Lactic Acid Generation During Pediatric Cardiopulmonary Bypass: A Comparison of Blood and Crystalloid Primes

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Abstract

With the increasing concern over patient exposure to donor blood, we undertook a study to determine whether the exclusion of red blood cells from the pump prime for pediatric cardiopulmonary bypass surgical procedures would contribute to the development of metabolic acidosis by either decreasing O_2 carrying capacity or diluting plasma buffers with a crystalloid solution. We compared a cellular (blood) prime (fresh-frozen plasma and red blood cells) and a non-cellular prime (Isolyte E and serum albumin).

Lactic acid and venous saturation levels were used to evaluate the effects of the two types of priming solutions. Lactic acid samples were drawn two minutes after bypass was initiated, and two minutes after cross clamp removal (or two minutes after bypass was resumed on circulatory arrest cases) and two minutes before discontinuing bypass. Venous saturation samples were taken at random times during the procedures. For cases using the clear prime, we were more aggressive in our blood conservation techniques.

Two-way analysis of variance revealed that there was a significant increase in lactic acid levels in both groups as a result of circulatory arrest ($p = .0000000887$, $n = 13$). There was not a significant difference in lactic acid levels between groups at any period during cardiopulmonary bypass ($p = .7756$). The only differences between groups 1($n = 15$) and 2 were the bypass hematocrits, number of donor blood exposures and patient cooling times. The two-way ANOVA "Interaction" p value ($p = .6117$) strongly suggests that this was a clean study. These findings are supported by the comparability of the exsanguination times and venous saturations.

Our study results indicate that an Isolyte E and serum albumin prime did not increase the pediatric patient's lactic acid levels compared to a blood prime, but it does reduce patient donor blood exposure.

Introduction

Average infant/pediatric bypass circuits require approximately 800 ml of priming solution.[1,2,3] This amount exceeds the blood volume of some patients by many times. The excess volume makes it necessary to use blood products to avoid excess hemodilution in all but the most polycythemic of children.

Growing parental concerns over blood-transmitted diseases, such as hepatitis and AIDS[4,5] prompted us to study whether cardiopulmonary bypass (CPB) could be done safely without using blood. One surgeon's patients (Group 1) were used as the control group for which blood was used to prime the pump. Another surgeon's patients (Group 2) were used as the study group. The purpose of the study was to determine whether the exclusion of red blood cells from the pump prime for pediatric cardiopulmonary bypass surgical procedures would contribute to the development of metabolic acidosis from either decreasing O_2 carrying capacity or from dilution of plasma buffers.[6,7] We also wanted to try and define the safe limits of hemodilution[8,9,10] for pediatric cardiac surgery patients at this altitude.

Arterial and venous blood gas determinations and lactic acid levels were used to evaluate the effects of the two priming solutions. In order to simplify the study we did not measure pyruvate levels.[11,12]

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Materials and Methods

Pulsatile bypass using a Cobe pulsatile pump[a] was used in all cases.[13] Terumo[b] Hollow Fiber Membrane Oxygenators (HFMO) were used as has been previously described.[14] The Alpha-Stat pH management technique was used.[15,16]In one group of patients (Group 1) the pump-oxygenator system was primed in the traditional way[14] using packed red blood cells (PRBC) and fresh frozen plasma (FFP) with the FFP being donor-matched to the red cells whenever possible. In a second group of patients (Group 2) the pump-oxygenator was primed with a non-cellular solution of Isolyte E[c] (250–600 ml.) and serum albumin[17] (100–250 ml. of 5%). We initially sequestered venous blood from (Group 2) patients from a port on the venous line withdrawing as much as half of their total blood volume while initiating bypass.[18,19]This method was discontinued because of the uncertainty about the resulting low hematocrits. We refined a "micro-prime" system[20] and with a further review of the scant literature on the subject decided to add red blood cells if the hematocrit dropped below 13%.[9]

Lactic acid samples were drawn two minutes after bypass was initiated, two minutes after crossclamp removal (or two minutes after bypass was resumed on circulatory arrest cases), and two minutes before coming off bypass. The 2 ml. venous samples were placed on ice and then transported to the laboratory via the pneumatic tube system. Lactic acid samples were measured in the laboratory with a Roche-Cobes-Bio[d] unit, using Behring Diagnostics "Stat Pac™" Rapid Lactate Test.[e] Arterial and venous blood gases were measured on a Corning IL.[f] Venous saturation samples were taken at random times during the procedure.

We employed three blood conservation techniques: 1) micro-prime circuits; 2) hemoconcentration; and 3) diuretics.

