Liquid ventilation(LV)

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- Introduction/History
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INTRODUCTION

- Preterm gas exchange-Ventilation perfusion mismatch
- Conventional Ventilation-VALI
- Search –To decrease VP Mismatch, VALI
- Liquid Ventilation in 1966
- Total Liquid ventilation/Partial

HISTORY

- In 1966, Clark and Gollan –perflurocarbon

(PFCs) in liquid ventilation in animal models.

- Over the past 40 years Perfluoroctyl bromide (PFOB)
  - Imaging
  - Experimental liquid ventilation
- Animal Studies-LV
  - Decrease inflammation
  - Improve pulmonary mechanics
  - Decreases Lung Injury

PROPERTIES OF PFC

Ideal fluid for LV should be

- Nontoxic
- Low surface tension
- Dissolving large amounts gases
- Minimal systemic absorption
- Chemically stable.

PROPERTIES

PFC fluids -

- Clear, colorless, odorless, and inert.
- Oxygen, carbon dioxide, and other gases are highly soluble in these fluids.
- Stable, insoluble in water,
- Stored at room temperature
- Do not wash out surfactant
- Radio-opaque

Physical properties Perfluoro-octyly bromide (PFOB)

- Backbone of 8 carbon molecules
- Carbon bound hydrogen atoms-replaced with fluorine atoms
- Bromide molecule at one end
- Carbon –fluorine bond are extraordinarily strong bond
- Flourine-Low polarizability and forms dense electron cloud
- Shields carbon backbone physically and from bonding

Physical properties Perfluoro-octyly bromide (PFOB)

- Kinetically and thermodynamically inert
- Can dissolve large amount of gases depending on partial pressure
- Bromine atoms provides radio-opacity
- Perflubron (LiquiVent), the only medical grade PFC available for use in human

PFOB AS A VENTILATORY MEDIA

- Ventilation perfusion mismatch
- Surface tension
- Gas exchange
- Inflammation
- Lavage
- Effect on pulmonary blood flow

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Ventilation perfusion mismatch

- PFC liquids are heavier than water (PFOB is twice as dense, 1.93 g/mL at 25°C)
- Because of gravity, PFC liquids tend to settle in the more dependent lung
- Dense column of noncompressible PFC liquid can act as liquid positive end-expiratory pressure (PEEP)
- Gently forcing open collapsed alveoli.

Surface tension

- Decreases surface tension
- Helping to prevent collapse of alveoli

Gas exchange

- Act as reservoir in which oxygen and carbon dioxide can be exchanged with pulmonary capillary blood

Inflammation

- Anti-inflammatory action
- Decreases levels of cytokines IL 6.TNF Alpha etc

Lung Lavage

- Mobilizing alveolar and airway debris and exudates

TEMPERATURE

- Functioning as a high efficiency heat exchanger

Technique

- Two methods :
  - **Total liquid ventilation**
  - **Partial liquid ventilation**

Total liquid ventilation

- Lung is filled with an oxygenated PFC liquid
- A liquid tidal volume of PFC -actively pumped into and out of the lungs.
- Specialized apparatus is required to deliver and remove the relatively dense, viscous PFC tidal volumes
- Initiated by insufflating the desired volume of pre-oxygenated PFC liquid (functional residual capacity plus tidal volume

Total liquid ventilation

- Low respiratory rate (eg, four to six breaths per minute)
- Tidal volumes and peak inspiratory and positive end expiratory pressures (PEEP) are adjusted
- Weaning
  - Period of partial liquid ventilation
  - Gas ventilation is begun
  - PFC fluid is not replaced or augmented
  - PFC Evaporates-generally requires one to seven days

Partial liquid ventilation

- Lungs slowly filled with a volume of PFC equivalent.
- Initiated by insufflating PFC liquid (approximately 20 to 30 mL/kg)
- PFC within the lungs is oxygenated and carbon dioxide is removed by means of gas breaths cycling in the lungs by a conventional gas ventilator

Partial liquid ventilation

- FRC is reached when a meniscus of PFC is present within the endotracheal tube at end-expiration.
- Replacement of PFC is done 2 to 8 mL/kg/hr
- PLV is discontinued by ceasing to replace the PFC that is lost through evaporation
- Intrapulmonary PFC evaporates in the next one to seven days, allowing a transition to gas ventilation

Comparision OF TLV vs PLV

- TLV allows the lavage and removal of lung secretions, meconium, or alveolar edema from the lower airways to a greater extent than PLV.
- TLV requires a specialized delivery apparatus where as does not require in PLV.

