FIRE EATER

Report

Use of Inergen for fire fighting purpose
- an assessment of personal and patient safety.
Special focus on effect of acute hypoxia healthy and sick individuals.

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Use of Inergen for fire-fighting purposes - an assessment of personal and patient safety. Special focus on the effect of acute hypoxia in healthy and sick individuals

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Purpose:

In this letter, the health aspects of short-term (less than 30 minutes) exposure to hypoxic gases will be highlighted. Hypoxic gas is considered inspiratory oxygen concentrations below 20.95% (normal oxygen concentration at 1 atmosphere) and in this context down to approx. 14%. It will also be highlighted how the addition of carbon dioxide (CO_2) to the inhaled air will affect the total oxygen supply to the body and brain. The recognized medical database www.pupmed.gov and textbooks in General Physiology and Biochemistry have been used for this letter.

Summary:

A review of published research indicates that shorter exposure (up to hours) to low inspiratory oxygen levels down to 14% O_2 is well tolerated by healthy individuals. The hypoxia experienced is similar to the hypoxia to which aviation passengers are exposed in commercial aviation. There are international guidelines and consensus for the transport of patients, which state that even quite ill patients can travel without further action.

By increasing the inspiratory carbon dioxide concentration to 3-4%, the tolerance for acute hypoxia is extended so that exposure to oxygen levels between 14% O_2 to 10% O_2 is also tolerated for a short time. Individual discomfort may be experienced in both general hypoxia and CO_2-compensated hypoxia.

At the case level, indications have been found that CO_2-compensated hypoxia in the range of 14-10% O_2 with 3-4% CO_2 may have a beneficial effect for patients with chronic obstructive pulmonary disease (COPD) as well as in patients with sequalae after acute vascular brain injury. These are areas that in the near future will be the subject of focused research at e.g. Department of Intensive Care for Brain and Nerve Diseases, Rigshospitalet, Copenhagen.

In practical terms, fire-fighting methods without the use of water are particularly relevant for intensive care and surgical sections, as immediate evacuation in connection with fire and fire alarms is very critical and practically impossible due to the patients' condition and connection to essential life support systems like respirators and cardiovascular inotropic agents.

Method:

For this document, the recognized medical database www.pupmed.gov has been used with keywords: hypoxia, gas, cerebral blood flow, auto-regulation, metabolism, hypercapnia, normocapnia, toxic, poison, hazard, safe, mitochondria, human, in vivo, in vitro, oxygen concentration, partial pressure and oxygen as well as carbon dioxide in various combinations. The document is not made as a systematic review. Relevant abstracts are read, and full text extracted and applied. In addition, textbooks in general physiology have been used.

Introduction:

The human being is basically physiologically adapted to life near the sea surface, where the air pressure around us is set at 1 atmosphere (atm). The air we breathe has a fixed distribution of Nitrogen (N) of 78.08%, oxygen (O_2) 20.95%, argon (Ar) 0.93%, carbon dioxide (CO_2) 0.04% and a number of noble gases such as Neon and Helium.

Despite our adaptation to life at sea level with pressures around 1 atm, man has always challenged physiology by moving up in altitude and down in depth. In the present review and discussion, it is the hypobaric environment (the low-pressure environment) that is in focus - the environment in which man finds himself in hiking to highlands and mountains and further with the help of various technological aids such as aircraft etc.

For many years, we have taken advantage of some of the opportunities that arises when changing the ordinary air composition and targeting the composition with regard to very specific needs and requirements for a desired effect. This is seen, among other things, in the very widespread altitude training among athletes as pre-competition preparations (1, 2). The lower oxygen concentration in high altitude stimulates the body to increased production of red blood cells which are essential in the oxygen-carrying capacity of the blood and thus energy to the cells. Under medical auspices, increased pressure has been used in i.e. hyperbaric medicine, where the increased partial pressure of oxygen leads to an increased solubility of oxygen in the blood and thus greater oxygen supply to acutely and chronically suffering cells as seen with carbon monoxide poisoning (3-5) and radiation damage after cancer therapy(6-8) .

Other technological possibilities for the use of manipulated air composition in the normobaric environment is seen, among other things, in firefighting/extinguishing.

