Symposium on HYPERBARIC MEDICINE

Physiological Aspects and Scope of Hyperbaric Oxygen Therapy

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Hyperbaric oxygen was introduced in clinical practice in the mid-fifties following the pioneering work of Boerema in Holland and Illingworth and Davidson in UK. In our country, it was first started at the Institute of Aviation Medicine, IAF, Bangalore in 1967, and a second centre followed shortly thereafter in Bombay. However, its use has remained restricted in India to these two centres and the general medical population is hardly conscious of the progress achieved in this field.

Hyperbaric oxygen (HBO) was originally introduced with the general idea that a large amount of oxygen could be made available deep into the tissues, specially in vital organs, for their survival in the event of and prior to circulatory arrest. Also, it could be of immense value in many pathological conditions where normal amount of oxygen is not available in the tissues while breathing air at atmospheric pressure (1 ATA).

From a physiological point of view, 3 areas need special consideration because important reactions take place in these regions. These are :—

a) the lungs

b) the blood, and

c) the tissue.

There are 3 gas laws which explain these reactions, viz.,

a) Boyle's law which relates gas volume inversely with pressure,

b) Dalton's Law which defines the partial pressure of a constituent gas in a mixture of gases, and

c) Henry's Law which identifies the volume of gases going into solution.

Although the above gas laws provide the physical basis for its application, by themselves they do not provide a physiological basis. Elevation of alveolar oxygen pressure several times will not necessarily raise the pressure throughout the body by the same value. The overall picture becomes modified by factors affecting lung diffusion, properties of haemoglobin, rates of oxygen uptake and blood flow, and by uncertainties concerning the diffusion of oxygen from capillaries into tissues.

Fresh air with 20.94% oxygen (O_2), on reaching the lung alveoli, contains 14.0% O_2 due to the presence of carbondioxide (CO_2) which is 5.6% by volume. On switching over to 100% oxygen breathing, a rapid rise in alveolar partial pressure of oxygen (pO_2) results. Initially, nitrogen wash out takes place at an exponential rate, reaching 98% by volume in approximately 7 minutes in normal lung. Alveolar pO_2 also changes simultaneously. The figures for alveolar gas compositions while breathing 100% oxygen at 1 atmosphere, 2 atmospheres, and 3 atmospheres are given in Table I.

Table-I

Alveolar gas tension (mm Hg) at 37°C

	Breathing AIR	Breathing OXYGEN		
	1 ATA	1 ATA	2 ATA	3 ATA
pN_2	570	0	0	0
pH_2O	47	47	47	47
pCO_2	40	40	40	40
pO_2	103	673	1433	2193
PB (Total)	760	760	1520	2280

Oxygen Uptake in the Lungs

Blood flow through the lung capillaries is very rapid. Oxygen passes from alveoli to the capillary blood by diffusion. As alveolar pO_2 is increased to several atmospheres, alveolo-pulmonary capillary oxygen transfer gets limited by a process of autoregulation. This limitation in oxygen transfer is reflected in a larger alveolar-arterial pO_2 difference which may reach as high as 100 mm Hg at 3 to 4 atmospheres of inspired oxygen pressure. This is responsible for a smaller than expected rise in arterial oxygen content. Following reasons are forwarded for such limitations of oxygen uptake :—

a) Greater increase of shunt above the normal (2%) via bronchial and pleural vessels.

b) Limitation in diffusion by difference between ventilation and perfusion.

c) Probable atelectasis of smaller lung units.

d) A response to increased oxygen tension, thereby increasing alveolar-blood barrier.

With rise in alveolar pO_2 from 1 to 5 ATA, a progressive decrease in pulmonary diffusion becomes evident as revealed by lowered diffusion constant for carbon monoxide and haemoglobin under high oxygen tension but it does not itself explain the observed interference with transpulmonary oxygen uptake.

Oxygen Transport in Blood

Oxygen is transported by the blood in two forms :—

a) chemically, as oxyhaemoglobin, and

b) physically in solution in plasma and in intracellular fluid in the erythrocyte.

