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Arterial Hyperoxia: Possible Risk and Outcome in Critically Ill Patients

Essay

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By

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Magid Gamil Reyad Kamel

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List of Abbreviations

ACC	:	The American College of Cardiology
ACS	:	Acute coronary syndrome
AHA	:	American Heart Association
ALI	:	Acute lung injury
ATA	:	Atmospheres absolute
ATP	:	Adenosine triphosphate
CaO_2	:	Oxygen content of blood
CAT	:	Catalase
CBF	:	Coronary blood flow
CBV	:	Coronary diastolic blood velocity
CF	:	Cystic fibrosis
CHF	:	Congestive heart failure
CNS	:	Central nervous system
COPD	:	Chronic obstructive pulmonary disease
CPAP	:	Continuous positive airway pressure
CVR	:	Coronary vascular resistance
DAMPs	:	Damage-associated molecular pattern molecules
DO_2	:	Oxygen delivery to the tissue
FiO_2	:	Fractional concentration of inspired oxygen
GSH	:	Glutathione peroxidase
HALI	:	Hyperoxic acute lung injury
Hb	:	Hemoglobin
HFNC	:	High-flow nasal cannula
ICU	:	Intensive care unit
IPPV	:	Intermittent positive pressure ventilation
LV	:	Left ventricle

List of Abbreviations (Cont.)

LVEDP	:	Left ventricular end diastolic pressure
NIV	:	Non-invasive ventilation
NO	:	Nitric oxide
NSTEMI	:	Non ST segment myocardial infarction
$PACO_2$	:	Alveolar levels of carbon dioxide
$PaCO_2$	:	Arterial carbon dioxide tension
PAO_2	:	Alveolar levels of oxygen
PaO_2	:	Partial pressure of oxygen in the blood
PIO_2	:	Inspired PO_2
PMNs	:	Polymorphonuclear neutrophils
PO_2	:	Partial pressure of O_2
$PtCO_2$	:	Transcutaneous carbon dioxide tension
RCT	:	Randomised controlled trial
RER	:	Respiratory exchange ratio
ROS	:	Reactive oxygen species
ROSC	:	Return of spontaneous circulation
SaO_2	:	Oxygen saturation level measured directly from an arterial blood sample
SOD	:	Superoxide dismutase
SpO_2	:	Oxygen saturation level measured from pulse oximeter
STEMI	:	ST segment myocardial infarction
SVR	:	Systemic vascular resistance
TTOT	:	Trans-tracheal oxygen therapy
UA	:	Unstable angina
V/Q ratio	:	Ventilation perfusion ratio
V_T	:	Tidal volume

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Introduction

Oxygen is a vital element in human survival and plays a major role in a diverse range of biological and physiological processes. In medical practice, it is among the most universally used agents for the treatment of critical illness and part of the routine treatment in acute shock and emergency medicine ***(Schultz et al., 2015)***.

While avoiding hypoxemia has long been a goal of critical care practitioners, oxygen therapy during mechanical ventilation, anesthesia, and resuscitation usually exceeds physiological level and less attention has been paid to the potential for excessive oxygenation ***(Gershengorn et al., 2014).***

Hyperoxia is a state of excess supply of O_2 in tissues and Organs. Oxygen toxicity occurs when the partial pressure of alveolar O_2 (PAO_2) exceeds that which is breathed under normal conditions. With continuous exposure to supra physiologic concentrations of O_2, a state of hyperoxia develops ***(Ciencewicki et al., 2008).***

Exposure time, atmospheric pressure, and fraction of inspired O_2 (FiO_2) determine the cumulative O_2 dose leading to toxicity. Oxygen is toxic to the lungs when high FiO_2 (>0.60) is administered over extended exposure time (≥ 24 hours) at normal barometric pressure (1 atmospheres absolute (ATA)). This type of exposure is referred to as low pressure O_2 poisoning, pulmonary toxicity, or the Lorraine Smith effect ***(Ciencewicki et al., 2008).***

In regard to oxygen toxicity, it is frequently assumed that it is not oxygen itself that exerts toxic effects but merely the reactive oxygen species (ROS) that are generated as an undesirable by-product of adenosine triphosphate synthesis during aerobic cellular metabolism. when the production of ROS exceeds the limit of counteraction by antioxidant responses, ROS concentrations reach high levels and a cellular state of oxidative stress manifests ***(Cornet et al., 2013)***.

Oxygen supplementation is a well-accepted therapy for hypoxaemic patients, because it increases the delivery of oxygen to cells and is thus believed to reverse the effects of hypoxia. Oxygen supplementation is a standard component of treatment in patients with acute heart disease. Hypoxaemic patients benefit from oxygen insufflation, because hypoxia can induce general and brain ischaemia. However, most patients who present with acute coronary syndrome (ACS) are not hypoxaemic ***(Bateman and Leach, 1998).***

Yet the use of supplemental oxygen is widespread in cardiac patients, inadvertent hyperoxia commonly occurs because of concerns to ensure sufficient oxygenation and because hyperoxia is not perceived to be detrimental. In recent years, there has been mounting evidence demonstrating the potential adverse effects of hyperoxia on the cardiovascular system ***(Lawrence and Raman, 2010)***.

Also, it has been long appreciated that hyperoxia has adverse consequences in patients with chronic obstructive lung disease or acute respiratory failure, as gas exchange may be worsened by de-nitrogenation atelectasis and increased intrapulmonary shunting ***(Kilgannon et al., 2011)***.

