Management of Acute Respiratory Distress Syndrome

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Abstract: **Since its first description, the acute respiratory distress syndrome (ARDS) has been acknowledged to be a major clinical problem in respiratory medicine. From July 2015 to July 2016 almost 300 indexed articles were published on ARDS. This review summarises only eight of them as an arbitrary overview of clinical relevance: definition and epidemiology, risk factors, prevention and treatment. A large international multicentre prospective coherent study including 50 countries across five continents reported that ARDS is under diagnosed, and there is potential for improvement in its management. Furthermore, epidemiological data from low-income countries suggest that a revision of the current definition of ARDS is needed in order to improve its recognition and global clinical outcome. In addition to the well-known risk-factors for ARDS, exposure to high ozone levels and low vitamin D plasma concentrations were found to be predisposing circumstances**.

Keywords: **Acute lung injury, Acute Respiratory Distress Syndrome.**

I. INTRODUCTION:

Acute respiratory distress syndrome (ARDS) is a permeability pulmonary edema characterized by increased permeability of pulmonary capillary endothelial cells and alveolar epithelial cells, leading to hypoxemia that is refractory to usual oxygen therapy. In a national study in Iceland, the incidence of ARDS almost doubled, but hospital mortality decreased during the 23 years of observation [1]. In a prospective study in Spain, despite use of lung-protective ventilation, overall ICU and hospital mortality of ARDS patients are still higher than 40% [2]. The aim of this review is to provide an update on ARDS.

II. ETIOLOGY:

The mechanical causes of ARDS fluid leaked from the smallest blood vessels in the lungs into the tiny air sacs where blood is oxygenated. Normally, a protective membrane keeps this fluid in the vessels. Severe illness or injury, however, can cause damage to the membrane, leading to the fluid leakage of ARDS.

Underlying causes of ARDS include:

*Sepsis [3] – The most common cause of ARDS is sepsis, a serious and widespread infection of the bloodstream.

*COVID -19 -People who have severe COVID-19 may develop ARDS.

*Aspiration pneumonitis.

*Infectious pneumonia [4]- [including Mycobacterial, Viral, Fungal, Parasitic]

Lung injury prevention score helps identify low-risk patients, but a high score is less helpful.

Some risk factors for ARDS include:

- Advanced age
- Female gender
- Smoking

Aortic vascular surgery

Cardiovascular surgery

Traumatic brain injury [5]

III. EPIDEMIOLOGY:

The incidence of ARDS was determined in a multicenter, population-based, prospective cohort study in the United States [6]. The study followed 1113 patients with ARDS for 15 months beginning in 1999 or 2000:

●The age-adjusted incidence was 86 per 100,000 person-years for individuals with an arterial oxygen tension to fraction of inspired oxygen (PaO_2/FiO_2) ratio ≤300 mmHg and 64 per 100,000 person-years for individuals with a PaO_2/FiO_2 ≤200 mmHg.

●Extrapolation of the data suggested that there are approximately 190,000 cases of ARDS in the United States each year [6].

CHILDREN:

From a systematic review of 29 paediatric studies [7] and the PARDIE cross-sectional study of 145 international paediatric intensive care units (PICUs) [8], the estimated population-based incidence of ARDS in children (2 weeks to 17 years of age) is 2.2–5.7 per 100,000 person-years; most of the children in these studies were <5 years of age. ARDS is diagnosed in 2.3–3% of PICU admissions, with an estimated mortality of 17–33% [7,8]; mortality is lower in highly resourced countries but was not associated with age. Over the past two decades, ARDS mortality in PICUs has been relatively stable.

IV. PATHOPHYSIOLOGY:

ARDS progresses through several phases after a direct pulmonary or indirect extrapulmonary insult. In the exudative phase, which may last seven to 10 days, alveolar macrophages secrete mediators that lead to accumulation of inflammatory cells in the lung. This accumulation, in surfaces and proinflammatory mediators and chemokines are released, leading to pathologic vascular permeability, gaps in the alveolar epithelial barrier, and necrosis of types I and II alveolar cells. Intravascular coagulation in the alveolar capillaries leads to microthrombi.

The end result of these changes is pulmonary edema, loss of surfactant, and deposition of dead cells and debris along the alveoli (hyaline membranes), which decrease pulmonary compliance and make gas exchange difficult [9-11]. Chest radiography may show changes from air space opacification to coarse reticular opacification during this phase [12] **(Fig.1)**.

