INTRODUCTION

Extracorporeal membrane oxygenation (ECMO) is a temporary life support technique, used to treat respiratory failure in critically ill patients. The aim is to increase oxygen levels in the blood. During the procedure, a tube carries blood from the right side of the heart then pumps it through an artificial lung where it picks up oxygen. This oxygen rich blood is then passed back into the person's blood system ***(Peek et al., 2009).***

Respiratory failure is a syndrome in which the respiratory system fails in one or both of its gas exchange functions, oxygenation and carbon dioxide elimination. In practice, it may be classified as either hypoxemic or hypercapnic respiratory failure ***(Ata et al., 2012).***

Hypoxemic respiratory failure (type I) is characterized by an arterial oxygen tension (PaO2) lower than 60 mm Hg with a normal or low arterial carbon dioxide tension (PaCO2). This is the most common form of respiratory failure, and it can be associated with virtually all acute diseases of the lung, which generally involve fluid filling or collapse of the alveolar unit. Examples of type I respiratory failure are cardiogenic and noncardiogenic pulmonary edema, pneumonia, and pulmonary hemorrhage ***(Ata et al., 2012).***

Hypercapnic respiratory failure (type II) is characterized by a PaCO2 higher than 50 mm Hg. Hypoxemia is common in patients with hypercapnic respiratory failure who are breathing room air. The PH depends on the level of bicarbonate, which, in turn is dependent on the duration of hypercapnia. Examples of type II respiratory failure are drug overdose, neuromuscular disease, chest wall abnormalities, asthma and chronic obstructive pulmonary disease ***(Noah et al., 2011).***

Respiratory failure can arise from abnormality in any of the components of the respiratory system, including the airways, alveoli, central nervous system (CNS), peripheral nervous system, respiratory muscles, and chest wall. Patients who have hypoperfusion secondary to cardiogenic, hypovolemic, or septic shock often present with respiratory failure. The pathophysiologic mechanisms that account for the hypoxemia are V/Q mismatch and shunt. These 2 mechanisms lead to widening of the alveolar-arterial PO2 gradient. V/Q mismatch is the most common cause of hypoxia. The low V/Q units contribute to hypoxemia and hypercapnia, whereas the high V/Q units waste ventilation but do not affect gas exchange unless abnormality is quite severe. Shunt is defined as the persistence of hypoxemia despite 100% oxygen inhalation. The deoxygenated blood (mixed venous blood) bypasses the ventilated alveoli and mixes with oxygenated blood that has flowed through the ventilated alveoli, consequently leading to reduction in the arterial blood content ***(Combes et al., 2008).***

Conventional treatment of respiratory failure involves maximum critical care support, including mechanical ventilation (for example, intermittent positive pressure ventilation). The high airway pressures and oxygen concentrations generated by this form of ventilation may exacerbate lung injury from the primary illness ***(Mols et al., 2000).***

Extracorporeal membrane oxygenation (ECMO) uses heart-lung bypass technology to provide gas exchange of carbon dioxide and oxygen outside the body, while the failing lung are kept inflated and resting by mechanical ventilation. The aims are to reduce ventilator-induced lung injury and improve patient outcomes ***(Beiderlinden et al., 2006).***

The idea of employing ECMO in patients with severe acute respiratory failure was first assessed in randomized controlled trials in the 1970s and 1980s. Poor rates of survival and major complications led to most intensvists believing that ECMO was inappropriate for adults. A small number of centers worldwide continued to refine the use of ECMO in small numbers of adult patients. Following the publication of their case series with improved results. Peak and colleges embarked upon a randomized controlled trial of conventional ventilation or ECMO in patients with acute severe respiratory failure (CESAR), the results of which have just been reported ***(Estenssoro et al., 2010).***

AIM OF THE WORK

To study the role of extracorporeal membrane oxygenation (ECMO) in treatment of acute severe respiratory failure, look for the cases suitable to be treated with, and study the risk/benefit ratio of its use.

Chapter 1

RESPIRATORY SYSTEM ANATOMY & PHYSIOLOGY

Knowledge of the respiratory anatomy provides a good foundation for understanding the complex process of respiration.

