MEASUREMENT OF 8-ISOPROSTANE IN EXHALED BREATH CONDENSATE OF COPD PATIENTS

Thesis

Submitted for Partial Fulfillment of Master Degree

In Chest Diseases and Tuberculosis

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2016

List of Contents

List of Tables

List of Figures

List of Abbreviations

Abb.	Description
AECOPD	acute exacerbations of Chronic Obstructive Pulmonary Disease
ATS/ERS	American Thoracic Society/European Respiratory Society
BALF	Bronchoalveolar lavage fluid.
BMI	body mass index
BODE	body mass index ,obstruction, dyspnoea, and exercise
CAT	COPD Assessment Test
CCLS	Copenhagen City Lung Study
CCQ	Clinical COPD Questionnaire
CF	cystic fibrosis
COPD	Chronic obstructive pulmonary disease
CPAP	continuous positive airway pressure
DM	Diabeitus mellitus.
EBC	Exhaled breath condensate
ENO	exhaled nitric oxide
EUROSCOP	European Respiratory Society Study on Chronic Obstructive Pulmonary Disease
FEV1	Forced expiratory volume in 1 second
FVC	Forced vital capacity

GOLD	Global Initiative for Chronic Obstructive Lung Disease
HCO3	Bicabonate
HRCT	high resolution computed tomography
HTN	Hypertension
ISOLDE	Inhaled Steroids in Obstructive Lung Disease in Europe
LLN	lower limit of normal
LTB4	leukotriene B4
LVRS	lung volume reduction surgery
mMRC	modified British Medical Research Council
NHLBI	National Heart, Lung, and Blood Institute
NMR	nuclear magnetic resonance
NO	nitric oxide
PaCo2	parital pressure of Co2 in arterial blood
PaO2	parital pressure of O2 in arterial blood
PG	prostaglandin
PH	Power of hydrogen
UACS	Upper Airway Cough Syndrome
VC	vital capacity

Abstract

Aim of the Work: *Measuring 8 isoprostane in exhaled breath condensate (EBC) of COPD patients as a biomarker of oxidative stress.*

Patients and Methods: *This study was conducted at Ain Shams University Hospitals and included patients with chronic obstructive pulmonary disease diagnosed according to the criteria of the Global Initiative for Chronic Obstructive Lung Disease. The cases were divided into two groups, group A (included 80 cases having COPD), group B (control group) included 16 healthy persons. All the patients were subjected to arterial blood gas analysis, spirometric lung functions, Spirometry was done at the same hour of measurement of the exhaled breath condensate 8_isoprostane using exhaled breath condensate apparatus was assessed.*

Results: *spirometry showed worsening of lung functions in COPD cases which increased with the severity of the disease.*

8-isoprostane increased in very severe COPD cases and correlated significantly to the severity of the disease.

Conclusion: *Measurement Of 8-Isoprostane In Exhaled Brreath Condensate is a promising non invasive biomarker in COPD patients.*

KEYWORDS: Exhaled breath condensate; *8_isoprostane*;

COPD;

Aim of the Work:

The aim of the present work is to measure the level of **8-Isoprostane** in Exhaled Breath Condensate of COPD patients and to compare it with normal individuals.

Definitions:

The definition of chronic obstructive pulmonary disease (COPD) and its subtypes (emphysema, chronic bronchitis, and chronic obstructive asthma) and the interrelationships between the closely related disorders that cause airflow limitation provide a foundation for understanding the spectrum of patient presentations. Severeal features of COPD patients identify individuals with different prognoses and/or responses to treatment. Whether these features identify separate "phenotypes" of COPD or reflect disease severeity remains unclear However, evaluation of these features can help guide clinical management, and their use in classification of patients is now recommended ***(Han et al., 2010).***

COPD - The Global Initiative for Chronic Obstructive Lung Disease (GOLD), a project initiated by the National Heart, Lung, and Blood Institute (NHLBI) and the World Health Organization (WHO), defines COPD as follows. "Chronic obstructive pulmonary disease (COPD), a common preventable and treatable disease, is characterized by 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 severeity in individual patients***."(Rennard et al., 2013).***

