Literature Review

Airway Mucus Hypersecretion in Chronic Obstructive Pulmonary Disease Patients: From Basic Pathophysiology to Rehabilitation Approaches

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ABSTRACT
Objective: This narrative review aimed to describe the pathophysiology of mucus accumulation and mucus expectoration disorders, rehabilitation assessments, and airway clearance techniques in chronic obstructive pulmonary disease (COPD) patients.
Methods: Articles were searched using relevant keywords in PubMed, Google Scholar, and CINAHL databases. Article searches were carried out without limiting the article types or year of publication. Only full-text articles in English and Indonesian were included for data synthesis.
Results: COPD causes physiological and structural changes in the airway including stiffness of the airway wall, impaired mucociliary clearance, and decreased cough ability due to respiratory muscle dysfunction. These changes then lead to mucus hypersecretion and mucus accumulation problems resulting in impaired airway clearance and worsened lung function. A rehabilitation assessment is important to assess cough ability and its impact on daily activities and quality of life. Various airway clearance techniques are used to reduce or eliminate airway occlusion and increase expiratory airflow and lung volume. Successful airway clearance can be supported by knowledge of the mechanisms by which mucus accumulates so that appropriate management can be provided.
Conclusion: COPD causes airway stiffness, impaired mucociliary clearance, and weakened cough due to respiratory muscle dysfunction, leading to mucus accumulation and worsened lung function. Airway clearance techniques aim to remove obstructions, improve expiratory flow, and enhance lung volume. Understanding mucus accumulation mechanisms is crucial for optimizing airway clearance management based on patient needs.

Keywords: *Chronic Obstructive Pulmonary Disease, Cough, Mucociliary Clearance, Mucus, Pulmonary Ventilation*

INTRODUCTION

Breathing difficulty, cough, and mucus hypersecretion are several persistent and progressive respiratory symptoms caused by chronic obstructive pulmonary disease (COPD). Clinical manifestations of mucus hypersecretion are recurrent cough and mucus expectoration disorders, which are considered the risk of progression and associated with COPD prognosis. Previous findings stated that around 50% of COPD patients experience mucus hypersecretion. The risk of death in COPD patients with mucus hypersecretion is 3.5 times greater than those without this symptom. COPD patients with chronic mucus hypersecretion also have poorer quality of life and psychological well-being.[1–3]

Quality of life impairment in COPD is primarily due to activity limitations caused by chronic cough with excessive sputum production and a severe high rate of dyspnea. Patients with COPD and chronic bronchitis generally have poor health status. Increased acute COPD exacerbations and hospitalization rates are associated with chronic airway mucus hypersecretion. Patients who experienced chronic cough and sputum production had a fourfold higher risk of acute exacerbations and hospitalization.[1,4]

COPD exacerbations are linked to reduced work productivity. A study found that job status differed significantly among 15.9% of employed subjects, with fewer patients working as disease severity increased. COPD-related work time loss was substantial, with employed subjects also reporting workplace impairments exceeding 40%.[4]

Psychological issues are among the major challenges faced by COPD patients during acute exacerbations. The emergence of psychological disorders, such as anxiety and depression, is attributed not only to acute exacerbations but also to increased mortality, prolonged hospital stays, and a decline in functional status and quality of life associated with COPD.[5] Exacerbations that necessitate hospitalization or even intensive care unit admission can lead to significant psychological disturbances. One study reported that the incidence of anxiety and depression in hospitalized COPD patients ranges from 10% to 55%, with generalized anxiety disorder, panic disorder, and specific phobias being the most commonly observed.[6] Furthermore, anxiety disorders were found to be 85% more likely to occur in COPD patients compared to control groups without COPD.[7]

Mucus hypersecretion in COPD is associated with respiratory tract infections, airflow obstruction, and more severe complaints, so airway clearance management plays an important role in improving symptoms.[8-10] Previous studies have shown that airway clearance techniques are associated with improvements in dyspnea, cough, and physical activity. Rehabilitation techniques aimed at airway secretion clearance are also linked to enhanced quality of life scores in both physical and mental domains. Reduced COPD exacerbations lead to improved work productivity and prevent actively working patients from occupational impairment caused by the disease.[1,4,10] Currently, many techniques and tools are used to manage airway secretions, so knowledge about the mechanisms underlying the hypersecretion and mucus discharge disorders found in COPD patients is needed. This knowledge is important for selecting appropriate airway clearance techniques.[8–10] This narrative review aimed to describe the pathophysiology of mucus accumulation and mucus expectoration disorders, the rehabilitation assessments, and airway clearance techniques.

