INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a disease characterized by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive, associated with an abnormal inflammatory response of the lungs to noxious particles or gases. COPD includes chronic bronchitis and emphysema. The disease is usually progressive, and is marked by dyspnea (Shortness of breath), which reduces patients ability to perform their daily activities, and decreases their health-related quality of life (HRQOL). COPD is the international preferred term chronic obstructive pulmonary disease encompassing, chronic bronchitis and emphysema. By definition COPD is a chronic slowly progressive disorder characterized by air flow obstruction (Forced expiratory volume FEV_1< 80%) and chronic respiratory failure ***(Haslett et al., 2002).***

Patients who benefit most from long term usually nocturnal nasal positive pressure ventilation (NPPV) are those with skeletal deformity specially kyphoscoliosis and neuromuscular disease, however NPPV can also be of value in some patients with central alveolar hypoventilation, it is now in wide spread use in the acute situation in patients with COPD and type II respiratory failure usually to try to avoid tracheal intubation, IPPV

(Intermittent positive Pressure Ventilation), but also in weaning such patients from mechanical ventilation ***(Haslett et al., 2002).***

Table (1): Classification and diagnosis of COPD ***(Haslett et al., 2002).***

Severity	**Spirometry**	**Symptoms**
Mild	FEV160-79% predicted	Smoker's cough exertional breathlessness
Moderate	FEV140-54% predicted	Exertional breathlessness wheeze, cough sputum
Severe	FEV1<40% predicted	Breathlessness, wheeze and cough predominant swollen leg

COPD imposes an increased load in respiratory muscle for three reasons, first because the increased air way resistance which is a characteristic of COPD, the inspiratory muscles have to generate a greater than normal change in pleural pressure to produce a given increase in lung volume. Second, although the emphysematous changes in lung architecture in COPD usually increase static pulmonary dispensability, the large inequalitits in the time constant are such that the effective complience during breathing may be lower than normal. Therefore, the elastic load may also be increased. Finally, emphysema increase

the relaxitive position of the respiratory system, which reduces the mechanical efficiency of the chest wall and requires the inspiratory muscle to operate at shorter than normal length ***(Haslett et al., 2002).***

The diaphragm is the most important respiratory muscle, whose motor function is supplied by phrenic nerve. The early clinical symptoms or signs of respiration dysfunction (RDF) resulting from neuromuscular disorders are often mild or easy to be overloaded. Phrenic nerve conduction study (PNC) may offer objective indication for evaluating RDF ***(Lassens, 1994).***

COPD and chronic hypoxemia will cause (PNP) peripheral neuropathy for longtime and neurophysiological changes in central nervous system as BAERIII (Brainstem evoked potential) and IPLs (interpeak latency) of it represent the pontomedullary portion of the brain, cigarette smoking and airway obstruction may not only cause PNP but also a delay responses o the brainstem by inducing chronic hyperapnia and inspirtory acidosis in patients with COPD ***(Kayacan, 2001).***

COPD is characterized by a long natural history and elevated costs for health care services. Depending on the individual patients with COPD present diverse degrees of dyspnea and deterioration exercise capacity in association

with impaired pulmonary and cardiovascular function weakness and reconditioning of respiratory and peripheral muscles are currently recognized in these patients as additional actors implicated in the reduction of exercise capacity as well as in the quality of life. The function of inpsiratory muscle is frequently found to be impaired ***(Sarmiessto et al., 2002).***

Rehabilitation for patients with chronic lung diseases is well established and widely accepted as means of enhancing standard therapy in order to alleviate symptoms of optimize function. The primary goal of rehabilitation to restore the patient to the highest possible level of independent function. This goal is accomplished by helping patients to increases their activity through exercise training and to reduce and gain control of symptoms ***(siafakas, 1995).***

Biofeedback has been used to assist breathing retraining in patients with COPD. Diaphragmatic and pursed lip are the most commonly used breathing retraining technique ***(Giardino et al., 2004).***

AIM OF THE WORK

The aim of the work is to:

1- Study the effect of hypoxemia and hypercapnia in COPD patients on neural conduction of peripheral and central nerves.

2- Evaluate the effect of pulmonary rehabilitation program of those cases using biofeedback training particularly on the neurophysiological changes of these nerves.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Chronic obstructive pulmonary disease (COPD) is a disease characterized by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive, associated with an abnormal inflammatory response of the lungs to noxious particles or gases. COPD includes chronic bronchitis and emphysema. The disease is usually progressive, and is marked by dyspnea (shortness of breath), which reduces patients ability to perform their daily activities, and decreases their health-related quality of life (HRQOL). By definition COPD is a chronic slowly progressive disorder characterized by airflow obstruction (forced expiratory volume FEV_1< 80%) and chronic respiratory failure ***(Haslett et al., 2002)***.

