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.\(^1\) 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.\(^2\) 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 \(\frac{1}{4}\)" 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).
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 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). These particular lines have a male leurr lock connection on one end and open $\frac{1}{16}''$ tubing on the other. The leurr 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 leurr either into the oxygenator or 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. While the idea of artificial hemofiltration was first discussed in 1928, 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. 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. 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. The use of HFT with CPB is a topic yet to be firmly established.

Hemofiltration is known by several names in the
Ultrafiltration, hemo-ultrafiltration, di­
afiltration, 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 differ­
ential 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.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 con­
centration polarization and thereby obtain high flux.12
Plates 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.4,6,9 High flux rates of 50 to 75
cc/min are also available.1,8

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 oxygen volume associated with ei­

cordis dow c-dak 2.5 or 3500, cordis-dow corp., concord, ca
49530
4 cf1500, travenol laboratories, inc., deerfield, ill., 92705
4 ppd 1.6m² cobe laboratories, lakewood, colo., 80215
4 gambro ultradiffuser, gambro, inc., barrington, ill., 60010
4 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. 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. 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.

There have been no reported changes in patient’s blood gas/acid base status as a result of HFT. 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. 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. Routine blood gas monitoring during bypass provides a constant monitoring of any possible acidemia.

Another point to make 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. 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. 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 even after six months of maintenance HFT. 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. Friedman has found the loss to be clinically "tolerable."

The phenomenon of rebound hyperkalemia has also been found to occur when HFT exceeds a total volume of three to five liters. The reason for such an effect is obscure. It is conceivable that such a hyperkalemia may be caused by excessive hemolysis, acute stimulation of alpha adrenergic receptors, 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 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-

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b Haemonetics Corporation, Braintree, MA, 02184
trated whole blood with formed elements. Centrifuga-
tion for bypass volume reduction yields only packed
cells. Both procedures help to eliminate plasma
and that this be achieved by maximizing the vacuum
to minimize hemolysis with resultant hyperkalemia.\(^2,3\)

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 mem-
brane surface and by varying the rate of plasma water
delivery to the membrane.\(^1\) The shear force is propor-
tional to the flow rate and should be held at this optimal
level giving maximal results with minimal trauma.

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