The statistics were performed on an IBM compatible computer using Microstat™ statistical package (Release 4.1),[h] and on an Apple Macintosh computer using the Statworks™ statistical package (Ver. 1.2).[g] The tests of significance were analysis of variance (ANOVA) and paired T-test.

a Cobe Laboratories, Lakewood, CO 80215
b Terumo, Piscataway, NJ 08954
c American McGaw, Irvine, CA 92714-5895
d Roche Analytical Instruments Inc., Nutley, NY 07110
e Behring Diagnostics, LaJolla, CA 92037
f Corning, Medfield, MA 02052
g Ecosoft, Inc., Indianapolis, IN 46220
h Cricket Software, Philadelphia, PA

Results

Table 1 shows the means and standard deviations of measured parameters. Those which reached significance were: cooling time ($p = .011$), hematocrit ($p = .026$), and donor exposures ($p < .001$). Total bypass time, arrest time, low flow, high flow, exsanguination S_vO_2, end of bypass S_vO_2, $NaHCO_3$ used, and patient weight did not reach significance. There was a highly significant increase of lactic acid in both groups ($p = .000000087$) (Table 2 and Figures 1 & 2), however, there was no difference in the increase between groups ($p = .6117$) (Figure 3).

Discussion

There were some differences in the clinical techniques used in managing the two groups of patients. In Group 2 there was decreased resistance due to decreased viscosity; we would have had to maintain higher flows to maintain pressures equal to those in Group 1, but because we were so concerned about adding volume we were not always able to increase flows.[21] The difference in flows between groups was not significant ($p = .54$). Correction of base deficits due to buffer dilution may have required addition of more buffer in Group 2 but there was no statistical difference between the two groups ($p = .07$). We were not able to achieve ideal pulse wave contours due to decreased viscosity and resistance.

Table 1.

	GROUP 1	GROUP 2	P Value
Cooling Time (min.)	11.27±3.17	7.13±4.93	p=.011 *
Bypass Time (min.)	73.4±30.06	60.8±33.01	p=.28
Arrest Time (min.)	45.53±17.34	35.73±22.19	p=.19
Low Flow (lpm)	0.89±0.3	0.89±0.3	p=.968
High Flow (lpm)	1.35±0.06	1.46±0.46	p=.54
S_vO_2 Exsanguination	93.31±8.6	87.5±12.6	p=.47
S_vO_2 End Bypass	72.86±19.9	76.1±10.9	p=.32
Hematocrit	26.61±4.3	18.8±5.2	p=.03 *
Donor Exposures	4.0±1.85	1.27±1.4	p<.001 *
NaHCO3 (mEq)	17.23±11.8	27.67±17.8	p=.07
Weight	8.3±5.03	8.0±2.95	p=.84

Table 2.

LACTIC ACID LEVELS

	SAMPLE 1	SAMPLE 2	SAMPLE 3	p
GRP. 1	25.62±12.55	43.99±8.54	50.62±13.57	P<.001
GRP. 2	26.94±23.43	49.14±21.29	47.18±27.21	P<.001

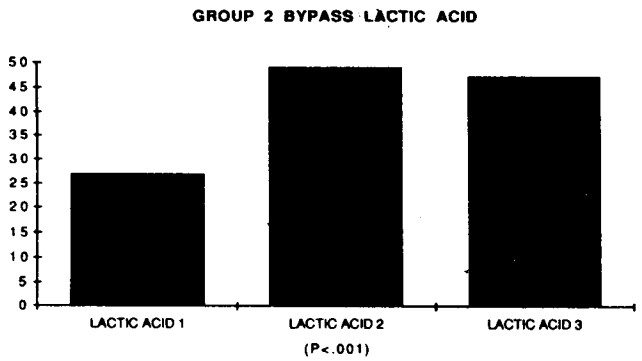

Figure 1

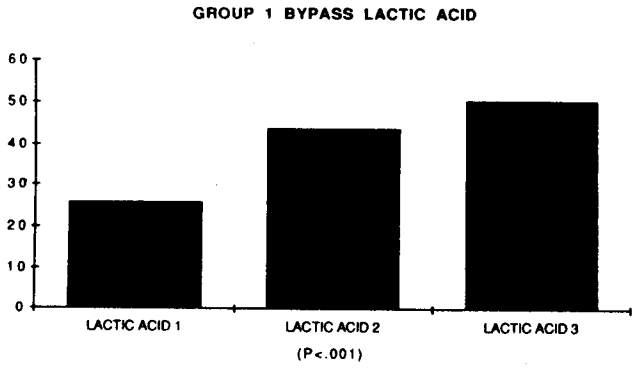

Figure 2

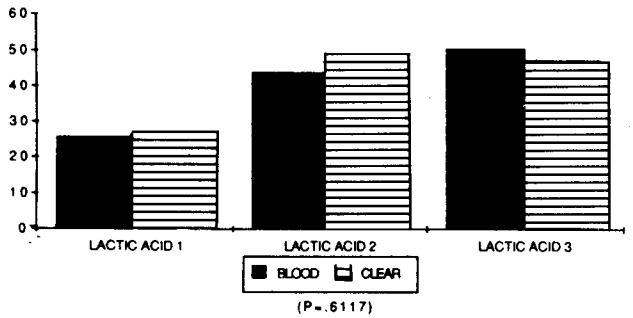

Figure 3

The benefits of the clear prime were small cooling gradients (difference between naso-pharyangeal and rectal temperature) cooling times, and decreased amounts of donor blood was used.

