
Hemoglobin P₅₀ Dynamics During Hypothermic Cardiopulmonary Bypass

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Abstract

The hemoglobin P₅₀ was ascertained prior to anesthesia and CPB and calculated during hypothermic CPB to track the change in hemoglobin affinity in fifty randomly selected cardiac disease patients.

The AMINCO Hem-O-Scan standardized P₅₀ averaged 32.1 $\pm$ 6.8 (1 SD) mmHg in the awake, slightly sedated CPB candidate. The awake patients were distributed into three significantly different ($p < .05$) groups: left-shifted oxy-hemoglobin dissociation curve (ODC), P₅₀ = 23.1 $\pm$ 1.4, $n = 5$; normal ODC, P₅₀ = 27.2 $\pm$ 1.3, $n = 13$; and right-shifted ODC, P₅₀ = 35.4 $\pm$ 6.1, $n = 32$. The three groups converged at the termination of hypothermic CPB to a single group calculated, mean P₅₀ = 30.7 $\pm$ 4.7 mmHg.

Unlike the previous studies of Woodson² (1970) and Wilkinson (1979), the Hem-O-Scan pre-CPB P₅₀ demonstrated a weak inverse correlation to ejection fraction, cardiac index and hemoglobin flow index in this patient group. The position of

the ODC prior to and during CPB may not be accurately predicted. Therefore, direct measurement of pO₂ and O₂ saturation of hemoglobin is recommended and calculator prediction of hemoglobin O₂ saturation from pO₂ assuming a beginning P₅₀ = 27 mmHg may not be trusted in cardiac diseased patients.

Introduction

Evaluation of tissue oxygenation during extracorporeal circulation has been through intermittent blood gas analysis. With the recent availability of continuous monitors of oxygen saturation of hemoglobin (O₂ SAT) and partial pressure of oxygen (pO₂), questions of accuracy, monitoring necessity and cost effectiveness have arisen. If pO₂ or O₂ SAT could be employed to predict the other, the problem would be simplified.

The single indicator that states the relationship between pO₂ and O₂ SAT is the hemoglobin P₅₀; the pO₂ at which an individual's hemoglobin is fifty percent saturated with oxygen.

The purpose of this study was to evaluate the predictability of the hemoglobin P₅₀ and track the P₅₀ change during hypothermic cardiopulmonary

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bypass in a random sampling of fifty cardiac disease patients undergoing open heart surgery.

Severinghaus and others report the normal adult hemoglobin P_{50} to be 27–28 mmHg with a standard deviation in the population equal to 1–2 mmHg.^{1,6}

Woodson, Kostuk, Agostoni, Shappell, Metcalfe, and others have correlated hemoglobin P_{50} inversely with cardiac index, hemoglobin concentration, hemoglobin flow index, arteriovenous oxygen content difference, and red blood cell 2, 3 DPG in their cardiac disease populations.^{1–9}

Patients in cardiogenic shock with severe acidosis have dramatically right-shifted oxyhemoglobin dissociation curves to enhance oxygen delivery to tissue during shock.⁴

Woodson and Valeri have documented the role of elevated red cell 2, 3 DPG in decreasing hemoglobin oxygen affinity and improving tissue oxygenation during compromised cardiac function.^{2,3} Valeri proposed that the hemoglobin P_{50} is “a functional biopsy of the status of tissue oxygenation.”¹³

It may be concluded that if hemoglobin P_{50} is known, then O_2 SAT may be predicted from pO_2 or the converse. Furthermore, the accurate prediction of an individual's P_{50} from his or her medical data base would allow the justification of the continuous monitoring of only pO_2 or O_2 SAT with accurate prediction of the other. However, these assumptions are unlikely in that investigators have demonstrated alteration in the hemoglobin P_{50} within an organ system (e.g. coronary sinus) compared to the individual's mixed venous hemoglobin P_{50} .⁶ In the resuscitation of severely impaired, low cardiac output patients with cardiopulmonary bypass, one might expect hemoglobin P_{50} to return to normal when the biochemical imbalances accompanying cardiogenic shock are corrected. Perhaps hemoglobin P_{50} change during cardiopulmonary bypass may be employed to monitor the adequacy of ECC tissue oxygenation.