Inhalation of air with lower oxygen composition is not a rare occurrence for people who do not reside in altitude. Every day, a large number of people are exposed to situations with lower oxygen supply (hypoxic level) through, for example, flights (9, 10) , fire protection systems, altitude training chambers (11) or stays in high altitude areas for work and leisure purposes(12, 13).

Oxygen is essential for energy production in the cells. The mitochondria are the cell's energy factory and can only function at an oxygen level above a given threshold. If the oxygen saturation in the blood falls below a given value (the threshold value), the energy-producing process in the mitochondria will initially switch to anaerobic metabolism and eventually stop.

Oxygenation of body tissues is the result of several factors: atmospheric pressure, blood oxygen levels, blood haemoglobin levels, heart rate, pumping capacity, tissue perfusion, and tissue oxygen consumption. The lowest acceptable limit for low inspiratory oxygen levels can therefore not be determined solely on the basis of oxygen levels in the air or oxygen supply in the blood but is a combination of all the above parameters.

If the oxygen concentration in the respiratory air (FiO2) is reduced at 1 atmospheric pressure, this is called isobar hypoxia.
Hypobaric hypoxia is achieved when atmospheric pressure is reduced. This is seen by flying, hiking in mountains and altitude chambers. There are some minor physiological differences between simulated isobaric hypoxia and hypobaric hypoxia. This is most notable by large pressure differences such as space travel, etc. In these circumstances of hypobaric hypoxia, a reduction in the amount of the dissolved oxygen just as the reduction in physically bound one is seen. Within ordinary atmospheric conditions, this connection is not relevant in relation to personal safety and health. Therefore, isobaric hypoxia and hypobaric hypoxia are considered equal situations in this review.

Hypoxia

Hypoxia is a condition with too little oxygen supply to the body's tissues. It is important to emphasize that mild hypoxia is not usually considered a health risk, thus prolonged intercontinental flights can be managed by the vast majority of people without this being associated with inconveniences or complications.

Factors such as atmospheric oxygen level, duration of exposure, workload during hypoxia, possibility of acclimatization/adaptation, possibility of rapid evacuation, genetic selection (indigenous peoples in the highlands) together with the elevation of stay will affect the risk profile of exposure to hypoxia. Individual risk factors and chronic diseases also play a role and will be discussed later.

The normal response of the human body to a sudden decrease in the oxygen supply to below 14.5%, corresponding to an altitude above 3000 m above sea level is of a compensatory nature. Resting heart rate and respiratory rate are increased to compensate for the reduced oxygen supply. Blood pressure usually remains unchanged(14).

Up to 5% of the population will respond to acute hypoxia with a decrease in blood pressure, slow heart rate and fainting, the so-called vasovagal syncope. This is often preceded by symptoms such as nausea, paleness and possibly cold sweats. In these people, fainting occurs more rapidly than in others at O_2 concentrations in the range of 14.5-9.7%. However, fainting (syncope) is considered by some to be a neuroprotective reaction, as fainting reduces the brain's oxygen consumption and thus has a protective effect in the short-term hypoxic situation (on a cellular level).

Short exposure to hypoxia

This review is limited to situations of extremely short hypoxia defined by the medical organization Union Internationale des Associations Alpinism (UIAA). UIAA is an umbrella organization for activities in environments with low oxygen levels (rated at pressures below 1 atm).

The term extremely short exposure to hypoxia covers situations such as civil aviation,

