Fluid Uptake by Patients During Cardiopulmonary Bypass: An Oxygenator Dependent Phenomenon

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INTRODUCTION:

It has been reported that wide discrepancies exist in the positive fluid balance to the patient after cardiopulmonary bypass utilizing crystalloid hemodilution[1]. With the advent of the hemodilution technique in cardiopulmonary bypass, volume loading of the patient has become a major concern to those involved in maintaining adequate fluid balance in the patient.

A significant difference in the amount of crystalloid solution necessary to maintain the patient with adequate perfusion was first noted between two bubble oxygenators being used clinically for the past two years at the Barnes Hospital, St. Louis, Missouri. This clinical study was established to determine the degree of difference of positive fluid balance to the patient as a result of cardiopulmonary bypass. The objective of this study was to test the hypothesis that positive fluid balance to the patient following cardiopulmonary bypass is a function of the type of oxygenator used, provided all other variables remain equal in standard, routine practice.

MATERIALS AND METHODS:

In this clinical study, one hundred four patients were alternated and equally divided into two groups: Group I was perfused with a Harvey H-1000 oxgenator*, and Group II was perfused with a Galen Optiflo 200 oxygenator**. Each group consisted of thirty-two patients who had valve replacements and twenty patients who had coronary vein bypass procedures (Table 1). All perfusions were identical with respect to the amount and type of prime solution used (2 liters of 5% Dex. in 0.9% NaCl). Furthermore, no patient received blood or colloid solutions during the perfusion. Any additional volume needed during the cardiopulmonary bypass procedure was crystalloid solution. During induction, all coronary vein bypass patients received fifty grams of salt poor albumin and one liter of Ringer's Lactate, while the valve patients received no colloid or crystalloid solutions. During the cardiopulmonary bypass procedures, all patients were maintained hypothermic at $29 \pm 1°C$. and all perfusions were greater than forty minutes in duration ($x = 103 \pm$ S.D. 35 min.). A net fluid gain was computed for each patient and normalized into terms of ml./minute of perfusion/square meter of body surface area (ml./min./M^2) (Appendix). There was a statistically equal distribution between the two groups of patients with respect to age, sex, weight, surface area, and length of perfusion.

During perfusion, the volume of additional crystalloid solution added to the extracorporeal circuit, the volume of additional crystalloid administered by the anesthesia team, and the losses of fluid from the suction, sponges, drapes, urine, and the volume remaining in the oxygenator at the termination of perfusion were recorded. Appropriate corrections and calculations were performed on these data. Additionally, mean arterial blood pressure, perfusion flow rate, duration of perfusion, blood gases, and serial hematocrits were measured and recorded. The results were tabulated and analyzed statistically using the unpaired Student T test.

TABLE I

Distribution of Type of Operation

Types of Cases	No. of Optiflo Cases	No. of Harvey Cases
AVR	14	12
MVR	11	11
Double Valve	6	6
Valve/CVBP comb.	1	3
CVBP × 2	12	11
CVBP × 3	7	8
CVBP × 4	1	1

RESULTS:

Use of the Galen Optiflo oxygenator resulted in less than half the positive fluid gain found with the Harvey oxygenator (5.78 ± 3.6 vs. 11.97 ± 4.3 ml./min./m^2) ($p<0.001$). A detailed statistical analysis of the two groups with respect to the type of operative procedure, sex, weight, length of perfusion, and fluid gain and loss is shown in Table II. The results indicate "volume uptake" is independent of patient weight, sex, and type of procedure. Patients perfused with the Harvey H-1000 oxygenator required 31% more crystalloid solution to maintain a mean blood pressure of 71.6 mmHg. at a mean flow rate index of 2.64 L./min./M^2 and had 30% less urine output than those perfused with the Galen Optiflo 200 oxygenator. A significant difference in positive fluid balance was found between the two study groups regardless of the length of perfusion. However, there appeared to be a gradual, though not statistically significant decrease in the amount of positive fluid balance with increasing length of perfusion within both groups. The differences in the central venous pressure during the perfusion and the pump flow indices between the two study groups were not statistically different. However, there was a significant difference in the mean arterial pressure between the two groups (Group I = 71.66 mmHg. vs. II=81.44 mmHg.) ($p<0.001$). Pre- and post-bypass hematocrits were statistically not significantly different between the two groups.