Our study results indicate that an Isolyte E and serum albumin prime did not increase the pediatric patients' lactic acid levels compared to a blood prime but does substantially reduce patient exposure to donor

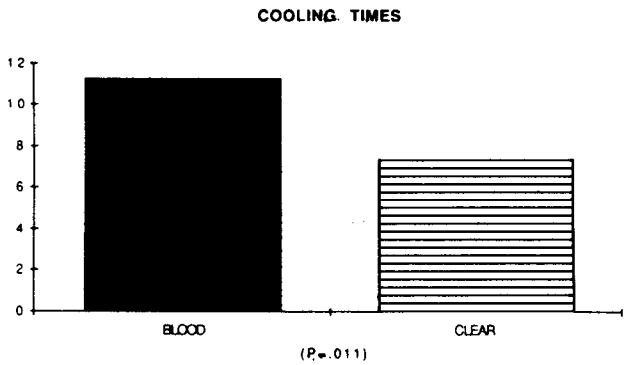

Figure A

blood. Although the mean level of hemotocrit in Group 2 was only 18.8%, individual patients were diluted more severely (as low as 12% hematocrit). These patients did not exhibit more lactic acidosis than those in Group 1. For this reason it seems reasonable to suggest that hematocrits in the low teens may be acceptable during hypothermic cardiopulmonary bypass. We have changed our priming protocols to exclude the use of blood unless the hematocrit will be below about 13% or 20% (according to the individual surgeon's preference) during bypass. These changes mean that we accept the management differences brought about by severe hemodilution, including lower hematocrits, use of a hemoconcentrator for every case, and smaller circulating volumes and reaction times. We now use the new priming protocols for their pediatric cases with certain adjustments for individual preferences.

Acknowledgements

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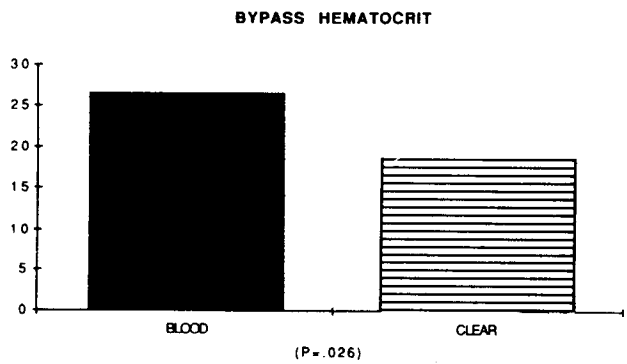

Figure B

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Questions from the Audience

Al Stammers, Ann Arbor, MI: Question: Did you by any chance normalize for the type of congenital abnormalities that you had between your groups? Were they within acceptable statistical norms?
Answer: I am not sure I can answer that question. In our altitude, the kids who were cyanotic are severely cyanotic. Most of these kids were not cyanotic. They do have slightly higher hemoglobins because of the higher altitude and are relatively dehydrated if they are older kids, but I could not say that that in any way influenced the results of the study.
Question: Is it the conclusion of your study that you are now using the clear prime?
Answer: In the cases that we do for the one surgeon that is very interested in staying away from using blood. The other surgeon lowered his limits, in other words, instead of wanting to come off the pump above 30, he is willing to come off the pump in the 25 range. Some of these kids in the crystalloid group, we originally took off up to half their volume as we went on the pump and we got down in the 5 and 6 range. We were real concerned about that because we are now treading in unchartered waters and when we looked at what little literature there was on the subject and decided we would treat anything below 13 as sort of a round number. We did not notice that there was any real difference because the kids were cold. They were arrested at temperatures of about 17 degrees rectal and then we were very careful about adding that blood as soon as we came off. We gave them the protamine and hemoconcentration. The kids often went to the unit with hemocrits in the high twenties and low thirties.
Question: Have you reduced your blood use then with the surgeon who was against the clear prime?
Answer: Yes. In fact, at this hospital before this study the average blood usage in the kids were 7½ units at the University Hospital. These kids were done at Childrens', where the average blood usage was 9½ units. That's donor exposure again. We have come down and that's really a lot in these patients.

Matt Tyndal, Denver, CO: I don't think there was any difference between the groups. We have substantially reduced the blood usage, the surgeon who prefers the higher hematocrit rather than priming the pump with three units of FFP or 2 units of packed cells–three or four donor exposures, now uses the units of whole blood. One donor exposure gets the same amount of volume with a little crystalloid except a little lower hematocrit. So, limiting the donor exposures, but still using some blood. As far as the cyanosis, I don't think there was any real difference. Even in the case where we used fresh frozen, we tried to get donor matched.