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The oxygen dissociation curve: quantifying the shift

Carole Hamilton[1], Barbara Steinlechner[2], Eva Gruber[2], Paul Simon[3] and Gregor Wollenek[3]

[1]Cardiac Perfusion Services, Life Systems, University Clinic of Tubingen, Tubingen, Germany; [2]Department of Cardiothoracic Anesthesia, University Clinic of Vienna, Vienna, Austria; [3]Department of Cardiothoracic Surgery, University Clinic of Vienna, Vienna, Austria

An oxyhaemoglobin dissociation curve (ODC) quantifies the most important function of red blood cells and that is the affinity for oxygen and its delivery to the tissues. Oxygen affinity for haemoglobin plays a critical role in the delivery of oxygen to the tissues and is changed by shifting to the left or right. A shift to the left implies an increased oxygen affinity and, hence, tighter binding due to the higher oxygen saturation in relation to the pO_2. On the other hand, a shift to the right corresponds to a decreased oxygen affinity and easier release of oxygen to the tissues. It is well known that the ODC shifts in response to changes in pH, pCO_2 and 2,3 diphosphoglycerate. However, how much the ODC shifts has never been quantified. Arterial and venous blood gases were taken during cardiopulmonary bypass and two indices were used to quantify the shift of the ODC; the p50 shift and the SO_2 difference. Arterial blood shifted to the right by 4 ± 0.1 mmHg at a pH of 7.24 and shifted to the left by −3.5 ± 0.05 mmHg at a pH of 7.51. The change in arterial saturation was minimal, rising by 0.8% and dropping by −5% and did not correlate to p50 shifting and changes in pH, but demonstrated changes dependent on the concentration of dyshaemoglobins. The venous blood exhibited a greater range of p50 shifting at each pH value. At a pH of 7.24, the p50 shifted to the right by 4.8 ± 2 mmHg and at a pH of 7.51 the p50 shifted to the left by −4 ± 1.8 mmHg. Unlike the arterial blood, the change in saturation correlated well to p50 shifting. It is shown here for the first time how much the curve shifts with changes in pH and how this may be used to evaluate treatment strategies. *Perfusion* (2004) **19,** 141–144.

Introduction

The oxyhaemoglobin dissociation curve (ODC) shifts to the left with increased pH, decreased pCO_2 and decreased 2,3 diphosphoglycerate. Normally, the p50 (pO_2 at 50% saturation) is a common value used to indicate horizontal right and left shifting. The p50 shift is defined as the reported p50 minus the normal p50 (26.6 mmHg) and is used to quantify either a left shift (negative number) or a right shift (positive number). Since there is also a corresponding fall or rise in oxygen saturation, a second index has been newly defined as the SO_2 difference. This takes into account the difference in SO_2 values at the same pO_2 value and is defined as the reported or measured SO_2 minus the normal SO_2 value at the same pO_2 when the ODC is in neutral position. The normal saturation is calculated from a predetermined standard ODC (Figure 1). At each pO_2, the saturation varies depending on the position of the curve. A higher than normal saturation at a given pO_2 (upward shift) is associated with a greater O_2 affinity and tighter binding of oxygen to haemoglobin, whereas a lower than normal saturation at a given pO_2 (downward shift) is associated with a reduced oxygen affinity and easier release to the tissues. The changes in oxygen affinity can now be further studied and used to quantify the shift of the ODC.

Materials and methods

The perfusion system consisted of a membrane oxygenator with an open-system venous reservoir. Arterial and venous blood gas samples were taken simultaneously during cardiopulmonary bypass (CPB) in 65 adult cases. Blood gas values were not corrected for temperature. A total of 500 samples were used to quantify the shift of the ODC using 1) p50 shift (p50−26.6) and 2) SO_2 difference (measured SO_2-SO_2 value at same pO_2 when the

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Address for correspondence: Carole Hamilton, Leitende Kardiotechnikerin, Klinik fuer Thorax-, Herz- und Gefasschirugie, UK Tubingen (UKT), Schnarrenberg Klinik, Ebene A02/OP, Hoppe-Seyker-Str. 3, 72076 Tubingen, Germany.
E-mail: carole.hamilton@gmz.net

