Technique

Avoiding Hyperoxemia at the Start of Cardiopulmonary Bypass While Optimizing Gas Flow and Temperature

Gerard J. Myers, RRT, CCP; Jean-Franç ois Ĺegaŕe, BSc, MD

QEII Health Sciences Center and IWK-Grace Health Center, Halifax, Nova Scotia, Canada

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ABSTRACT

There seems to be a wide range of practice in relation to the optimum oxygen setting before, and at the start of, cardiopulmonary bypass. Even manufacturers of blood oxygenators vary in their suggestions for this phase of extracorporeal circulation. Most of these suggestions are based on peak performance, Association for the Advancement of Medical Instrumentation (AAMI) standards, experience, and legal considerations. Therefore, suggested gas:blood flow ratios will vary from no gas flow at the start of bypass, to a ratio setting of 1:1. On the other hand, suggested inspired oxygen concentrations will generally vary between 0.80 to 1.0 at the start of cardiopulmonary bypass. In regard to perfusate temperatures before going on bypass, there are no clearly defined standards other than those of clinical preference. The manufacturer of the oxygenator used in this study clearly states in the operating instructions that gas flow should be proportional to blood flow at the start of bypass, and gas flow should be turned off when there is no fluid flow through the oxygenator.

The presence of hyperoxic perfusates and wide patient/perfusate temperature gradients at the start of bypass has been suspected in the appearance of gaseous microemboli during this critical period. Hyperoxemia during the bypass period is also implicated in the introduction of oxygen free radicals and nitric oxide into the hypoxic myocardium during cardioplegia delivery.

Presented here are the results of a randomized clinical study involving 39 adult patients undergoing cardiopulmonary bypass for the surgical treatment of coronary artery disease. All patients were randomly selected into five groupings. The first group had 1 L of gas flow through the perfusate before bypass, and bypass was then started with an FIO_2 of 0.80. The second two groups had no gas flow through the perfusate prior to bypass and a starting FIO_2 of 0.21. Groups 4 and 5 had 1 L of gas flowing through the perfusate and a starting FIO_2 of 0.21.

Results indicate that gas flow through Normosol R/Albumin perfusates will prevent the acidosis that is found in this solution when the system is previously flushed with carbon dioxide. Also, suggested high FIO_2 settings will produce hyperoxic perfusates at the start of cardiopulmonary bypass. However, the use of an FIO_2 of 0.21 at the start of bypass will produce normoxemic conditions that are both safe and reliable for the conduct of initiating cardiopulmonary bypass.

Address correspondence to:
Gerard J. Myers, RRT, CCP
Cardiovascular Perfusion
5th Floor O.R., QE II Health Sciences Center
NHI Site, 1796 Summer Street
Halifax, Nova Scotia, Canada B3H 3A7

INTRODUCTION

The process of cavitation is considered to be the spontaneous formation of gaseous vapor in a liquid that becomes stressed. Several factors are known to be part of this cavitation process, where gas is readily taken out of supersaturated solutions during cardiopulmonary bypass (CPB). These factors are temperature, oxygen content, Reynold's number, kinetic energy, hydrostatic pressure, cannula size, and flow rate (1). Temperature and partial pressure of oxygen (PO_2) of perfusates are two of the most frequently overlooked, but easily controlled, parameters that contribute to the cavitation process.

When such fluids as blood are supersaturated with oxygen, they are known to contain gaseous nuclei (1). Under such conditions, the cavitation process may occur at the aortic cannula tip as bypass begins. This may in part be attributable to the Bernoulli effect in the presence of laminar flow at this tip, or it may be created in the vortices of turbulent flow as blood leaves the cannula (1).

