Therapeutic Thresholds for Acute and Chronic Alterations in Arterial O₂ Concentration

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Introduction

The maintenance of the O₂ supply to an organ requires both an adequate O₂ concentration and perfusion (O₂ availability), i.e., convective transport to the organ, and a sufficient O₂ partial pressure, i.e., diffusive transport. An adequate arterial O₂ concentration almost always guarantees the diffusion of a sufficient amount of O₂ from the blood into the tissue. Only under extreme conditions can the O₂ in the blood not be extracted, i.e., cannot be consumed by the tissue. A limiting value for the arterial O₂ concentration that supports the physiological supply of O₂ to all human organs in a resting state must be logically centered around the organ with the greatest O₂ utilization, i.e., O₂ extraction with a single passage of blood through the capillary bed.

The Myocardium as Limiting Organ

The arteriovenous O₂ difference (avDO₂), expressed in concentration units (e.g., ml/dl, ml O₂/100 ml blood), is the parameter used to assess O₂ utilization. From Table 1 it is evident that the heart is the organ with the greatest avDO₂ and can therefore be considered as the limiting organ. Apart from the fact that the myocardium shows the greatest avDO₂ among all the organs (12 ml/dl), the table also illustrates a further unique
Table 1. Oxygen consumption (\(\dot{V}O_2\)), perfusion (\(\dot{Q}\)) and arteriovenous O\(_2\) difference (avDO\(_2\)) in human organs at rest.

<table>
<thead>
<tr>
<th>Organ</th>
<th>Weight (g)</th>
<th>(\dot{V}O_2) (ml/min)</th>
<th>(\dot{Q}) (ml/min)</th>
<th>avDO(_2) (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>2,500</td>
<td>55 (55)</td>
<td>1,400 (1,200)</td>
<td>0.06 (0.026)</td>
</tr>
<tr>
<td>Kidneys</td>
<td>300</td>
<td>18 (18)</td>
<td>1,200 (1,800)</td>
<td>0.015 (0.01)</td>
</tr>
<tr>
<td>Brain</td>
<td>1,400</td>
<td>50 (50)</td>
<td>775 (1,165)</td>
<td>0.065 (0.063)</td>
</tr>
<tr>
<td>Heart</td>
<td>300</td>
<td>30 (45)</td>
<td>250 (375)</td>
<td>0.12 (0.12)</td>
</tr>
<tr>
<td>Muscle</td>
<td>30,000</td>
<td>60 (60)</td>
<td>450 (1,275)</td>
<td>0.06 (0.047)</td>
</tr>
<tr>
<td>Other</td>
<td>35,500</td>
<td>62 (62)</td>
<td>1,025 (1,540)</td>
<td>0.06 (0.040)</td>
</tr>
<tr>
<td>Total</td>
<td>70,000</td>
<td>275 (290)</td>
<td>5,500 (2,255)</td>
<td>0.05 (0.035)</td>
</tr>
</tbody>
</table>

Values in brackets: Increase in cardiac output by 90% as a result of hyperemia.

\(\dot{V}O_2\): Values for the heart with an additional 100% increase in coronary perfusion.

characteristic of this tissue. If, for instance, the cardiac output increases to compensate for a decrease in arterial O\(_2\) concentration, the avDO\(_2\) of all other organs falls to a similar extent. This is shown in table 1 in the case of an increase of 50% in cardiac output, which results in avDO\(_2\) values around 5% of the initial values. The exception is the myocardium since this has to perform more work in order to produce the increase in cardiac output, resulting in an increased O\(_2\) consumption. The myocardial avDO\(_2\) therefore remains practically constant under these conditions. An increase in coronary perfusion alone, however, leads to a decrease in the myocardial avDO\(_2\); doubling the coronary perfusion, for instance, halves the avDO\(_2\) from 12 to 6 mmHg.

A decrease in O\(_2\) availability to the myocardium is the strongest known stimulus for coronary dilatation; the healthy heart can thus increase its perfusion by a factor of 3- to 4-fold.