The proliferative phase begins the process of lung repair over the next two to three weeks. Anti-inflammatory cytokines deactivate inciting neutrophils, which then undergo apoptosis and phagocytosis. Type II alveolar cells proliferate and differentiate into type I cells, re-establishing the integrity of the epithelial lining.

Alveolar ion channels and aquaporins are re-expressed, drawing fluid out of the alveoli and into the pulmonary microcirculation and lung lymphatics. Simultaneously, alveolar cells and macrophages remove debris from the alveoli, and endothelial cells re-establish vascular integrity, allowing the lungs to recover [9-11].

The fibrotic phase, which does not occur in all patients, is characterized by ongoing inflammation, extensive basement membrane damage, persistent edema, intra-alveolar and interstitial fibrosis, and microvascular damage. Shear forces associated with mechanical ventilation may promote the development of the fibrotic phase, although lung protective ventilation is thought to ameliorate this effect [13]. Progression to the fibrotic phase is associated with prolonged mechanical ventilation and increased mortality [9-11].

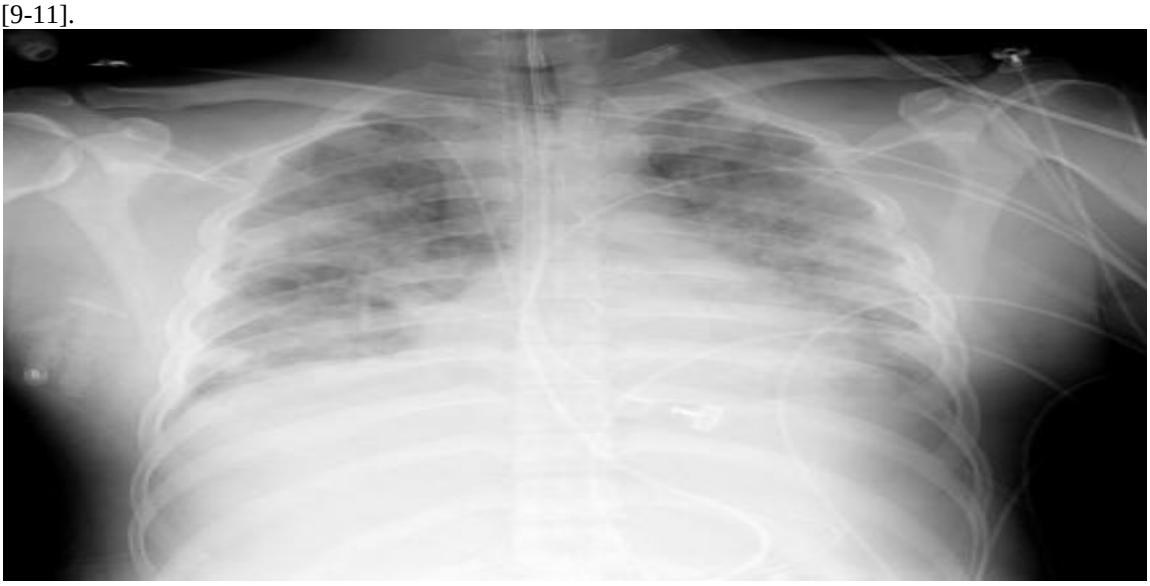

Figure 1: Chest radiograph of a patient with acute respiratory distress syndrome. Note the bilateral air space opacification and lack of obvious vascular congestion.

V. CLINICAL SIGNS AND SYMPTOMS:

The person with ARDS may initially appear agitated as a result of breathing difficulty (rapid breathing or shortness of breath), but later may become lethargic and or even comatose. The patient may appear pale, and the hands and feet may have a bluish-grey tone because of the diminished level of oxygen in the blood.

Underlying causes of ARDS include:

*****Sepsis [14] – Fever, hypertension, leucocytosis, lactic acidosis, infectious source.

*Severe trauma – History of trauma or fractures within the last week.

*Pulmonary contusion – History of chest trauma (blunt or penetrating) chest pain.

The signs and symptoms of ARDS can vary in intensity, depending on its cause and severity, as well as the presence of underlying heart or lung disease. They include:

- Severe shortness of breath
- Low blood pressure
- Confusion and extreme tiredness.

VI. DIAGNOSIS:

The diagnosis of ARDS is made based on the following criteria: acute onset, bilateral lung infiltrates on chest radiography of a non-cardiac origin, and a PaO/FiO ratio of less than 300 mmHg. It is further sub-classified into mild (PaO2/FiO2 200 to 300 mmHg), moderate (PaO2/FiO2 100 to 200 mmHg), and severe (PaO2/FiO2 less than 100 mmHg) subtypes. Mortality and ventilator-free days increase with severity. A CT scan of the chest may be required.