METHODS

Synthesizing data was based on articles searched using PubMed, Google Scholar, and CINAHL databases. The inclusion criteria of the studies included in this review were all types of articles that met the search criteria and discussed the study objectives. Authors also included textbooks and other types of literature like proceedings or editorials that support the discussion of this study. The exclusion criteria were articles that were not in English or Indonesian and those without full-text availability. The search strategy used keywords with the combination of “airway clearance” or “airway secretion;” “airway mucus” or “airway mucus secretion;” “airway secretion management” or “airway clearance techniques;” “pulmonary rehabilitation” or “respiratory rehabilitation” or “chest physical therapy;” and “chronic obstructive pulmonary disease” or “COPD” or “airway obstruction.” The authors screened the search results by first reviewing article titles and then abstracts. Articles with titles and abstracts aligned with the study objectives underwent full-text review. References and the citations of the articles included were also further explored to meet and enrich the review’s purpose.

RESULTS

The article search was based mainly on the research objectives. Nine articles, consisting of seven review articles and two original articles, were found relevant to explain different aspects of COPD pathophysiology, which include various mechanisms of airway clearance disorders and respiratory muscle dysfunction in COPD. As for the rehabilitation aspect, two main sections of the assessment approach and airway clearance techniques were discussed. Eight articles, consisting of four reviews and four original articles, were reviewed to elaborate the rehabilitation assessment approach in COPD patients which includes comprehensive steps from general anamnesis to cough ability assessment. Later ten articles, consisting of five reviews and five original articles, were included to explain various airway clearance techniques. The included study is then summarized and presented as a narrative review that elaborates comprehensive discussion about COPD from its pathology to its rehabilitation approach, especially on the airway clearance aspect.

DISCUSSION

PHYSIOLOGY OF MUCUS, MUCOCILIARY CLEARANCE, AND COUGH

The terms sputum and mucus are often considered the same but they are different. Mucus is a secretion produced by goblet cells and mucous glands as well as serous cells that attach to cell membranes, which is then carried by the movement of the cilia to the upper part of the airway to be coughed up. The mucus that is coughed up is called sputum.[10–12]

Goblet cells are the main secretory cells in the superficial layers of the large airways. The number of goblet cells along the airways decreases over time and disappears before entering respiratory bronchioles. The number of mucus glands also decreases when they reach the bronchioles.[10-12]

A surface layer consisting of ciliated-columnar epithelial cells is called mucosa. Cilia movement allows upward mucociliary movement to move mucus, inhaled fluids, and particles including dissolved chemicals and pathogens from proximal airways. After ascending the trachea, the laryngeal ciliary epithelium is moved from the airway to the vocal cords. Subsequently, mucus reaches the vocal cords, causing them to close. This closure generates sufficient pressure to propel the mucus. If the pressure is adequate, the vocal cords will open, leading to mucus expulsion.[10,13,14]

Mucus consists of a mixture of mucin, electrolytes, fluids, metabolites, and proteins, with varying compositions. Mucus production is stimulated by inflammation and environmental exposure and serves as a lung barrier against foreign particles and microorganisms. The mucus also facilitates the clearance of inflammatory products from the lungs.[11,12]

Mucin plays a role in forming viscoelastic mucus gel and preventing dehydration of the mucosal layer as well as producing carbohydrate ligands with pathogens absorber function. Mucin, which binds to other secretory components, also acts as a sink for protective proteins and peptides. Mucin is also found on the surface and attached to the microphilia or cilia of the airway epithelium which acts as a barrier that maintains the periciliary layer and regulates the movement of the cilia. These two forms of mucin interact to maintain epithelial function and airway surface moisture and provide mucociliary clearance. Disruption of mucin regulation will cause mucociliary transport disorders. Under normal conditions, mucin production can maintain efficient airway function, but if hyperplasia and/or metaplasia occurs, excess production occurs which causes pathological conditions.[10,12]

