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Status of Lipid Peroxidation and Iron Levels in Bronchial Asthma

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Abstract

Introduction: The *Oxidative stress*, specifically *lipid peroxidation*, is believed to contribute to the pathophysiology *of asthma*. Low antioxidant levels and oxidative stress due to airway inflammation may be determinant of asthma severity. Level of plasma malondialdehyde (MDA) was used as index of lipid peroxidation. Even elevated iron levels also contribute for production of ROC and free radicals which causes inflammation in bronchial asthma. So the present study was aimed to reveal the relationship between lipid peroxidation and bronchial asthma.

Method: The FEV1% was measured to categorize the asthmatic patients and controls. Later MDA and serum iron levels were measured in thirty asthma cases and 30 healthy volunteers aged between 18-45 years. All the procedures were performed in the morning after their light breakfast in a less noise and illuminated room.

Results: The results showed serum MDA and iron levels significantly increased in bronchial asthmatic patients were suggestive of lipid peroxidation and oxidative stress in asthmatic patients compared to controls.

Conclusion: Therefore, Oxidative stress and lipid peroxidation are the key factors to produce ROC and free radicals which aggravates bronchial asthma.

Keywords: *Oxidative stress, Body Mass Index, Bronchial asthma, Lipid peroxidation.*

Introduction

Asthma is defined as chronic inflammatory process characterized by reversible and variable air flow obstruction due to bronchial hyper responsiveness secondary to multiple external stimuli in which genetic factors interact with environmental factors[1.] Symptomatically asthma is characterized by recurrent attacks of cough, wheeze and breathlessness. It is a major public health problem across the globe. Asthma does not respect age or gender, affecting both children and adults from kinder garden and school through work to retirement[2]. According to WHO estimates that 300 million people are affected by asthma globally with 2.5 lakhs of deaths every year[2]. It is the commonest chronic disease contributing a third of all chronic disorders. In India alone the prevalence is 2-3.5%. At least 25 to 35 million Indians are asthmatics and the economic burden of this disease in India is thus huge[3]. Now it is recognized as a major cause of disability, medical expense and preventable death. Pathophysiologically asthma involves many different cells and cellular elements like basophils, eosinophils, lymphocytes, mast cells, macrophages and mediators like cytokines, chemokines, histamine, leucotreines, reactive oxygen species and thromboxanes. Although asthma is multifactorial in origin, inflammation is believed to be the corner stone of the disease[4]. Airway inflammation and remodeling are critical components of asthma; furthermore environmental exposures throughout life can modulate the expression of asthma susceptibility genes, making asthma a dynamic disease[5].

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Asthma has attracted the full spectrum of biochemical investigations from studies of the prevalence of asthma in different populations[6]. These studies continue to refine the scientific understanding of asthma and suggest new approaches to diagnosis and treatment[3]. Bronchial asthma is one of the free radical mediated inflammatory condition of the air ways (oxidative stress) [7]. Oxidative stress is a unique pathophysiological condition resulting from the disrupted balance between oxidants and antioxidant levels and may be determinant of severity of asthma. Increased level of free radicals may cause oxidative damage of all biomolecules like nucleic acids, proteins, lipids and saccharides[8]. The inflammatory reaction is initiated by the formation of allergen antigen complex. Inflammatory cells are activated during inflammation and produce variety of chemicals along with free radicals[9]. These free radicals induce lipid peroxidation leading to chain of reactions causing increased level of lipid peroxidation products like malondialdehyde (MDA). MDA is most important and frequently used biomarker providing an indication of the overall lipid peroxidation level in the blood[10]. So one of the purpose of the present study is to monitor the extent of lipid peroxidation and severity of bronchial asthma as measured by FEV1 (forced expiratory volume in the first second). It has been reported that high iron stores increase the free radical production and may elevate the asthma risk[11]. Another experimental study shows, overloading the rats by giving iron dextran injection increase lipid peroxidation[12]. In view of this the present study is under taken to know the effect of iron stores in the production of free radicals and correlate the same with the severity of the disease as it is less studied.