The patients develop airway wall inflammation, hypertrophy of the mucus secreting glands and an increase in the number of goblet cells in the bronchi and bronchioles with a consequent decrease in ciliated cells. There is therefore less efficient transport of the increased mucus in the airways. Airflow limitation reflects both mechanical obstruction in the small airways and loss of pulmonary elastic recoil. Loss of alveolar attachments around such

airways makes them more liable to collapse during expiration ***(Haslett et al., 2002)***.

Emphysema increases the relaxative position of the respiratory system, which reduces the mechanical efficiency of the chest wall and require the inspiratory muscle was to operate at shorter length ***(Gandevia et al., 1996).***

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Pathology of COPD:

The most prominent pathological and pathophysiological changes seen in COPD are progressive airflow limitation and peripheral airway inflammation. Airflow limitation results from the loss of elastic recoil of the parenchyma and from the increase in airway resistance ***(Curkendall et al., 2006)***.

Table (2): Cellular and structural changes in the lung in chronic obstructive pulmonary disease ***(Curkendall et al., 2006)***.

Central airways wall	Increase in marcophages and T lymphocytes (particularly $CD8^+$ T lymphocytes). Neutrophils in severe disease.
Lumen	Neutrophils
Peripheral airways	Goblet cell metaplasia and mucous plugging smooth muscle cell hypertrophy. Fibrosis. Inflammation (particularly $CD8^+$ T lymphocytes). All inflammatory cells including neutrophils in severe disease.
Parenchyma	Inflammation (particularly CD^+ Tlymphocytes). Destruction (centriacinar and panacinar emphysema). Fibrosis
Pulmonary arteries	Endothelial dysfunction. Intima thickening medial thickening (less frequently). Adventitial inflammation (particularly CD8+ T lymphocytes)

Central airways:

Patients with COPD exhibit enlarged bronchial mucous glands and an increased number of goblet cells. These morphological changes may lead to mucus hypersecretion, although an increase in the number of goblet cells has not been consistently observed. The accepted definition of chronic bronchitis chronic or recurrent excess secretion of muocus into the bronchial tree. Since the main source of bronchial mucous was thought to be the submucosal glands, the enlargement of these glands was considered to be a histological hallmark

of chronic bronchitits. The degree of mucous gland enlargement is measured as the ratio of the thickness of the bronchial mucous glands to the thickness of the bronchial wall ***(Nagai et al., 1989)***.

Developments in bronchoscope have enabled inflamed central airways to be more closely observed. Consequently, predominant inflammatory cellular infiltrations in the subepithelial region of the bronchial wall have been identified as activated CDS T-lymhocytes and macrophages. A number of neutrophils have been found in the bronchial lumen, and some neutrophil infiltrates have been identified near bronchial epithelium and submucosal glands ***(Sauled et al., 1998)***.

Peripheral airways:

The peripheral airways are considered to be the major sites of increased airway resistance in patients with COPD. Various structural changes can be observed in these regions, including goblet cell metaplasia, squamous metaplasia, inflammatory cellular infiltrations, an increased amount of smooth muscle, fibrosis and pigmentation. Mucous plugging is also frequently observed in the airway lumen. These pathological changes may lead to an increase in airway wall thickness and the subsequent narrowing of the airway lumen ***(Nagai et al., 1989).***

Knowledge of how inflammation leads to structural changes is important for an understanding of the relationship between pathological changes and the severity of airflow limitation. Inflammation appears to be the earliest stage of lesion formation and by it self, can cause mild chronic airflow limitations. Fibrosis and goblet cell metaplasia are thought to follow inflammation and cause irreversible airflow limitations ***(Sauled et al., 1998).***

Lung parenchyma:

In patients with emphysema, the lung parenchyma is characterized by an enlargement of the air spaces accompanied by alveolar destruction. Conventionally, three types of emphysema have been described: centriacinar emphysema, panacinar emphysema and distal acinar emphysema. As distal acinar emphysema is not associated with airflow limitations, only centriacinar and panacinar emphysema will be described here. Centriacinar emphysema.is characterized by alveolar destruction in the respiratory bronchioles in the central area of the acinus. These lesions are predominantly found in the upper lobes of smokers. Panacinar emphysema involves the dilatation of the entire acinus, with the lower lobe dilated to a larger degree than the upper lobe, deficiency of a 1 -antitrypsin and an early onset are associated with panacinar emphysema. Both types of emphysema are characterized

by alveolar destruction with loss of the capillary bed ***(Naggi, 2002)***.

Clinical Features of COPD:

The clinical state as table (3) is dictated largely by the severity of disease. The initial symptoms are usually repeated attacks of productive cough, usually after colds during the winter months, which show a steady increase in severity and duration with successive years until cough is present all the year round. Thereafter, patients suffer recurrent respiratory infections exertional breathlessness, regular morning cough wheeze and occasionally chest tightness. Sputum may be scanty mucoid tenacious and occasionally streaked with blood during infective exacerbations. Frankly purulent sputum is indicative of bacterial infection, which often occurs in these patients. Breathlessness is aggravated by infection, excessive cigarette smoking and adverse atmospheric conditions ***(Haslett et al., 2002)***.

