Laboratories Catalog Number 26-750-000).^b These particular lines have a male leur lock connection on one end and open $\frac{3}{16}$ " tubing on the other. The leur lock end should be connected to a stopcock where the arterial filter bleed line is also fed. The open end should then be connected to the diafilter and the outflow of the diafilter connected the same way with the remaining leur either into the oxygenator or

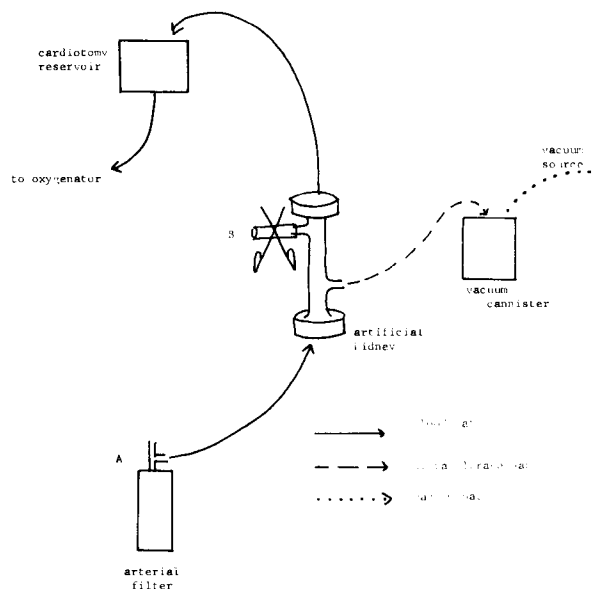


FIGURE 2. This is a block diagram of a circuit used to retrieve blood from the arterial filter for hemofiltration during cardiopulmonary bypass. A large bore dialysis monitoring line is connected to a stopcock (A) directly on the arterial filter. The stopcock is turned to allow blood to flow from the filter to the artificial kidney. The upper dialysate port is sealed with a piece of clamped $\frac{1}{2}$ " tubing (B) and the lower dialysate port is connected to a vacuum cannister where the ultrafiltrate is measured. The hemoconcentrated blood leaves the diafilter and then is either returned to a cardiotomy reservoir or directly into the oxygenator.

cardiotomy reservoir. Blood flow through the diafilter is then a function of the arterial line pressure. Vacuum should be connected to one of the dialysate ports and the other port sealed off.

Discussion

The glomerulus of the natural kidney is a hemofilter and all metabolites which traverse it and which are not reabsorbed or secreted by the tubules are cleared from the bloodstream at the same rate.⁵ While the idea of artificial hemofiltration was first discussed in 1928,^{6,7} the application of this technique for the replacement of renal function has awaited the availability of synthetic membranes with appropriate hydraulic permeability and solute retention properties.⁵ In 1947, Alwall described the first artificial kidney in which the principles of HFT were applied for removal of water and sodium from over-hydrated patients.⁸ The use of HFT as it is known today for the treatment of fluid overload and blood toxemia in end-stage renal failure was pioneered by Henderson *et al* in 1967.^{9,10} The use of HFT with CPB is a topic yet to be firmly established.

Hemofiltration is known by several names in the

^a Cordis Dow C-Dak 3500, Cordis-Dow Corp., Concord, CA 94520

^b Cobe Laboratories, Lakewood, Colorado, 80215

literature. Ultrafiltration, hemo-ultrafiltration, diafiltration, or hemodiafiltration are all terms meaning the same thing. Hemofiltration is the name preferred due to its establishment in scientific literature and is therefore the term we will use.¹¹

Hemofiltration is fundamentally different from conventional dialysis. Dialysis is a diffusive process where smaller molecules diffuse more rapidly than larger molecules. HFT is a convective process where all the solutes transfer at the same rate. The driving force for HFT is the transmembrane pressure differential across the membrane. The value of TMP is determined from the sum of the positive pressure applied to the blood path and the absolute value of the applied vacuum. The limiting factor for solute removal in HFT is the membrane pore size. Large proteins and albumin will be retained on the blood side of the diafilter.

