Oxygen and carbon dioxide transport via colloids?

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Introduction

When a patient loses blood the reduction in volume is far more difficult to compensate for, even under acute conditions, than the loss of hemoglobin. This fact has been responsible for the justified and widespread use of plasma volume expanders in recent years.

A question that arises again and again in this context concerns the minimum hemoglobin concentration tolerated under acute and chronic conditions. We therefore need to consider the hemoglobin functions that are significant for O_2 and CO_2 transport:

- O_2 transport in the form of O_2Hb to the heme groups (up to a maximum of 1.39 mL O_2/g Hb);
- CO_2 transport to the NH_2 groups of the globin residue in the form of CO_2Hb (carbaminohemoglobin); and
- CO_2 transport in the form of HCO_3^- (bicarbonate) when the globin residue of Hb has buffered the H^+ ions deriving from H_2CO_3 ($CO_2 + H_2O$)—Hb as the respiratory and non-respiratory buffer of the blood.

The limiting factor in the use of colloidal plasma volume expanders, in cases in which hemodilution is necessary, as in hemorrhage, or in which it is therapeutic, as in iatrogenic hemodilution, is the minimum Hb concentration necessary to supply O_2 and/or remove CO_2 from tissue.

O_2 supply and CO_2 removal from tissue

The determinants of O_2 supply to tissue are the circulation, on the one hand, and the arterial O_2 concentration, on the other (Fig. 1), the product of both parameters giving the oxygen available to the tissue. As far as the blood is concerned, in addition to an adequate O_2 concentration, the necessary CO_2 partial pressure must also be available to ensure diffusion of O_2 from the blood into the tissue.

O_2 supply to tissue ($\dot{Q}O_2$) is ensured when the O_2 delivery ($\dot{A}O_2$), i.e., the product of circulation ($\dot{Q}$) and arterial O_2 concentration (caO_2), is sufficient, and the necessary O_2 partial pressure difference (ΔpO_2) is reached. CO_2 removal from the tissue is ensured when the product of circulation and venous CO_2 concentration ($cvCO_2$) is sufficient. The CO_2 partial pressure difference ($\Delta pCO2$) and local pCO_2 remain low.

There may be rare instances where, despite the presence of an adequate O_2 concentration, the necessary O_2 partial pressure is lacking. This could be the case in CO intoxication, where tissue supply is endangered not by a reduction in the arterial O_2 concentration, but because of the extreme displacement of the O_2 binding curve to the left (reduction in O_2 partial pressure). It is much more common for the O_2 concentration and O_2 partial pressure to be reduced,

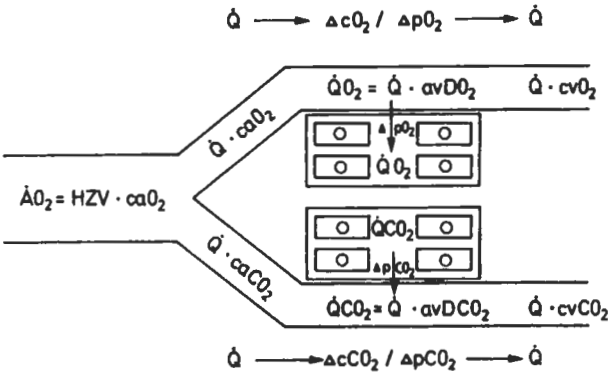

Fig. 1 Determinants of O_2 supply and CO_2 removal from tissue

and the O_2 partial pressure determines the O_2 concentration here, as can be seen from the O_2 content curve.

Finally, an attempt can be made to improve the delivery of O_2 to tissue in cases of hypoxia by administering pure oxygen to raise the O_2 partial pressure until an adequate O_2 concentration is achieved.

Since the O_2 concentration in the blood is determined by the large proportion of O_2 bound to Hb (the product of O_2 saturation, Hb concentration, and the Hüfner factor of 1.39 mL/g) and the relatively small proportion of physically dissolved O_2 (the product of O_2 partial pressure and O_2 solubility), hemodilution will reduce the amount of chemically bound O_2. The relationship between O_2 concentration and O_2 partial pressure or Hb concentration is shown in Figure 2.