Table (3): Classification and diagnosis of COPD

Severity	Spirometry	Symptoms
Mild	FEV1 60-79% predicted	Smoker's cough exert ional breath lessens
Moderate	FEV1 40-54% predicted	Exert ional breath lessens wheeze, cough sputum
Severe	FEV1 < 40% predicted	Breath lessens, wheeze, cough predominate, swollen leg

(Haslett et al., 2002)

Chronic bronchitis:

Chronic bronchitis is defined clinically by a productive cough lasting for at least 3 months, recurring in at least 2 consecutive years, if it cannot be attributed to other pulmonary or cardiac condition. Chronic bronchitis results from mucus hyperscretion, which does not always lead to airway obstruction. In pathology, chronic bronchitis also means certain microcopic and macroscopic changes in the airway structure, such as mucus production, epithelial changes, airway inflammation, smooth muscle cell hypertrophy and submucosal bronchial gland enlargement ***(Curkendall et al., 2006).***

Macroscopically, mucus overflow is observed that affects mainly the intermediate bronchi, 2-4mm in diameter. Microscopically, mucus is present in lumen and goblet cell hyperplasia is observed in the bronchial wall. In chronic bronchitis, goblet cells, expense of ciliated epithelial cells, serous and Clara cells ***(Curkendall et al., 2006).***

Obstructive broncholities:

Obstructive bronchiolitis is an inflammatory condition that involves small and peripheral airways (<2 mm in diameter).

The typical histological feature of the disease is collapsed lumen with increased mucus, unlike in asthma where the lumen is maintained. Lumen closure is due to high surface tension and small airway instability caused by mucus hypersecretion. Mucus hypersecretion is a result of goblet cell metaplasia. Goblet cells replaces clara and serous cells in the small airways, and mucus production dominates over surfactant secretion. The destabilized bronchioles collapse.

Macrophages and $CD8^+$ T-lymphocytes dominate small airway inflammation ***(Laghi et al., 2005).***

Emphysema

Emphysema is defined by permanent air space enlargement involving, the distal to terminal bronchioles, respiratory bronchioles and occasionally the alveoli. The mechanism of the disease involves unregulated inflammation associated with release of large amounts of proteolytic enzymes. However, the exact mechanism that results in parenchyma destruction, fibrosis and remodeling is not well understood ***(Kim et al., 1993)***.

Two distinct forms of emphysema are described in the literature. Centrilobular emphysema is common in cigarette smokers. The main site of inflammation and destruction is the respiratory bronchioles but in advanced

disease the capillary bed can also be involved. The enlargement and confluence of respiratory bronchioles is most frequent in the 3rd order respiratory bronchioles, however, alveolar ducts and sacs may also be involved. Third form of emphysema is more frequently observed in the upper lobes in its mild form. The reason for the localization is not known. Pancinar emphysema is typically seen in α-antitrypsin (α-AT) deficiency. This quite rare genetic disease counts for approximately 1% of all emphysema cases. In pancinar emphysema respiratory bronchioles, alveolar ducts and sacs are equally involved in the disease process. Pancinar emphysema is mostly localized to the lower lung lobes ***(Laghi et al., 2005).***

Pulmonary vascular disease:

Secondary pulmonary hypertension is common in very severe COPD. Tobacco smoke itself can cause endothelial dysfunction in pulmonary vessels, most likely mediated through endothelial derived relaxing factor. Furthermore, patients with mild to moderate COPD have increased pulmonary vascular pressure following exercise. Intimal thickening, smooth muscle hypertrophy and inflammation was detected in patients with COPD ***(Sauled et al., 1998)***.

Intimal thickening occurs first when lung function is still normal and pulmonary vascular pressure is physiological. Later increase in smooth muscle hypertrophy follows which is moderate, but may expand to small vessels where the smooth muscle layer normally is not present. $CD8^+$ T-lymphocytes and macrophages dominate pulmonary vessel inflammation. Pulmonary vessel remodeling is also noticed in advanced COPD. Proteoglycan and collagen deposition further reduces vessel lumen and fibrosis may obliterate smaller vessels. Endothelinl (ET-1) shows increase expression in pulmonary vessels exposed to hypoxia ***(Santtos et al., 2003)***.

Effect of COPD on:

(1) Respiratory muscles:

COPD imposes a severe strain on the respiratory muscles for several reasons. First, because of the increased on flow resistance and reduced dynamic pulmonary compliance, the resistive and elastic loads are greater than normal, and hence the inspiratory muscle have to generate a greater reduction in pleural pressure to inflate the lung ***(Andre et al., 1997).***

Second the emphysematous changes in the lung cause hyperinflation, which makes the inspiratory muscles operate at a shorten the normal length reduces their ability