Despite careful and meticulous cannulation, microembolic events (MEE) have been recorded at the inception of CPB (2, 3). It is difficult to differentiate between gaseous or particulate microemobli during these periods, but the most likely cause of this activity is felt to be gaseous microemboli, created by supersaturated solutions and wide temperature gradients (4). In a randomized study of 48 patients undergoing CPB, Belboul and co-workers (5) showed a significant increase in morbidity when using hyperoxic PO_2s (190–300 mmHg), as compared to those cases using normoxemic PO_2s (80–112 mmHg) on bypass. In comparison to the normoxemic group, those managed with high PO_2s had a significantly increased period of postoperative ventilator support, increased bleeding, and increased blood product usage. This hyperoxemic group had a significant increase in arrhythmias, myocardial infarctions, and respiratory insufficiency. Liver enzymes and creatinine levels were found to be significantly lower in the group managed with low PO_2s. When compared to normoxemic management of CPB, the use of hyperoxic management has lead to reductions in vital capacity (VC) and the forced 1-second expiratory volume (FEF_1) during the postoperative period (6).

Abbruzzese and co-workers (7) used transesophageal echocardiography (TEE) to examine microbubble release in 20 patients. Results showed a constant flow of microbubble activity at both the start of CPB and throughout the entire bypass period when bubble oxygenators were used. When using membrane oxygenators, the release of microbubble activity was confined to the first 2 min after starting bypass. More specifically, that period during the infusion of priming fluid. Several other authors have noted the benefits of providing physiological PO_2s at the start of, and during the maintenance of CPB (4–6, 8–10).

Hyperoxemia was also found to be harmful during that phase of extracorporeal circulation when delivery of cardioplegia is taking place. Ihnken and co-workers (6, 9, 10) found that the reintroduction of hyperoxic blood (PO_2 of 400 mmHg) into hypoxic piglet hearts produced highly cytotoxic substances such as nitric oxide, peroxynitrite, and oxygen free radicals. Their conclusions were that reoxygenation of hypoxic hearts with hyperoxic blood (PO_2s > 150 mmHg) causes oxidant related damage to the mocardium that is characterized by lipid peroxidation.

Table 1: Study groups

Group	Pre-Gas Flow 4 min	Start-FIO_2	Bypass FIO_2	Bypass-Q/B
1	1	80%	80%	0.76:1.0
2A	Zero	21%	50%	0.75:1.0
2B	Zero	21%	80%	0.75:1.0
3A	1	21%	50%	0.78:1.0
3B	1	21%	80%	0.82:1.0

To maintain PO_2s greater than 250 mmHg, most present day practitioners initiate and maintain CPB with inspired oxygen concentrations (FIO_2) between 0.50 and 1.0. Perfusate temperatures before bypass can be anywhere between 25° and 37°C, depending on perfusionist preference to recirculate or turn off the main pump head after the arteriovenous loop is divided. Most clear or blood perfusates that are circulated in the arteriovenous loop before bypass are generally warmed to near normothermic temperatures. If manufacturer recommendations are then followed, these perfusates may be ventilated with FIO_2s of 0.8 to 1.0. When recirculation is then stopped to wait for the start of bypass, these supersaturated perfusates will rapidly drop in temperature and create ideal conditions for the creation of MEE at the start of bypass as cold hyperoxic fluid enters a warm body (3, 4). Under these conditions, release of emboli from the cannulation site can persist for as long as 2 to 10 min after CPB has started (11, 12). What we attempted to do was demonstrate that physiological PO_2s in the range of 100 to 200 mmHg are obtainable in prebypass perfusates with the use of an FIO_2 of 0.21, and that these PO_2s are also safe for the initiation and maintenance of CPB (13).

