Hypophosphatemia and weaning of Mechanically Ventilated patients with Chronic Obstructive Pulmonary Disease during acute exacerbations

Thesis

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List of Contents

List of Tables

List of Figures

List of Abbreviations

Abb.	Full term
TIRADS	Thyroid Imaging Reporting And Data System

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common pulmonary disease. It is currently the third leading cause of death in the United State and is predicted to be the third leading cause of death worldwide by 2020 ***(CDC, 2010)***.

The American Thoracic Society (ATS) and European Respiratory Society (ERS), defined COPD as "a preventable and treatable disease characterized by irreversible progressive airflow limitation, associated with an abnormal inflammatory response of the lungs towards toxic particles or gases, derived from tobacco smoke, air pollution, or occupational exposures ***(GOLD, 2018)***.

The pathogenesis of COPD is strongly linked to smoking. All smokers develop variable degrees of lung inflammation ***(Willemse et al., 2004)***. Although the mechanism is still poorly understood, there are some factors suspected to be involved such as infections, genetic factors and altered immune and inflammatory regulation ***(MacNee, 2007)***.

The pathologic changes of COPD are widely variable either occur in both large and small airways (chronic bronchitis and bronchiolitis) or in the lung parenchyma (emphysema) ***(Hogg et al., 2009)***. Chronic bronchitis is describing symptoms of cough and excess sputum production for ≥ 3 months per year

in two consecutive years. Emphysema is a pathological term describing destruction of gas exchanging surfaces of lung (alveoli) ***(GOLD, 2018)***.

- **Symptoms**

Early cases are often asymptomatic. Symptoms of dyspnea, wheezing, cough and sputum production, become more prominent along with disease progression.

Dyspnea is mild and only with exertion early in COPD, then becomes progressive and limiting patients' daily activities with progression of the disease. The mechanism for dyspnea in COPD is multifactorial, however exercise-induced air trapping which known as "dynamic hyperinflation" is suspected to play a significant role ***(Rennard et al., 2002)***.

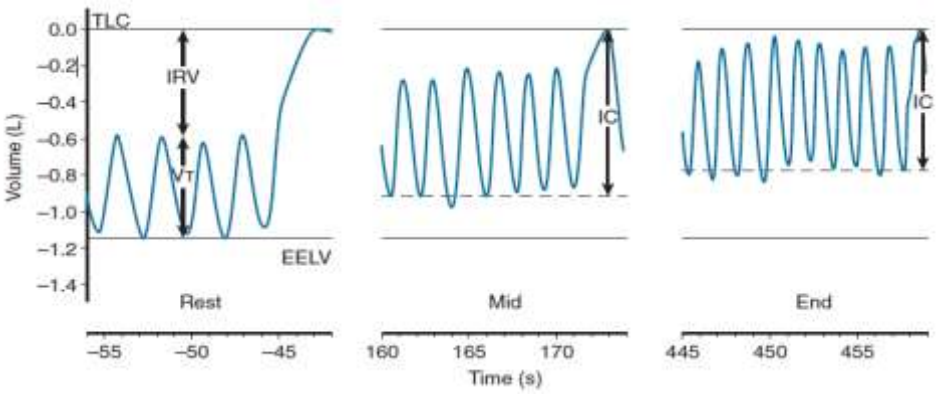

Figure (1): Dynamic hyperinflation ***(Dolmage et al., 2013)*** Volume tracing from a patient with severe COPD who demonstrated ventilatory dependent dynamic hyperinflation. Inspiratory capacity (IC) decreases and end-expiratory lung volume (EELV) increases as ventilation increases during exercise. IRV, inspiratory reserve volume, TLC, total lung capacity, VT, tidal volume.

The presence of cough and sputum production in COPD is variable and can significantly impact quality of life. Sputum usually tends to be mucoid, clear to white in appearance, and more purulent with exacerbations. Smokers have more sputum production, which paradoxically increase after smoking cessation ***(Rennard et al., 2002)***. Excessive sputum production may indicate the presence of bronchiectasis, with a prevalence between (29-52)% is reported in moderate to severe COPD cases ***(Martínez-García et al., 2013)***.

- **Physical Examination**

There are no specific abnormalities noted on physical examination early in the course of the disease. Wheezes may or may not be present and does not necessarily relate to the severity of airflow obstruction. Prolonged expiratory time is a more consistent finding in COPD, particularly as the disease progresses. A forced expiratory time > 6 seconds corresponds to a *forced expiratory volume (FEV1)*/*forced vital capacity* (FVC) ratio of < (50-60) %.

- **Pulmonary Function Testing and the Diagnosis**

  - **Spirometry**

Spirometry is essential to establish a diagnosis of COPD. Spirometry can be performed in the physician's office and should be done for any patient with symptoms (e.g., cough, sputum, dyspnea) and risk factors. When performing

spirometry, a subject exhale forcefully and the FEV1 is compared against the total air exhaled, which is the FVC. COPD is defined by a reduction in the FEV1/FVC ratio. The degree of FEV1 reduction defines the severity of airflow obstruction. The flow volume loop in COPD typically has a concave appearance and the volume time curve demonstrates a prolonged expiratory time ***(Nelson et al., 2012)***.

The American thoracic Society (ATS) and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommend that post-bronchodilator values be used to help distinguish COPD from asthma. GOLD set a value of FEV1/FVC < 0.70 as the threshold for presence of airflow obstruction ***(Celli et al., 2004)***.

