Oxygen transport and doubts about PEEP

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Three factors in particular govern the transport of oxygen to the tissues, namely cardiac output (probably the most important), the hemoglobin content of the blood and hemoglobin saturation, as expressed in the formulas[1]

$$\text{oxygen transport } (TO_2) = \text{cardiac output} \times \text{arterial oxygen content}$$

$$\text{arterial oxygen contents} = \text{hemoglobin concentration percent} \times \text{saturation} \times 1.34 + \text{arterial oxygen tension} \times 0.003$$

These three factors may be termed the "coarse adjustment" for oxygen transport and delivery, as opposed to "fine adjustments" such as pH, temperature, 2, 3 dpg and individual variations in the oxyhemoglobin dissociation curve, though these may be significant factors in disease. There is a linear relationship between oxygen transport and cardiac output (*Fig. 1*), and its range is not as restricted by physiologic limits as are hemoglobin concentration and saturation.

Severe impairment of oxygen transport is commonly a major problem in patients with lung failure after cardiac surgery. Positive end-expiratory pressure (PEEP) has become an established technique for improving arterial oxygenation in this situation and in similar conditions that belong to the family

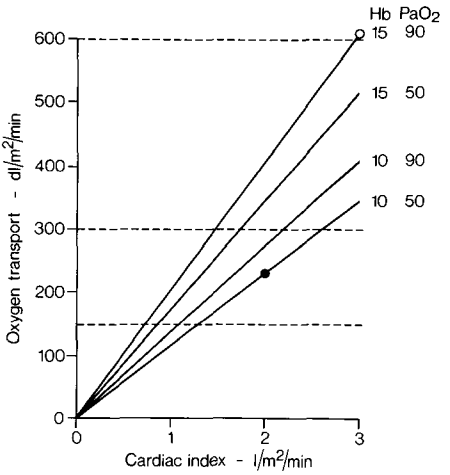

Fig. 1. The slope of the line especially depends on the hemoglobin concentration of the blood and on the arterial oxygen tension (PaO_2). The influence of these two factors increases as the cardiac output rises. The basal oxygen consumption in an average healthy adult is about 150 $dl/m^2/min$, though tissue oxygen supply should be at least twice this (300 $dl/m^2/min$) since venous blood is never fully desaturated.[1] Some workers suggest it should even be 600 $dl/m^2/min^2$ in the sick patient and certainly if he has sepsis or pyrexia. The solid dot and circle refer to the example shown in *Figure 2* before and after correction of a reduced cardiac output, anemia, and hypoxemia.

of lesions termed the adult respiratory distress syndrome (ARDS). But despite current enthusiasm for PEEP and its various degrees and a widespread belief in its therapeutic value, there have been few controlled studies and there is little or no evidence that it is ultimately beneficial in terms of morbidity and mortality in ARDS, however dramatically it improves a low arterial oxygen tension (PaO_2), and even though it can delay a fatal outcome.[2,3] The apparent decrease in the mortality of ARDS since the introduction of PEEP, which is claimed by some centers may be due to other factors, including other and simultaneous advances in therapy, more skilled management, and changes in diagnostic criteria. Moreover, there is still no generally accepted definition of ARDS in terms of physiological parameters, or any agreed classification of its degrees of severity, though some workers have described their own criteria.[4] This makes it very difficult to compare results. Nonetheless, PEEP may have some prophylactic effect in patients who are at risk of ARDS developing, by reducing the incidence and/or the severity of this condition.[4-7]

There are several possible reasons for its disappointing influence on the outcome of established ARDS. First, it cannot reduce the underlying alveolar-capillary damage and it is not likely that it can prevent the escape of proteinaceous fluid into the alveoli.[8] Second, with mechanical ventilation and oxygen therapy, patients generally die not from hypoxia, which is severe only terminally, but from multiple organ failure and in particular heart failure, with sepsis as an important aggravating factor. Third, unless anemia and a reduced cardiac output are corrected, the rise in oxygen transport may be slight despite a dramatic rise in PaO_2 (*Fig. 2e*). Correction of these abnormalities alone can produce marked improvement in oxygen transport (*Fig. 2a, b, c*). Moreover, the rise in PaO_2 with PEEP may be associated with a paradoxical fall in oxygen transport if there is an associated reduction in cardiac output (*Fig. 2d*), and this reduction may not be reflected by a fall in systemic blood pressure,[9] although the compensatory rise in peripheral resistance could be detected by a fall in peripheral temperature. A fall in cardiac output will also aggravate the effect of the high physiological shunt in this situation if it leads to a fall in mixed venous oxygen tension.[10] PEEP must be used with great care if there is brain damage.[11]