The ultrafiltration rate (UFR) is the rate at which effluent is removed from the blood in the diafilter. UFR is dependent upon TMP and the surface area of the diafilter. There is a linear increase in UFR with increasing TMP to a point. This point is where the UFR levels off as a function of the surface area of the particular diafilter. All toxins and solutes smaller than the cut-off of the membrane pore size are passed and those larger are retained.¹²

The choice of hemofiltration unit is usually made from parallel plate or hollow fiber diafilters.² Hollow fiber diafilters are the membrane of choice for HFT because of their intrinsically high ratio of surface area to volume, relatively low end-to-end pressure drop, and because they provide a simple and convenient method of obtaining thin channels required to minimize concentration polarization and thereby obtain high flux.¹² Plate or hollow fiber dialyzers can produce a medium HFT flux rate of about 25 to 35 cc/min with a TMP of about 500 mmHg.^{c,d,e} High flux rates of 50 to 75 cc/min are also available.^{f,g}

The application of HFT to CPB can be divided into pre, during, and post-bypass indications. Pre-bypass indications include oliguria or anuria and acute/chronic renal failure with resultant over-hydration and/or blood toxemia. During bypass, HFT is indicated with excessive oxygenator volume associated with ei-

ther a normal or abnormal hematocrit. Removal of cardioplegia volumes or simple hemoconcentration prior to the termination of bypass are other reasons to use HFT. A post-bypass indication is the hemoconcentration of the remaining pump circuit blood. There are no absolute contra-indications for use of HFT during bypass.

As an example of post-bypass hemoconcentration, if the termination hematocrit is 20% with 1000 cc of blood remaining in the circuit, then simple proportions can be used to make calculations. The red cell volume can be determined as twenty percent of 1000 cc, yielding 200 cc of RBC's. If the desired hematocrit is 60% with the 200 cc of RBC's, then the final blood volume would be 200 cc divided by 60% or 333 cc of blood. Thus 667 cc of effluent needs to be removed from the original 1000 cc. If the diafilter used has a flux rate of 50 cc/min, then the removal of 667 cc will take about thirteen and a half minutes of recirculation.

The effluent removed from the blood, referred to as either the filtrate, ultrafiltrate, or hemofiltrate, has been the subject of much investigation. This filtrate contains molecules with a molecular dimension below the membrane pore size. The concentration of the molecules is the same in both the filtrate and the plasma because this is a convective mass transport mechanism.^{5,13,14} The composition of this ultrafiltrate is entirely analogous to glomerular filtrate.¹ Leakage of some small proteins across the membrane has been documented.^{1,8,13}

Many advantages of HFT with respect to its application in renal failure have been documented.^{2,3,15,16,17,18,19} Of these, most can be inferred to be advantageous for use during CPB, although the theory and clinical application of HFT to CPB is not to be found in the literature.

The most obvious advantage of HFT is hemoconcentration. With hemodilution included among modern bypass techniques, diafiltration provides a simple method of reversal, when indicated. The removal of plasma water results in increased hematocrit, plasma albumin concentrations and plasma colloidal osmotic pressures.^{15,16,17,18} Plasma and extracellular volumes can be reduced.^{19,20}

Third spacing, which is physiologically similar to overhydration subsequent to renal failure is common to CPB. Ing *et al.* have proposed that the increased plasma oncotic pressure secondary to the increased concentration of plasma proteins promotes the absorption of edematous fluids.²

^c Cordis Dow C-Dak 2.5 or 3500, Cordis-Dow Corp., Concord, CA 94520

^d CF1500, Travenol Laboratories, Inc., Deerfield, Ill., 92705

^e PPD 1.6m² Cobe Laboratories, Lakewood, Colo., 80215

^f Gambro Ultradiffuser, Gambro, Inc., Barrington, Ill., 60010

^g Amicon Diafilter 66, Amicon Corp., Lexington, MA, 02173

Another complication associated with hemodilution during bypass is the ultimate dilution of the circulating clotting factors. Hemoconcentration of these factors may lead to a decrease in peri-, and post-operative blood losses and thus a decrease in the use of bank blood. Aside from removing the risks to the patient associated with blood administration, a tremendous cost advantage could develop.

In addition to the hemoconcentration virtue of HFT is the subsequent removal of small and middle molecular weight uremic toxins.³ In the instance of acute renal failure (ARF) on CPB, control of these toxins may alleviate further ARF and other toxic systemic complications.