/ train traffic in high mountain areas, skiing, cable cars, altitude training chambers and therefore includes oxygen levels which is seen in fire containment/extinguishing.
These activities occur most frequently at altitudes of 1800-2600 m above sea level, which corresponds to 17.4% -15% isobaric oxygen concentration applicable to outdoor activities and down to 9-13% isobaric oxygen concentration for research/training and altitude chambers. The time of exposure to hypoxia in these situations is limited; from a few minutes up to hours. The International Civil Aviation Organization (ICAO), has set a maximum limit for pressure corresponding to an equivalent altitude of 2400 meters, equivalent to isobar 15.2% O_2, for cabin pressures in passenger aircraft. However, there is data to support the fact that airlines operate at lower than this, especially with modern aircraft (15).
If people stay in an environment with a persistent oxygen level between 17.0-14.8% (+/- 0.2), the body shows an immediate slight adaptation to hypoxia with increased heart rate at rest. During prolonged stay, there is an increased production of the hormone erythropoietin in the blood. The level of when the body begins to adjust varies 17.4-15.5% O_2, corresponding to 1500-2400m above sea level (16, 17). In summary, research shows that occupational exposure to oxygen concentrations down to 13% does not pose a health risk given short exposure times if defined precautions are followed (18, 19).
In the context of acute hypoxia, the term "time for useful attention" is used to indicate how long you can expect to act rationally at a given elevation or oxygen concentration (20).
For people who are professionally exposed to acute hypoxia, functional limits for exposure time and oxygen concentration have been set. It is not relevant in terms of time for usable awareness of extremely short exposure to equivalent altitudes/oxygen concentration up to 5000 m above sea level, corresponding to 11.1% O_2. An important point is that the hypoxic environment can be abandoned by in situations of simulated hypoxia. At 5500 m above sea level, corresponding to 10.4% O_2, a functional time limit for usable attention has been set to about 30 minutes (21).
People with medical conditions may experience discomfort and problems at such oxygen concentrations/heights (in addition to physiological compensation such as faster breathing and heart rate increase), while healthy individuals should tolerate this exposure without any problem. The duration of exposure here is too short to develop acute altitude sickness, and it is below the limit for when significant neurological risks occur. From the aeronautical literature, a limit of about

6,000 m above sea level has been set, corresponding to 9.7% O2, where one wants to maintain consciousness. This applies to healthy, young people who are sedentary and are suddenly exposed to elevation. At 8.5% O2, corresponding to 7000 m above sea level, the functional attention is estimated at 3-5 minutes (21). In normal individuals, tolerance to acute hypoxia improves with concomitant supply of CO2 to the inhaled air within these values (12.7-10% O2)(22).

Physical work capacity during hypoxia

Physical work increases the cellular oxygen demand and the hypoxia tolerance is consequently reduced (the threshold for when anaerobic metabolism is activated occurs earlier). At rest and at normal cardiac output, it takes each red blood cell (erythrocyte) approx. 0.75 second to pass the pulmonary capillaries, where gas exchange (carbon dioxide is excreted and oxygen is absorbed) takes place.

This passage time is consequently reduced in connection with physical activity and is measured at extreme physical activity down to approx. 0.25 seconds. To saturate the blood with oxygen at a hypoxic oxygen concentration down 11.9% is approx. 0.50 second pass time required as a minimum. With increasing altitude and decrease in atmospheric pressure and consequently decrease in the inspired oxygen concentration (FiO2), the maximum physical performance decreases by 10-15% per 1000 m above sea level, depositing at about 1500 m above sea level. Studies also show that healthy individuals are able to perform hard physical exertion (defined as work > 200 W) for several minutes at isobar 11% oxygen concentration equal to approx. 5000 m above sea level (23-30).

In commercial aircraft, altitude travel, etc., it is rare that hard physical work is sustained, and most activities are of very limited scope (estimated power 0.5-1.0 W/kg body weight). In these situations, there is no reason to believe that reduced FiO2 experienced in, for example, aircraft, will affect the human organism.

Hypoxia - how do patients with acute and chronic diseases respond?

Cardiac disease

Contrary to many people's beliefs, the heart is not the organ that carries the greatest risk when exposed to hypoxic situations. While heart muscle cells handle a high degree of hypoxia, it is the lungs that can become a limiting factor in a combined heart and lung failure (21)
The chronic ischemic heart disease patient will experience a marginally reduced physical performance and a somewhat earlier onset of symptoms with chest pain (angina pectoris) than non-heart disease individuals exposed to equivalent hypoxia (31).
Studies in patients with stable chronic heart disease have concluded that exposure to altitudes between 3000-3500 m above sea level (O2 concentration 14.5-13.6%) combined with moderate physical activity is generally safe (31-34). The International Air Transport Association (IATA) has prepared a manual for the transport of patients with chronic and acute illness. These are largely based on the hypoxic conditions a patient is exposed to during flight. For cardiac patients, flight without medical assistance or oxygen can be done in stable angina 10 days after a myocardial infarction and 2 days after coronary stenting of a cardiovascular disease (35). Thus, there is no evidence that hypoxia in the range within the scope of this paper is the acutely dangerous component for cardiac patients.