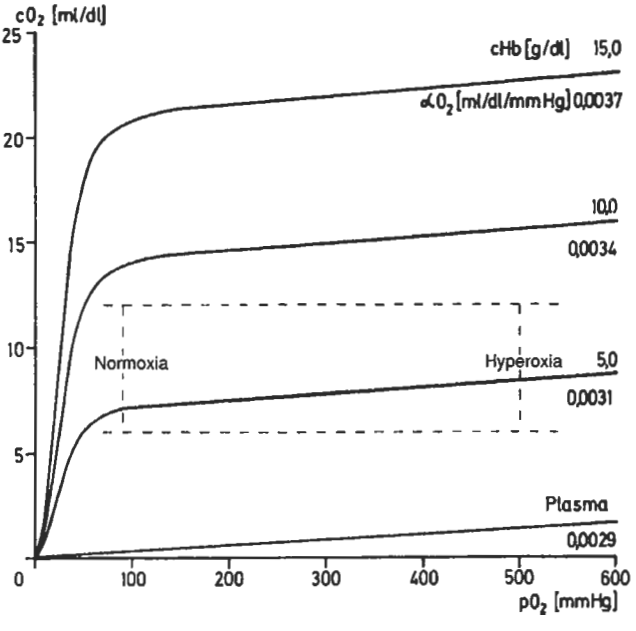

Fig. 2 O_2 content curve of the blood as a function of Hb concentration

The oxygen content in the blood (cO_2) is determined by the O_2 partial pressure, and depends, on the one hand, on the Hb concentration (cHb) (chemically bound O_2), and, on the other, on O_2 solubility (αO_2) (physically dissolved O_2). Physically dissolved O_2 is of greater significance in hyperoxia (art. pO_2 e.g., = 500 mmHg), if the Hb concentration is reduced e.g., from 15 to 5 g/dL, than it is in normoxia (art. pO_2 = 90 mmHg).

Even though it might appear that physically dissolved O_2 is negligible, there are some exceptions to this general observation:

1. If colloids care capable of exerting any influence at all on the O_2 supply to tissue, this can only be via a change in the concentration of physically dissolved O_2.
2. One characteristic of the microcirculation is that different sections very close to each other can have very different hematocrit values. The dynamics of the tone of the smooth muscles of vessels not only bring about a continuous change in the blood circulation in individual capillaries, but also cause a redistribution of erythrocytes amongst the individual capillaries (cf. [2]). For this reason, the physically dissolved O_2 of the plasma is important as the "baseline O_2 concentration".
3. Together with local pCO_2 and pH, the physically dissolved O_2 determines the tone of the vessel smooth musculature via local pO_2, and therefore plays a decisive role in adjusting the overall peripheral resistance.
4. In cases of hyperoxia, i.e., where there is an increase in inspiratory and thus in arterial O_2 partial pressure to values in the region of 400–6000 mmHg, the physically dissolved O_2 takes on increased significance, since both the O_2 concentration and the O_2 partial pressure of the plasma can be markedly increased.

The determinants of CO_2 removal from tissue are once again the circulation and the venous CO_2 concentration of the blood, or the increase in the concentration of arteriovenous CO_2. The larger this concentration increase, the lower the resulting venous CO_2 partial pressure (cf. Fig. **1**). Apart from circulation, the venous CO_2 partial pressure also determines the blood's ability to transport CO_2.

The blood's means of transporting CO_2, namely in the form of HCO_3^-, carbaminohemoglobin and in physically dissolved form, are all a function of the CO_2 partial pressure, as can be seen from the CO_2 binding curve for the blood. A small section of this CO_2 binding curve is shown in Figure **3** which, compared with the O_2 content curve, additionally describes the dependence on Hb concentration. This dependence of the CO_2 binding curve of the blood on Hb concentration is derived from various data in the literature (Zander, unpublished data).

The CO_2 concentration in the blood (cCO_2) is determined by the CO_2 partial pressure (pCO_2), and depends, on the one hand, on the Hb concentration (cHb) and the O_2 saturation (sO_2)—chemically bound CO_2 (HCO_3^- + carbaminohemoglobin)—and, on the other hand, on the CO_2 solubility in blood (αCO_2)—physically dissolved CO_2. Assuming an arterial pCO_2 of 40 mmHg, venous pCO_2 depends on the CO_2 production ($avDCO_2$) and cHb and sO_2 (O_2 consumption). Only if cHb has an extremely low value can unphysiologically high venous pCO_2 values result (Fig. **3**).

Since the formation of carbaminohemoglobin also depends on the oxygenation of hemoglobin (the so-called Haldane effect), not only the decrease in O_2 saturation but also CO_2 production (derived from O_2 consumption via the RQ) has to be taken into consideration when determining the resulting venous CO_2 partial pressures.

An example from Figure **3** may clarify this. Assuming an Hb concentration of 10 g/dL and an arterial O_2 saturation approaching 100%, then, if the CO_2 production was 5 mL/dL ($avDO_2$ = 6 mL/dL), CO_2 partial pressure would rise from 40 to 47.5 mmHg, and O_2 saturation would drop to 55%. With an $avDCO_2$ of 10 mL/dL, venous pCO_2 would rise to 56.5 mmHg, and venous O_2 saturation would drop to just 12 % ($avDO_2$ = 12 mL/dL).