In the post-resuscitation phase, there is evidence that patients surviving initial resuscitation may be managed more safely with 30% oxygen than with 100% oxygen. Clinically, hyperoxia is associated with poor neurological outcome following resuscitation ***(Kilgannon et al., 2011)***.

Aim of the Essay

The aim of this essay is to provide a comprehensive overview of the effects of hyperoxia on the clinical outcome of critically ill patients.

Chapter 1
Oxygen therapy

Oxygen therapy is the administration of oxygen as a medical intervention, which can be for a variety of purposes in both chronic and acute patient care. Oxygen is essential for cell metabolism, and in turn, tissue oxygenation is essential for all normal physiological functions (***Roston, 2014***).

Oxygen is probably the commonest drug to be used in the care of patients who present with medical emergencies. Currently, ambulance teams and emergency department teams are likely to give oxygen to virtually all breathless patients and to a large number of patients with other conditions such as ischaemic heart disease, sepsis or trauma ***(Davison et al., 2008).***

O_2 in blood exists in 2 forms:

1- In physical solution (0.3cc/100cc.blood)

Although it is very small in amount, it is very important in determining the direction and rate of diffusion of O_2 from the blood.

2- In chemical combination with haemoglobin:

Normally blood contains 15 gms of Hb/100cc. Each 1 gm Hb carries 1.34 cc O_2. So arterial blood when fully saturated with O_2 contains 20 cc O_2 ***(Davison et al., 2008).***

As there is a fixed amount of haemoglobin circulating in the blood, the amount of oxygen carried in the blood is often expressed in terms of how saturated with oxygen the circulating haemoglobin is. This is what is meant by ‘‘oxygen saturation level’’. If this is measured directly from an arterial blood sample, it is called the SaO_2. If the measurement is calculated from a pulse oximeter it is called the SpO_2. The normal SaO2 in healthy adults at sea level is maintained within a narrow range of about 95–98%. Alternatively, one can measure the oxygen tension of the blood (PaO_2), known as the ‘‘partial pressure of oxygen’’ in the blood. This measurement can be expressed in kilopascals (kPa) (normal range 12.0–14.6 kPa) or in millimetres of mercury (normal range 90–110 mm Hg for young adults) ***(Crapo et al., 1999)***.

Hypoxia:definition and types :

Definition:

Hypoxaemia refers to low oxygen tension or partial pressure of oxygen (PaO_2) in the blood. Most authors who have studied this area have defined hypoxaemia as PaO_2<60 mm Hg (8 kPa) or SaO_2 90% ***(Considine, 2005).*** There is no known risk of hypoxic tissue injury above this level and many guidelines on critical care set 90% as the minimum below which SaO_2 should not be allowed to fall ***(Jubran and Torban, 1990)***.

Types:

1- Hypoxaemic hypoxia:

Hypoxaemic hypoxia (sometimes also referred to as hypoxic hypoxia) is present when the oxygen content in the blood is low due to reduced partial pressure of oxygen. This occurs naturally at altitude and in many diseases such as emphysema which impair the efficiency of gas exchange in the lungs ***(Slutsky, 1994)***.

2-Anaemic hypoxia:

Anaemic hypoxia results from a reduced level of haemoglobin available for oxygen transport. Although the patient may not be hypoxaemic (with a normal PaO_2 and oxygen saturation measured by oximetry (SpO_2), the reduced oxygen content of the blood may lead to tissue hypoxia. Carbon monoxide poisoning may also produce a form of anaemic hypoxia by impairing the ability of haemoglobin to bind oxygen, thereby reducing oxygen-carrying capacity ***(Slutsky, 1994)***.

3- Stagnant hypoxia:

Stagnant hypoxia is a low level of oxygen in the tissues due to inadequate blood flow (either globally or regionally). This condition may occur in the extremities if a person is exposed to cold temperatures for prolonged periods of time and it is the cause of gangrene in tissue that is deprived of blood in severe peripheral vascular disease. Stagnant hypoxia may occur in low cardiac output states ***(Slutsky, 1994)***.

4- Histotoxic hypoxia:

Histotoxic hypoxia is an inability of the tissues to use oxygen due to interruption of normal cellular metabolism. The best known example of this occurs during cyanide poisoning which impairs cytochrome function. It is increasingly thought that mitochondrial dysfunction may lead to decreased oxygen utilization in sepsis despite adequate oxygen delivery. This has also been termed ‘‘cytopathic dysoxia’’ ***(Brealey and Singer, 2003).***

Pathophysiology of hypoxaemia:

Hypoxaemic hypoxia in blood as regards the alveolar capillary unit in the lung may be induced by alveolar hypoxia or incomplete gas exchange. The alveolar gas equation calculates the oxygen level in the alveolus using the following formula:

$$PAO_2 = PIO_2 - PACO_2/RER$$

Where PAO_2 and $PACO_2$ represent alveolar levels of oxygen and carbon dioxide, RER is the respiratory exchange ratio or the ratio of carbon dioxide production to oxygen consumption and inspired PO_2 (PIO_2). Considering this equation, alveolar hypoxia can be induced by decreased PIO_2 or increased $PACO_2$.

If an alveolar capillary unit is relatively underventilated for its degree of perfusion (low V/Q ratio), $PACO_2$ will rise due to inadequate clearance and thus PAO_2 will fall. In diseases that cause global hypoventilation such as respiratory muscle weakness, effectively all areas of lung have low V/Q ratios and this explains the hypercapnia and hypoxaemia associated with these conditions.

An extreme form of low V/Q pathophysiology occurs in intrapulmonary and extrapulmonary shunt where no gas