Mucociliary clearance is carried out through ciliary movement. The movement of the cilia when pushing mucus is called ciliary stroke which consists of three phases, namely effective stroke, resting state, and recovery stroke. During the effective stroke phase, the cilia will move forward, so that they are positioned perpendicular to the cell surface. The maximum speed reaches 1 mm/sec at the peak and forms an arc at an angle of approximately 110 degrees. The cilia peak will penetrate the mucus layer to a depth of ± 0.5 µm and push the mucus forward. Next, the cilia entering a resting state before entering stroke recovery. During the recovery stroke, the cilia will swing almost 180 degrees backward to approach the cell surface and after that, the cilia will enter the effective stroke again. This movement will bring mucus to the proximal airway so it can be expelled.[10,15]

Coughing is a body defense reflex to clear secretions and debris from the airway through four phases, namely receptor, inspiration, compression, and expulsion phases. In the receptor phase, cough receptors are stimulated, activated, and then transmit impulses through the vagal nerve to the center. The inspiratory phase consists of the glottis opening so that air enters the lungs and increasing the air volume accompanied by closing the glottis. Closure of the glottis results in an increase in intratracheal pressure up to 66 mmHg and this phase is called the compression phase. Simultaneously, the abdominal muscles and other expiratory muscles contract strongly which causes intrapulmonary pressure to increase and the alveoli and bronchioles compressed. Next, a sudden opening of the glottis accompanied by high-speed expulsion of air occurs, so that it can clear the airway lumen.[14,16,17]

The determining factor for cough effectiveness is an operational lung volume, which depends on the respiratory and laryngeal muscles coordination and strength, and also the mechanics of the lung. Incoordination and/or weakness of these muscles can reduce driving pressure in the alveoli and bronchial airways. Reduced driving pressure causes low expiratory volume and flow during the coughing process. Airflow limitations and lung hyperinflation also result in a decrease in the lung's operational volume.[17]

STRUCTURAL AND FUNCTIONAL CHANGES OF THE LUNG DUE TO COPD

Changes in Goblet Cell and Mucus

Persistent airflow limitation due to COPD is associated with increased chronic response to inflammation caused by noxious gases or particle stimulation. The increase in chronic inflammatory response causes increased mucous glands and goblet cell production presented as chronic sputum production or chronic bronchitis and mucus hypersecretion (Table 1). The change that occurs in goblet cells due to COPD is called hyperplasia. In smokers, there is an increase in goblet cell density and mucin volume. This affects airway remodeling, which disrupts homeostasis and dehydration due to poor mucus clearance.

Table 1. Pathophysiology of Airway Mucus Hypersecretion in COPD

Pathophysiology of Airway Mucus Hypersecretion	
Structural and Functional Changes	**Airway Clearance Disorders**
Change in Goblet Cells and Mucus • Hyperplasia of goblet cells • Airway remodeling • Homeostasis changes • Dehydration Changes in Airway Wall • Stiffness of airway wall • Decrease recoil ability of lung parenchyma	Mucus hypersecretion • Inflammatory processes • Oxidative stress • Viral and bacterial infections Impaired mucus elimination • Poor cilia function • Lower airway occlusion • Decreased peak expiratory flow (PEF) • Ineffective coughing (a secondary

• Reduction in ability to exhale air and perform gas exchange • Decrease in forced expiration volume in one second (FEV1)	consequence of decreased PEF) • Weakness of the respiratory muscles

Apart from remodeling disorders, hyperplasia also occurs due to inflammatory processes and infections. The influence of cigarette smoke also causes an increase in viscosity.[12]

Changes in Airway Wall

Airway wall stiffness is also a change that occurs due to COPD (Table 1). The stiffness of the airway wall is determined by passive components such as airway blood vessels, glands, smooth muscle, cartilage, and extracellular matrix as well as active components in the form of airway smooth muscle activity. [18]

Structural changes of the airway smooth muscle are reduced stretching and thickening abilities of the epithelial layers of the lamina propria and adventitia. Thickening occurs in up to 20% of the smooth muscle layers of the large and small airways. Smooth muscle thickening results from hyperplasia or hypertrophy or both simultaneously.[18]

The lung parenchyma and blood vessels change in patients with COPD occur in the extracellular matrix in the form of a decrease in elastin number. The amount of elastin in the alveoli decreases and causes a decrease in the recoil ability of the lung parenchyma and a reduction in the ability to exhale air and gas exchange. Decreased elasticity in the alveoli and airways results in a decrease in the patient's expiratory volume which can be assessed through the forced expiratory volume in one second (FEV1). Another extracellular matrix change is an imbalance in collagen structure with a reduction in mature collagen composition.[18]