Oxygen tension in the arterial blood is the primary factor which governs the volume of oxygen to be carried in both these forms. Considering that 1.34 ml of oxygen can combine with each gram of haemoglobin in chemical combination, 20.1 ml (normal Hb=15 g%) of oxygen will be carried per 100 ml of blood. Peculiarity of the pulmonary circulation and oxygen dissociation curve normally produce 98% saturation of Hb. Thus, increased oxygen tension under HBO can hardly increase the volume of oxygen in this form. However, the amount of dissolved oxygen increases linearly with increasing pressure and at 3 ATA can reach 6.6 vol% at 100 mm Hg. Thus, volumetrically, it is equivalent to more than 25% increase in arterial oxygen content.

Hyperbaric oxygen therapy is based on the following physiological principles :

a) increased volume of oxygen per unit of blood volume.

b) increased oxygen tension in the plasma and thereby in the tissue fluid around the vessel.

c) Increased oxygen tension gradient from the capillary blood to the metabolising cells, and

d) increased volume rate of "oxygen flow" (i.e., the amount of oxygen perfusing the tissue per minute) through the tissue.

Tissue Oxygen Tension

As oxygen is metabolised in the tissues, an increase in the pressure of oxygen in the inspired air does not necessarily produce corresponding rise in pO_2 in the tissue capillaries. The induced rise in pO_2 along a brain tissue capillary is not uniform from one end to the other unless the flow of oxygen is very much higher relative to the actual demand. At the extreme arterial end pO_2 may be elevated to that of inspired oxygen level. Average arterial

oxygen tension of 90 mm Hg may rise to 550 mm Hg when breathing 100 percent oxygen. At 3 ATA the average value may stay between 1550 and 1700 mm Hg. After decompression, the value drops to pre-compression values. Venous oxygen tension rises to high level in several instances shortly after compression. This rise may later be followed by some fall but still remains significantly above the precompression values.

Actual change of pO_2 that may occur in any particular organ depends on the tissue activity, amount of normal blood flow and oxygen consumption in each tissue. This, of course, is based on the conventional assumption that oxygen depletion from the blood occurs uniformly along the capillaries. Even in normal subjects for any particular pressure of inspired oxygen the "dose" of oxygen will differ from organ to organ and from tissue to tissue. Irregularities of blood flow and metabolism may cause local differences in oxygen tension within an organ or tissue. In pathological states, greater discrepancies occur between one gross or microscopic region to another. Other factors like temperature and drugs can cause further changes by affecting tissue metabolism.

Interference in CO_2 Transport

Under hyperbaric condition increased oxygen tension would prevent reduction of haemoglobin. This may affect CO_2 transport from the tissues. Fully oxygenated Hb is less effective than reduced Hb as a buffer for H+ ion. Thus, the transport of CO_2 and the H+ ion produced by its hydration in the tissue capillaries occurs at higher level of pCO_2 and an increase in arterial pO_2 under HBO leads to a rise in pCO_2 and acidity.

While breathing air at sea level, 90 percent of CO_2 molecules diffusing into the capillary blood become bound and are transported as bicarbonates or in carbamino forms. For each CO_2 molecule thus bound, one hydrogen ion is liberated in the red cell. Again, under air breathing state, the deoxygenation of Hb makes available enough basic groups to transport the entire amount of CO_2 with a respiratory quotient of 0.7 without change in pH. Hyperoxygenation inactivates this process. It is often thought *that extreme degree of CO_2 retention in tissues* would result under hyperbaric oxygen. Experimental studies have shown that at 3 ATA the increase in oxygen tension would prevent deoxygenation of Hb and may lead to a rise of 5 mm Hg in pCO_2 in organs like brain. The central hypercapnoea by oxygen is self-limiting. Increase of central pCO_2 by 5 mm is approximately equal to inhalation of 6 percent CO_2 in air at sea level. However, where narcosis, inefficient pulmonary ventilation, respiratory failure or other pathological states affecting CO_2 elimination exist, these may add to the effects of CO_2 retention produced by failure of the Hb deoxygenation.