There is no way of measuring the

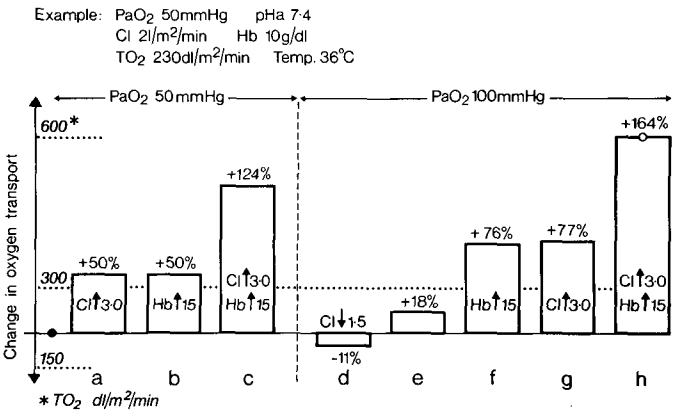

Fig. 2. Diagram illustrates changes in oxygen transport, which may be achieved by correcting hypoxemia, a reduced cardiac output, and anemia. Even if the PaO_2 remains unchanged (50 mm Hg) oxygen transport may be more than doubled simply by raising the cardiac output to normal and correcting anemia (c). Correcting hypoxemia alone does not produce a marked rise in oxygen transport until the cardiac output is raised and anemia treated (f, g, h).

cardiac output by clinical examination, though a cool periphery in a warm room when the central temperature is normal strongly suggests it is significantly reduced. This is a common finding in the critically ill with ARDS.[12] An inotropic agent will not only improve heart action, cardiac output and hence oxygen transport (*Fig. 2*), but it will also reduce the pulmonary vascular resistance,[13] which is generally raised in ARDS and is probably one of the factors leading to right heart failure in this condition.[14] While inotropic agents also increase physiological shunting and oxygen consumption, factors which can impair arterial oxygenation (*Fig. 3*) have less impact on oxygenation and oxygen transport than the rise in cardiac output.[15] Fresh blood is preferable for the correction of anemia because of its normal 2,3 dpg content and viable red cells. Although moderate hemodilution has a beneficial effect on oxygen transport, improving tissue flow and cardiac work by reducing blood viscosity,[16] and although some workers advise it,[17] its place in severe ARDS is uncertain, since the necessarily associated rise in cardiac output may not certainly occur in this situation. There is little reason to aim for a PaO_2 in excess of 90 or even 80 mm Hg in treating hypoxemia, since the dissociation curve is almost flat above these levels of PO_2. Although a high PaO_2 (> 200 mm Hg) can significantly increase the amount of oxygen physically dissolved in the blood, the dangers of adding oxygen poisoning to an already damaged lung debar this approach, even if it feasible. It is still uncertain whether or not existing lung damage has a protective effect against oxygen damage.

Current therapy tends to emphasize the need to improve oxygen supply to the tissues. Some workers have recently emphasized the equal importance of reducing oxygen consumption in patients with severe hypoxemia from lung damage who are candidates for membrane oxygenation. They recommend a combination of hypothermia to 34 C, sedation and profound muscle paralysis.[18] We have recently successfully treated an 18-month-old child in this manner. She

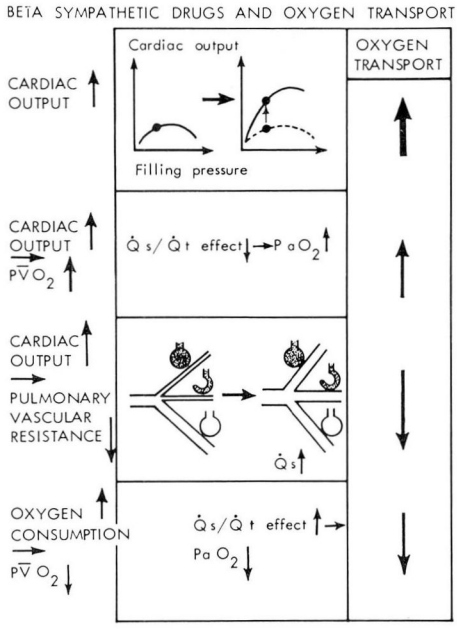

Fig. 3. Diagram illustrates four ways in which beta-sympathetic (inotropic) drugs can affect oxygen transport through their effects on the "quantity" ($\dot{Q}_s/\dot{Q}_t$, shunt fraction) and the "quality" (PVO_2, mixed venous oxygen tension) of the physiological shunt.[10] The dominant effect is a rise in oxygen transport, despite changes that tend to produce a fall.

had suffered a cardiac arrest and developed gross pulmonary edema, severe heart failure requiring inotropic therapy, and severe hypoxemia following respiratory obstruction after surgical repair of a cleft palate. Her condition was swiftly deteriorating despite mechanical ventilation until this therapy, which lasted 4 days, was instituted. A reduction in oxygen demand is clearly not only desirable in severe hypoxemia, but it also reduces heart work, an important gain if there is cardiac failure. It may also markedly improve arterial oxygenation, as was observed in this and the reported cases, perhaps by raising the mixed venous oxygen tension and so reducing the impact of the gross physiological shunt, in a manner similar to inotropic support and even PEEP.[10] The fall in temperature may perhaps also inhibit further development of the pulmonary lesion and allow swifter recovery. Steroid therapy appears to be of slight value in severe hypoxemia.[19]

Summary

Current therapy for hypoxemia caused by acute lung damage has tended to emphasize improvement in arterial oxygenation as a goal rather than correction of the quantitatively more important factors such as a reduced cardiac output and anemia. It has yet to be shown that PEEP is a significant advance in therapy, despite widespread belief in its value. It may also impair oxygen transport, rather than improve it. Reduction of oxygen consumption with a combination of mechanical ventilation, sedation, profound muscle relaxation, and hypothermia may prove to be a much more valuable approach to the problem of severe hypoxemia in ARDS than PEEP.

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