THE MECHANISM OF AIRWAY CLEARANCE DISORDERS IN COPD

Impaired airway clearance is caused by an imbalance between mucus secretion and expulsion. The main mechanisms contributing to impaired airway clearance in COPD are hypersecretion of mucus by the goblet cell and reduced elimination of mucus by the cilia. In addition, submucosal gland hypertrophy that is associated with airway inflammation severity occurred (Table 1). The hypertrophy is measured with the ratio of submucosal glands thickness and the cartilage covering the bronchi.[12,19]

Mucus hypersecretion is caused by inflammatory processes, oxidative stress, and viral or bacterial infections.[10] Impaired mucus elimination in COPD patients is influenced by several factors including poor cilia function, lower airway occlusion, and ineffective coughing as a secondary consequence of decreased peak expiratory flow (PEF) and weakness of the respiratory muscles.[10,13]

Mucus Hypersecretion, Impaired Mucociliary Clearance, and Airway Occlusion

Chronic productive cough and mucus hypersecretion are consequences of exposure to cigarette smoke, bacterial or viral infections, or inflammatory cell activations due to the mucin gene transcription. These conditions are exacerbated by reduced mucus-clearing ability. Mucus hypersecretion may play a greater role than mucociliary disorders alone in triggering lung inflammation and remodeling (Table 1).[10,11]

Mucus blockage-induced pro-inflammatory effects are related to epithelial necrosis resulting from hypoxia in a blocked airway. Mucin that accumulates in the airway lumen causes an immunomodulatory effect which then triggers macrophage activation and the release of proteolytic substances that damage lung tissue. Mucus hypersecretion and impaired mucociliary clearance also cause accumulation and retention of irritants or allergens that worsen lung function. Airway occlusion is also caused by thickening of the smooth muscle layer which results in narrowing of the airway lumen. Airflow obstruction increases susceptibility to infection due to airways chronic inflammation and lung structure damage that can occur with or without the presence of bacterial infection.[18]

Respiratory Muscle Dysfunction

In COPD, there are qualitative and quantitative changes in the respiratory muscles. Qualitative changes occur due to the transition of respiratory muscles from muscles with aerobic metabolism and slow type fiber composition to anaerobic metabolism and fast type fiber composition. Quantitative changes occur due to loss of respiratory and peripheral muscle mass.[20]

There is also neurohumoral activation which can aggravate inflammation, cachexia, and skeletal muscle dysfunction. This process occurs repeatedly, causing inflammation and chronic respiratory muscle dysfunction.[16] Decreased muscle strength in COPD patients is also caused by malnutrition, deconditioning, heart failure, electrolyte imbalance, myopathy, and systemic inflammation due to long-term corticosteroid treatment. Inspiratory muscle weakness is also caused by pulmonary hyperinflation which places the inspiratory muscles in a non-optimal condition during contraction. Expiratory muscle weakness can occur due to general muscle weakness.[21]

The inspiratory muscle weakness also affects the effective coughing process. High volume during inspiration will increase the elasticity of chest wall recoil which can maximize pressure during expiration or expulsion. Inspiratory muscle strength will also be optimal with increasing chest wall expansions so that it reaches optimal volume to produce a high air flow rate.[22]

REHABILITATION ASSESSMENT IN AIRWAY MUCUS HYPERSECRETION MANAGEMENT

Anamnesis, Physical Examination, and Supporting Examination

A clinical and functional assessment of COPD is described in Table 2. The most common complaint in COPD patients is a cough with excessive mucus production. A cough history is taken to assess the frequency, duration, impact, causes, family history, and symptoms associated with disorders of the throat, chest, and digestive tract. In the cough history, it is also necessary to identify other risk factors that can cause coughing, such as angiotensin-converting enzyme inhibitor use, smoking, and sleep apnea. Coughs can be categorized as acute and chronic coughs. Coughing for

≥4 weeks in patients aged less than 14 years or ≥8 weeks in older patients is considered a chronic cough.[23]

The clinical history regarding mucus production is important to know before carrying out therapy. Mucus production in normal adults is approximately 20-30 ml/day. Mucus can be expelled involuntarily or through a cough mechanism. The mucus production can easily assess if the patient experienced a productive cough. In coughs that are not accompanied by mucus expectoration, a deeper history is needed. A dry cough does not indicate a cough without mucus production, as it tends to be swallowed when the mucus has reached the pharynx. The sound made when coughing can also help in determining the amount of mucus. Other assessments in productive cough are the frequency and physical characteristics of the sputum to estimate the disease severity.[24]

