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Review Article

Review of 8 Hydroxy 2 Deoxyguanosine and 8-Isoprostane as Biomarkers of Oxidative Stress in Respiratory Diseases

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Abstract

Lately, the emphasis has been given to the importance of oxidative stress as the determinants of respiratory diseases like Asthma, Chronic Obstructive Pulmonary Disease (COPD) and allergic rhinitis. Oxidative stress is a very important caution signal, fundamental for early diagnosis and treatment of respiratory illness. The significance of oxidative stress on the pathogenesis and development of respiratory diseases is partly recognized, as the mechanisms and importance of the process are still unknown. The increasing oxidant pollutant exposures have detrimental effects on public health as inhaled oxidants stimulate pathologic processes like airways inflammation and aggravation of airways disease. Hence it is critical to understand the mechanisms of oxidants and their impact on respiratory illness. This study aims to review 8 hydroxy 2 deoxyguanosine and Isoprostane biomarkers of oxidative stress in respiratory diseases. Measurement of these biomarkers of oxidative stress explores the role of free radicals in the pathogenesis, risk stratification and prognosis of conditions associated with oxidative stress in respiratory diseases. Thus, the incidence of oxidative stress has vital consequences in the pathogens of asthma, allergic rhinitis, and COPD.

Keywords: *Oxidative Stress; Biomarkers; 8 Hydroxy 2 Deoxyguanosine; 8-Isoprostane; Chronic Obstructive Pulmonary Disease; Asthma; Rhinitis*

Introduction

Asthma, chronic obstructive pulmonary disease (COPD) and allergic rhinitis are robustly related respiratory diseases [1-3] and they substantially contribute to morbidity and mortality in adults and are challenging to health systems and considered as a social burden [4]. Interaction between individual/genetic susceptibility and the environment is commonly seen in these diseases. The environmental determinants of respiratory diseases such as air pollution, occupational exposures, active and passive smoking, alcohol consumption, diet, etc. induce oxidative stress [5], which is seen in the pathogenesis and progression of chronic and allergic respiratory diseases [6] and also as the result of an imbalance between antioxidants and oxidants in the lung cells and which may induce damage to DNA, lipids, and proteins. Lungs, when compared to other organs, come directly in contact with environmental oxidants and are more prone to develop this imbalance. Several clinical studies have documented increased expression of biomarkers of oxidative stress in COPD, asthma [7] and allergic rhinitis [8] patients in comparison with healthy subjects [7].

8-hydroxy-2 deoxyguanosine (8-OHdG) and 8-isoprostanes biomarkers of oxidative stress

Understanding the role of free radicals is important in human diseases [1]. 8-Hydroxy-2 deoxyguanosine (8-OHdG) which is a nucleoside and the oxidative derivative of guanosine the most predominant free radical-induced product of oxidative DNA damage and serve as a marker of DNA oxidative stress. Another commonly used biomarker of oxidative stress is 8-isoprostane, lipid oxidation byproducts that can be found in plasma or urine along with oxidized phospholipids as they can cause systemic and local inflammatory responses [9]. An elevated level of 8-isoprostanes is found in breath condensates as well as in the urine [5].

The 8-isoprostanes biomarkers stimulate biological responses in many cell types in the lungs and act as potent constrictors of pulmonary vascular smooth muscle and airway smooth muscle. 8-Isoprostanes are also raised in cystic fibrosis, chronic obstructive pulmonary disease, interstitial lung diseases, sarcoidosis, pulmonary hypertension, acute lung injury, and respiratory failure, etc [19]. Increased F2

isoprostane levels are seen in hypercholesterolemia, diabetes mellitus, smoking, renovascular hypertension, and hyperhomocysteinemia patients [20]. Statins may marginally reduce isoprostane levels [21].

8-Isoprostane is used as markers of oxidative stress in both asthma and COPD [7]. Oxidation of uric acid by reactive oxygen species results in the formation of allantoin, which can then be measured in various body fluids as a marker of oxidative stress. 8-Isoprostane is proven to be elevated in exhaled breath condensate of asthmatic patients, reflecting the underlying airway redox imbalance. Even in allergic rhinitis patients have increased local oxidative stress, as expressed by high levels of 8- isoprostane in nasal lavage and higher FeNO levels. During pollen season, cysteinyl leukotrienes levels and LTB4 gets more elevated in the exhaled breath condensate of allergic rhinitis patients [8]. Smokers who consume more ascorbate show a decreased level of F2-isoprostane lipid peroxidation. Levels of 8-isoprostane or F2- isoprostanes are found in Bronchoalveolar lavage (BAL) fluid of asthma patients.