Formal diagnostic criteria for ARDS were not widely accepted until the 1994 American–European Consensus Conference (AECC). The AECC criteria include the acute onset of hypoxemia, the presence of noncardiogenic, bilateral infiltrates on chest radiographs and the absence of left atrial hypertension. The presence of hypoxemia was quantified using the ratio of partial pressure of arterial oxygen and the fraction of inspired oxygen (Pao_2/FiO_2), with a $Pao_2/FiO_2 < 200$ mm Hg required for diagnosis of ARDS.

Assessment of left ventricular function may be required to differentiate from or quantify the contribution of congestive heart failure to the overall clinical picture. This assessment can be achieved via invasive methods such as pulmonary artery catheter measurements or non-invasively, such as cardiac echocardiography or thoracic bioimpedance, or pulse contour analysis. However, the use of pulmonary artery catheters (PAC) is controversial and should be avoided if clinically possible, and noninvasive measures for assessment should be exhausted first; the use of PAC is discouraged by the new definition. The practice of using bronchoscopy may be required to assess pulmonary infections and obtain material for culture [5].

In 2012, the clinical criteria for diagnosis of ARDS were refined to address these limitations, resulting in the Berlin definition [15]. For diagnosis of ARDS, the patient must have new or worsening symptoms within 1 week of a known clinical insult; bilateral opacities observable on anteroposterior chest radiographs that are not due to effusions, nodules or lobar or lung collapse; and hypoxemia, defined by a Pao_2/FiO_2 < 300 mm Hg and a minimum positive end-expiratory pressure ≥ 5 cm H_2O, that is not fully explained by cardiac failure or fluid overload (**Fig. 2**).

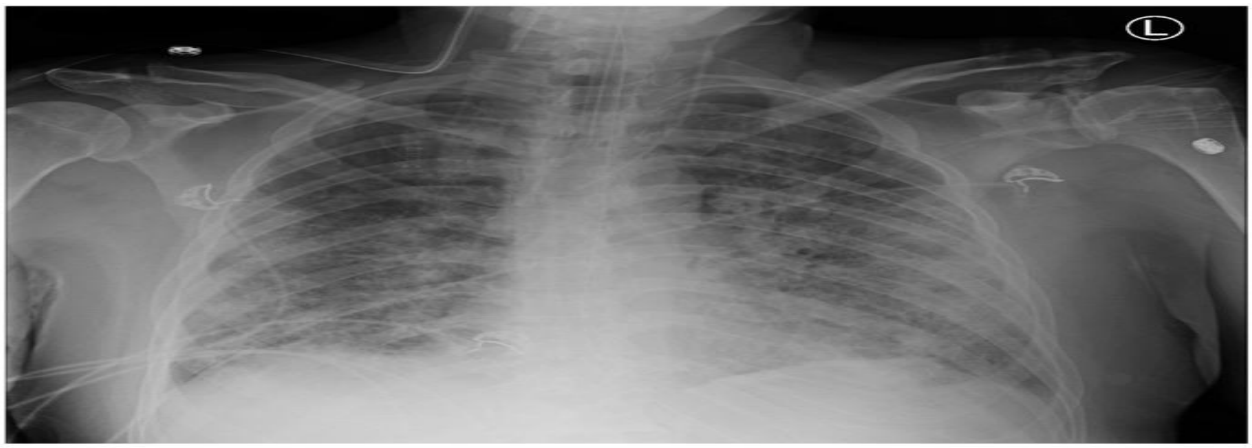

Figure 2: Anteroposterior chest radiograph showing bilateral pulmonary infiltrates, consist with acute respiratory distress syndrome.

The Berlin definition also identified mutually exclusive categories of ARDS severity based on the degree of hypoxemia, including mild (Pao_2/FiO_2 200–300 mm Hg), moderate (Pao_2/FiO_2 100–200 mm Hg) and severe (Pao_2/FiO_2 < 100 mm Hg) ARDS. These categories correspond to prognosis, with higher severity associated with increased mortality rates in the data sets used for derivation of the criteria [15,16]. (**Fig. 3**).