The physical examination includes cardiovascular and respiratory examinations along with an examination of the ears, neck, and throat. The purpose of the physical examination is to determine the presence or absence of mucus and the location and possible causative factors.[23,24] Supporting examinations as an initial assessment of COPD include spirometry and chest radiology examinations. In patients who experience chronic cough with normal chest x-rays, a lung CT-Scan is not recommended because of the low probability of finding and the risk of radiation exposure.[23]

Table 2. Rehabilitation Assessment and Airway Clearance Modalities in Managing Airway Mucus Hypersecretion in COPD

Rehabilitation Assessment
Clinical Examination • Anamnesis: cough with excessive mucus production • Physical examination: cardiovascular, respiratory, and ear, nose, and throat examinations • Supporting examination: spirometry, chest x-ray, lung CT-scan Functional Examination • Cough frequency: recording devices • Cough impact on QoL: St. George Respiratory Questionnaire (SGRQ) and the Leicester Cough Questionnaire (LCQ) • Cough ability: gastric pressure, peak cough flow (PCF), and expiratory volume during maximal and voluntary coughing
Airway Clearance Modalities
• Postural drainage. A technique to mobilize mucus from the peripheral to the central airway using gravity • Manual technique. Applying pressure to the chest using the hands (clapping and vibration) provides positive pressure on the chest wall resulting in increased expiratory flow • Active cycle of breathing techniques (ACBT). Consists of 3 phases (breathing control, chest expansion exercises, and forced expiration) that facilitate collateral ventilation to encourage secretion and expand the area of occlusion; also, to produce maximum expiratory airflow which can reduce airway collapse • Autogenous drainage (AD). Consisting of 3 phases (release, collection, evacuation) which will cause changes in lung volume, break down mucus adhesions, and move mucus proximally in the airways • Positive expiratory pressure (PEP). Flutter or oscillatory positive expiratory pressure (OPEP), a technique of exhalation against resistance at threshold resistance will generate positive airway pressure during the expiratory phase. This results in the accumulation of a larger volume of air to push the expulsion • Continuous chest wall vibration. This technique will clear the airway, stimulate respiratory muscles, and reduce shortness of breath • Intrapulmonary percussive ventilation (IPV). A high-pressure airflow generator with a valve to stop airflow. It creates small bursts of air with a high frequency that causes vibration or internal percussion in the lungs • Expiratory flow accelerator (EFA). A vacuum method to accelerate expiratory flow causing secretion to reach the upper airway so that the patient expels mucus physiologically via mucociliary mechanisms • Manual assisted cough (MAC). A technique to provide compression to the chest or stomach to increase expiratory flow (chest) and increase cough flow (abdomen) which will increase mucus clearance • Cough assist (Mechanical insufflator-exsufflator). This technique mimics the coughing process. It increases the inspiratory pressure and then converts to negative pressure resulting in higher expiratory airflow which will increase peak cough flow and further increase cough effectiveness and mucus clearance

Assessment of Cough and Its Effect on Daily Activities and the Quality of Life

Assessment of cough frequency can be done with cough recording devices which are often used in research but are not effective in clinical practice. One valid tool for measuring cough frequency is an electronic audio and video recording device which is at least carried out in the laboratory using manual calculations as a reference standard. Devices for electronic recording are found to be more valid in assessing the frequency of cough compared to manual calculations. The score of the visual analog scale (VAS) can assess both the frequency and impact of coughing. The cough impact can also be assessed as a part of the quality of life assessment, but the data on the validity of this score is limited.[25,26]

The impact of cough on quality of life can be assessed with the St. George Respiratory Questionnaire (SGRQ) and the Leicester Cough Questionnaire (LCQ). Coughing can also cause urinary incontinence, falter speech, and depression. The use of the LCQ to assess the impact of cough on daily activities and the health status of the general population has also been well-validated. This questionnaire can also assess the response to the treatment given.[25,26]

The 19 questions and statements in the LCQ are divided into three groups to assess physical, mental psychological, and social disorders. The assessment uses a Likert scale of 1-7 and is used to assess the impact of coughing in the last two weeks. The range of scores for this questionnaire is 3-21. A better result on the patient's quality of life is shown by a higher LCQ score.[27]