Measurement of 8-hydroxy-2-deoxyguanosine biomarkers of oxidative stress

Analysis of 8-OHdG is measured in urine, human organs, leukocyte DNA as a biomarker of oxidative stress, aging, and carcinogenesis [10]. Floyd (1986) offered an analytical method for sensitive detection for 8- OHdG by High-Pressure Liquid Chromatography with an electrochemical detector (HPLC-EC) in cellular DNA [10]. DNA repair results in the 8-OHdG excretion in urine and 8-OHdG can be measured as a non-invasive biomarker that reflects whole-body oxidative damage [11]. Urinary 8 OHdG is affected by neither diet nor cell turnover [12]. The biomarker 8-oxodG OR 8-OHdG is a significant marker for measuring endogenous oxidative damage to DNA [10].

The measurement of 8-OHdG rationale in urine is based on the concept of specific repair systems for the removal of oxidative DNA damage. The 8-OHdG dietary contribution is less than 2% of the total 8-OHdG detected in the excretion which makes it less significant. However, the nucleotide pool contribution of 8-OHdG in urine at present is not clear. 8-OHdG levels are higher in smokers than non-smokers. Smoking characteristically determines urinary excretion of 8-OHdG and is linked with a 50% rise in oxidative DNA damage. Smoking cessation results in a decrease in urinary 8-OHdG levels. There is a strong correlation between the excretion of 8-OHdG and the daily cigarette consumption in smokers [13]. In healthy men within ten minutes after smoking two cigarettes, there is a 1.5 fold raise in leukocyte 8-OHdG [14].

The preferred methods of measuring 8-hydroxy-2-deoxyguanosine (8-OHdG), are High- performance liquid chromatography (HPLC) with electrochemical detection (EC) or GC-mass spectrometry in urine [13] and HPLC tandem mass spectrometry [10]. 8-OHdG (ng/ml) can also be quantified by ELISA competitive assay kits. Frequently, spot urine samples collected for creatinine have been used for the analysis of 8-OHdG. However, the correlation between the 8-OHdG to creatinine ratio in spot samples and the 24h excretion of 8-OHdG is poor [13]. In some studies 24 hours urine is collected, while in others only spot urine. Some studies have explored the chance of using morning urine samples, to analyze morning spot urine samples in substitution of those collected during 24 hours, due to the consistent correlation between the two measurements [15-18].

Measurement of isoprostane biomarkers

F2 isoprostanes can be measured with high sensitivity and specificity and can be measured using a gas chromatographic/negative ion chemical ionization mass spectrometric approach employing stable isotope dilution. Mass spectrometry is a highly sensitive method to measure IsoPs and yields good quantitative results in the low pictogram range. Antibodies and immunoassay kits are commercially available.

Results

Urinary 8-OHdG concentration is affected by the confounding effect of smoking and multiple other complex factors. This finding is similar with the previous studies done by Pilger., *et al.* [22] were the intraindividual variability (17 - 106%) in urinary 8 OHdG was found greater than the increase in excretion levels due to smoking and thus highlighting the confounding effect of many confounding factors

on urinary 8 OHdG levels. Higher levels of 8-OHdG are seen in COPD in a study reported by Igishi., *et al.* [23] that the median 8OHdG was significantly ($p < 0.05$) elevated in COPD patients as compared to control group. In many other studies, there was no distinct correlation between smoking and urinary 8-OHdG levels [24-26]. On contrary, other studies showed increased levels of more 8OHdG in smokers than non-smokers [27-31]. Prieme., *et al.* [32] reported that 4 weeks of smoking cessation resulted in a decrease in 8 OHdG levels by 21%.

The most common methods used for measurements of 8OHdG are spectrometric method and immunoassays [33,34]. The correlation in the results of these two methods for the measurement of 8 OHdG levels was found good in one study [35]. When Isoprostane was considered as a marker of oxidative stress the values are higher for allergic rhinitis patients and lower in controls. This finding is supported by studies done by Montuschi., *et al.* [36], Pratico., *et al.* [37] and Jason., *et al* [19].