Upper airway:

The upper airway consists of the nasal passages, the sinuses, the pharynx, the epiglottis, and the larynx. its functions are to conduct air to the lower airway, to protect the lower airway from foreign matter, and to warm, filter, and humidify the inspired air ***(Bercker et al., 2005).***

Lower airway:

The lower airway consists of a series of tubes that divide like the branches of a tree, becoming narrower, shorter, and more numerous as they penetrate deeper into the lung. Its functions are to conduct air, provide mucociliary defense, and, most important, perform external gas exchange ***(Alhazzani et al., 2013)***

Conducting airways:

Nonalveolate region:

In the lung, the right main bronchus divides into three lobar bronchi that supply the upper, middle, and lower right

lung lobes. Two lobar divisions of the left main-stem bronchus supply the two lobes of the left lung: the upper and the lower ***(Bercker et al., 2005).***

Respiratory zone:

Alveolate region:

The terminal respiratory unit, or amicus, is that portion of the lung arising from a single terminal bronchiole. The acinus is the primary gas-exchanging unit of the lung, consisting of the respiratory bronchiole, alveolar ducts, alveolar sacs, and the alveoli. The respiratory zone makes up most of the lung; its volume is approximately 3000 ml. The surfactant prevents the alveoli and bronchioles from collapsing, especially during expiration, by reducing surface tension. Surface tension is caused by the liquid lining the alveoli. The lung therefore consists of hundreds of millions of relatively unstable bubbles, each 0.3 mm in diameter. Surfactant makes it easier to expand the lung (increase compliance), thereby reducing the work of breathing ***(Levitsky, 2003).***

Lungs: lobes and segments:

The lobes of the lung are further divided into bronchopulmonary segments. Understanding the location of the various pulmonary segments is useful in applying the pulmonary hygiene techniques of postural drainage, percussion, and vibration and for anatomically defining and describing areas of abnormality ***(Ruppel, 2003).***

Pleura and pleural space:

The lungs and the thoracic cavity are lined with the pleura, a continuous sheet of elastic and collagenous fibers that described in two portions: the visceral pleura and the parietal pleura. The visceral pleura is a thin, delicate lining around the lungs, lung fissures, and hilar bronchi and vessels ***(De Chazal and Hubmayr, 2003).***

Respiratory muscles:

The principle muscle of respiration is the diaphragm. The accessory muscles of respiration are called into play with increased effort breathing. During inspiration the scalene muscle contracts to elevate the first two ribs. The sternocleidomastoid muscle assists in elevating the sternum. Expiration during normal quiet ventilation is passive activity that occurs because of relaxation of the inspiratory muscles and recoil of the lung parenchyma. During forceful expiration the internal intercostal muscles contract, these muscles lie under the external intercostals and have similar points of attachment but differ in that they have fibers that pass downward and backward. The abdominal muscles used for increased effort expiration include the internal and external oblique muscles, the rectus muscle, and the transverse abdominus muscle ***(West, 2004).***

Physiological aspects of the respiratory system:

Mechanics of spontaneous ventilation:

The basic principle of the movement of gas is that it travels from an area of higher to lower pressure. Physiologic pressures related to the flow of gases into and out of the lung are atmospheric pressure, intrapulmonary (intraalveolar) pressure, and intrapleural (intrathoracic) pressure. The difference between two pressures is called a pressure gradient. The three important pressure gradients related to ventilation are trans respiratory, trans pulmonary, and transthoracic pressure ***(Combes et al., 2008).***