Cough Ability Assessment

Assessment of cough effectiveness can be done with gastric pressure, peak cough flow (PCF), and expiratory volume during maximal and voluntary coughing measurements. Measuring gastric pressure is an invasive method by inserting a balloon catheter connected to the manometer through the nose into the stomach. The patient is asked to cough 3-6 times starting from maximum inspiration. Normal gastric pressure values are ≥100 cmH2O and ≥130 cmH2O in women and men, respectively.[17]

PCF assessment is an alternative for examining expiratory muscle strength, which is one of the determining factors for cough effectiveness. PCF examination is carried out by asking the patient to cough through a facemask and starting with maximum inspiration. The facemask is connected to a pneumotachograph. The test is done 3-6 times. The normal PCF value in healthy male or female individuals is ≥360 L/minute. Variation of average PCF based on previous studies in healthy Caucasian Europeans was >300 L/minute and in healthy Indonesians was 477 L/minute. Patients with a PCF value <160 L/minute may have an ineffective cough ability and therefore require manual or mechanical cough assistance.[17,22,28]

Cough assessments should be carried out routinely in patients who are suspected to have ineffective coughing. Apart from expiratory volume and PCF measurements, the vital capacity and respiratory muscle strength measurements are also considered for the cough ability assessment. Maximum inspiratory pressure (MIP) and maximum expiratory pressure (MEP) values represent respiratory muscle strength. In healthy individuals, the expiratory volume value is usually >1 L (an average value of 2.4 L). Clinical evaluation of PCF can be used as a parameter of overall cough effectiveness. In these patients, it is also necessary to examine the respiratory muscle function, which is carried out by measuring vital capacity in standing and supine positions.[17]

AIRWAY CLEARANCE TECHNIQUES IN COPD

Airway clearance techniques (Table 2) aim to reduce airway occlusion due to mucus to prevent the emergence of airway infections and the development of collapsed lung parenchyma. These techniques can help gas exchange and reduce the risk of inflammation. There are several mechanisms used to reduce or eliminate airway occlusion such as increased expiratory flow, airflow oscillations, and increased lung volume.[8]

Postural Drainage (PD)

PD is a technique for mobilizing mucus from the periphery to the central airway using gravity so that it is easier to cough up. The PD technique has no effect or minimal effect in patients with minimal mucus secretion. The PD technique is recommended to be used in patients with mucus production >30 ml per day. A side effect that may arise from the application of the PD technique is shortness of breath. The use of intermittent positive airway pressure or noninvasive ventilation simultaneously can reduce shortness of breath and help increase positive expiratory pressure for mucus expulsion. Evidence regarding the effectiveness of PD is limited, and the effect of gravity on the small airway remains questionable.[8,9]

Manual Technique

The manual technique is carried out by applying pressure to the chest using the hands. This technique consists of percussion (clapping) and vibration. Percussion is given with the hand cupped on the patient's chest which is then moved quickly and rhythmically. This technique is given to the area to be treated during inspiration and expiration. The percussion strength is adjusted to suit the patient's comfort with a percussion frequency between 4.6 and 8.5 Hz. Vibration is carried out with back-and-forth movements combined with chest compressions during exhalation. The pressure applied to the chest wall must be sufficient to increase expiratory flow but must not cause discomfort to the patient.[8]

Manual techniques provide positive pressure intermittently on the chest wall and transmit it to the airway which results in increased expiratory flow. Currently, no evidence has been found to support or refute the superiority of manual techniques compared to other techniques. A previous study found that manual techniques did not show a significant impact on airway clearance.[8,9]

Active Cycle of Breathing Techniques (ACBT)

The ACBT (Figure 1) is an option in airway clearance management because it can be done by the patient themselves without equipment. This technique consists of three phases, namely breathing control, chest expansion exercises, and forced expiration. Breathing control is a breathing technique with diaphragmatic breathing at a tidal volume that is adjusted to the patient's respiratory volume and frequency. Patients are allowed to rest if they experience fatigue, desaturation, or signs of shortness of breath while performing this technique.[8]

Chest expansion exercises consist of three or four breathing cycles of slow, deep inspiration (a volume greater than the tidal volume) with a pause of approximately three seconds at the end of the inspiration and followed by passive expiration. Deep inspiration must be able to facilitate collateral ventilation which then flows the air through the intrabronchial, bronchoalveolar, and interalveolar canals as well as the interalveolar pores. This technique will encourage secretion and expand the area of occlusion.[8]