Each subset within an oxygenator group was examined and no statistically significant differences were noted between subsets. The Galen Optiflo 200 oxygenator group demonstrated no significant difference in the results with respect

TABLE II

Analysis of Positive Fluid Balance for Patients in the Galen and Harvey Oxgenator Groups

(ml./min./M²)

Variable	*Galen (n=52)*	*Harvey (n=52)*	*Probability (p)*
	(n) Mean ± S.D.	(n) Mean ± S.D.	(p)
Total Cases	(52) 5.78 ± 3.66	(52) 11.97 ± 4.37	<0.001
Coronaries	(20) 5.41 ± 3.12	(20) 11.92 ± 4.26	<0.001
Valves	(32) 6.13 ± 4.13	(32) 12.00 ± 4.50	<0.001
Males:			
Coronaries	(17) 5.74 ± 2.61	(18) 12.46 ± 4.14	<0.001
Valves	(16) 5.47 ± 4.22	(13) 13.39 ± 4.38	<0.001
Females:			
Coronaries	(03) 2.37 ± 2.40	(02) 14.55 ± 2.47	<0.01
Valves	(16) 5.24 ± 2.06	(19) 11.05 ± 4.44	<0.01
Patient Wgt. (kg):			
21-40	(02) 5.05 ± 1.34	(0)	
41-60	(11) 5.59 ± 3.70	(21) 12.32 ± 3.73	<0.001
61-80	(23) 6.63 ± 4.10	(20) 10.37 ± 4.45	<0.01
≥81	(16) 4.79 ± 3.09	(11) 14.17 ± 4.57	<0.001
Length of Perfusion (min.):			
<60	(03) 3.63 ± 2.76	(03) 16.47 ± 2.83	<0.01
60-90	(22) 7.37 ± 4.05	(16) 12.88 ± 4.65	<0.001
91-120	(18) 5.27 ± 2.41	(16) 12.28 ± 4.31	<0.001
<120	(09) 4.62 ± 3.84	(17) 10.03 ± 3.65	<0.01
Fluid into Patient	(52) 18.56 ± 5.74	(52) 24.25 ± 6.39	<0.001
Urine out of Patient	(52) 7.51 ± 5.63	(52) 5.35 ± 2.84	<0.05
Avg. Arterial Blood Pressure (mmHg.)	(52) 81.44 ± 13.77	(52) 71.66 ± 11.39	<0.001
Pump Flow Index (L./min./M)	(52) 2.74 ± 0.46	(52) 2.64 ± 0.38	N.S.*
Avg. Pump Time (min.)	(52) 98.39 ± 27.92	(52) 107.28 ± 42.13	N.S.
Avg. Pre-bypass Hct. (%)	(52) 35.00 ± 5.49	(52) 36.57 ± 6.22	N.S.
Avg. Post-bypass Hct. (%)	(52) 26.33 ± 5.19	(52) 25.79 ± 4.14	N.S.

*N.S. = p value >0.05

to the type of operation performed (Coronary cases = 5.41 ± 3.12 vs. valve cases = 6.13 ± 4.13 ml/min./M^2) nor was there a difference in the Harvey H-1000 oxygenator group (Coronary cases = 11.92 ± 4.26 vs. Valve cases = 12.00 ± 4.50 ml/min./M^2). Fluid uptake was not sex dependent for patients undergoing valve replacement. (Galen group - male valve cases = 5.74 ± 2.61 vs. female valve cases = 5.24 ± 2.06 ml/min./M^2). (Harvey group - male valve cases = 13.39 ± 4.38 vs. female valve cases = 11.05 ± 4.44 ml/min./M^2).*** Additionally, the distribution of patient weight within the same oxygenator group did not reveal any significant differences.