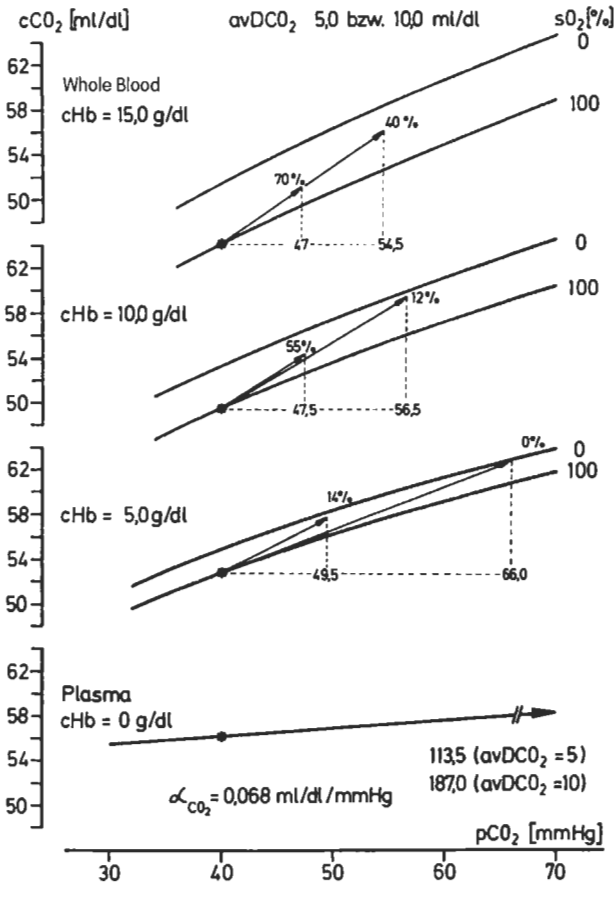

Fig. 3 CO_2 content curve for blood as a function of Hb concentration

This rise in venous CO_2 partial pressure can be seen as relatively normal, and does not pose a problem.

If, however, a capillary is perfused solely with plasma, then the venous pCO_2 would still be 113.5 mmHg at an $avDCO_2$ of 5 mL/dL, or 187.0 mmHg at an $avDCO_2$ of 10 mL/dL ($avDO_2$ = 12 mL/dL, e.g., myocardial), an extreme plasma pCO_2 value corresponding to a plasma pH of approximately 6.8–6.9.

As soon as the O_2 saturation of venous blood approaches zero (O_2 consumption = O_2 delivery), this being dependent solely on the Hb concentration, venous pCO_2 rises very markedly, and the pH falls correspondingly.

Since local tissue pCO_2 and pH are decisive for the adjustment of the tone of the vessel smooth musculature, the CO_2 solubility in plasma assumes particular importance, since it represents the "baseline CO_2 concentration," and is therefore the sole determinant of venous pCO_2, in the event that perfusion is carried out using plasma alone.

Whenever hemoglobin is to be replaced with a colloidal plasma volume expander, therefore, not only the O_2 solubility, but also the CO_2 solubility, in the volume expander should be high, in order to ensure a baseline level of CO_2 removal.

O_2 and CO_2 solubility in plasma volume expander solutions

The O_2 and CO_2 solubility at 37 °C was measured for various plasma volume expanders. The solutions were allowed to equilibrate with defined gas mixtures (pO_2, pCO_2) using a precision gas mixing apparatus (Ciba Corning 192). The resulting O_2 concentration was measured using the so-called O_2 cuvette (cf. [3]) and the CO_2 concentration was measured using a CO_2 analyzer (Ciba Corning 965) and expressed as mL/dL/mmHg. The results are shown in Table **1** for O_2 and Table **2** for CO_2.

Table 1: solubility values at 37°C in various media in mL/dL/mmHg and as percentages of the corresponding solubility in a 0.9% NaCl solution (100%)

Substance		αO_2 (mL/dL/mmHg)	(%)
H_2O		0.0032	106
0.9 % NaCl		0.0030	100
Plasma		0.0029	95
Dextran 60	6 g/dL	0.0027	91
Dextran 40	10 g/dL	0.0025	84
HES 450	6 g/dL	0.0028	92
Oxypolygelatin	5.5 g/dL	0.0027	91
Polypeptide	3.5 g/dL	0.0028	93

As has already been demonstrated to some extent [2], the O_2 solubility of very different plasma volume expanders does not differ much from that of plasma or physiological NaCl solution. The situation changes, however, when the colloid concentration is markedly increased. The O_2 solubility drops considerably with a 10 g/dL solution of dextran 40, compared to the value with plasma (only 84% of the value for 0.9% NaCl).

