Evaluation of The Maximal Inspiratory Mouth Pressure In COPD Patients

Thesis

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in Chest Diseases and Tuberculosis

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Waleed Hussein Awad

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List of Abbreviations

ABG	:	Arterial Blood Gases.
ATS	:	American Thoracic Society.
BAL	:	Bronchoalveolar lavage.
BLVR	:	Bronchoscopic lung volume reduction
BMI	:	Body-Mass Index.
BODE	:	Body-mass index, airflow Obstruction, Dyspnea and Exercise capacity index
cmH٢O	:	Centimeter Water.
CO	:	Carbon monoxide.
CO٢	:	Carbon dioxide.
COPD	:	Chronic Obstructive Pulmonary Disease.
COX	:	Cyclo-Oxygenase;
CT	:	Computed tomography
DLCO	:	Carbon Monoxide Gas Diffusing Capacity
DNA	:	Deoxyribonucleic acid
ECG	:	Electrocardiography
EGF	:	Epidermal Growth Factor
EMG	:	Electromyography
ERS	:	European Thoracic Society.
ET-١	:	Endotheline-١.
FEV ٦	:	Forced Expiratory Volume after ٦ s.
FEV١	:	Forced Expiratory Volume in ١ s.
FGF	:	Fibroblast Growth Factor.
FRC	:	Functional Residual Capacity.
GINA	:	Global initiative for Asthma.
GM-CSF	:	Granulocyte Macrophage Colony Stimulating Factor.

GOLD	:	Global initiative for Chronic Obstructive Lung Disease.
GRO	:	Growth-Related Oncogene.
$H^{٢}O^{٢}$	:	Hydrogen Peroxide.
HIV	:	Human Immune Deficiency Virus.
HS	:	Highly Significant.

List of Abbreviations (Cont.)

HT	:	Height.
IFN	:	Interferon.
IL	:	Interleukin.
IP-١٠	:	Activated protein-١٠.
KCO	:	CO transfer coefficient.
kPa	:	Kilopascal.
L٠	:	Optimal length.
LPS	:	Lipopolysaccharides.
LT	:	Leukotriene.
LVRS	:	Lung volume Reduction Surgery.
M	:	Muscarinic.
MCP	:	Monocyte chemoattractant protein.
MIP	:	Macrophage inflammatory protein.
MMHG	:	Millimeter Mercury.
MMP	:	Matrix metalloproteinase.
mRNA	:	Messenger Ribonucleic Acid.
NE	:	Neutrophil Elastase.
NF- κB	:	Nuclear Factor- kabba B.
NK	:	Natural killer (cell).
NO	:	Nitric oxide.
$NO^{٢}$	:	Nitrogen dioxide
NS	:	Non Significant.
$O^{٢}$	:	Oxygen.
$O_{٢}^{-}$	:	Superoxide anion.
$O^{٣}$	:	Ozone
OH	:	Hydroxyl Radical.

P.A	:	Posteranterior.
P٢١	:	Protein ٢١
PaCO٢	:	Partial Carbon dioxide pressure.
PAF	:	Platelet Activating Factor.
PaO٢	:	Partial oxygen pressure.
Pdi,sn	:	Transdiaphragmatic pressure during sniff.
PEEP	:	Positive End-Expiratory Pressure.

List of Abbreviations (Cont.)

PEEPI	:	Intrinsic Positive End-Expiratory Pressure.
PEMAX	:	Maximum Expiratory Pressure.
Pes	:	Esophageal pressure.
PFT	:	Pulmonary function test.
PG	:	Prostaglandin.
Pga	:	Gastric pressure.
Pga, co	:	Cough gastric pressures.
PGF٢	:	Prostaglandin F٢.
PI MAX	:	Maximum Inspiratory Pressure.
PI,di,max	:	Maximum static transdiaphragmatic pressure.
PiZZ	:	Homozygous phenotype of α١ AT.
Pmus	:	Pressure developed by the respiratory Muscles.
Ppl	:	Pleural pressure.
Prs	:	Transrespiratory system pressure.
Pthmax	:	Maximum threshold pressure.
ROS	:	Reactive Oxygen Species.
RV	:	Residual volume.
SaO٢	:	Arterial Oxygen Saturation.
SD	:	Standard Deviation.
SER CA	:	Sarco-Endoplasmic Reticulum Calcium-Adenosine triphosphatase.
SLPI	:	Secretory Leukoprotease Inhibitor;
SNIP	:	Sniff Nasal Inspiratory Pressure.
SO٢	:	sulpher dioxide

TGF	:	Transforming Growth Factor.
TIMP	:	Tissue Inhibitor of MMPs
TLC	:	Total Lung Capacity.
TNF α	:	Tumor Necrosis Factor Alpha.
VC	:	Vital capacity.
WT	:	Weight.

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Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and is associated with an abnormal inflammatory response of the lungs to noxious particles or gases. Worldwide cigarette smoking is the overwhelming risk factor for COPD, although in many countries, air pollution resulting from the burning of wood and other biomass fuels has also been identified as a COPD risk factor ***(GOLD, ٢٠٠٧)***.

Although COPD affects the lungs, it also produces significant extra pulmonary effects that may contribute to disease severity in individual patients ***(Agusti, ٢٠٠٥)***.

COPD is a major cause of chronic morbidity and mortality throughout the world; many people suffer from this disease for years and die prematurely from it or its complications. COPD is currently the fourth leading cause of death in the world and is predicted to be the third most frequent cause of death in the world by ٢٠٢٠ ***(celli et al, ٢٠٠٤)*** .

COPD is associated with extrapulmonary effects that contribute to limit the exercise capacity of these patients and to worsen prognosis, independent - of their pulmonary function ***(Oudijk et al, ٢٠٠٣)***.

