Quality Of Life, Fatigue, Changes In Insulin Like Growth Factor 1, Bone Mineral Density And Muscle Mass In Elderly Patients With COPD

Thesis

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Hazem El-Sayed Hussein

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List of Abbreviations

ATP	:	Adenosine triphosphate
BMD	:	Bone mineral density
BMI	:	Body-mass index
COPD	:	Chronic obstructive pulmonary disease
CS	:	Sex, corticosteroid
CSA	:	Cross-sectional area
DXA	:	dual-energy X-ray absorptiometry
DVT	:	Deep venous thrombosis
FEV1	:	Forced Expiratory volume in the first second
FFM	:	Fat free mass
FRC	:	Functional residual capacity
GH	:	Growth hormone
GOLD	:	Global Initiative for Chronic Obstructive pulmonary disease
ICS	:	Inhaled corticosteroid
IGF-1	:	Insulin-like growth factor-1
IGFs	:	Insulin-like growth factors
LTOT	:	Long-term oxygen therapy
MMPs	:	Matrix Metalloproteinases
NHANES	:	National Health and Nutrition Examination Survey
OPG	:	Osteoprotegerin

List of Abbreviations (Cont.)

PH	:	Pulmonary Hypertension
PTH	:	Parathyroid hormone
RANKL	:	Receptor activator of nuclear factor-κB (RANK)-ligand
ROS	:	Reactive oxygen species
SD	:	Standard deviation
VCFs	:	Vertebral compression fractures
WHO	:	World Health Organization

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Abstract

Backgroud: COPD is a highly prevalent systemic disease in the elderly population and it is considered as a major health problem in Egypt, However information on its prevalence, morbidity, and mortality is still lacking.COPD has a variety of extrapulmonary manifestations and our study was conducted to determine the changes in insulin like growth factor-1, Bone mineral density and muscle mass in elderly people with COPD.

Material and Methods: case control study conducted on 90 elderly participants and they were classified into two groups:

Cases Group:

Forty five patients diagnosed to have COPD either mild or moderate.

Control Group:

Forty five healthy subjects, age and gender matched to cases recruited from the community Both groups were subjected to detailed history taking and clinical examination, comprehensive geriatric assessment, spirometry , measurement of serum IGF-1, DXA scan to determine BMD and muscle mass.

Results: The study showed that elderly COPD patients had a lower level of IGF-1 (106.1) compared with control group (184.6) which is lower by 42%and a lower BMD in the cases group (1.15) compared to the control group (1.52) and also a lower muscle mass (47465) when compared to normal elderly(49400).

Conclusion: the study concluded that COPD patients had a lower mean level of IGF- 1, BMD and Muscle mass than normal elderly.

Introduction

Chronic obstructive pulmonary disease (COPD) is defined as a preventable and treatable disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases, primarily caused by cigarette smoking. Although COPD affects the lungs, it also produces significant systemic consequences **(Celli et al.,2004).**

COPD is a major cause of morbidity and mortality in countries of different levels of income. Estimates from WHO that COPD was the fifth leading cause of death in developed countries, accounting for 3.8% of total deaths, and it was the sixth leading cause of death in developing countries, accounting for 4.9% of total deaths. In this same report, COPD was also estimated to be the seventh and tenth leading cause of disability-adjusted life years in developed and developing countries respectively **(Lopez et al., 2006).**

The consequences of COPD include a high risk to exacerbation of clinical symptoms, severely impaired functional capacity, poor health status and hence a low quality Of life. Endocrine disorder, systemic inflammation, oxidative stress and hypoxia contributes to the various effects of COPD **(Rabe et al.,2007),** they promote a hyper-metabolic state and an overall catabolic/anabolic imbalance, leading to the depletion of endogenous energy stores **(Laghi et al., 2009).**

Weight loss resulting from tissue wasting is a serious and common manifestation in COPD and leads to cachexia, a serious comorbidity associated with an advanced disease state (**Sergi et al.,2006).**

Beside the progressive loss of lung function COPD has a several extra-pulmonary co morbidities, and these include osteoporosis, cardiovascular disease and low skeletal muscle mass and function with an adverse effect on health outcomes **(Sin et al., 2006).**

The importance of skeletal muscle dysfunction may increase over time as the deterioration in exercise capacity is not only related to the progression of airflow limitation **(Oga et al., 2005).**