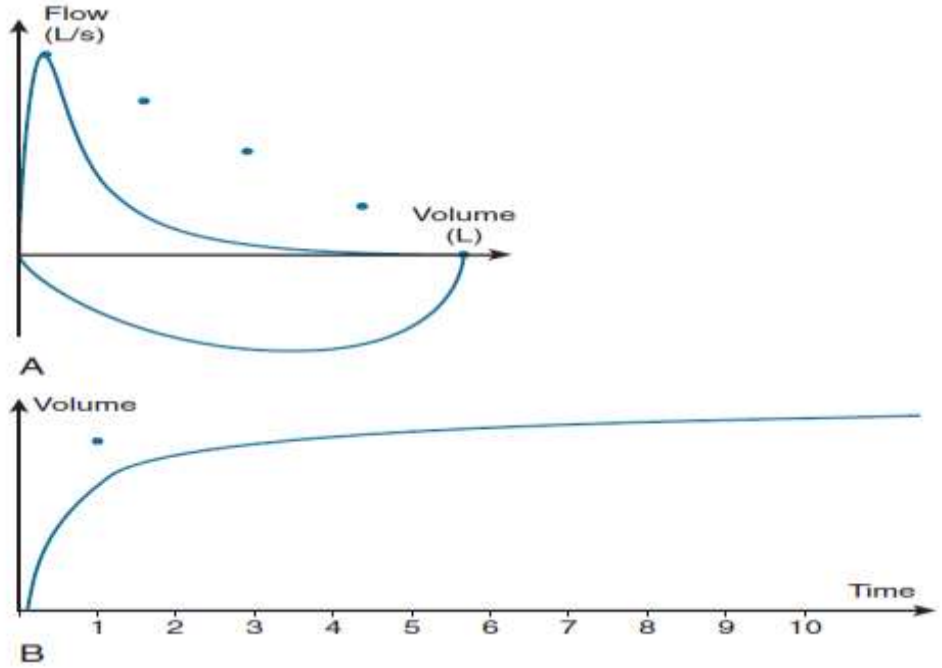

Figure (2): Flow volume loop in COPD. ***(Broaddus et al., 2015)*** A, *the tracing shows a concave flow volume loop with reduction of flow at all lung volumes. The dots indicate the expected flow at various lung volumes. B, the volume-time curve shows a prolonged expiratory time. The dot demonstrates the predicted FEV1.*

While COPD severity has typically been graded based on FEV1% predicted, which is part of the GOLD and ATS/ERS recommendations, recent updates to the GOLD recommendations now incorporate symptoms and exacerbation risk as part of disease staging.

Table (1): GOLD Classification of Severity of Airflow Limitation in COPD ***(GOLD, 2018)***

Severity	**FEV1**
GOLD 1 (Mild)	≥ 80% predicted
GOLD 2 (Moderate)	50%-80% predicted
GOLD 3 (Severe)	30%-50% predicted
GOLD 4 (Very severe)	< 30% predicted

COPD, chronic obstructive pulmonary disease, FEV1, forced expiratory volume in 1 second.

- **Lung Volumes**

The plethysmography is used to measure lung volumes including total lung capacity (TLC) and residual volume (RV). TLC is increased in COPD, particularly in the presence of emphysema where there is significant loss of elastic recoil, resulting in lung hyperinflation. RV tends to increase to a greater extent than TLC, leading to an increase in the RV/TLC ratio. Vital capacity in COPD is decreased because of hyperinflation ***(GOLD, 2018)***.

- **Diffusing Capacity**

Diffusing capacity for carbon monoxide (DLCO) reflects the alveolar capillary blood volume. It is decreased in emphysema, and other abnormalities that affect the alveolar capillary bed including pulmonary fibrosis. Near-normal

spirometry and lung volumes with severely reduced diffusing capacity and radiographic evidence of emphysema would be suggestive of combined pulmonary fibrosis emphysema syndrome ***(Jankowich et al., 2012)***.

- **Exercise Testing**

The *6-minute walk test* (6-MWT) is the most frequently employed exercise test in COPD, which was first described in the early 1960s ***(Laboratories, 2002)***. Its advantage replies on it requires little training to be done and doesn't need a specialized equipment ***(Balke, 1963)***.

- **Imaging**

Chest radiography (CXR) and computed tomography (CT) are the most commonly used imaging modalities used in COPD. CXR is frequently used to investigate dyspnea, hemoptysis, pneumonia, heart failure, lung cancer, and pneumothorax, however it is not sensitive or specific for the diagnosis of COPD. CXR features of hyperinflation seen in COPD involve radiolucency, diaphragmatic flattening, and increased airspace on the lateral radiograph ***(Broaddus et al., 2015)***.

- **Laboratory Testing**

Erythrocytosis

Polycythemia may be seen in COPD, caused by chronic hypoxemia. A hemoglobin value is also helpful in excluding dyspnea due to anemia ***(Broaddus et al., 2015).***

Sputum

Sputum examination in stable COPD cases typically reveals a predominance of macrophages and few bacteria. During exacerbations, the number of organisms on Gram stain typically increases. The most common pathogens identified on sputum culture include *Haemophilus influenzae, Moraxella catarrhalis* and *Streptococcus pneumoniae.* Less frequently identified organisms include *Staphylococcus aureus, Pseudomonas aeruginosa*, and other gram-negative rods ***(Patel et al., 2002)***.

Arterial Blood Gases

Arterial blood gases (ABGs) can provide data to assess hypoxemia and hypercapnia, in severe respiratory disease or during an acute exacerbation of COPD. ABG abnormalities also tend to worsen during exercise and sleep. Early in the disease course, mild to moderate hypoxemia without hypercapnia is typically seen. Later on, hypercapnia may develop, particularly with FEV1 < 1 L ***(GOLD, 2018)***.