Zander, Mertzlufft (eds.): The Oxygen Status of Arterial Blood,
pp. 233–237 (Karger, Basel 1991)

Therapeutic Thresholds for Acute and Chronic Alterations in Arterial O_2 Concentration

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Introduction

The maintenance of the O_2 supply to an organ requires both an adequate O_2 concentration and perfusion (O_2 availability), i.e. convective transport to the organ, and a sufficient O_2 partial pressure, i.e. diffusive transport. An adequate arterial O_2 concentration almost always guarantees the diffusion of a sufficient amount of O_2 from the blood into the tissue. Only under extreme conditions can the O_2 in the blood not be extracted, i.e. cannot be consumed by the tissue. A limiting value for the arterial O_2 concentration that supports the physiological supply of O_2 to all human organs in a resting state must be logically centred around the organ with the greatest O_2 utilization, i.e. O_2 extraction with a single passage of blood through the capillary bed.

The Myocardium as Limiting Organ

The arteriovenous O_2 difference ($avDO_2$), expressed in concentration units (e.g. ml/dl, ml O_2/100 ml blood), is the parameter used to assess O_2 utilization. From table 1 it is evident that the heart is the organ with the greatest $avDO_2$ and can therefore be considered as the limiting organ. Apart from the fact that the myocardium shows the greatest $avDO_2$ among all the organs (12 ml/dl), the table also illustrates a further unique

Table 1. Oxygen consumption ($\dot{Q}O_2$), perfusion ($\dot{Q}$) and arteriovenous O_2 difference ($avDO_2$) in human organs at rest.

Organ	Weight (g)	$\dot{Q}O_2$ (ml/min)	$\dot{Q}$ (ml/min)	$avDO_2$ (ml/ml)
Liver	2,500	55 (55)	1,400 (2,100)	0.04 (0.026)
Kidneys	300	18 (18)	1,200 (1,800)	0.015 (0.01)
Brain	1,400	50 (50)	775 (1,165)	0.065 (0.043)
Heart	300	30 (45)	250 (375)	0.12 (0.12)
		45*	750*	0.06*
Muscle	30,000	60 (60)	850 (1,275)	0.07 (0.047)
Other	35,500	62 (62)	1,025 (1,540)	0.06 (0.040)
Total	70,000	275 (290)	5,500 (8,255)	0.05 (0.035)

Values in brackets: Increase in cardiac output by 50% as a result of hypoxemia.

* 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 ⅔ 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 ml/dl.

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 pathologocial conditions (cf. [2]). This would give a minimum necessary myocardial $avDO_2$ of 9 ml/dl. 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 $avDO_2$ (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

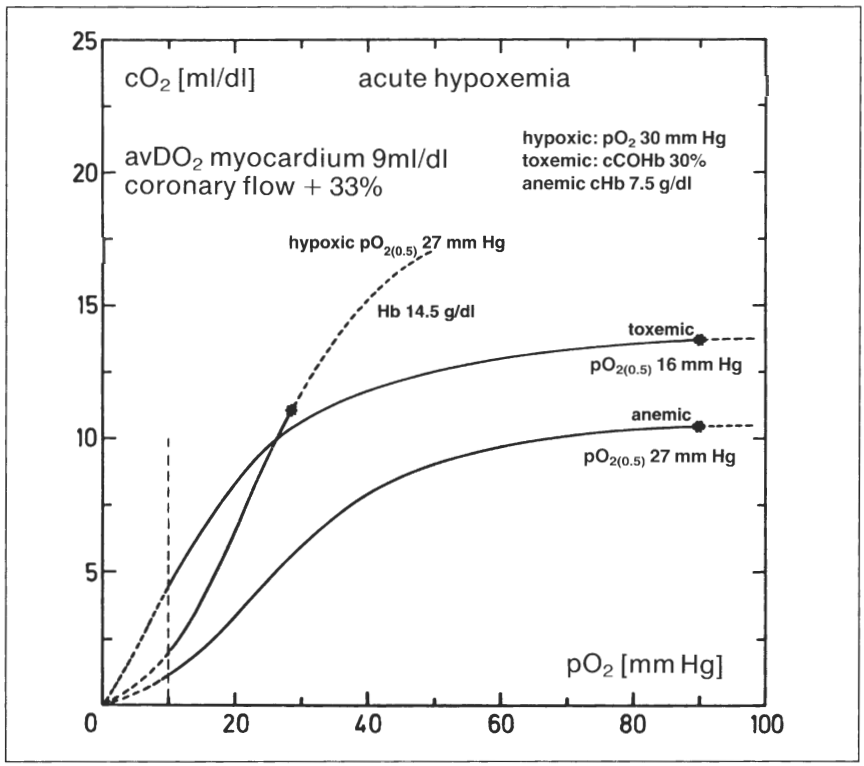

Fig. 1. O_2 content curves (cO_2 as a function of pO_2) for various forms of acute hypoxemia. The figure should underline the fact that, at an O_2 extraction of blood to a coronary pO_2 of 10 mmHg, the myocardium maintains its $avDO_2$ of 9 ml/dl (increased coronary flow of around 33%) in different ways: Hypoxic hypoxemia can be tolerated up to a paO_2 of 30 mmHg, toxemic hypoxemia up to a cCOHb of 30% and anemic hypoxemia up to an Hb concentration of 7.5 g/dl.

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 O_2 content curve.

The differences in O_2 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 O_2 concentration:

In toxemia caO_2 = 13.7 ml/dl (30% COHb),
in hypoxia caO_2 = 11.0 ml/dl (paO_2 = 30 mmHg), and
in anemia caO_2 = 10.4 ml/dl (cHb = 7.5 g/dl).

It must be emphasized at this point that these threshold values for the O_2 concentration include a series of safety factors as mentioned above (coronary dilatation only 33%, cHb only 14.5 g/dl, critical coronary venous pO_2 10 mm Hg). This is especially the case in anemic hypoxemia, where critical O_2 concentrations of only 6 ml/dl 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 O_2 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 O_2 binding curve (reduced affinity) due to a change in intraerythrocytic 2,3-DPG concentration, an increase in blood Hb concentration and an improved microcirculation (capillarization, vasodilation). In the myocardium (limiting organ) there is thus a partial improvement in arterial hypoxemia, a decrease in the necessary $avDO_2$ as well as an improvement in O_2 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 ⅓. This would result in the case of chronic anemic hypoxemia, for example, in a critical O_2 concentration of around 7 ml/dl, representing an Hb concentration of approximately 5 g/dl; clinical experience suggests that this value is not only valid for recumbant patients (at rest).

Summary

A therapeutic threshold value for the arterial O_2 concentration (caO_2) must be centred 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 (33%), 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 hypoxemias are derived of 13.7 ml/dl in toxemia, 11.0 ml/dl in hypoxia and 10.4 ml/dl in anemia. Under chronic conditions these values should be reduced by about ⅓.

References

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