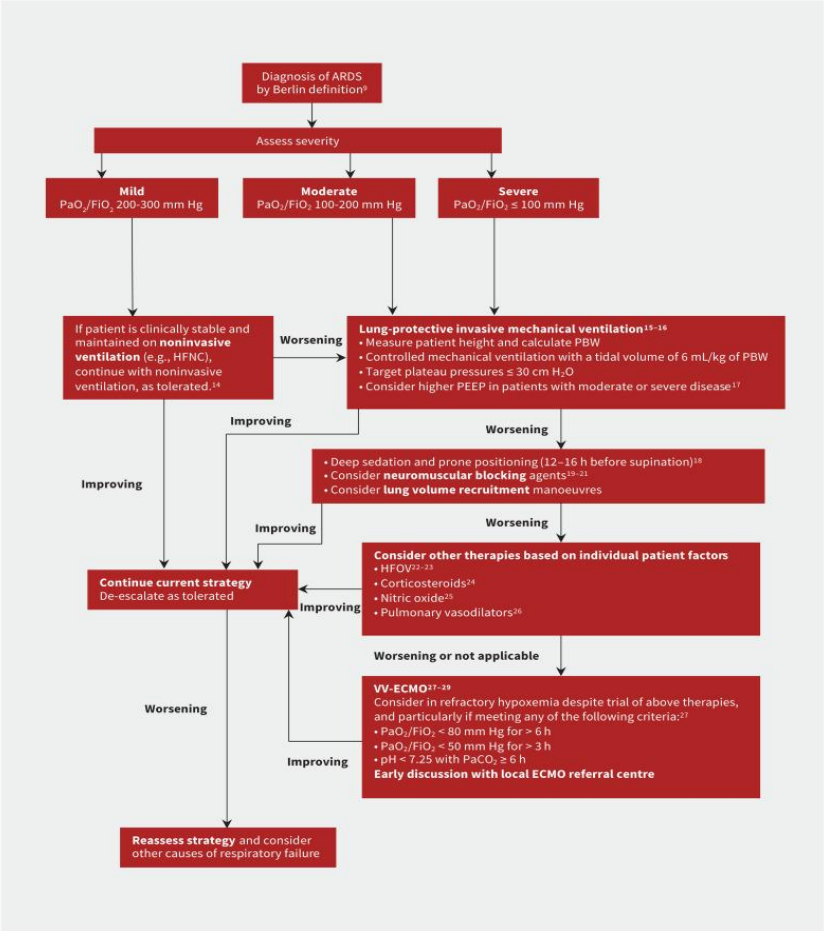

Figure 3: Diagnosis according to Berlin definition.

Suggested treatment algorithm showing risk stratification and tiered approach to therapy for patients with acute respiratory distress syndrome (ARDS). Note: HFNC = high-flow nasal cannula, HFOV = high-frequency oscillatory ventilation, PEEP = positive end-expiratory pressure, PBW = predicted body weight, VV-ECMO = venovenous extracorporeal membrane oxygenation.

Other diagnostic tests for the causes of ARDS include:

- Diagnosis of exclusion, lung biopsy occasionally helpful – Drugs (chemotherapeutic agents, Amiodarone, Radiation).
- Appropriate clinical content and positive cultures – Sepsis.
- Elevated amylase & lipase, with or without abnormal imaging – Pancreatitis.
- Appropriate clinical content and positive respiratory cultures – Infectious pneumonia.
- Diagnosis of exclusion – Transfusion related acute lung injury and massive transfusions, HSCT, Inhalation injuries other than smoke, Thoracic surgery.

VII. TREATMENT:

NON-PHARMACOLOGICAL TREATMENT:

Treatment of ARDS is generally supportive, consisting of mechanical ventilation, prevention of stress ulcers and venous thromboembolism, and nutritional support while addressing the underlying etiology. *Table 1* summarizes the management of ARDS.

Table 1: Management of ARDS

Management of ARDS

General measures

Nutritional support

Prevention of stress ulcers and venous thromboembolism

Reevaluate ventilation parameters and therapeutic measures at least every 24 hours

Ventilator parameters

Choose any mode, such as volume assist

Inspiratory to expiratory ratio of 1:1 to 1:3

PEEP ≥ 5 cm H_2O; higher PEEP (> 12 mm Hg) preferred for moderate to severe ARDS (F_{IO_2} ≤ 200 mm Hg)*

Respiratory rate ≤ 35 breaths per minute

Tidal volume of 4 to 8 mL per kg predicted body weight (start at 6 mL per kg)