Blood damage has been a point of concern when using HFT due to high TMP and high shear rates. However, in studies performed from conventional hemofiltration for renal failure the fact that plasma free hemoglobin has not been detected in significant amounts in either the effluent or the plasma would alleviate the concern.²¹ Silverstein has stated that the hemolysis encountered during HFT is in fact less than that encountered when using occlusive pumps currently in wide clinical use in hemodialysis.¹

There have been no reported changes in patient's blood gas/acid base status as a result of HFT.^{2,22} However, our results demonstrate a vacuum-induced respiratory alkalemia when the residual CPB circuit blood is repeatedly recirculated post-bypass for the purpose of hemoconcentration. We have observed no clinical effects on patient's acid-base status when the concentrated blood is returned. This is a point that may warrant further investigation.

Keshaviah *et al* have reported the use of HFT for more than one to two hours may result in a mild metabolic acidemia.²³ The pathophysiology of this acidemia has been suggested to be a depletion of plasma bicarbonate due to preferential movement of the anion into the ultrafiltrate. This movement is thought to be related to the Gibbs-Donnan phenomenon as a result of an HFT induced increase in plasma protein concentration. Lactic acidosis due to excessive HFT cannot be excluded.² Routine blood gas monitoring during bypass provides a constant monitoring of any possible acidemia.

Another point to be made is that concerning heparin. When using a conventional hemodialyzer modified for HFT, the membrane pore size is less than the size of the heparin molecule. However, if using a true diafilter (membrane pore size 40,000–45,000 mw) the heparin

molecule (16,000 mw) is cleared at the UFR.^{12,18} Therefore, if HFT via a true diafilter is used during CPB, especially during the rewarming phase of the procedure, the perfusionist should be even more acutely aware of the anticoagulation status of the patient. Some allowance for this heparin clearance should be made at that time and also during post-bypass hemoconcentration.

The loss of amino-acids and proteins by HFT has received much attention. The protein loss problem raises many questions about the loss of intermediate molecular weight solutes normally retrieved by the kidney as well as their importance to metabolism.^{14,25,26,27} This protein loss is really only significant if they are irreplaceable. Dog and goat studies performed in attempt to correlate any depletion syndromes to the protein loss have yielded no clinical significance^{28,29} even after six months of maintenance HFT.³⁰ The total protein loss during forty-five minutes of HFT on bypass does not even approach that of six months of maintenance HFT. Quellhorst has found the amino-acid loss to be dependent only on plasma levels, as expected, amounting to a loss smaller than by peritoneal dialysis and insignificantly higher than hemodialysis.²⁴ Friedman has found the loss to be clinically "tolerable."¹¹

The phenomenon of rebound hyperkalemia has also been found to occur when HFT exceeds a total volume of three to five liters.³¹ The reason for such an effect is obscure. It is conceivable that such a hyperkalemia may be caused by excessive hemolysis,² acute stimulation of alpha adrenergic receptors,³² or the exit of potassium from the intracellular compartment as a result of extracellular dehydration. Regardless of cause, serial potassium levels should be closely monitored, especially in conjunction with the use of a hyperkalemic cardioplegia during bypass.

The use of HFT has certain advantages over external cell centrifugation/processing devices. First, from a cost point of view, HFT requires only the dialyzer, vacuum cannister, tubing and connectors amounting to less than thirty-five dollars per case. No capital expense is required. This is about ten dollars less per procedure than for the Haemonetics Cell Saver^h disposables alone. Both HFT and centrifugation require about the same set-up time. The true distinction lies in the final product. HFT yields a product of re-concen-

^h Haemonetics Corporation, Braintree, MA, 02184

trated whole blood with formed elements. Centrifugation for bypass volume reduction yields only packed red cells. Both procedures help to eliminate plasma toxin build-ups.

In addition to the points made in the Methods and Materials section; the authors have compiled some practical guidelines for use. First, the transmembrane pressure should be limited to a maximum of 700 mmHg to minimize hemolysis with resultant hyperkalemia.^{2,33} Ing has suggest that this TMP not exceed 500 mmHg and that this be achieved by maximizing the vacuum of Zhe negative pressure side of the diafilter, as opposed to increasing the positive pressure with a screw clamp on the outflow side. Blood will not be excessively squeezed through constricted channels and, therefore, less trauma to the red cells will result.² Increasing the positive pressure increases the shear force, which is more hemolytic.

Finally, the blood flow rate should be limited to about 200 cc/min. Blood flow rate influences the UFR by both altering the shear force at the luminal membrane surface and by varying the rate of plasma water delivery to the membrane.¹ The shear force is proportional to the flow rate and should be held at this optimal level giving maximal results with minimal trauma.

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