DISCUSSION:

There are a number of important reasons for regulating the amount of hemodilution. Patients who develop edema prior to or during cardiopulmonary bypass need to be diuresed strenuously to avoid a possible circulatory overload, as described by Neville[2]. Strenuous diuresing of edmatous patients may produce electrolyte imbalances which are difficult to control[3]. Excess hemodilution during cardiopulmonary bypass can dilute the clotting factors enough to cause a coagulopathy[17]. Excess hemodilution of the vascular compartment could lead to a hemoglobin level low enough to produce an insufficient arterial blood oxygen content, leading to a hypoxemic condition in the tissues, especially in those patients exhibiting a limited cardiac reserve[19]. The lower limit of safety is a hematocrit level of 20% at normothermia[4]. Below this hematocrit at 37°C., the oxygen supply may be less than the amount of oxygen needed to replenish the oxygen consumed by the tissues. Other than the addition of red blood cells, the best way to ameliorate this condition during cardiopulmonary bypass is to either increase the perfusion flow rate or to decrease the body temperature.

Fluid movement in and out of the vascular compartment is controlled primarily by two factors during cardiopulmonary bypass: central venous pressure and colloid osmotic pressure. With increasing hemodilution of the patient, the colloid osmotic pressure in the vascular compartment will decrease causing the movement of fluid out of the vascular system in order to restore the balance of oncotic pressure in the system[5]. Also, any increase in the central venous pressure during cardiopulmonary bypass which usually occurs as a result of a change in the hydrostatic pressure gradient from the patient to the pump or a restriction of the outflow of the caval cannulae, creating peripheral pooling, will cause fluid movement into the interstitial compartment[6,7]. One additional cause of the interstitial fluid build up is the sluggish activity of the peripheral lymphatic system occurring during cardiopulmonary bypass. With the patient anesthetized and paralyzed, and perfused with non-pulsatile blood flow and hypothermia, the lymphatic pump is nearly inoperative due to a lack of muscle contraction, normal body movements, pulsatile blood flow, and tissue motion. Additionally, the lymphatic system is the only way to return plasma protein leakage into the interstitial compartment back to the circulation[8]. A slow build up of protein can occur in the interstitium due to the sluggish lymph flow[9]. As the cardiopulmonary bypass patient becomes more edematous, the interstitial fluid pressure rises from −7.0 mmHg. to 0 mmHg., and any additional increase in the interstitial fluid pressure above 0 mmHg. causes an extremely rapid increase in the interstitial fluid volume[10].

The results of this clinical study demonstrate highly significant differences between the two oxygenators with respect to positive fluid balance to the patient. The conclusion that is made from these results is that the Galen Optiflo 200 oxygenator resulted in approximately half the positive fluid uptake compared to those patients who had a Harvey H-1000 oxygenator used during perfusion. Thus, the type of oxygenator used during cardiopulmonary bypass can exert great influence on the positive fluid balance to the patient during perfusion.

The two variables which played the key role in the net fluid gain to the patient were the fluid into the patient and the urine output of the patient. The Galen Optiflo 200 oxygenator group required significantly less fluid to the patient ($p<0.001$) and these patients excreted significantly more urine ($p<0.05$) than did the Harvey H-1000 oxygenator group.

A conclusion that can be definitely drawn about the results of the variables examined within a given oxygenator group is that the type of operation, patient sex and weight, and the length of perfusion does not significantly govern the amount of positive fluid balance of the patient.

A significant difference between the mean arterial blood pressures of the two groups deserves comment. Hemodilution generally reduces mean arterial blood pressure by decreasing viscosity of the blood; hence, reducing the systemic vascular resistance[14,15,16]. Although it is generally known that low mean arterial blood pressure and use of a non-pulsatile flow will cause an increase in the rate of movement of fluid into the interstitial region, there have been no animal or clinical studies which demonstrate that, under the conditions of these perfusions, there is a significant difference in the rate of interstitial fluid volume accumulation at a mean blood pressure of 71 versus 81 mmHg.