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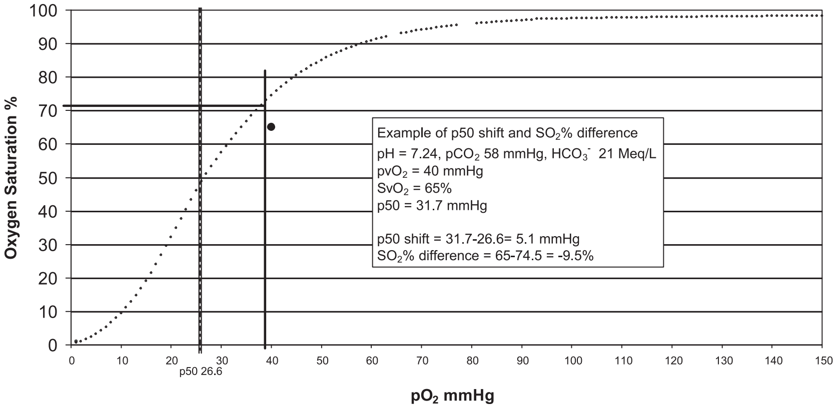

Figure 1 Oxygen dissociation curve in normal position (37°C, pH 7.4, pCO_2 40 mmHg); p50 (26.6 mmHg at 50% saturation).

ODC is in neutral position). The blood gas measurements included; pH, pCO_2 mmHg, pO_2 mmHg, HCO_3^- mEq/L, base excess (BE) mEq/L, haemoglobin (Hb) g/dL, SO_2%, p50 mmHg and the dyshaemoglobins; carboxyhaemoglobin (COHb), methaemoglobin (MetHb) and reduced haemoglobin (HHb). All values, including patient data, were entered into an Excel program.

Results

For ease of interpretation, blood gases were divided into arterial and venous samples.

Influence of pH on p50 shifting

Arterial blood: the p50 shift correlated linearly with the pH ($r^2 = 0.97$) (Figure 2). The maximum p50 left shift was −6.1 mmHg at a pH of 7.61, and the maximum p50 right shift was 4.1 mmHg at a pH of 7.24.

Venous blood: the correlation of p50 shift versus pH in the venous blood was ($r^2 = 0.61$) (Figure 3), in which each pH value displayed a wide range in p50 shifts. At a pH of 7.47, the maximum p50 left shift was −6.4 mmHg (range −6.4 mmHg to −0.6 mmHg) and at a pH of 7.24, the maximum p50 right shift was 7.5 mmHg (range 2.9 mmHg to 7.5 mmHg).

Correlation of p50 shift on SO_2 difference

The arterial blood SO_2% difference changed very little with respect to p50 shift (Figure 4). The SO_2% difference ranged from 0.81% to −5.1%, with the greatest fall due to a high concentration of dyshaemoglobins. The higher the percentage of dyshaemoglobins (carboxyhaemoglobin and methaemoglobin), the lower was the arterial saturation (Figure 5). Only 3.6% of arterial samples showed a rise in saturation difference (higher saturation at the same pO_2) and these cases had zero concentration of methaemoglobin. The venous blood, however, showed a linear correlation between SO_2 difference and p50 shift ($r^2 = 0.86$) (Figure 6). With a right shift of 7.5 mmHg at a pH of 7.24, the fall in SO_2 difference was −13%. At the same pH of 7.24, a right shift of 3 resulted in a SO_2 fall of −7.8%. At a pH of 7.47, the maximum

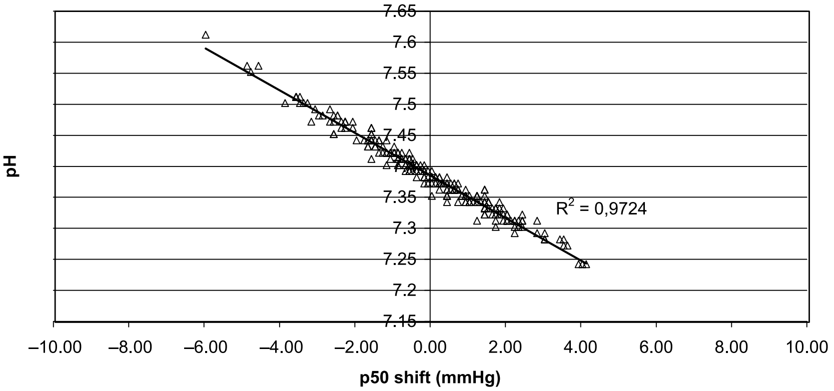

Figure 2 pH versus p50 in arterial blood.