Arterial pH of 7.30 to 7.45

Monitoring parameters

Oxygen saturation of 88% to 95%

P_{AO_2} of 55 to 80 mm Hg

Plateau pressure < 30 cm H_2O

Adjunctive measures

Conservative fluid therapy

Neuromuscular blockade for early severe ARDS (some guidelines also recommend for early moderate ARDS)

Prone positioning for all patients with severe ARDS (some guidelines also recommend for moderate ARDS)

Spontaneous breathing trials and weaning protocols

Consider corticosteroids (controversial)

Consider extracorporeal membrane oxygenation for severe ARDS

Consider inhaled nitric oxide (controversial)

Consider recruitment maneuvers (temporary elevations of applied lung pressures)

ARDS = acute respiratory distress syndrome; F_{IO_2} = fraction of inspired oxygen; P_{AO_2} = partial pressure of arterial oxygen; PEEP = positive end-expiratory pressure.

*—Sample F_{IO_2} and PEEP protocol from the National Heart, Lung, and Blood Institute's ARDS Network:

F_{IO_2}	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5	0.5	0.5-0.8	0.8	0.9	1.0	1.0
PEEP	5	8	10	12	14	14	16	16	18	20	22	22	22	24

Adapted with permission from Saguil A, Fargo M. Acute respiratory distress syndrome: diagnosis and management. Am Fam Physician. *2012;85(4): 355, with additional information from references 25-28.*

MECHANICAL VENTILATION

Although mild cases of ARDS may respond to noninvasive ventilation, most patients require sedation, intubation, and ventilation while the underlying injury is treated. Any ventilator mode may be used, and there are multiple guidelines to inform therapy. The respiratory rate, expiratory time, PEEP, and Fio_2 may be set according to protocols from the National Heart, Lung, and Blood Institute's ARDS Network.

Settings should be adjusted to maintain an oxygen saturation of 88% to 95%, an arterial pH of 7.30 to 7.45, and a plateau pressure of no more than 30 cm H2O to avoid barotrauma. Starting with low tidal volumes of 6 mL per kg of predicted body weight is superior to starting with traditional volumes of 10 to 15 mL per kg (number needed to treat to prevent death before discharge and for a patient to breathe independently = 11).

Guidelines recommend initiating ventilation with low tidal volumes. However, low volumes are associated with higher partial pressures of arterial carbon dioxide ($Paco_2$), and while some hypercapnia is permissible, $Paco_2$ of 50 mm Hg or higher is independently associated with mortality. Patients should be followed closely, and adjustments should be made while balancing the preference for low tidal volumes with the risk of excessive increases in arterial carbon dioxide levels.

Higher PEEP values (12 cm H_2O or higher) are associated with decreased mortality when compared with values of 5 to 12 cm H_2O (number needed to treat = 20) and should be used in patients with moderate or severe ARDS. Conservative fluid therapy (limiting fluid intake and considering the use of diuretics and albumin) may have some benefit but is not universally recommended.

PRONE POSITIONING

The incidence of ventilator-induced lung injury may be reduced by placing patients in the prone position. Mechanical ventilation in the supine position can result in atelectasis and derecruitment of the most dependent lung regions.

Prone positioning redistributes mechanical forces through the injured lung, resulting in more homogeneous lung inflation and recruitment of alveoli in the dependent lung regions. In patients with ARDS and a Pao_2/FiO_2 < 150 mm Hg, high-quality evidence shows that prone positioning reduces the risk of death without an increase in serious complications [17]. Therefore, use of routine prone positioning in patients with severe ARDS is recommended by guidelines.

VENTILATOR WEANING

Patients with ARDS spend an average of 16 days (standard deviation = 15.8) in the ICU and a total of 26 days (standard deviation = 27.7) in the hospital. Patients with an anticipated ventilation requirement of more than 10 days may benefit from tracheostomy. Early tracheostomy (up to eight days after ICU admission) is associated with fewer ventilator days but not reduced long-term mortality.

The American Thoracic Society and American College of Chest Physicians recommend a ventilator liberation protocol (also known as a weaning protocol) for patients who have been on mechanical ventilation for more than 24 hours. As the underlying illness resolves and the patient improves, spontaneous breathing trials are indicated; these protocols can reduce the duration of mechanical ventilation and weaning, and can shorten ICU stays. *Table 2* outlines a set of criteria that can be used to determine whether patients can be weaned from ventilation.

Table 2: Example Spontaneous Breathing Trail: Eligibility and Weaning Parameters.