Hemoglobin P_{50} dynamics prior to and during moderate hypothermic cardiopulmonary bypass were studied employing the following method.

Methods

Fifty adult open heart patients undergoing various cardiac surgical procedures were randomly

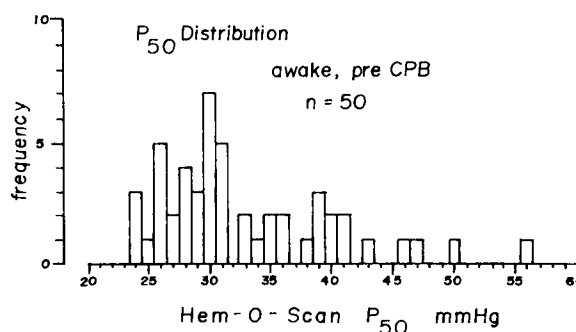


FIGURE 1. The frequency distribution of the *IN VIVO* hemoglobin P_{50} for fifty randomly selected cardiopulmonary bypass candidates.

selected, and their medical records were reviewed to evaluate history, biochemistry, hematology, and cardiac function. Pre-operative ejection fraction, cardiac index (L/minute/ M^2) and hemoglobin flow index ($Gm\%/L \times \text{minute}/M^2$) were collected to correlate to hemoglobin P_{50} .

A radial artery blood sample was drawn from each lightly sedated, awake CPB candidate breathing room air. The sample was analyzed for pH, pO_2 , pCO_2 and base excess via the Corning 175.^a The sample was also analyzed for % Hb · CO and % Methemoglobin (% Met Hb) by the IL282 Co-oximeter^b and the oxyhemoglobin dissociation curve constructed with the Hem-O-Scan^c employing the manufacturer's instructions. The Hem-O-Scan 100% relative saturation (O_2 SAT Max) was adjusted for the %Hb · CO and % Met Hb with the following equations:

$$F = \frac{\%HbCO + \%Met Hb}{SAT Max}$$

$$ADJUSTED O_2 SAT MAX = \frac{INITIAL O_2 SAT MAX}{F}$$

The resulting P_{50} was reported as the *IN VIVO* P_{50} .

The *IN VIVO* P_{50} was standardized (STD P_{50}) to pH equal to 7.4, pCO_2 equal to 40 mmHg, and temperature equal to 37°C by the following equation.¹

^a Corning, Medfield, MA 02052

^b Instrumentation Laboratory, Lexington, MA 02173

^c American Instrument Co., Jessup, MD 20794

^d American Bentley Laboratories, Irvine, CA 92714

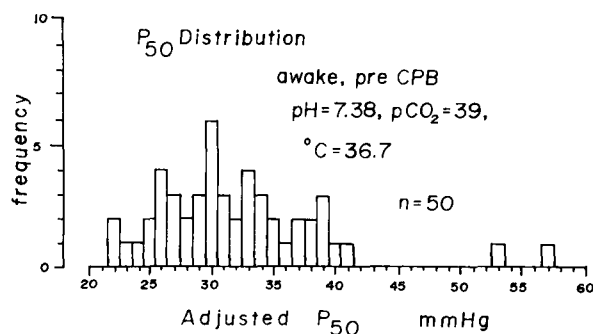


FIGURE 2. The frequency distribution of the standardized hemoglobin P_{50} for fifty randomly selected cardiopulmonary bypass candidates.

$$\begin{aligned} \text{STD } P_{50} = & \text{Hem-O-Scan } P_{50} + .0755 \\ & \times (40 - p\text{CO}_2) + 26.66 \times (\text{pH} - 7.4) \\ & + 1.25 \times (37^\circ\text{C} - \text{Temp}) \end{aligned}$$

Anesthesia was obtained with 50–100 ug/kg fentanyl citrate or 1–2 mg/kg morphine sulfate. Muscle relaxation was established with about .15 mg/kg pancuronium hydrochloride. Bypass was initiated with a cardiac index of 2.2 to 2.7 L/min/ M^2 and 28°C hypothermia was instituted. The perfusionist attempted to maintain the temperature corrected pH and blood gases within 37°C normal ranges. Donor blood was employed to maintain the hematocrit above 22%.