When oxygen is administered in normal subjects breathing air at sea level, a transient decrease in ventilation occurs since increased oxygen tension tends to depress the chemo reflex activities. However, this shortly gives way to a light respiratory stimulation. This increased pulmonary ventilation is apparently a consequence of the rise in central pCO_2 and hydrogen ion concentration which again reduce arterial pCO_2. The slope of ventilatory response to CO_2 decreases concurrently. Thus, both stimulant and depressent effects of oxygen can co-exist. The respiratory response to CO_2 is diminished more by oxygen inhalation at 2 to 3 ATA than at 1 ATA. Where the respiration is depressed by drugs, injury or disease, administration of HBO decreases pulmonary ventilation by removing the normal hypoxaemic chemoreflex drive.

Circulatory Effects

At 1 atmosphere the circulatory effects of oxygen are mostly due to suppression of tonic activity of peripheral chemoreceptors, resulting in decrease in pulse rate and cardiac output. Rise in central pCO_2 leads to a stimulation of vagal centre. Changes in circulation in regional vascular beds are produced by oxygen. Vasoconstriction has been noticed in cerebral, coronary, eye and renal vessels. This vasoconstriction may be due to direct action of oxygen on vascular smooth muscles. Relationship of tissue oxygen tension to auto-regulation is well established. When the oxygen saturation falls from 100% to 30% the blood flow is found to increase to 25%. In contrast, HBO produces a

decrease in flow. The theory of auto regulation should explain both these phenomena. It has been suggested that diminished oxygen availability lowers oxygen supply to the smooth muscles of arteriolar wall which in turn weakens the wall and allows the pressure head to cause a dilation and increased flow. Lack of oxygen also causes blood vessels to dilate because of decreased ATP and other oxygen dependent substances that are required to maintain contraction. Vasoconstriction effect on oxygen can, however, be simply explained on the basis of direct effects on the vessel wall cells, increasing the strength of contraction of the local vessels and thus constriction. Oxygen, however, at a reasonable dose might do one thing, while a very high dose might begin to exert powerful biochemical poisoning of arteriolar smooth muscle cells. It may be that there are more than one dose-dependent curves for effects of oxygen on vessels, one based on the physiological influence and the other on toxicological influence. These could produce overlapping effect with one giving way to another under increasing tension. Besides the direct effect, the influence of central hypercapnoea, neurogenic factors and local chemical influences have also to be considered. It has been found that when arterial pCO_2 is held constant under O_2 administration to normal subjects at 1 ATA, cerebral vasoconstriction does not occur. It is, thus seen that a new balance develops with increase in arterial oxygen tension, increased tissue carbon-di-oxide and changes in hydrogen ion concentration.

Scope

Considering the various physiological aspects of the use of hyperbaric oxygen, its scope can be broadly defined in some of the clinical applications :-

a) Increase in oxygen capacity can be utilised in conditions where haemoglobin is lost or inactivated as in CO poisoning.

b) Increase in oxygen content can be effectively utilised to compensate for decreased blood flow in otherwise normal vascular beds. This can be of much use in peripheral vascular trauma or disease.

c) Increase in oxygen tension gradient between capillaries and tissues extends the distance of effective oxygen diffusion and thus can be effective in localised tissue ischaemia like frostbite. This can be of use in conditions where acute involvements of vital organs like brain may lead to permanent damage. HBO is likely to be of some value in such situations.

d) Ability of hyperbaric oxygen to increase the tissue pO_2 can create dramatic improvement in anaerobic infections like gas gangrene by creating hostile environment for their destruction, inhibiting further multiplication and promoting a possible neutralisation of toxin.

e) Elevated tissue pO_2 inside the tumour cells under HBO can enhance the effect of chemotherapeutic and radiation therapy in malignant conditions.

f) Inhibitory effects on lepra and tubercle bacilli have also been reported in some studies.

g) Oxygen toxicity is closely related to dose-duration of the therapy and this limits the use of hyperbaric oxygen, its duration of exposure and the magnitude of pressure.