Discussion and Conclusion

The plasma and urine biomarkers of oxidative damage are the fundamental indicators used to identify high-risk groups and to monitor the progression of chronic diseases. Biomarkers of oxidative stress offer the benefit of being risk-free, less expensive, and appropriate to a large range of populations at risk. Measurement of biomarkers can be performed in outpatient settings and can be used for follow up assessments and also used for preventive interventions. Biomarkers of oxidative stress can be used along with novel imaging modalities in high-risk populations which help physicians to intervene early in the disease process and reduce mortality and morbidity from medical conditions linked with oxidative stress.

It is possible to identify smokers with faster decline in FEV1 who are at high risk of COPD development and in asthma cases who are more likely to experience disease worsening or disease remission when exposed to different indoor environments [6], rhinitis subjects who are more prone to develop diseases of the lower respiratory tract like asthma or COPD.

Bibliography

1. Guerra S. "Overlap of asthma and chronic obstructive". *Current Opinion in Pulmonary Medicine* 11 (2005): 7-13.
2. Fabbri L., *et al*. "Allergic Rhinitis, Asthma, Airway Biology, and Chronic Obstructive Pulmonary Disease in AJRCCMin 2004". *American Journal of Respiratory and Critical Care Medicine* 171.7 (2005): 686-698.
3. Bousquet J., *et al*. "Consensus statements, evidence-based medicine and guidelines in allergic diseases". *Allergy* 63.1 (2007): 1-4.
4. Mannino DM. "Global burden of COPD: risk factors, prevalence, and future trends". *The Lancet* 370 (2007): 365-373.
5. Ciencewicki J., *et al*. "Oxidants and the pathogenesis of lung diseases". *Journal of Allergy and Clinical Immunology* 122.3 (2008): 456-468.
6. Ito K and Barnes PJ. "COPD as a Disease of Accelerated Lung Aging". *Chest* 135.1 (2009): 173-180.
7. Kirkham P and Rahman I. "Oxidative stress in asthma and COPD: Antioxidants as a therapeutic strategy". *Pharmacology and Therapeutics* 111.2 (2006): 476-494.
8. Tanou K., *et al*. "Inflammatory and oxidative stress biomarkers in allergic rhinitis: the effect of smoking". *Clinical and Experimental Allergy* 39.3 (2009): 345-353.
9. Sharma G and Goodwin J. "Effect of aging on respiratory system physiology and immunology". *Clinical Interventions in Aging* 1 (2006): 253-260.

10. Valavanidis A., *et al*. "8-hydroxy-2′ -deoxyguanosine (8-OHdG): A Critical Biomarker of Oxidative Stress and Carcinogenesis". *Journal of Environmental Science and Health* 27.2 (2009): 120-139.

11. Feng S., *et al*. "Evaluation of urinary 1-hydroxypyrene,S-phenylmercapturic acid, trans, trans-muconic acid, 3-methyladenine, 3-ethyladenine, 8-hydroxy-2′-deoxyguanosine and thioethers as biomarkers of exposure to cigarette smoke". *Biomarkers* 11.1 (2006): 28-52.

12. Pan CH., *et al*. "Effects on Chinese Restaurant Workers of Exposure to Cooking Oil Fumes: A Cautionary Note on Urinary 8-Hydroxy-2'-Deoxyguanosine". *Cancer Epidemiology Biomarkers and Prevention* 17.12 (2008): 3351-3357.

13. Pilger A. "8-Hydroxy-2′-deoxyguanosine as a marker of oxidative DNA damage related to occupational and environmental exposures". *International Archives of Occupational and Environmental Health* 83 (2006): 1-15.

14. Kiyosawa H., *et al*. "Cigarette Smoking Induces Formation of 8-Hydroxydeoxyguanosine, One of the Oxidative Dna Damages in Human Peripheral Leukocytes". *Free Radical Research Communications* 11.1-3 (1990): 23-27.

15. Poulsen HE., *et al*. "Oxidative DNA damage *in vivo*: Relationship to age, plasma antioxidants, drug metabolism, glutathione-S-transferase activity and urinary creatinine excretion". *Free Radical Research* 29.6 (1998): 565-571.

16. Poulsen HE., *et al*. "Oxidative DNA damage *in vivo*: Relationship to age, plasma antioxidants, drug metabolism, glutathione-S-transferase activity and urinary creatinine excretion". *Free Radical Research* 29.6 (1998): 565-571.

17. Moller P., *et al*. "Dietary antioxidants and beneficial effect on oxidatively damaged DNA". *Free Radical Biology and Medicine* 41 (2006): 388-415.

18. Boyle S., *et al*. "Bioavailability and efficiency of rutin as an antioxidant: a human supplementation study". *European Journal of Clinical Nutrition* 54.10 (2000): 774-782.