Venous hemoglobin O_2 SAT was continuously monitored with the Oxy Sat Meter^d and maintained greater than 65% at 37°C and greater than 87% at 28°C . Base deficit was not corrected during hypothermia.

Blood gas analyses were obtained every 15–20 minutes during CPB and just prior to termination. The P_{50} during bypass was estimated employing Severinghaus' method.⁵

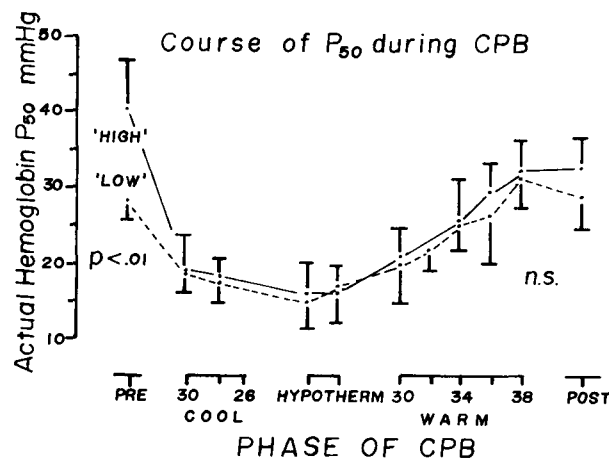


FIGURE 3. The course of the calculated *IN VIVO* hemoglobin P_{50} for two groups, P_{50} greater than 32 mmHg (High) and P_{50} less than 32 mmHg (Low).

Results

Figures 1 and 2 display the distribution of the *IN VIVO* P_{50} (32.9 ± 7.2 mmHg) and the STD P_{50} (32.1 ± 6.8 mmHg) pre-anesthesia. The STD P_{50} 's were divided into three groups: Normal STD P_{50} = 25 to 29 mmHg; high STD P_{50} greater than 29 mmHg and low STD P_{50} less than 25 mmHg. Table 1 lists the group statistics. Confidence intervals were constructed for the unequal patient groups to test for significant differences at $p < .05$.

Figure three depicts the hypothermic ODC left shift with hypothermic CPB. The three groups converge during CPB warming to demonstrate no significant difference at termination of CPB. The STD P_{50} post CPB averaged 30.7 ± 4.7 mmHg.

Table 2 exhibits the weak predicting power of preoperative medical record physiologic parameters. In this group, ejection fraction averaged $.63 \pm .13$ (1 SD) and was as low as .35 and as great

TABLE 1

The mean $\pm$ one standard deviation for each resulting study subgroup prior to CPB and at the termination of CPB. The significance between groups and rows was tested by constructing confidence limits for each cell.

HEMOGLOBIN P_{50} GROUP	PRIOR TO CPB	END OF CPB	SIGNIFICANCE BETWEEN ROWS
Right Shifted (n = 32)	35.4 $\pm$ 6.1	31.2 $\pm$ 5.4	p < .01
between groups:	p < .01	N.S.	
Normal (n = 13)	27.2 $\pm$ 1.3	31.2 $\pm$ 2.9	p < .01
between groups:	p < .05	N.S.	
Left Shifted (n = 5)	23.1 $\pm$ 1.4	27.8 $\pm$ 4.2	p < .05

TABLE 2
The linear correlation of various preoperative indices of cardiac function versus the standardized hemoglobin P₅₀ pre or post CPB.

CARDIAC FUNCTION INDEX	CORRELATION COEFFICIENT
% Ejection fraction	-.24
Hemoglobin flow index (Gm% × CI)	-.24
Preoperative CI	-.25
Postoperative CI	-.12

as .87. Pre-CPB hemoglobin flow averaged 34.4 ± 16.5 (1 SD) and spanned the limits of 17.5 to 75.2 Gm%/L × min/M². Pre-operative CI was $2.45 \pm .73$ L/min/M² and varied from 1.33 to 4.95 in those 50 patients. Post-CPB CI was $2.66 \pm .27$ L/min/M².