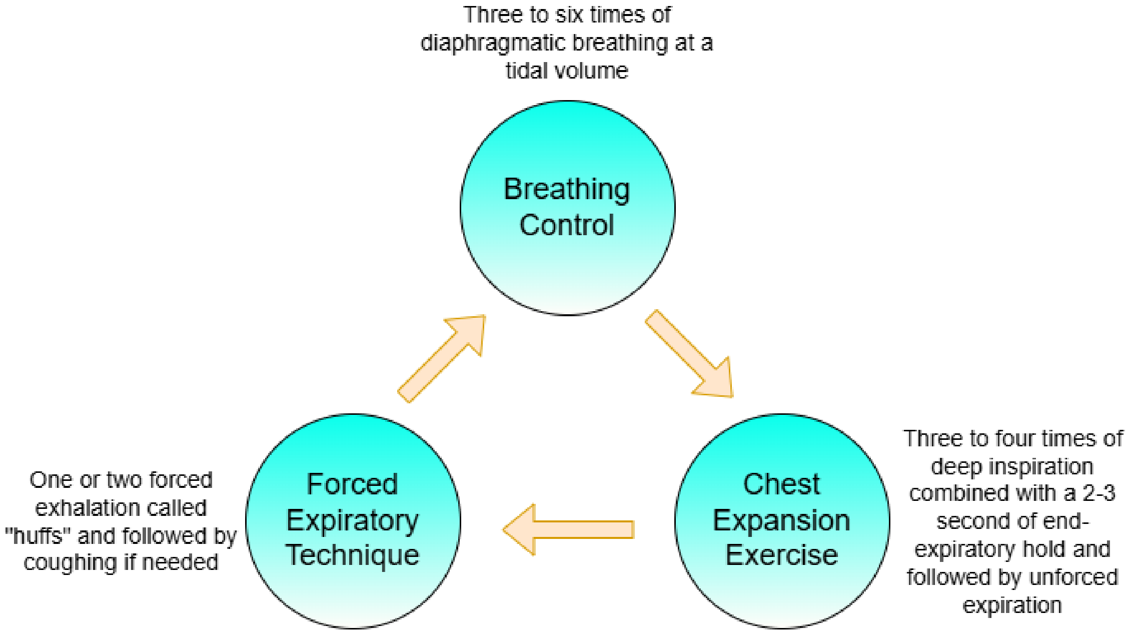

Figure 1. Active Cycle of Breathing Technique

The final stage of ACBT is the forced expiratory technique, which is a combination of one or two forced expirations called "huffs" and breathing at tidal volume. When the huff length and expiratory muscle contraction strength are sufficient to produce maximum expiratory airflow which can reduce airway collapse, the expiration will be most effective.[8]

ACBT can be performed in several positions such as supine, upright, or prone. Combination with other tools and/or positions or together with manual techniques can also be done. Horizontal position ACBT in patients with mucus production >20 grams a day resulted in better airway clearance. Evidence of the superiority of ACBT compared to other techniques is scarce.[8,9]

Autogenous Drainage (AD)

The AD technique is also an airway clearance technique that does not require tools. This technique consists of three phases, namely release, collection, and evacuation. Each phase causes changes in lung volume with the largest volume occurring in the collection phase. Changes in volume will break down mucus adhesions, release mucus from the walls, and move mucus proximally in the airways. This technique can be done in a sitting position. Research showed that this technique is equivalent to other methods and the AD technique is superior to ACBT in cases of chronic hypercapnia.[8,9]

Positive Expiratory Pressure (PEP)

The PEP technique consists of exhalation against the resistance at threshold resistance or flow to generate positive airway pressure during the expiratory phase. The airflow against obstruction will increase through the collateral canal and thereby accumulate a larger volume of air to push the expulsion.[8]

One type of PEP used in COPD patients is flutter or oscillatory positive expiratory pressure (OPEP). Daily use of OPEP in COPD patients with sputum production improves proximal sputum mobilization, the force vital capacity (FVC), the 6-minute walk test distance (6MWD), and the quality of life. Increased ventilation which provides a mechanical effect in the form of sputum mobilization to the proximal part is the mechanism underlying the changes that occur after OPEP administration.[8,29]

This technique must also be able to create a pressure gradient to oppose the obstruction so that it can push mucus toward the center. Positive pressure during exhalation will prevent the premature collapse of the peripheral airway. A study found no significant difference in patients' quality of life after administration of PEP compared with other clearance techniques (ACBT, PD, and AD).[8]

Continuous Chest Wall Vibration

Initially, the vibration technique with the device was used in pulmonary rehabilitation programs to clear the airway.