Lung disorder

Humans have a significant pulmonary reserve capacity, understood in such a way that even with very reduced functional lung volume, we can maintain a normal oxygen saturation in the blood. As a passenger and as a patient, people with lung disease have been subjected to extensive research in whit in the field of commercial aviation, which works with hypoxic environments and oxygen percentages down to approx. 15%. (36-44).
In the Medical Manual of IATA a comprehensive guideline for transporting the lung sick patient. It is recommended (based on research and consensus in the organization) that COPD (chronic obstructive pulmonary disease) patients can fly unaccompanied and without oxygen if they can

walk > 50 meters on land without experiencing dyspnoea or shortness of breath (35). Mild lung disease also does not appear to limit the possibility of mountain sports, even for the elderly. This accounts up to altitudes above 2500 m above sea level, corresponding to 15.4% O2 (45). In patients with severe COPD, they have been shown to have an increased incidence of dyspnoea during flights than healthy individuals exposed to similar oxygen concentrations (46-48).
For COPD patients with severe disease who experience reduced oxygen saturation under normal oxygen and pressure conditions, the following applies: if oxygen saturation <92% at sea level and/or who develop peripheral oxygen saturation drops to ≤84% after six minutes of gait test, use oxygen during flight. Scientific experiments from aviation confirm that patients with severe COPD may experience a decrease in O2 saturation, which is unacceptable. This is supported by clinical research where the significance of the partial pressure is considered significant. Thus, COPD patients may better tolerate isobar hypoxia than hypobaric hypoxia, allegedly due to the marginally reduced paO2 in hypobaric hypoxia (49)

Anaemia

The oxygen-carrying capacity of the blood can be affected by a number of different factors. Significant to the cells is that enough oxygen is delivered for the mitochondrial processes to run. Reduced transport capacity of oxygen in the blood may be due to blood loss, lower concentration of haemoglobin, poisoning with toxins that bind to both haemoglobin and cytochromes - (carbon monoxide and cyanide) that bind at the expense of oxygen. IATA's guideline recommends that passengers and patients have > 5.9 mmol/l haemoglobin in flight. A number of diseases that cause structural changes in the erythrocyte also affect its ability to bind and transport oxygen to the cells. Sickle-cell anaemia is a disease that must always have oxygen supplementation during flight due to the severely reduced oxygen-carrying capacity of the blood (35).
Tobacco smokers have a chronically elevated carbon monoxide (CO) in their blood. The concentration can fluctuate from 1-10% without affecting the smoker. Carbon monoxide binds to haemoglobin approx. 300 times better than oxygen. This applies to the adult smoker. Foetal haemoglobin binds CO approx. 600 times better than oxygen but can better absorb and release oxygen to the foetal cells in hypoxic environment. Smokers are thus disadvantaged in acute

hypoxia, but the degree of hypoxia must be high, as many smokers fly commercial flights and earlier while smoking, without this having affected them.

CO_2 compensation

Carbon dioxide (CO_2) is a metabolically active gas and is regulated in several different ways in the human organism. CO_2 has significant vasoactive effects on the cerebral vascular bed and thus significant for blood flow and oxygen supply to the brain. The regulation is controlled by central chemoreceptors which are sensitive to changes in the body's pH level (acid/base ratio) and thus react to the level of among other things H^+ ions. Recorded pH shifts rapidly induce compensatory respiratory changes and later initiates the renal compensatory mechanisms. Oxygenation at 1 atm generally passively follows these effects dictated by CO_2. In case of acute hypobaric hypoxia, the peripheral oxygen-sensitive chemoreceptors will stimulate the respiratory centre for increased activity. The increased respiration causes alveolar hyperventilation. This hypoxic hyperventilation, and its benefits at the alveolar level of O_2, partially compensates for the lower supply at the lung and artery level. Nevertheless, the hypoxia-induced blood flow to the brain is partially limited, and in some cases exceeded due to the hypocapnic vasoconstriction of the cerebral vessels and thus significant reduction of the partial pressure of CO_2 in the blood (50-53). CO_2 has a direct effect on the cerebral arterioles (54). A decreasing $paCO_2$, so-called hypocapnia, reduces the blood flow (the cerebral blood flow) due to vasoconstriction (55, 56). Significant hypocapnia can trigger flow-compromising vasoconstriction to an extent that triggers reduced oxygen supply to the brain leading to unconsciousness and, in severe cases, irreversible infarctions. In neuro-trauma patients with increased intracranial mass action and thus increased intracranial pressure, $paCO_2$ is significant and very controlling for the pressure in the brain. With reduced CO_2, the intracerebral volume is reduced due to reduced intracranial blood volume. Therefore, it has previously been an obvious treatment strategy to hyperventilate patients, thereby reducing life-threatening pressure increases in the brain. However, studies paradoxically show that although intracerebral pressure decreases with hyperventilation, overall morbidity and mortality increase. Therefore, the treatment strategy is relevant to keep $paCO_2$ tightly controlled around normal values in the seriously ill neurotrauma patient and allow increased $paCO_2$ in non-pressure threatened patients.