Discussion

The individual cardiac disease patient's oxyhemoglobin curve position may not be known or confidently predicted prior to CPB. However, in this study, 64% of patients arrived in the operating room suite with right-shifted ODC's.

Patients with compromised cardiac function compensate to facilitate oxygen transfer by decreasing hemoglobin oxygen affinity.^{1-4,6,8} Elevated P₅₀ is common in patients in chronic CHF, cardiogenic shock, post MI, anemia, and cardiomyopathies.¹⁻⁴ Change in red cell 2,3 DPG largely mediates change in hemoglobin P₅₀ in conjunction with acid base effects on the ODC.²⁻⁴

It is reasonable to hypothesize that an individual's hemoglobin P₅₀ may be predicted by cardiac function parameters. However, only weak, inverse correlations were observed in this patient group between P₅₀ and ejection fraction, cardiac index, and hemoglobin flow index.

The initiation of increased cardiac index CPB and corrective measures (e.g. surgery, acid base imbalance correction) probably reverse the processes elevating P₅₀ and return the ODC toward a

normal position. The minute relationship between decrease in P₅₀ pre to post CPB with change in cardiac index and the total group mean P₅₀ equal to 30.7 ± 4.7 mmHg at CPB termination support the role of increasing blood flow shifting the ODC to the left.

The position of the oxyhemoglobin dissociation curve can not be accurately predicted and changes dynamically prior to and during hypothermic CPB. Therefore, direct measurement of pO₂ and saturation is indicated during CPB. Calculator prediction of O₂ SAT from pO₂ assuming a beginning P₅₀ equal to 27 mmHg can not be trusted.

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References

1. Woodson, R. D.: Oxygen Transport: DPG and P₅₀, *Basics of RD*, 5(4), 1977.
2. Woodson, R. D., Torrance, J. D., Shappell, S. D., and Lenfant, C.: The Effect of Cardiac Disease on Hemoglobin-Oxygen Binding, *J. Clin. Invest.* 49:1349-1356, 1970.
3. Valeri, C. R.: Blood Banking and use of Frozen Blood Products, CRC Press, Cleveland, p. 153, 1976.
4. Agostini, A.: Hemoglobin Oxygen Affinity in Patients with Acute Myocardial Infarction and Angina Pectoris, in *Physiological and Clinical Aspects of Oxygenator Design*, Dawids, S.G., and Engell, H.C. (Ed.), Elsevier, Amsterdam, pp. 235-241, 1976.
5. Severinghaus, J. W.: Simple Accurate Equations for Human Blood Oxygen Dissociation Computations, *J. Appl. Physiol.: Respir. Environ. Exercise Physiol.* 46(3):599-602, 1979.
6. Wilkinson, P. L., Graham, B. H., Moyers, J. R., Hamilton, W. K., Ports, T. A., Ulyot, D. J., and Chatterice, K.: Changes in Mixed Venous and Coronary Sinus P₅₀ Secondary to Anesthesia and Cardiac Disease, *Anes. and Analg.* 59(10):751-758, 1980.
7. Aberman, A., Cavanilles, J. M., Weil, M. H., and Shubin, H.: Blood P₅₀ Calculated From a Single Measurement of pH, pO₂, and SO₂, *J. Appl. Physiol.* 38(1):171-176, 1975.
8. Shappell, S. D., and Lenfant, C. J. M.: Adaptive, Genetic, and Iatrogenic Alterations of the Oxyhemoglobin-Dissociation Curve, *Anesthesiology*, 37(2):127-139, 1972.
9. Steinbach, J. H., Blackshear, P. L., Varco, R. L., and Buchwald, H.: High Blood Cholesterol Reduces IN VITRO Blood Oxygen Delivery, *J. Surgical Research*, 16:134-139, 1974.