This technique then developed to stimulate respiratory muscles and reduce shortness of breath. The application of vibration with a device in healthy patients facilitates respiratory muscle work, increases respiratory drive, and reduces the sensation of shortness of breath and the effort associated with inspiration.[30]

The application of vibration with a continuous chest wall vibration device along with aerobic exercise is found to increase pulmonary rehabilitation program effectiveness. There was an increase in exercise capacity in COPD patients who were given chest wall vibration, but no effect of this technique was found on shortness of breath, respiratory muscle function, and quality of life.[30]

Intrapulmonary Percussive Ventilation (IPV)

A high-pressure airflow generator and a valve to stop the airflow are the components of this tool. In normal breathing, this tool creates small bursts of air with a high frequency (5-520 cycles per minute), which then causes vibration or internal percussion in the lungs. This tool can also be used as a ventilation aid.[8]

In COPD patients, IPV is administered to improve gas exchange and exacerbation-related parameters. It has been suggested that IPV may be more effective as a method to assist ventilation compared to other techniques. It was also found that in stable COPD patients and during exacerbations, IPV administration had immediate and long-term effects on gas exchange and peripheral oxygen saturation due to better lung recruitment.[8,31]

A combination of IPV with conventional physiotherapy increased the ratio of PaO_2/FiO_2 and MEP and reduced pneumonia incidence. The use of this technique in daily practice in patients with COPD is not supported by sufficient evidence. However, it may be beneficial during COPD exacerbations as it shortens the length of hospital stays and improves gas exchange.[8]

Expiratory Flow Accelerator (EFA)

EFA is a device that uses a vacuum method to accelerate expiratory flow, increasing mucus clearance without placing pressure on the airway in patients with or without an ineffective cough. Secretions can reach the upper airway so that the patient can expel them physiologically via mucociliary mechanisms. This process occurs in the expiratory phase and is comparable to the airflow in spontaneous breathing following the patient's respiratory rhythm.[8,32]

The administration of EFA in stable severe COPD patients improves blood gas analysis and results in increased MIP and greater 6MWT results. Research by Zampogna et al. found that the use of EFAs improved bronchial clearance in post-exacerbation severe COPD patients with symptoms of hypersecretion and decreased cough efficiency.[32]

Manual Assisted Cough (MAC)

MAC is a technique for clearing the airway by providing compression on the chest or stomach that is adjusted to the cough cycle to increase expiratory ability. Strong chest compressions simultaneously with expiration increase expiratory flow, thereby increasing mucus clearance.[33]

Compression of the abdomen results in increased abdominal pressure so that the intra-abdominal organs push against the diaphragm and cause an increase in cough flow. The MAC technique requires patient cooperation and should not be performed 1-1.5 hours after eating. Research showed an increase in PCF after MAC administration.[34] In healthy subjects, mucus could be easily cleared by coughing without the MAC technique, but in COPD patients with neuromuscular disease, it can be difficult. In addition, in COPD alone patients, the effect of MAC is minimal.[35]

Cough Assist (Mechanical Insufflator-Exsufflator)

The cough assists device produces airflow changes within the bronchial tree. This technique is generally used in neuromuscular pathology and respiratory muscle weakness, resulting in ineffective cough.[8] The mechanism of action of this device mimics the cough mechanism by increasing the inspiratory pressure in the airway. Inspiratory pressure is quickly converted to negative pressure to create a higher expiratory airflow. This process increases peak cough flow resulting in increased cough effectiveness and better mucus clearance.[8,36]

CONCLUSION

COPD causes physiological and structural changes in the airways including stiffness of the airway walls, impaired mucociliary clearance, and decreased ability to cough due to respiratory muscle dysfunction. These changes then lead to mucus hypersecretion and accumulation which cause impaired airway clearance and worsen lung function.

In the implementation of airway clearance procedures, assessment is carried out to assess the ability to cough and its impact on daily activities and quality of life. Various airway clearance techniques are used to reduce or eliminate airway occlusion and increase expiratory flow and lung volume. We assumed that the success of airway clearance techniques is supported by knowledge of the mechanisms by which mucus accumulates so that airway clearance management can be provided according to the patient's condition.

Conflict of Interest

The authors declare there is no conflict of interest.

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Author Contribution

The authors contributed to all concepts, design, writing preparation, editing, and review of this manuscript.

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