Example Spontaneous Breathing Trial: Eligibility and Weaning Parameters

Eligibility for starting trial

Able to meet oxygen requirement with noninvasive methods
Hemodynamically stable
Minute ventilation ≤ 15 L
Positive end-expiratory pressure ≤ 5 cm H_2O

Parameters for ventilator weaning*

Airway can be protected
Hemodynamically stable
No agitation
Oxygen saturation ≥ 90%
Respiratory frequency to tidal volume ratio ≤ 105
Respiratory rate ≤ 35 breaths per minute

Note: This is one example of a spontaneous breathing trial and weaning parameters. A spontaneous breathing trial tests whether a patient is able to breathe for themselves with or without a low level of pressure support while still attached to the ventilator circuit.

*—Determined during a one- to two-hour spontaneous breathing trial.

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MOBILIZATION THERAPY

Patients on ventilators should be encouraged to participate in mobilization therapy consisting of range-of-motion or resistance activities, sitting, or standing. It may be necessary to reduce sedation to allow patients to participate. Mobilization therapy is associated with fewer ventilator days and a greater likelihood of being able to walk at hospital discharge.

PHARMACOLOGICAL THERAPY:

BALOXAVIR MARBOXIL

Trade name- Xofluza.

Class- Antivirals.

Type of Administration- Oral route [Take orally as a single dose, May be taken with or without food.]

Dosage form- Tablet-40mg,80mg

Granules for oral suspension- 40mg/20ml, reconstituted solution 2mg/ml

Tablet

- 20 kg to <80 kg: 40 mg PO as a single dose
- ≥80 kg: 80 mg PO as a single dose

Oral suspension

- <20 kg: 2 mg/kg PO as a single dose
- 20 kg to <80 kg: 40 mg (20 mL) PO as a single dose
- ≥80 kg: 80 mg (40 mL) PO as a single dose.

Mechanism of action- Inhibits cap-dependent endonuclease; it is thought to inhibit viral replication activity of the viral polymerase. Inhibition accomplished by a method called cap snatching, where viruses hijack the host mRNA transcription system to allow viral RNA synthesis.

Storage-Store at controlled room temperature of 20-25ºC (68-77ºF); excursions permitted to 15-30ºC (59-86ºF).

- Granules: Store at room temperature 20-25ºC (68-77ºF) and keep in original bottle; excursions permitted to 15-30ºC (59-86ºF).
- Reconstituted suspension: Store at room temperature 20-25ºC (68-77ºF) no longer than 10 hr once reconstituted; discard suspension if not used within 10 hr of preparation or if suspension has been stored at >25ºC (77ºF).

Adverse effects- Diarrhoea (3%),
Bronchitis (2%),

Nausea (1%),
Nasopharyngitis (1%),
Headache (1%)

Pharmacokinetics – Absorption
Effect of food: Decreased peak plasma concentration by 48% and AUC by 36%
Peak plasma time: 4 hr
Peak plasma concentration: 96.4 ng/mL (40-mg dose); 107 ng/mL (80-mg dose)
Distribution- Protein bound: 92.9-93.9%, Vd: 1180 L
Metabolism- Metabolized by UGT1A3 (major) and CYP3A4 (minor)
Metabolites: Baloxavir marboxil is a prodrug and is almost completely converted to baloxavir (active metabolite)
Elimination - Half-life: 79.1 hr, Clearance: 10.3 L/hr. Excretion: Faeces (80.1%), urine (14.7%)

BERACTANT

Trade names-Survanta
Class- Lung surfactants
Type of administration- Intratracheal route
Dosage form- Not indicated for adults.
Pediatric-intratracheal suspension

- 25mg/mL

Mechanism of action- Natural bovine pulmonary surfactant; replaces deficient endogenous lung surfactant in neonates with respiratory distress syndrome. Surfactant prevents the alveoli from collapsing during expiration by lowering surface tension between alveolar surfaces and air.
Frequency- 4 doses can be administrated in the first 48hrs of life. Doses should be given no more frequently than every 6hrs. The need for additional doses is determined by evidence of continuing respiratory distress.
Storage- It is stored refrigerated (2-8°C). Date and time need to be recorded in the box on front of the carton or vial, whenever it is removed from the refrigerator. Before administration, it should be warmed by standing at room temperature for at least 20 minutes or warmed in the hand for at least 8 minutes.
Adverse effects-Transient bradycardia (12%),
O2 desaturation (10%),
Apnea, Endotracheal tube blockage,
Endotracheal tube reflux, Hypotension,
Hypercarbia, Sepsis, Vasoconstriction.
Pharmacokinetics - Excretion: Rapid.