The reasons for the observed differences in positive fluid balance between the two oxygenator groups is not clear. One hypothesis is that a greater production of microemboli may have occurred with the Harvey oxygenator as compared to the Galen Optiflo oxygenator[11]. Vascular blockade, i.e. ischemic injury, is associated with interstitial and intracellular edema in all organs. A second hypothesis is that there was a difference in the amount of damage to the cellular components and proteins in the blood. An increase in the concentrations of histamine, serotonin, or other vasoactive polypeptides during cardiopulmonary bypass have been reported[17,20]. These substances, in sufficient quantity, can affect the transport of fluid across the capillary membrane in two different ways. First, they cause a dilatation of the capillary pores which would cause an increase in the movement of protein across the capillary membrane into the interstitium[13]. Second, they have a powerful vasodilatory effect on the arteriolar end of the capillary bed with concurrent constriction of the venules[13]. Also, the release of significant quantities of serotonin has been shown to cause a vasoconstriction of the renal blood vessels, thereby reducing the urine output[17], p. 265; 18.

SUMMARY:

On the hypothesis that positive fluid balance of the patients following cardiopulmonary bypass is a function of the type of oxygenator used, a study was undertaken with one hundred four patients. Each of two equal groups were per-

fused with a bubble oxygenator. Group I was perfused with the Harvey H-1000 oxygenator and Group II was perfused with the Galen Optiflo 200 oxygenator. Both groups were otherwise similar in all respects. It was found that the use of the Galen Optiflo 200 oxygenator resulted in less than half the positive fluid gain than when the Harvey H-1000 oxygenator was used. The Galen oxygenator group had a mean positive balance rate of 5.78 ± 3.66 ml./min./M^2 versus a mean positive balance rate of 11.97 ± 4.37 ml./min./M^2 for the Harvey oxygenator group ($p<0.001$).

Two hypothetical explanations are suggested to account for this phenomenon: a higher mecroemboli blockage, on the one side, and a large histamine-like substance release from a higher blood damage.

APPENDIX

Calculation for the net fluid gain or loss during perfusion: These data were recorded only for the time period of perfusion.

Crystalloid into the Patient

1) Prime solution; composition and volume
2) Additional crystalloid fluid to the pump; composition[5] and volume
3) Intravenous fluids given by anesthesia[1]; composition and volume

Crystalloid from Patient

1) Urine
2) Insensible loss[2]
3) Sponges and Drapes[3]
4) Volume remaining in the pump[4]
5) Suction[3]

[1]The volume of intravenous fluids given by anesthesia during perfusion was that required to maintain the monitoring catheters patent with a constant infusion rate system. This volume was 3.0 ml./hr./catheter, and was considered insignificant; therefore, these data were not used in the calculation.

[2]Insensible loss was considered insignificant with the use of hypothermia, humidity in the ventilation system, and topical myocardial hypothermia. Therefore, it was not included in the calculations.

[3]In the sponges, drapes and suction, the water loss was calculated from the hematocrit. The net loss for sponges and drapes during perfusion was less than 1% in all cases; therefore, it was used as a constant for all cases (200 ml./case for sponges and drapes).

[4]The volume left in the pump was measured and all but the red cell volume was considered crystalloid. Crystalloid volume = Total volume in the pump × (1 - Hct. in% × 10^{-2}). There was no statistical significant difference between the two groups for this variable.

[5]The composition of additional fluid was either 0.9% NaCl or Ringer's Lactate.

Example of a calculation for the net fluid gain or loss during perfusion

Crystalloid into the Patient

Priming Volume	= 2000 ml.
Additional Volume	= 2000 ml.
Intravenous Volume from Anesthesia - negligible	
Total Volume	= 4000 ml.

Crystalloid out of Patient

Urine Output	= 750 ml.
Insensible loss	= negligible
Sponges and Drapes	= 200 ml.
Suction	= 500 ml.
Volume left in Pump	= 400 ml.
Total Volume	= 1850 ml.

Fluid balance to the Patient = 4000 ml. − 1850 ml. = 2150 ml.

Perfusion time = 100 min.

Patient Body Surface Area = 1.5 M^2

Fluid Uptake Rate for this Patient = (2150 ml./100 min./1.5 M^2) = 14.33 ml./min./M^2

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***A comparison of the coronary patient cases between the sexes was not included in the results due to the very small number of female coronary patients in both oxygenator groups.