19. Morrow JD and Roberts LJ. "The Isoprostanes". *American Journal of Respiratory and Critical Care Medicine* 166.1 (2002): S25-S30.

20. Tsimikas S., *et al*. "C-Reactive Protein and Other Emerging Blood Biomarkers to Optimize Risk Stratification of Vulnerable Patients". *Journal of the American College of Cardiology* 47.8 (2006): C19-C31.

21. Tsimikas S. "*In Vivo* Markers of Oxidative Stress and Therapeutic Interventions". *The American Journal of Cardiology* 101.10 (2008): S34-S42.

22. Pilger A., *et al*. "Longitudinal study of urinary 8-hydroxy-2′-deoxyguanosine excretion in healthy adults". *Free Radical Research* 35.3 (2001): 273-280.

23. Igishi T., *et al*. "Elevated urinary 8-hydroxydeoxyguanosine, a biomarker of oxidative stress, and lack of association with antioxidant vitamins in chronic obstructive pulmonary disease". *Respirology* 8.4 (2003): 455-460.

24. Van Zeeland AA., *et al*. "8-Hydroxydeoxyguanosine in DNA from leukocytes of healthy adults: relationship with cigarette smoking, environmental tobacco smoke, alcohol and coffee consumption". *Mutation Research/Genetic Toxicology and Environmental Mutagenesis* 439.2 (1999): 249-257.

25. Rie Yoshida., *et al*. "Moderate Alcohol Consumption Reduces Urinary 8-Hydroxydeoxyguanosine by Inducing of Uric Acid". *Industrial Health* 39.4 (2001): 322-329.

26. Sakano N., *et al*. "Plasma 3-nitrotyrosine, urinary 8-isoprostane and 8-OHdG among healthy Japanese people". *Free Radical Research* 43.2 (2009): 183-192.

27. Kiyosawa H., *et al*. "Cigarette Smoking Induces Formation of 8-Hydroxydeoxyguanosine, One of the Oxidative Dna Damages in Human Peripheral Leukocytes". *Free Radical Research Communications* 11.1-3 (1990): 23-27.

28. Loft S., *et al*. "Oxidative DNA damage estimated by 8-hydroxydeoxyguanosine excretion in humans: influence of smoking, gender and body mass index". *Carcinogenesis* 13.12 (1992): 2241-2247.

29. Loft S., *et al*. "Prospective study of 8-oxo-7,8-dihydro-2′-deoxyguanosine excretion and the risk of lung cancer". *Carcinogenesis* 27.6 (2005): 1245-1250.

30. Pourcelot S., *et al*. "Urinary 8-oxo-7,8-dihydro-2′-deoxyguanosine and 5-(hydroxymethyl) uracil in Smokers". *Free Radical Research* 30.3 (1999): 173-180.

31. Asami S., *et al*. "Increase of a Type of Oxidative DNA Damage, 8-Hydroxyguanine, and Its Repair Activity in Human Leukocytes by Cigarette Smoking1". *Cancer Research* 56 (1996): 2546-2549.

32. Prieme H. "Effect of smoking cessation on oxidative DNA modification estimated by 8-oxo-7,8-dihydro-2'-deoxyguanosine excretion". *Carcinogenesis* 19.2 (1998): 347-351.

33. Frenkel K., *et al*. "Quantitative high-performance liquid chromatography analysis of DNA oxidized *In vitro* and *In vivo*". *Analytical Biochemistry* 196.1 (1991): 126-136.

34. Yin B., *et al*. "Determination of 8-hydroxydeoxyguanosine by an immunoaffinity chromatography-monoclonal antibody-based ELISA". *Free Radical Biology and Medicine* 18.6 (1995): 1023-1032.

35. Shimoi K., *et al*. "Comparison between high-performance liquid chromatography and enzyme-linked immunosorbent assay for the determination of 8-hydroxy-2'-deoxyguanosine in human urine". *Cancer Epidemiology, Biomarkers and Prevention* 11 (2002): 767-770.

36. Montuschi P. "Review: Analysis of exhaled breath condensate in respiratory medicine: methodological aspects and potential clinical applications". *Therapeutic Advances in Respiratory Disease* 1.1 (2007): 5-23.

37. Praticò D., *et al*. "Chronic Obstructive Pulmonary Disease is associated with an increase in urinary levels of Isoprostane F2 α-III, an index of oxidant stress". *American Journal of Respiratory and Critical Care Medicine* 158.6 (1998): 1709-1714.

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