Materials and Method

It is an analytical cross-sectional study undertaken by the authors in Department of Physiology, Narayana medical college, Nellore. The study protocol was reviewed and approved by Institutional ethical committee of the same college. The test group subjects were Bronchial asthmatic patients, who were otherwise normal, attending outpatient department, and central laboratory of Narayana Medical College and Hospital. The non-random sampling procedure was executed for recruitment of cases and controls. The cases were included in both genders with less than 2 years duration of bronchial asthma without other confounding factors. The controls were recruited from the primary investigator acquaintances from Narayana medical college. All the participants were fully explained about the procedures were carried out in the day time at ambient room temperature and written consent was obtained from each participant as per the declaration of Helsinki. The tests were conducted in 30 Bronchial asthmatic patients and compared with 30 age matched controls. A detailed history was taken including personal, medical, past history, drug history and duration of disease.

Spirowin: The bronchial asthma was determined by different spirometric parameters carried out with a computerized spirometer (Spirowin Version 2.0) and the following lung function parameters were recorded

Demographic measurements: In each subject height in centimeters measured by stadiometer and weight in kilograms were measured by electronic weighing machine. Body Mass Index (BMI) for each subject was calculated using the formula BMI = Weight (Kgs) /Height (m^2).

Spirometric parameters: The test procedure was explained to the subjects and a demonstration of the test procedure was given. They were allowed to sit quietly for 10 minutes to become mentally and physically relaxed prior to testing. Subjects were asked to inspire as much as possible and hold the sterile mouth piece in the mouth, with the lips forming a tight seal around the mouth piece, and asked to inspire maximally, expire maximally and inspire with maximum effort again. After preliminary trials, the test was performed three times in the standing position and the best recording was taken. The FEV1% was obtained from the digital spirowin automatically.

Blood parameters: Venous blood was taken from the each participant mixed with EDTA. The plasma was separated by centrifugation and malondialdehyde (MDA) which indicate the status of lipid peroxidation, total iron levels were estimated using spectrophotometry.

Statistical analysis: The data sets were analyzed by graph pad prism & data was represented as mean and SD. Normality of data was tested using Kolmogorov-Smirnov test. A p value of > 0.05 indicated normal Gaussian distribution. As the data sets were skewed, Mann-Whitney test was performed and Spearman correlation were done to find out associations.

Results: The obtained values from the protocol were expressed as mean ± SD in the tables.

Table: 1

Participants	Age	BMI
Cases	29.48±7.68	24.8±2.64
Controls	30.46±6.22	25.02±4.53
P value	>0.05	>0.05

Table 1 shows Age distribution in Obese and Non-obese diabetic patients.

Table: 2

Test	Cases	Controls	P value
FEV1%	89.58± 7.55	55.24± 13.13	<0.001
MDA (μ mol/L)	5.09± 1.08	3.06± 0.84	<0.001
Plasma Iron (μ mol/L)	25.97±6.10	15.13±4.59	<0.001

Table 2 shows FEV1, MDA and iron levels in asthmatics and controls.

Discussion

The main theme of the present study protocol was to evaluate lipid peroxidation, plasma levels in bronchial asthmatic patients. The asthma status was determined by FEV1% (p value<0.001) and enquiry of history of illness from the each participant and divided in to cases and controls. Later plasma MDA and iron levels in cases were compared with age matched controls.

In our study there is significant increase of plasma MDA (p value<0.001) and iron levels (p value<0.001) in cases as compared with controls. Plasma MDA levels are increased due to elevated oxidative stress and inflammation which enhances lipid peroxidation resulting in loss of structural integrity of plasma membranes. Asthma attacks are associated with aggravation of the inflammatory status with a significant increase in reactive oxygen species (ROS) and free radicals. Iron is an essential elements in all tissues and cells. However an excess of liable iron is deleterious and causes cellular injury. This two phase behaviour is also shared by ROS at low levels as a beneficial signaling species, but at higher concentrations, specific free radicals may cause damage. Labile redox active iron serves as a catalyst in the production of hydroxyl radicals via the Fenton reaction which is the key part in ROS–induced injury.