Inspiration is an active process that requires the expenditure of energy. Contraction of the inspiratory muscles enlarges the thoracic cavity. The lungs expand because they are pulled outward, along with the movement of the thoracic wall. Negative pressure normally within the intrapleural space becomes even more negative on inspiration (from -50 cm H2O to -8 cm H2O); thus the trans pulmonary pressure gradient widens, causing the alveoli to expand. As the alveoli expand, intraalveolar pressure also becomes sub-atmospheric (-1cm H2O); therefore air at atmospheric pressure flows into the lung. Inspiration continues until intraalveolar pressure rises equal to the atmospheric pressure. So, air does not have to drawn into the lung. Expiration is a passive process that occurs because of the elastic recoil of the lung. When contraction of the

inspiratory muscles ceases, the thoracic cage and lungs recoil to their original size. Intrapleural pressure become less negative. Intraalveolar pressure become slightly positive on expiration, which ends when intraalveolar and atmospheric pressures equalize. When individual is placed on a positive-pressure ventilation, the normally low intrathoracic pressures are disrupted in that they become positive ***(Stenqvist, 2003)***

Lung volumes and capacities: Some lung volumes and capacities are important. They can be measured by a spirometer.

Tidal volume (VT):

Is the volume of gas moved into or out of the lung in a single normal inspiration or expiration. It averages 500 ml, or 5-8 ml/kg. It represents the volume reaching the alveoli, approximately 350 ml, plus the volume in the conducting airways, known as the anatomic dead space, which is approximately 150 ml, or 2 ml/kg ***(Yoshida et al., 2013)***.

Inspiratory reserve volume (IRV):

Is the volume of air that can be inspired at the end of a normal tidal inspiration. The IRV is called on when increased tidal breathing is necessary, as in exercise. Average volume 3000 ml ***(Fink, 1999).***

Expiratory reserve volume (ERV):

The expiratory reserve volume (ERV) is the maximal volume of gas that can be exhaled after a normal exhalation. Average volume 1200 ml ***(Ruppel, 2003).***

Residual volume (RV):

The volume of gas remaining in the lungs after a maximal expiration. It is obtained by using the helium dilution test, nitrogen washout method, or body plethysmography to determine the functional residual capacity (FRC). Average volume 1300 ml. RV = FRC - ERV ***(Alhazzani et al., 2013).***

Inspiratory capacity (IC):

Is the maximal volume of gas that can be inspired after a normal expiration. Average volume 3500 ml. IC =IRV +VT ***(Yoshida et al., 2013)***.

Vital capacity (VC) = IRV + VT + ERV:

Is the maximal volume of gas exhaled after the deepest possible inspiration. It is clinically useful in that it tells us the patient's maximal ventilatory capacity. VC may be measured and trended as an indicator of a patient's ventilatory capacity when respiratory muscles are compromised, as may be after a new spinal cord injury. Average volume 4700 ml ***(De Chazal and Hubmayr, 2003).***

Functional residual capacity (FRC) = ERV + RV:

Is the volume of air remaining in the lungs at the end of a normal expiration. This is the volume where gas exchange is constantly taking place. In many pathologic conditions, such as atelectasis, secretion or fluid collection in the lungs, or pleural effusion, the FRC is reduced and thus gas exchange is affected. Average volume 2500 ml ***(Kackmarek et al., 2005).***

Total lung capacity (TIC) = IC + FRC:

Is the maximal volume of air in the lungs after a maximal inspiration. Average volume 6000 ml ***(Combes et al., 2008).***

Closing volume (CV):

Is that volume on expiration where small airways in the lung base begin to close. It is normally 10% of the VC. When lung elasticity or volume decreases, the intrapleural pressure at the base of the lungs may become positive, compressing the lung. This causes the CV to increases and alveolar ventilation decreases, which lead to impaired gas exchange ***(West, 2004).***

Factors affecting ventilation:

Compliance:

Compliance is the opposite, or inverse, of what is called elastance (e): C = 1/e or e = 1/C. The compliance of any structure is the relative ease with which it distends. A balloon that is easy to inflate is very compliant. Elastance is the

tendency of a structure to return to its original form after being stretched or acted on by outside force ***(Ruppel, 2003)***.