When considering threshold values for therapy, an increase of coronary perfusion of only 33% will be assumed for safety reasons; this value can also be safely assumed for the heart under pathologic conditions (cf. [2]). This would give a minimum necessary myocardial avDO\(_2\) of 9 mmHg. The question to which coronary venous O\(_2\) partial pressure oxygen can be extracted has been extensively investigated in the past (cf. [2]). In this case, also for safety reasons, a critical value for the coronary venous pO\(_2\) of 10 mmHg is assumed rather than that of 4-7 mmHg described in the literature.
Thresholds for \( O_2 \) Concentration in Acute Hypoxemia

On the basis of the minimum acceptable myocardial \( \text{avDO}_2 \) (9 ml/dl), the critical coronary venous \( pO_2 \) (10 mm Hg) and the actual \( O_2 \) content curve (\( cO_2 \) as a function of \( pO_2 \), it is possible to derive the therapeutic thresholds for arterial \( O_2 \) concentration. The results are illustrated in figure 1. Although a normal \( O_2 \) content curve can be assumed in acute hypoxic and anemic hypoxemia (half saturation pressure \( pO_2 \) [0.5] = 27 mm Hg), a significant leftward shift in the \( O_2 \) content curve is observed.

![Fig. 1. O2 content curves (cO2 as a function of pO2) for various forms of acute hypoxemia. The figure should underline the fact that, at an \( O_2 \) extraction of blood to a coronary \( pO_2 \) of 30 mmHg, the myocardium maintains its \( \text{avDO}_2 \) of 9 ml/dl (increased coronary flow of around 33%) in different ways: Hypoxic hypoxemia can be tolerated up to a \( pO_2 \) of 30 mmHg, tensive hypoxemia up to a \( cO_2Hb \) of 30% and anemic hypoxemia up to an Hb concentration of 7.5 g/dl.](image)
in CO intoxication (toxic hypoxemia). In this case a half saturation pressure of around 16 mm Hg can be assumed [1]. Again for safety reasons, an Hb concentration of 14.5 g/dl has been assumed in all cases described here for determining the O2 content curve.

The differences in O2 content curves and the different regions of these curves that are relevant during the passage of blood through the tissue lead to different threshold values for the arterial O2 concentration:

- In normocapnia, ca\textsubscript{O2} = 13.7 m\textsubscript{mol/L} (39% COHb),
- in hypocapnia, ca\textsubscript{O2} = 11.0 m\textsubscript{mol/L} (pa\textsubscript{CO2} = 30 mm Hg), and
- in anemia, ca\textsubscript{O2} = 10.4 m\textsubscript{mol/L} (Hb = 7.5 g/dL).

It must be emphasized at this point that these threshold values for the O2 concentration include a series of safety factors as mentioned above (coronary dilatation only 33%, Hb only 14.5 g/dL, critical coronary venous pO2 (10 mm Hg). This is especially the case in anemic hypoxemia, where critical O2 concentrations of only 6 m\textsubscript{mol/L} can readily be justified [2].

It must also be mentioned that these threshold values are only valid for single cases and not for combinations of two or more disorders. The therapeutic threshold value for a hypoxic plus anemic hypoxemia, for example, must be set more carefully, i.e. higher, than that for anemia alone.

**Thresholds for O2 Concentration in Chronic Hypoxemia**

Compensation mechanisms will be brought into play depending upon the severity and duration of chronic hypoxemia. This involves primarily a rightward shift in the O2 binding curve (reduced affinity) due to a change in intracapillary 2,3-DPG concentration, an increase in blood Hb concentration and an improved microcirculation (capillarization, vasodilatation). In the myocardium (limiting organ) there is thus a partial improvement in arterial hypoxemia, a decrease in the necessary in\textsubscript{v}DO\textsubscript{2} as well as an improvement in O2 utilization. Since these factors can hardly be assessed, the threshold values in chronic hypoxemia must be set carefully. It is certainly justified to adjust the thresholds for the chronic situation downwards by about 1/3. This would result in the case of chronic anemic hypoxemia, for example, in a critical O2 concentration of around 7 m\textsubscript{mol/L}, representing an Hb concentration of approximately 5 g/dL; clinical experience suggests that this value is not only valid for recumbent patients (at rest).
Summary

A therapeutic threshold value for the arterial $O_2$ concentration ($cO_2$) must be centered around the human myocardium at rest since the heart, due to its large $avDO_2$, must be considered as the limiting organ. Under the conservative assumptions of only little coronary dilatation (35%), a critical coronary venous $pO_2$ of 10 mm Hg, an Hb concentration of only 14.5 g/dl, and using a normal or (in the case of CO intoxication) a leftward shifted $O_2$ binding curve, therapeutic threshold values in acute hypoxemia are derived of 13.7 mmHg in isoxemia, 11.0 mmHg in hypoxia and 10.4 mmHg in anemia. Under chronic conditions these values should be reduced by about 1/3.

References


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