METHODS

After applying this technique in the laboratory setting and internal medical review, a prospective randomized clinical study was conducted on 39 adult patients undergoing CPB for ischemic heart disease. These cases were placed in 5 different groups (Table 1). All cases were done by the same perfusionist, using a clear prime and the Sorin Monolyth[a] hollow fiber oxygenator, which has been shown to have reliable and consistent oxygen transfer capabilities (8). Arterial filtration with the

a Sorin Biomedical, Irvine, CA

Table 2:

Group	Weight (kg)	Age Years	Oxy. Consump L/min	Patient Temp (C)	Perfusate Temp (C)
1	88.3 ± 29.7	69.8 ± 19.2	121.5 ± 67.5	34.8 ± 1.2	36.4 ± 0.2
2A	77.1 ± 36.9	65.9 ± 16.9	124.3 ± 71.7	35.0 ± 1.0	36.5 ± 1.0
2B	69.8 ± 7.2	66.3 ± 21.3	99.4 ± 31.6	34.8 ± 1.5	36.8 ± 0.8
3A	78.3 ± 19.7	68.6 ± 19.6	114.5 ± 34.9	34.9 ± 0.9	36.2 ± 1.6
3B	85.3 ± 26.3	58.4 ± 15.6	128.5 ± 59.2	35.2 ± 0.5	36.2 ± 0.8
Mean	79.8 ± 24.0	65.8 ± 18.0	117.6 ± 53.0	34.9 ± 1.0	36.4 ± 0.9

Autovent Plus (40 micron)[b] was used in all cases, and carbon dioxide (CO_2) was used to flush the entire bypass circuit for 3 min before priming.

The total priming volume for each CPB case was 1600 mL, which consisted of 1350 mL. Normosol R[c] and 250 mL of 5% normal serum albumin. No active cooling was used, and all patients were allowed to drift to a temperature of 30° to 32°C, while blood cardioplegia was delivered at a ratio of 4:1 and a temperature of 10° to 13°C.

Samples of the perfusate solution were drawn and analyzed just before going on bypass. Arterial blood gases were measured using the Alpha Stat method of blood gas analysis, with the exception of all PO_2s, which were corrected for temperature. Blood gases and electrolytes were analyzed using the Corning 278 Blood Gas Analyzer.[d] A bypass flow of 2.5 L/m^2/min was reached within 1 min after the start of bypass, and was maintained for the duration of the sampling period. Arterial blood gases were measured at the 1 min and 2 min interval after starting CPB. Arterial and venous blood gases were also taken 8 min after the start of bypass. Arterial and mixed venous saturations were constantly measured using the CDI 100 in line saturation monitor.[e]

GROUP 1 (N = 8)

CPB was started with a gas flow of 1 L/min and an FIO_2 of 0.8. After the start of bypass, the FIO_2 was maintained at 0.8, and the gas flow was adjusted to a mean gas:blood flow ratio (Q/B) of 0.76:1.0 (±0.12).

GROUP 2A (N = 8)

CPB was started with no (zero) gas flow and an FIO_2 of 0.21. Ten to 30 sec after the start of bypass, the FIO_2 was increased to 0.50, and the Q/B was adjusted to 0.75:1.0 (±0.07).

GROUP 2B (N = 7)

CPB was started with no (zero) gas flow and an FIO_2 of 0.21. Ten to 30 sec after the start of bypass, the FIO_2 was increased to 0.80 and the Q/B was adjusted to 0.75:1.0 (±0.06).

b Pall Biomedical, East Hills, NY
c Abbott Laboratories, North Chicago, IL
d Corning
e Sarns/3M Healthcare, Ann Arbor, MI

GROUP 3A (N = 8)

CPB was started with a gas flow of 1 LPM and an FIO_2 of 0.21. Ten to 30 sec after the start of bypass, the FIO_2 was increased to 0.50, and the Q/B was adjusted to 0.78:1.0 (±0.07).

GROUP 3B (N = 8)

CPB was started with a gas flow of 1 LPM and an FIO_2 of 0.21. Ten to 30 sec after the start of bypass, the FIO_2 was increased to 0.80, and the Q/B was adjusted to 0.82:1.0 (±0.14).