Clinical assessment of the global function of the respiratory muscles is often performed by measuring maximum inspiratory and expiratory mouth pressures (PImax and PEmax) ***(MacNee, ٢٠٠٠)***

Maximal inspiratory pressure (PImax) is the maximum negative pressure that can be generated from one inspiratory

effort, starting from functional residual capacity (FRC) or residual volume (RV) ***(ATS/ERS ٢٠٠٥).***

The mouth pressure recorded during these maneuver is assumed to reflect the respiratory muscle strength. ***(Epstein et al, ١٩٩٤)***

It is known that a reduction of PImax has been associated with several neuromuscular diseases, but it is also possible to point up lower values in patients with chronic obstructive pulmonary disease (COPD) **(Iandell et al, ٢٠٠١)**

The factors contributing to respiratory muscle weakness in many patients with COPD are: a) malnutrition related to biochemical, anatomical and physiological changes; b) muscular atrophy; c) steroid-induced myopathy; d) pulmonary hyperinflation with increased residual volume; e) reduced blood flow to the respiratory muscles and the measurement of PImax is indicated in any of these situations or when dyspnea or hypercapnia is not proportional to FEV_1 reduction. ***(ATS/ERS ١٩٩٩).***

Aim of the Work

To evaluate the possible correlation between airway obstruction and the maximal inspiratory pressure (PImax) values and to describe PImax variation in the different stages of COPD according to GOLD criteria.

Chronic Obstructive Pulmonary Disease (COPD)

Definition:

The definition of COPD has been always a concern to chest physicians. It was changed several times from the first trials in ١٨١٩, when Laennec first described the pulmonary catarrh as an 'inf١ammation of the mucous membrane' of the bronchi and emphysema as an increase in the size of the airspaces in the lungs to the latest GOLD (global initiative for obstructive lung disease) definition ***(Fletcher et al., ٢٠٠٦)***

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious Particles or gases. ***(GOLD, ٢٠٠٧).***

As it can be noticed, the most recent of definitions implies the most prominent risk factor, the spectrum of affection of the syndrome and a hint about the management.

Other attempts at defining COPD with reference to spirometric functional criteria were undergone e.g. The BTS functional definition; Chronic obstructive pulmonary disease (COPD) is characterized by airflow obstruction defined as a reduced forced expiratory volume in one second (FEV١) and a reduced FEV١ / FVC Ratio (where FVC-is forced Vital capacity), such that FEVl is less Than ٨٠% predicted and FEV١ / FVC is less than ٠.٧. The airflow obstruction is usually progressive, not fully reversible and does not change markedly over several months. The disease is predominantly caused by smoking. ***(BTS, ٢٠٠٤)***

It was always believed that COPD is comprised of two conditions namely: Chronic bronchitis and Emphysema. Chronic bronchitis is defined- clinically as chronic productive cough for ٣ months in each of tow successive years in patients in whom other causes of productive chronic cough have been excluded. Emphysema is defined pathologically as the presence of permanent enlargement of the airspaces distal to the terminal bronchioles, accompanied by destruction of their walls and without obvious fibrosis ***(Snider et at, ١٩٨٥)***

Lastly, a line must be drawn as sharp as possible between very Close entities to COPD: Bronchial asthma. Asthma is defined as a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role, in particular, mast cells, eosinophils, T lymphocytes, macrophages, neutrophils, and epithelial cells. In susceptible individuals, this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread but variable airflow treatment. The inflammation also causes an associated increase in the existing bronchial hyperresponsiveness to a variety of stimuli. ***(GINA, ٢٠٠٧)***

Asthma differs from COPD in its pathogenic and therapeutic response, and should therefore be considered a different clinical condition. The high prevalence of asthma and COPD in the general population results in the co-existence of both disease entities in many individuals. Asthma is characterized by significant airflow limitation and a large response to bronchodilators. In COPD patients, the forced expiratory volume in one second (FEV١) does not return to normal and frequently worsens over time. There is a great need to design studies aimed at determining the prevalence, natural history, clinical course and therapeutic response in these patients ***(Thomson et al., ٢٠٠٤)***.

Some patients with asthma develop poorly reversible airflow limitation. These patients are indistinguishable from patients with COPD but for practical purposes are treated as asthma ***(Pawels, ٢٠٠١).***

Epidemiology

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide, and results in an economic and social burden that is both substantial and increasing. COPD is the fourth leading cause of death in the USA and Europe. By the year ٢٠٢٠, it is expected to rank among the first three diseases to claim the maximum number of lives. According to recent estimates, ٦٠٠ million people suffer from COPD all over the world. The disease claims ٢.٧٥ million lives every year. COPD mortality in females has more than doubled over the last ٢٠ yrs and this may be attributed to the fact that smoking rates are almost the same for men and women over the past ١٠-١٥ years. ***(Halbert et al., ٢٠٠٦).***

COPD is a more costly disease than asthma. The direct costs of COPD are the value of health care resources devoted to diagnosis and medical management of the disease. Indirect costs reflect the monetary consequences of disability, missed work, premature mortality and caregiver or family costs resulting from the illness ***(Sullivan et al., ٢٠٠٠).***

Risk factors

A)*Host factors:*

These are the minor part of the risk factors; and are caused mainly due to the genetic risk factor that is best documented, a severe hereditary deficiency of α١-antitrypsin (α١ AT) (a major circulating inhibitor of serum proteases). It is well-Known that the homozygous deficiency of α١ AT, phenotype PiZZ is associated with an increased risk of COPD. Also recent studies have shown that in the general population the contributory genetic factors seem to extend beyond the