The plasma MDA levels shows significantly increased in cases due to oxidative stress and lipid peroxidation. They reflects imbalance between the ROC and decline in detoxification abilities in the bronchial asthma. The redox state of cells can cause toxic effects and damages all major components of the cell. Lipids are the predominant susceptible components as they are rich in cell membranes. These MDA levels are high in asthmatic cases when compared with controls. Our results are in accordance with paul Kirkham et. al[13] and hee sunpark et. al[14] observed asthmatic patients has elevated MDA levels. Umith M sahiner et. al along with lipid peroxidation parameter levels, they studied antioxidant defenses which also supports to our study[15]. Sharma A et. al was estimated MDA levels in asthmatic children three times. They observed significant decrease in MDA levels after treatment[16]. But still higher than control group indicating chronic inflammation. P. Hemachandra Reddy revealed in his research that mitochondrial dysfunction and oxidative stress are involved and plays an important role asthma[17].

The iron levels in the current study was significantly increased in asthmatic group as compared to control group. Iron is stored along with ferritin is surrounded by a protein shell. Unless it is in the free ionic form, it is unable to cause oxidative damage. In bronchial asthma of increased oxidative stress, proteins are also affected by excessive free radicals along with other biomolecules. In this event protein surrounding the iron core in ferritin could have damaged and free iron is released from ferritin. The presence of such metals in biological systems in an uncomplexed form can significantly increase the level of oxidative stress. This is thought to induce Fenton reactions and the Haber–Weiss reaction, in which hydroxyl radical is generated from hydrogen peroxide. The hydroxyl radical then cause lipid peroxidation of biomolecules. It also leads to irreversible modification of certain amino acids.

Our results were obtained is correlated with Haim Bibi et. al was studied the role of iron and iron catalyzed oxidative injury in asthmatic inflammatory process[18]. They were observed elevated ferritin levels in the non-treated asthmatic group. L. S. Greene also stated in their study high iron stores increases free radical production and may also elevate asthma risk[19]. Egil Bakkeheim et. al also observed higher ferritin levels, reduced albumin in poorly controlled asthma with allergic rhinitis as compared with controls[20]. Al Obaidi et. al estimated calcium, VLDL, LDH and creatinine kinase in addition to serum iron levels were significantly lower stable asthmatic group as compared to that in acute asthmatics[21]. However our study results are retrospectively correlates with the study of Reznichenko L et. al who had observed that prior to treatment, there was increased level of iron

which was decreased after using iron chelating agents with simultaneous decrease of inflammation [22]. Both iron and lipid peroxidation products increased in the research of Ekmekci were studied that oxidation of lipoproteins is facilitated by iron and copper in bronchial asthma cases[23]. The findings of our study are in contradictory with the findings of Vural H et. al who showed no changes in serum iron and ferritin levels in bronchial asthma cases when compared with control group[24].

Limitations: In our study the sample size was limited and it addresses the population of this geographical area, separate study in males and females was not conducted. A multicentric study with larger sample size will be carried out in future to understand the relation between MDA and iron levels in asthmatics.

Conclusion

The present study concludes that, there is increased lipid peroxidation in bronchial asthma cases due to inflammation which is evidenced by increased levels of malondialdehyde. There is also concomitant increase in plasma iron levels which may be due to release of iron from iron stores which further aggravate lipid peroxidation by Fenton and Heberwiess reactions. Thus there is significant positive correlation between MDA and iron levels. The asthma can be controlled by biofeedback mechanism which alters the visceral responses[25].

Conflict of Interest: On behalf of all authors, the corresponding author states that there is none declared any type of conflict regarding this research work.

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