The mean age of this study group was 65.8 ± 18 years, and the mean body weight was 79.8 ± 24 kg (Table 2). After 8 min of CPB, using the following formula, mean oxygen consumption for the 39 patients was found to be 117.6 ± 53 mLO_2/min:

$$\text{Oxygen Consumption} = \text{Pump Flow} \times (aO_2 \text{ Content} - vO_2 \text{ Content}) \times 10$$

The temperature of all perfusate solutions was maintained at, or slightly above, the patient's body temeprature before going on bypass. As seen in Table 2, the mean perfusate temperature was 36.4 ± 0.9°C, and the mean nasopharangeal temperature was 34.9 ± 1.0°C.

STATISTICS

For statistical analysis, all PO_2 and pH values from groups 2A/2B and groups 3A/3B were compared to Group 1, which was considered to be our control group. These continuous variables were compared using Student's *t* test, with a *p* value of less than .05 considered to be significant. No adjustments were made for repeated comparisons.

RESULTS

Before going on bypass with Group 1, the perfusate was continuously circulated with a gas flow of 1 L/min and an FIO_2 of 0.8 (Table 3). This produced a prebypass solution that was not only hyperoxic (PO_2 499 ± 47.0 mmHg), but exhibited a normal pH of 7.39 ± 0.16, despite the acidic nature of albumin (pH 6.8). One, 2, and 8 min after the start of bypass, the pH

Table 3: (Group 1)

	pH	PO_2	PCO_2	HCO_3	B.E.	A.Sats.	V.Sats.
Perfusate	7.39 ± 0.2	499 ± 47.0	0	0	0	100 ± 0	0
Art 1 min	7.42 ± 0.1	332 ± 81	29 ± 12	20 ± 4	−3.0 ± 4	98 ± 1	78 ± 8
Art 2 min	7.45 ± 0.1	354 ± 81.0	30 ± 5.0	21 ± 3.0	−2.0 ± 6.0	98 ± 1.0	0
Art 8 min	7.47 ± 0.1	336 ± 71.0	37 ± 11.0	23 ± 4.0	1.0 ± 4.0	98 ± 1.0	0
Ven 8 min	7.43 ± 0.1	36 ± 3.0	36 ± 7.0	25 ± 3.0	1.0 ± 4.0	0	83 ± 3.0

Data are shown as the mean ± the standard error of the mean.

Table 4: (Group 2A)

	pH	PO_2	PCO_2	HCO_3	B.E.	A.Sats.	V.Sats.
Perfusate	6.88 ± 0.1	147 ± 13.0	17 ± 3.0	3.0 ± 1.0	−31 ± 3.0	97 ± 1.0	0
Art 1 min	7.39 ± 0.1	149 ± 68.0	34 ± 11.0	21 ± 4.0	−3.0 ± 3.0	97 ± 3.0	72 ± 12.0
Art 2 min	7.41 ± 0.1	149 ± 60.0	34 ± 10.0	22 ± 4.0	−2.0 ± 2.0	97 ± 3.0	0
Art 8 min	7.45 ± 0.1	132 ± 84.0	35 ± 9.0	24 ± 3.0	1.0 ± 4.0	97 ± 3.0	0
Ven 8 min	7.41 ± 0.1	34 ± 8.0	40 ± 6.0	25 ± 2.0	1.0 ± 4.0	0	76 ± 13.0

Data are shown as the mean ± the standard error of the mean.

Table 5: (Group 2B)

	pH	PO_2	PCO_2	HCO_3	B.E.	A.Sats.	V.Sats.
Perfusate	6.88 ± 0.1	153 ± 6.0	19 ± 8.0	4 ± 1.0	−30 ± 3.0	98 ± 1.0	0
Art 1 min	7.44 ± 0.3	311 ± 162	31 ± 9.0	19 ± 6.0	−5.0 ± 9.0	98 ± 5.0	78 ± 15
Art 2 min	7.40 ± 0.2	320 ± 83.0	32 ± 10	20 ± 4.0	−3.0 ± 3.0	98 ± 2.0	0
Art 8 min	7.44 ± 0.1	325 ± 33.0	34 ± 9.0	23 ± 5.0	0.0 ± 8.0	98 ± 1.0	0
Ven 8 min	7.41 ± 0.2	37 ± 12	38 ± 9.0	24 ± 5.0	0.0 ± 3.0	0	83 ± 9.0