Potential Neonatal applications-

1.Respiratory distress syndrome –.

- LV may facilitate more uniform endogenous surfactant distribution,
- May be of use in surfactant-unresponsive cases.

Potential Neonatal applications-

2.Meconium aspiration –

- May be useful in MAS as a lavage therapy
- Remove meconium from the airways more effectively than conventional measures .

3.Persistent pulmonary hypertension of the newborn –

- Improving ventilation/perfusion matching and facilitating pulmonary vasodilation.

Other Potential Neonatal applications-

- Congenital diaphragmatic hernia -may provide mechanical stimuli (eg,pressure transduction) that favor neonatal lung growth
- Temperature control-heat exchange characteristic of PFCs may be helpful in maintaining temperature in preterm babies
- Lung protection during cardiopulmonary bypass - Anti-inflammatory effects, alveolar distention, oxygen-carrying capacity, and surfactant-like properties may protect the lung before and during cardiopulmonary bypass.

FUTURE

- The future of liquid ventilation (LV) is unclear. There are no current human LV trials, though basic science research using in vitro and animal lung models

Quiz

1. Perfluorooctyl bromide (PFOB) has been studied as a potential compound to facilitate liquid ventilation in neonates. Which of the following statements about PFOB is correct?

A. It belongs to the polychlorophospholipid family.

B. The backbone of the compound is composed of carbon-hydrogen bonds.

C. It is inert and can carry large amounts of dissolved oxygen and carbon dioxide.

D. Carbon-fluorine bonds are very weak, allowing for quick uptake and release of oxygen.

E. Fluorine has low electron affinity, leading to a very stable structure that will not interact with human tissue

Quiz

2. For the application of liquid ventilation, PFOB may be used in a mode of partial or total liquid ventilation. Which of the following statements regarding the properties of PFOB interacting with the lungs is correct?

A. PFOB is half as dense as water and, therefore, will distribute evenly throughout the lung space.

B. PFOB may help improve ventilation-perfusion matching and recruit alveoli by providing additional distending pressure.

C. PFOB has high surface tension and acts as a pseudosurfactant.

D. Both partial and total liquid ventilation require the adjunctive use of conventional mechanical ventilation. E. Because of its low density, gravity does not affect the distribution of PFOB and similar perfluorochemicals. 3. Although the mechanisms of action

Quiz

3 Although the mechanisms of action are not well understood, PFOB appears to have antiinflammatory properties. Studies have shown various effects of PFOB in in vitro or animal studies on inflammatory markers. Which of the following has been shown to be decreased with PFOB administration?

A. Interleukin 6.
B. Interleukin 10.
C. Interleukin 13.
D. Interferon a.
E. Transforming growth factor b

Quiz

4. Liquid ventilation studies have used various perfluorochemicals (PFCs). Animal studies have shown potential applications for neonatal respiratory disease. Which of the following statements regarding human studies of PFCs is correct?

A. Because of the experimental nature of PFCs in respiratory function, studies on PFCs and ventilation have only been performed in neonates with normal lungs but other life-threatening conditions such as congenital heart disease or lethal genetic disease.

B. Informed consent is not necessary when performing research on PFCs for neonates, because mechanical ventilation is a life-saving procedure.

C. Although further research is needed, studies in newborns have demonstrated an increase in dynamic pulmonary compliance and improvement in oxygen and ventilation in some patients.

D. A common adverse event and life-threatening complication has been persistent hypocapnia.

E. Thus far, human studies have used only 1 type of PFC, called PFC-16, which has been the most promising one used to date in animal studies.

Quiz

5. Although animal and human studies have shown potential promise of PFCs in liquid ventilation, there are limitations to both practical application and study designs to demonstrate efficacy. Which of the following characteristics describes one of these limitations accurately?

A. While the safety profile is well established, the PFCs studied thus far have not had the ability to carry respiratory gases.

B. PFCs are highly conducive for microorganism growth, leading to high infection risk.

C. PFCs are only stable in a range that is below normal human temperatures, and therefore, may primarily be used for patients undergoing therapeutic hypothermia.

D. Because of its highly evaporative quality, PFCs need to be continuously infused into the lungs, making the mechanics of ventilation difficult.