Symptoms of COPD:

The most common symptoms of COPD include chronic and progressive breathlessness, cough, sputum production, wheezing, and chest congestion. In addition to the airflow restriction and changes to the lung, COPD is associated with systemic effects and comorbidities. Systemic effects include weight loss, nutritional abnormalities and malnutrition, and skeletal muscle dysfunction. Common comorbidities are ischemic heart disease, osteoporosis, respiratory infection, bone fractures, depression and anxiety, diabetes, sleep disorders, anemia, glaucoma, cataracts, and cancer ***(Quality-Based Procedures, 2015).***

COPD is a progressive disease. The rate of progression varies and may occur over severeal years or severeal decades, depending on factors such as continued exposure to noxious particles (e.g., tobacco smoke). There are severeal systems for classifying the severeity of COPD; one of the most widely used is the Global Initiative for Chronic Obstructive Lung Disease (GOLD) staging criteria, which are based on postbronchodilator spirometry (forced expiratory volume in 1 second [FEV1]). In the GOLD system there are 4 stages, which range from mild to very severe (Table 1) ***(Quality-Based Procedures. 2015).***

Severeity scores:

The COPD Assessment Test (CAT) is a new scoring system for COPD patients, which provides a simple method for assessing the impact of COPD on the patient`s health. The validation studies have shown that it has similar properties as St. George`s Respiratory Questionnaire (SGRQ) ***(Jones et al., 2011a; 2011b).***

The CAT and FEV_1 are complementary measurements for assessment and management of COPD **(*Jones et al., 2011a; 2011b).***

The CAT is a standard and validated test containing eight items for the evaluation of the impact of COPD on health status ***(Jones et al., 2009; 2011a)*.**

It is a tool for the measurement of disease impact on health status, but FEV_1 is essential to establish a diagnosis and to confirm the severeity of airway obstruction in symptomatic COPD patients ***(Celli et al., 2004).***

CAT score:

After history taking and physical examination, all patients completed the Persian version of CAT respiratory questionnaire. The total CAT score was calculated for each individual by summing the points for each variable.CAT has a scoring range of zero to 40. The CAT score was classified into four groups of low ***(Funk et al., 2009)***, medium ***(GOLD., 2008),*** high ***(Fabbri et al., 2007)*** and very high ***(Ong et al.,***

2006) based on the impact level of disease on health status as shown in Table (1).

Table (1): Impact level of COPD on health status

CAT score	Impact level
< 10	Low
10 – 20	Medium
21 - 30	High
> 30	Very high

Severeity of COPD was assessed by the COPD Severeity Score (COPDSS), which includes questions that comprise five overall aspects of COPD severeity: respiratory symptoms, systemic corticosteroid use, other COPD medication use, previous hospitalisation or intubation for respiratory disease, and home oxygen use. Each item was assigned an a priori weight based on clinical aspects of the disease and its expected contribution to overall COPD severeity. Missing values for medication use and other questions were defined as zero. Possible total scores range from 0 to 35 and higher scores reflect more severe COPD ***(Eisner et al., 2009).***

Table (2): GOLD SPIROMETRIC CRITERIA FOR COPD SEVEREITY *(GOLD., 2010)*.

I: Mild COPD	• FEV1/FVC < 0.7 • FEV1 ≥ 80% predicted	At this stage, the patient may not be aware that their lung function is abnormal.
II: Moderate COPD	• FEV1/FVC < 0.7 • 50% ≤ FEV1 < 80% predicted	Symptoms usually progress at this stage, with shortness of breath typically developing on exertion.
III: Severe COPD	• FEV1/FVC < 0.7 • 30% ≤ FEV1 < 50% predicted	Shortness of breath typically worsens at this stage and often limits patients' daily activities. Exacerbations are especially seen beginning at this stage
IV: Very Severe COPD	• FEV1/FVC < 0.7 • FEV1 < 30% predicted or FEV1 < 50% predicted plus chronic respiratory failure	At this stage, quality of life is very appreciably impaired and exacerbations may be life-threatening