It is important, therefore, to know how muscle function is affected, to identify the factors that contribute to the muscle dysfunction and the mechanism of muscle wasting in COPD so as to improve the management of the disease. (**Tisdale, 2005).**

Insulin-like growth factor-1 (IGF-1) is released systemically in response to autocrine/paracrine signalling actin by binding to and activating the IGF-1 receptor, triggering growth-promoting and anti-apoptotic pathways. Moreover, IGF-1 improves nitrogen balance and have anabolic effects. Some studies have suggested that inappropriately decreased IGF-1 levels occur in clinically stable COPD **(Kythreotis et al.,2009) (Coskun et al.,2009)**.

A low bone mineral density (BMD), leading to osteoporosis is common in COPD with previous studies reporting osteoporosis in 24-44% of patients with COPD **(Biskobing 2002).** The causes of this loss is multifactorial including female sex, corticosteroid (CS) therapy, smoking, physical de-conditioning, vitamin D deficiency, hypogonadism and chronic systemic inflammation **(Bolton et al.,2004).**

The impact of inhaled CS on bone status is unclear with conflicting findings in terms of the rate of loss of BMD, the risk of osteoporosis and the risk of fractures. Many studies on the effect of inhaled CS are limited by difficulties in quantifying the varying and often intermittent use of oral CS and few take in to account the potential for a disease specific component in BMD loss **(Lee and Weiss,2004), (Etminan et al.,2008).**

Fatigue is a common symptom that inhibits normal functional performance of Chronic Obstructive Pulmonary Disease (COPD) patients in daily activities and has a great impact on their quality of life **(Theander and Unosson, 2004)**.

Fatigue together with dyspnoea is the most prominent disabling symptoms in COPD. There is growing interest and attention on the substantial impact of fatigue on COPD patients (**Man et al., 2003) (Kapella et al., 2006).**

Aim of the Work

To determine the effect of COPD on Insulin growth factor 1, muscle mass, bone mineral density, quality of life and fatigue in elderly people.

Chronic Obstructive Pulmonary Disease (COPD)

I. Definition.

Chronic obstructive pulmonary disease (COPD), is a common preventable and treatable disease, characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients (**Global Initiative for Chronic Obstructive pulmonary disease, 2015).**

Worldwide, cigarette smoking is the most common risk factor for COPD, however in many Countries, air pollution resulting from the burning of wood and other biomass fuels have also been identified as a COPD risk factor **(Global Initiative for Chronic Obstructive pulmonary disease, 2015).**

A systemic review and meta-analysis in studies carried out in 28 countries between 1990 and 2004 provide evidence that the prevalence of COPD is significantly higher in smokers and ex-smokers that non-smokers, in those over 40 than those under 40 and in men than women (**Halbert et al., 2006).**

The chronic airflow limitation characteristic of COPD is multifactorial and it is composed of a mixture of small airway disease (obstructive bronchiolitis) and parenchymal destruction (emphysema), the relative contributions of which vary from person to person.

Chronic inflammation narrows and structurally changes the small airways, furthermore it destructs the lung parenchyma and the alveloar attachment to the small airways is lost, the destruction of lung parenchyma also decreases the lung recoil. These changes decreases the ability of the airways to remain open during expiration **.**Airflow limitation is best measured by spirometry, as this is the most widely available, reproducible test of lung function **(Global Initiative for Chronic Obstructive Lung Disease, 2006).**

II. Burden of COPD

COPD is a major cause of morbidity and mortality worldwide and results in an economic and social burden that is both huge and elevating (**Lopez et al., 2006).**

Morbidity

In most countries, consultations for COPD greatly outnumbered consultations for asthma, pneumonia, lung and tracheal cancer, and tuberculosis. In the United States in 2000, there were 8 million physician office/ hospital outpatient visits for COPD, 1.5 million emergency department visits, and 673,000 hospitalizations **(CDC. 2002).**

Another way of estimating the morbidity burden of a disease is to calculate years of living with disability (YLD). The Global Burden of Disease Study estimates that COPD results in 1.68 YLD per 1,000 populations, representing 1.8% of all YLDs, with a greater burden in men than in women (1.93% vs. 1.42%) (**Lopez et al., 2006).**