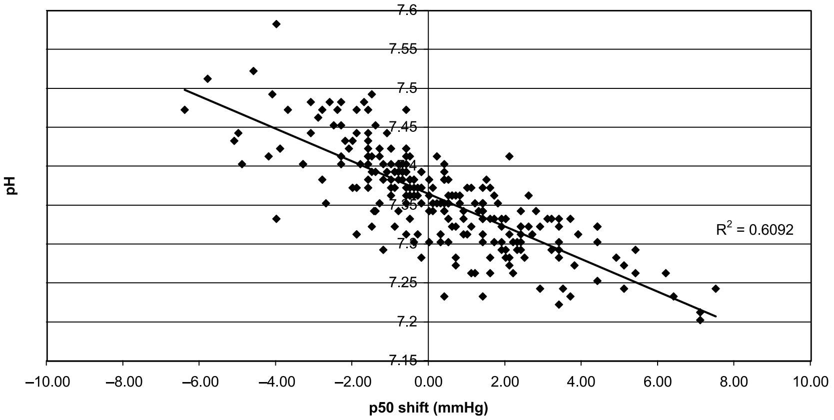

Figure 3 pH versus p50 in venous blood.

left shift was −6.4 mmHg corresponding to a rise in SO_2% by 6.8%. At the same pH of 7.47, the ODC shifted to the right by 0.6 mmHg and showed no change in saturation.

Discussion

Since the early work of Bohr, Hasselbach and Krogh in the early 1900s,[1] the position of the curve has been used as a relative indicator of oxygen affinity and discussed only in terms of either shifting to the right or left. Since the greater percentage of oxygen binding or release is from haemoglobin, the saturation change is also of major importance.

The amount of p50 shifting and the changes in saturation reacted differently in arterial and venous blood. The venous blood displayed a greater range of p50 shifting when the pH was the same, indicating that factors other than pH influence oxygen uptake. In the venous blood, there was a good correlation between the SO_2% difference and p50 shifting. The greater the p50 shift, the greater was the SO_2% difference. Therefore, the amount of shifting varied depending on how much the saturation dropped.

In the arterial blood, there was no correlation of SO_2% difference to p50 shifting, confirming the flat upper part of the ODC with little to no change in saturation with large pO_2 changes. The greater drop in SO_2% was noted with an increased concentration of dyshaemoglobins reducing the affinity of oxygen for haemoglobin.

It is shown here for the first time how much the curve shifts in a quantitative manner and the various influences on the saturation drop or rise in arterial and venous blood. Evaluation of venous blood gases along with arterial blood gases allows the detection of early metabolic changes and should be used to evaluate future treatment strategies.

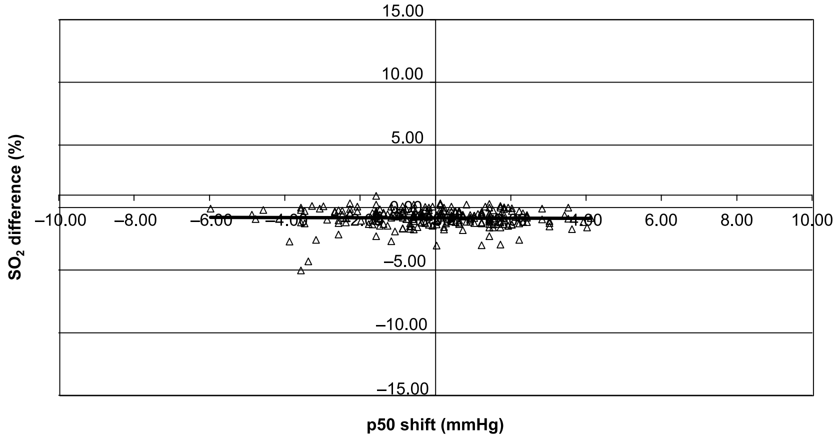

Figure 4 SO_2 difference versus p50 in arterial blood.