Pulmonary physiology uses the term compliance to describe the elastic forces that oppose lung inflation. Compliance is defined as the change (A) of volume (V) that corresponds to the change in pressure (P): C = AV/AP. Volume typically is measured in liters or milliliters and pressure in centimeters of water pressure. The compliance of the respiratory system is the sum of the compliances of both the lung tissue and the surrounding thoracic structures. Two forms of compliance can be measured, static and dynamic. Static compliance is the truest of compliance of the lung tissue. In a spontaneously breathing individual, the total compliance is about 0.1 L/cm H2O. The value for compliance varies considerably, depending on a person's posture, position, and active breathing. It can range from 0.05 L/cm H2O to 0.17 L/cm H2O (50 to 170 mL/cm H2O) ***(Rubenfeld et al., 2005).***

For patients on mechanical ventilatory support, compliance calculations can be measured as:

$$CST = \frac{\text{Exhaled tidal volume}}{\text{Plateau pressure - PEEP}}$$

Technically this calculation includes the recoil of the thoracic wall, so that the compliance value includes both the lungs and the thorax. However, thoracic compliance generally

does not change significantly in a ventilated patient. Dynamic compliance is a measurement taken while gases are moving in the lungs, therefore it measures not only compliance of the lung tissue but also resistance to gas flow. It is easier to measure because it does not require the use of the inspiratory hold maneuver. The formula for dynamic compliance:

$$CDYN = \frac{\text{Exhaled tidal volume}}{\text{Peak inspiratory pressure - PEEP}}$$

(Shneerson and Simonds, 2002)

Resistance:

Resistance, or frictional forces, associated with ventilation are the result of the anatomical structure of the conductive airways and the tissue viscous resistance of the lungs and adjacent tissues and organs. As the lungs and thorax move during ventilation, the movement and displacement of structures such as the lungs, abdominal organs, rib cage, and diaphragm create resistance to breathing. During mechanical ventilation, resistance of the airways (Raw) is the factor most often evaluated. The ability of air to flow through the conductive airways depends on the gas viscosity, the gas density, the length and diameter of the tube, and the flow rate of the gas through the tube ***(Putensen et al., 2009).***

In clinical situations, viscosity, density, and tube or airway length remain fairly constant. Careful attention is paid

to the diameter of the airway lumen and the flow rate of the gas. The diameter of the airway lumen and the flow of gas into the lungs can decrease as a result of bronchospasm, increased secretions, mucosal edema, or kinks in the endotracheal tube. The rate at which gas flows into the lungs can be controlled on most mechanical ventilators. Resistance can be measured by the following physiologic formula:

$$\text{Raw} = \frac{\text{Peak pressure - plateau pressure}}{\text{Flow}}$$

(Dreher et al., 2010)

Work of breathing (WOB):

Breathing requires mechanical work, which is performed by the respiratory muscles, and metabolic work, which is the expenditure of energy and is reflected by the oxygen consumption of the respiratory muscles. It is the work that the respiratory muscles must perform to expand the lung to overcome elastic and nonelastic forces: compliance and resistence. When compliance decreases or resistance increases, a greater force is required to expand the lung, that is the WOB increases. The WOB imposed by the breathing apparatus consists of work imposed by the circuit and work imposed by the endotracheal tube ***(Terragni et al., 2007).***

Perfusion:

It is the movement of blood through the pulmonary capillaries. The distribution of perfusion in the lung is uneven. This uneven distribution of blood flow is explained by hydrostatic pressure differences in the pulmonary arterial system from the base to the apex of the lung. Pressure within the alveoli easily influences the adjacent pulmonary capillaries because they have such thin walls. Indeed, the capillaries may become compressed during mechanical ventilation when alveolar pressure is high ***(Leaver and Evans, 2007).***

The apices of the lungs represent zone I, a region above the heart and therefore not well perfused. If the alveolar pressure rises, as may occur with positive pressure ventilation, or if arterial pressure falls, as in hemorrhage or other causes of decreased perfusion pressure, no flow occurs in zone I. Zone II is the middle portion of the lung. Perfusion through zone II lung areas is dependent on the pressure difference between the pulmonary arteries and the alveolar pressure. In zone III, venous pressure exceeds alveolar pressure; perfusion is therefore determined by the usual mechanism of the arterial-venous pressure difference. The distribution of perfusion is influenced by several therapies used in critically ill patients, such as PEEP, vasodilators, and inotropic agents ***(Martí et al., 2010).***