LUCINACTANT

Trade name- Surfaxin
Class- Lung surfactants
Type of administration- For intratracheal use only.
Dosage form- Not indicated for adults.
Pediatric - intratracheal suspension

- 8.5mL/vial
- Each mL contains 30mg phospholipids (22.5mg dipalmitoylphophatidylcholine and 7.5mg palmitoyloleoyl-phosphatidylglyerol, sodium salt), 4.05mg palmitic acid, and 0.862mg sinapultide.

Mechanism of action- Endogenous pulmonary surfactant lowers surface tension at the air-liquid interface of the alveolar surfaces during respiration and stabilizes the alveoli against collapse at resting transpulmonary pressures; deficiency of pulmonary surfactant in premature infants results in RDS. Lucinactant compensates for the deficiency of surfactant and restores surface activity to the lungs of these infants.
Frequency- The recommended dose is 5.8 mL per kg birth weight. Up to 4 doses can be administered in the first 48 hours of life. Doses should be given no more frequently than every 6 hours.
Storage - Refrigerate at 2C to 8C (36F to 46F) and protect from light until ready for use. The manufacturer product information should be consulted.
Adverse effects - ETT reflux (18%),
Pallor (9%),
Dose interruption (9%), ETT obstruction (6%)

METAPROTERENOL

Also referred as Orciprenaline.
Trade name – Alupent
Class – Beta2 agonists
Type of Administration – oral route
Dosage form – Tablet- 10mg,20mg
Syrup – 10mg/5ml
Mechanism of action - Beta-2 receptor agonist with some beta-1 activity; stimulation of beta2 receptors may result in bronchial smooth muscle relaxation.
Frequency - Adults—Two teaspoonfuls (10ml) three or four times a day. Your doctor may adjust your dose as needed.
Pediatric - <2 years old: 0.4 mg/kg PO q8-12hr

- 2-6 years old: 1-3.5 mg/kg/day divided q6-8hr PO; not to exceed 10 mg/dose
- 6-9 years old: 10 mg PO three/four times daily
- >12 years old: 20 mg PO three times daily.

Storage - Store it at controlled room temperature (15°C- 25°C). Avoid excess humidity.
Adverse effects - Tremor (2-17%),
Tachycardia (6-17%),
Nervousness (5-20%),
Diaphoresis increased (4%),
Headache (4%),
Heartburn (4%),
Palpation (4%),
Pharyngitis (4%),
Dizziness (1-4%),
Insomnia (2%),
Weakness (1%),
Nausea (1-4%),
Exacerbation of asthma (2%),
Chest pain,
Hypertension,
Weakness, Syncope, Spasms.
Pharmacokinetics - Onset: 30 min (oral), Peak effect: 1 hr, Duration: 2-6 hr.
Metabolism: Liver, Metabolites: Metaproterenol-O-sulfate, Excretion: Urine (40%).

MOLGRAMOSTIM

Trade name – Leucomax, Macrogen
Class – immunomodulators
Type of Administration – Intravenous and subcutaneous
Dosage form and Frequency –

Intravenous - Adult: 10 mcg/kg (110,000 IU/kg) daily by infusion over 4-6 hr beginning on the day after the procedure and continued for 30 days depending on the neutrophil count. Max: 10 mcg/kg (110,000 IU/kg) daily.

Subcutaneous - Adult: 5 mcg/kg (60,000 IU/kg) daily. After the 5th dose, adjust dose according to neutrophil count. Max: 10 mcg/kg (110,000 IU/kg) daily.

Mechanism of action - Molgramostim is a granulocyte-macrophage colony-stimulating factor (GM-CSF) that influences the growth, differentiation and function of the granulocytes, macrophages and eosinophils. It helps in the separation of granulocyte and macrophage pathways and also enhances cell function.
Storage - Store at 2-8°C. Do not freeze. Protect from light.
Adverse effects - Fever and chills, nausea, dyspnoea, diarrhoea, rash, rigors, vomiting, fatigue, anorexia, bone and musculoskeletal pain, asthenia, transient hypotension, non-specific chest pain, stomatitis, headache, increased sweating, abdominal pain, pruritus, dizziness, peripheral oedema, paraesthesia and myalgia.

PERAMIVIR

Trade name – Rapivab
Class – antivirals (Neuraminidase inhibitors)
Type of Administration – intravenous
Dosage form - IV solution

- 200mg/20mL (10mg/mL)
- Dilute to recommended final volume before administering.

patients who have been symptomatic for ≤2 days- 600 mg IV as a single dose.