Data are shown as the mean ± the standard error of the mean.

remained within normal values, and the arterial PO_2 was hyperoxemic throughout. Arterial saturations never dropped below 98%, and the venous saturation was 78 ± 8.0% after 1 min of bypass. The 8-min mixed venous sample indicated excessively high saturations at 83 ± 3.0%, which was most likely because the supply of oxygen was exceeding the patient's metabolic demands.

The perfusate in Group 2A (Table 4) showed a normal PO_2 (147 ± 13 mmHg) but was acidotic in nature with a pH of 6.88 ± 0.05. Despite the perfusate's acidic nature before bypass, the pH at 1, 2 and 8 min was normal, and the arterial PO_2 was consistently within the normal (normoxemic) values. The base excess and bicarbonate values follwed the same pattern as in Group 1, and the arterial saturations were 98% at all three sampling periods. Venous saturations after 1 min of bypass were 72 ± 12.0%, and after 8 min of bypass, they were recorded at 76 ± 13.

In Group 2B (Table 5), no gas flow was delivered to the prebypass perfusate, and the FIO_2 was adjusted up to 0.80 after going on bypass. This demonstrated an acidic perfusate (pH 6.93 ± 0.32) with a normoxic range for PO_2s. One, 2, and 8 min after the start of bypass, the pH was normal, but the PO_2 was hyperoxemic at all three periods. Arterial saturations were 98% at 1, 2, and 8 min, and the venous saturations were 78 ± 15.0% after 1 min of bypass. The 8-min venous saturation was 83 ± 9.0%.

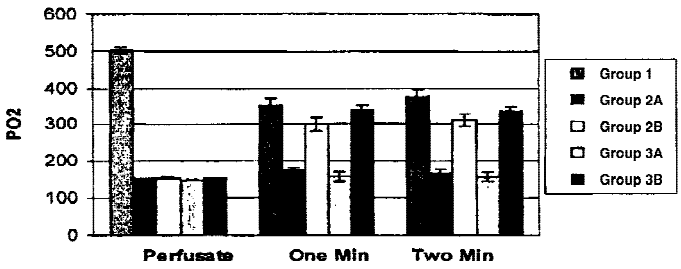

Figure 1.

Group 3A (Table 6) had a gas flow of 1 L/min being delivered through the perfusate prior to bypass at an FIO_2 of

Table 6: (Group 3A)

	pH	PO_2	PCO_2	HCO_3	B.E.	A.Sats.	V.Sats.
Perfusate	7.44 ± 0.1	152 ± 3.0	0	0	0	100 ± 0.0	0
Art 1 min	7.42 ± 0.1	161 ± 56	32 ± 4.0	21 ± 2.0	−3.0 ± 2.0	98 ± 1.0	72 ± 4
Art 2 min	7.43 ± 0.1	155 ± 69.0	33 ± 3.0	22 ± 2.0	−2.0 ± 2.0	98 ± 1.0	0
Art 8 min	7.46 ± 0.1	151 ± 73.0	34 ± 5.0	24 ± 3.0	1.0 ± 2.0	98 ± 1.0	0
Ven 8 min	7.43 ± 0.1	34 ± 5.0	38 ± 8.0	24 ± 2.0	1.0 ± 1.0	0	78 ± 5.0

Data are shown as the mean ± the standard error of the mean.