CO_2 solubility resembles O_2 solubility, with no appreciable changes observed between a 0.9% NaCl solution and colloidal plasma volume expander solutions. Only if the concentration is markedly increased (e.g., 10 g/dL HES 200) does the solubility drop noticeably (only 92% of the value for 0.9% NaCl).

Comparison of the measured values with data in the literature [1] shows that this method delivers reliable data.

It appears that oxypolygelatin has a markedly higher CO_2 solubility value, compared with 0.9% NaCl and plasma. This finding is even clearer if the value is measured at a smaller pCO_2 (in this case 100 mmHg). Both Haemaccel (based on polypeptides) and Gelifundol S (based on oxypolygelatin) show twice the CO_2 solubility of plasma at physiological pCO_2 (40 mmHg).

To be more precise, this is not an increase in the CO_2 solubility in the physiological pCO_2 range of the above preparations, but the fact that they have isolated NH_2 groups with a low buffering ability. This property leads to a buffering of H^+ from H_2CO_3, thereby forming

Table 2 solubility values at 37 °C in various media in mL/dL/mmHg and as percentages of the corresponding solubility in a 0.9% NaCl solution (100%), compared with data in the literature

Substance		αCO_2 (mL/dL/mmHg)	(%)
Literature data			
H_2O		0.0732	103
0.9 % NaCl		0.0710	100
Plasma		0.0681	96
Measured data (pCO_2 = 700 mmHg)			
0.9% NaCl		0.0715	101
Dextran 60	6 g/dL	0.0697	98
Dextran 40	10 g/dL	0.0672	95
HES 200	6 g/dL	0.0701	99
HES 450	6 g/dL	0.0672	95
HES 200	10 g/dL	0.0655	92
Oxypolygelatin	5.5 g/dL	0.0866	122
Measured data (pCO_2 = 100 mmHg)			
0.9% NaCl		0.0690	97
Oxypolygelatin	5.5 g/dL	0.1220	172
Polypeptide	3.5 g/dL	0.1180	166

HCO_3^- and leading to an apparent increase in CO_2 solubility. This does not, however, affect the desired CO_2 transport, as the CO_2 transport capacity of the preparations is markedly raised.

Conclusions

Colloidal plasma volume expanders not only exert an influence on the O_2 supply and CO_2 removal from tissue by virtue of their ability to transport O_2 and CO_2 in physically dissolved form, but they also thereby influence the value of the total peripheral resistance, depending on whether there is a local pO_2 fall or pCO_2 rise.

Measurements of O_2 and CO_2 solubility in plasma volume expanders have shown that appreciable differences from plasma or 0.9% NaCl are only to be expected if the colloid concentration is of the order of 10 g/dL.

Oxypolygelatin and polypeptide-based solutions exhibit a markedly increased CO_2 transport capacity in the physiological pCO_2 range.

References

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3 Zander R. Photometrische Messung der arteriellen O_2-Konzentration. In: Zander R, Mertzlufft B, eds. Der Sauerstoff-Status des arteriellen Blutes. Basle: Karger, 1988:216.

Discussion

Boldt: What influence does the change in viscosity have on the peripheral resistance?

Zander: I did not go into the role of viscosity. Naturally, the molecular weight and concentration of the colloid play a part. I am quite certain that the viscosity exerts a marked influence on the value of the peripheral resistance.

We will certainly have an opportunity during this meeting to discuss which colloid is optimal from the point of view of "water-binding" and "concentration".

Kiesewetter: What is the importance of the increased removal of CO_2 within the context of hemodilution and vasoconstriction? Is the high CO_2 transport capacity desirable?

Zander: It is not known whether the limiting factor for hemodilution is oxygen or CO_2. The physiological balance is inevitably destroyed by the reduction of hemoglobin.

Boldt: You maintain that the improvement seen with gelatin preparations is due to a lower change in peripheral resistance. That is not in the least desirable. An improvement in the microcirculation, especially in view of the Hb reduction, is of clinical significance. This is so, for instance, in patients with myocardial disease and coronary heart disease. It is exactly these patients who benefit from a reduction in resistance.

Zander: In those cases in which vasodilation occurs where we want it to, then I agree. Generally, though, hemodilution cannot be influenced in such an isolated way. One can suddenly come up against a threshold at which the peripheral resistance falls apart. From a theoretical viewpoint, there is no evidence to date of how far one can proceed with hemodilution without reaching this threshold.

Buzello: Is oxygen transport through colloids possible?

Zander: Oxygen transport through colloids is not possible to any appreciable extent, except under hyperbaric conditions.