Frequency - The recommended dose of Rapivab in adult and adolescent patients 13 years of age or older with acute uncomplicated influenza is a single 600 mg dose, administered via intravenous infusion for 15 to 30 minutes.
Storage - Each single-use vial contains 200 mg per 20 mL (10 mg/mL) of peramivir in a clear glass vial. Rapivab injection is supplied in cartons containing three single-use vials (NDC # 61364-181-03). Store vials of Rapivab injection in original cartons at 20° to 25°C (68° to 77°F).
Mechanism of action - Elicits antiviral activity by inhibiting influenza virus neuraminidase, an enzyme that releases viral particles from the plasma membrane of infected cells.
Adverse effects - Adults- Neutrophils (8%),
Increased serum glucose (5%),
Constipation (4%),
Insomnia (3%),
Diarrhoea (8%),
Hypertension (2%).

Aged 6 months to 17 years- Generally, similar to adults, except Vomiting (3%), Proteinuria (3%)

Pharmacokinetics – Absorption- Rapid
Distribution- Protein bound: <30%.

Metabolism - Not significantly metabolized, it is not a substrate for CYP enzymes, does not affect glucuronidation, and is not a substrate or inhibitor of P-gp
Elimination - Half-life: 20 hr (single 600-mg IV dose), Clearance: ~90% (renal).
Excretion: Urine ~90%

PIRBUTEROL ACETATE

Trade name – Maxair
Class – Beta2 agonists
Type of Administration – it is an aerosol that is inhaled my mouth.
Dosage form – Adult (Given to an age more than 12yrs) - metered dose inhaler

- 200mcg/actuation (14g canister; ~400 actuations)

Mechanism of action - The pharmacologic effects of beta-adrenergic agonist drugs, including pirbuterol, are at least in proof attributable to stimulation through beta adrenergic receptors of intracellular adenyl cyclase, the enzyme which catalyzes the conversion of Adenosine triphosphate (ATP) to cyclic-3† ,5†-adenosine monophosphate.
Frequency - The usual dose for adults and children 12 years and older is two inhalations (400 mcg) repeated every 4-6 hours. One inhalation (200 mcg) repeated every 4-6 hours may be sufficient for some patients. A total daily dose of 12 inhalations should not be exceeded.
Storage - Store it at room temperature, away from heat or an open flame.
Adverse effects - Frequency Not Defined, but sometimes includes Nervousness, Restlessness, Serum glucose increased, Serum potassium decreased, Trembling, Palpitations, Tachycardia, Cough, Headache, Dizziness, Light headedness, Taste changes, Vomiting, Nausea, Paradoxical bronchospasm.
Pharmacokinetics - Half-Life: 2 hr, Onset: <5 min; 0.5-1 hr (peak effect), Duration: 5 hr
Metabolism: Hepatic, Excretion: Urine (10%)

SULFADIMIDINE

Class – sulfonamides
Type of Administration – Oral route
Dosage form – tablet- 500mg
Frequency - 2-4 g/day divided 3-6x/day PO.
Prophylaxis of Recurrent Rheumatic Fever - >30 kg: 1 g/day, <30 kg: 500 mg/day
Mechanism of action - Exerts bacteriostatic action through competitive antagonism with para-aminobenzoic acid (PABA). Microorganisms that require exogenous folic acid and do not synthesize folic acid are not susceptible to the action of sulfonamides.
Storage- Stored at room temperature, away from light and moisture.

- Keep out of reach of children.

Pharmacokinetics - Absorption: well absorbed.
Distribution- sulfadiazine is distributed into most body tissues; appears to cross cell membranes freely; at a plasma concentration of 100 mcg/mL, Protein Bound- approximately 32-56%.
Elimination- largely in urine; urinary concentrations usually are 10-25 times those attained in serum.

VIII. CONCLUSION:

Acute respiratory distress syndrome causes respiratory failure that most commonly occurs secondary to pneumonia, sepsis, trauma or aspiration. Increasing severity of hypoxemia in ARDS is associated with high risk of mortality. Management of ARDS is largely focused on supportive management, lung-protective ventilation and minimizing iatrogenic forms of lung injury, with extracorporeal life support as an option for patients who continue to deteriorate despite these supportive therapies. Acute respiratory distress syndrome that is associated with COVID-19 does not appear to be distinct from the conventional syndrome, and existing therapies should remain the mainstay of treatment.

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