Table 7: (Group 3B)

	pH	PO_2	PCO_2	HCO_3	B.E.	A.Sats.	V.Sats.
Perfusate	7.43 ± 0.2	153 ± 11	0	0	0	100 ± 0.0	0
Art 1 min	7.42 ± 0.1	285 ± 91	29 ± 7.0	19 ± 3.0	−4.0 ± 3.0	98 ± 1.0	74 ± 10
Art 2 min	7.43 ± 0.1	293 ± 82.0	31 ± 6.0	20 ± 3.0	−2.0 ± 2.0	98 ± 2.0	0
Art 8 min	7.46 ± 0.1	297 ± 12.8	32 ± 4.0	23 ± 2.0	1.0 ± 3.0	98 ± 0.0	0
Ven 8 min	7.42 ± 0.1	36 ± 12	39 ± 6.0	25 ± 3.0	1.0 ± 2.0	0	81 ± 12

Data are shown as the mean ± the standard error of the mean.

0.21. After going on bypass, the FIO_2 was adjusted to 0.50, whichresulted in normoxemic PO_2s at the start of bypass and throughout the sampling period. The pH remained normal throughout the sampling period and HCO_3/B.E. were the same as in the Group 1. Arterial saturations were found to be 98% at all times, and the 1-min venous saturation was normal at 72 ± 4.0%. Venous saturations after 8 min of bypass were 78 ± 5.0%.

Group 3B (Table 7) provided a gas flow through the perfusate of 1 L/min, with an FIO_2 of 0.21 before, and at the start of CPB. The PO_2 of the perfusate was within normal ranges, but after going on bypass and increasing the FIO_2 to 0.80, the arterial PO_2s were in the hyperoxemic range. Once again, pH values were normal throughout, and the arterial saturation was found to be 98% at all times. Venous saturations after 1 min of bypass was found to be 74 ± 10.0%, and after 8 min, they were at 81 ± 12.0%.

When all perfusate pH values were compared, most were found to be within normal physiological range before bypass and at the 1 and 2 min mark following bypass. The only abnormal pH values obtained were from Groups 2A and 2B, where no gas flow was passed through the perfusate before going on bypass, resulting in a pH of 6.88 ± 0.07 for group 2A ($p < .001$), and a pH of 6.88 ± 0.05 for group 2B ($p < .001$). However, within 1 min of going on bypass and adjusting gas flows, both pH values had returned to physiological levels, with pH values of 7.39 and 7.44, respectively (Figure 2) range. Once again, pH values were normal throughout, and the arterial saturation was found to be 98% at all times. Venous saturations after 1 min of bypass was found to be 74 ± 10.0%, and after 8 min they were at 81 ± 12.0%.

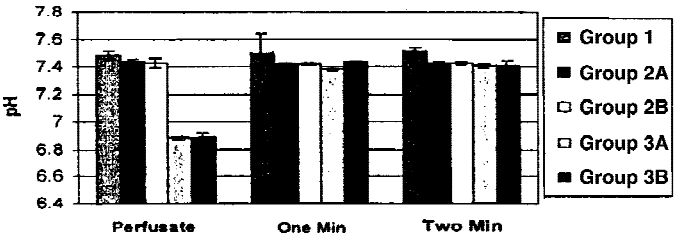

Figure 2.

CONCLUSIONS

In the pursuit of optimal patient care during CPB, we must not overlook some of the simple, yet obvious, avenues to this care. Some of these avenues, such as perfusate temperatures before bypass, may seem irrelevant. However, it is well established that perfusate temperatures much lower than the patient's body temperature at the start of CPB may lead to the creation of gaseous microemboli at the cannulation site through the cavitation process (1, 3, 4). Especially if that perfusate is also unnecessarily hyperoxic at the start of CPB.

As seen with this study, creation of large temperature gradients between the perfusate and the patient is an entirely avoidable situation before bypass. Once the priming and deairing of the entire circuit is complete, the perfusate is maintained at or near body temperature by recirculation through the oxygenators recirculation line. In the 39 patients studied, the mean patient temperature at the start of bypass was 34.9 ± 0.4°C, and the mean perfusate temperature at the start of CPB was 36.4 ± 0.4°C.