If the patient has lung disease at the same time, the addition of CO2 overall can reduce the complications in this type of patient (57, 58). An addition of CO2 to inspired hypoxic gas (air) can reduce hypocapnic vasoconstriction and thus maintain cerebral blood flow and oxygen supply to brain tissue (55, 59).

Research - Perspectives.

Exciting research and treatment aspects within the use of hypoxic/normoxic gases supplemented with increased inspiratory CO2 are evident. There is quite good scientific evidence for the effect of CO2 on intracranial pressure and intracerebral blood volume, auto-regulation and flow (60, 61). At the Department of Intensive Care for Brain and Nerve Diseases, University Hospital of Copenhagen, Rigshospitalet, preparations have been initiated for formalized human and animal experimental research in the areas of cerebral thromboembolism (both acute and secondary to cerebral haemorrhage) in combination with CO2-enriched inspiratory air. There will also be a focus on variations in the so-called penumbra zone (marginal tissue around an infarction) and the association with inspiratory CO2. In addition, a project is planned with a focus on late effects after blood clots in the brain and treatment with CO2-enriched air. The work is thought of as interdisciplinary research between Neuroanesthesiologists, Neurologists, Neurosurgeons and Veterinarians.

As a format for the research, 1-2 PhD´s are planned at the University of Copenhagen, SUND

On the technical side, a research project with a focus on Intensive treatment and firefighting is envisaged. The Innovation Laboratory under Neuroanesthesia may here be a close collaborator as it has 2 full-scale intensive care units for conducting experiments with firefighting in an environment with potentially high oxygen concentrations. This is increasingly relevant in line with increasing treatment needs at Covid-19 patients, which needs high flow oxygen treatment in often closed isolation rooms.

Conclusion

Based on the review of the general human physiology with a focus on the effect of oxygen and carbon dioxide on vessels in the brain and heart, in both healthy and in people with various medical conditions, it must be concluded that: Acute, short-term exposure to a hypoxic atmosphere with FiO2 down to about 14% is well tolerated by most people. As long as there is no simultaneous sustained hard physical exertion. There are implicitly significant individual tolerances for hypoxia (genetic, altitude adaptation, diseases, etc.) and differences in physiological response in acute hypoxia should therefore be expected. Research on the human response to FiO2 around 14-12% has been thoroughly investigated, as it is the oxygen concentration of inspiratory air in commercial passenger flights. International consensus guidelines for both regular passengers and patient transports with significant co-morbidity have been made and emphasize the safety of regular air traffic. Thus, few conditions require oxygen supplementation during flight.
The importance of total oxygen supply to the brain as well as the importance of paCO2 (FiCO2) is thoroughly elucidated in the neurosurgical and neuroanaesthesiological research. Thus, it is primarily patients with severe traumatic brain injuries, including increased intracranial pressure, who tolerate increased inspired CO2 poorly. For all patients not in risk of increased intracranial pressure, alveolar hyperventilation leading to vasoconstriction in the vessels of the brain in isolation poses a greater risk of morbidity and mortality.

Based on the above, it must be considered probable that the risk of neurological and cardiac complications is minimal with short-term (30 minutes) exposure to CO2 compensated hypoxia within the limits seen in commercial aviation, altitude chambers and fire extinguishing systems (FiO2 about 14-10% O2).

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