When gaseous microemboli are generated in hyperoxic solutions, these oxygen microbubbles are generally more soluble in blood and less persistent in vivo. However, they can lead to an increase in postoperative morbidity by initiating microthrombus formation, activating platelets/leukocytes, causing adsorption and denaturation of proteins, and accelerating the activation of Factor XII (3, 4, 5). In addition to reducing cerebral blood flow by 15% through the process of autoregulation (4), hyperoxia has been demonstrated to produce numerous unwanted effects during the delivery of CPB. As stated before, the effects of hyperoxia were shown to produce oxidative myocardial damage by the increased presence of oxygen free radicals and nitric oxide. This oxidative damage may be most prevalent during the delivery of blood cardioplegia after prolonged ischemic periods (9, 12, 13). It is during this time that reoxygenation of a myocardium with hyperoxic blood will produce myocardial damage through the process of lipid peroxidation.

This present study demonstrates that without the use of at least 1 L of gas flow through the Normosol R/Albumin perfusate, these primes will be very acidic at the start of CPB. This is most likely because of the combination of the neutral pH of Normosol R, the acidic pH of Albumin (6.8), and the presence of extraneous CO_2 used for flushing the circuit. This correction of an acidotic perfusate may not occur when the main priming solution is not pH balanced, and thereby previously acidic in nature (Lactated Ringers, Normosol, etc.). However, regardless of the FIO_2, 1 L of gas flow through Normosol R/albumin perfusates will provide a balanced pH without the addition (or cost) of sodium bicarbonate. When that gas flow is delivered with 0.21 oxygen, it will consistently result in the delivery of normoxic perfusates at the start of CPB. FIO_2s of 0.50 or greater will always produce hyperoxic perfusates that may be implicated in the occurrence of MEE through temperature gradients and intra-aortic cavitation at the aortic cannula tip.

Throughout all stages of this study, when bypass was started with an FIO_2 of 0.21, there was no acid base indication of inadequate oxygen delivery at 1, 2, or 8 min of CPB. In their assessment of the management of acid base balance on bypass, Swan and co-workers (14) described the importance of monitoring mixed venous PO_2. They concluded that when venous PO_2s fell below 30 mmHg, there was a significant increase in lactic acid production because of inadequate tissue oxygenation. However, when venous PO_2s were found to be above 35 mmHg, there were very small, if any, increases in the production of lactic acid. The mean venous PO_2 after 8 min of CPB in all cases started with an FIO_2 of 0.21 was 35.2 ± 9.2 mmHg, and the mean mixed venous saturation after 1 min of bypass was 74 ± 10%. The mean venous PO_2 in the Group 1 after 8 min of bypass was 36.0 ± 3.0 mmHg, and the 1 min mixed venous saturation was 78 ± 8.0%.

Published literature suggests that normoxemic management of PO_2 is safer for the entire course of CPB, because it eliminates the possibilities of microemboli production and the inadvertent delivery of nitric oxide and oxygen free radicals. In addition, it was found that starting CPB with an FIO_2 of 0.21 is both safe and reliable in the delivery of adequate perfusion at the start of bypass, if the FIO_2 is adjusted upward 10 to 30 sec after starting CPB.

Since the conclusion of this study, the technique of going on bypass with an FIO_2 of 0.21 and adjusting this FIO_2 upward 10 to 30 sec after the start of CPB has been used successfully in over 700 cases to date. The latter cases were also used in conjunction with maintaining arterial PO_2s between 100 mmHg and 200 mmHg throughout the bypass period.

Keeping PO_2s between 100 mmHg and 200 mmHg throughout bypass will provide adequate tissue oxygenation and avoid the potential problems associated with hyperoxemia, wide temperature gradients, gaseous microemboli, nitric oxide, and oxygen free radicals.

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