

Cigarette Smoking Induced Human Cellular Oxidative Deregulations

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Abstract

Cigarette smoke contains numerous unsafe chemical molecules, most of them at such low levels that they are unnoticeable to the people those who smoking their senses. The level of damage by these compounds is very dangerous, therefore deciphering the molecular mechanisms underlying cigarette smoke induced oxidative toxicity is one of the major task in modern biology. Now, there is substantial confirmation that cigarette smoke can cause both irreparable changes to the genetic structure of DNA. A vast script pertaining to the toxicological effect of cigarette smoke and other such type of carcinogens has been focused but, mechanisms behind the predisposition and development of oxidative damage to our genetic integrity by cigarette smoke is still mysterious. On this premises we made a current account of consequence of cigarette smoke leading to various molecular upsets leading to oxidative damage and oxidative burst. This mechanistic review will provide an existing supervision of smoke contributing to oxidative damage and molecular alterations confronts assorted human complaints. This fiery knowledge would help in superior sympathetic of better diagnostics, safety assessments, therapeutic strategies and interventions.

Keywords: Cigarette smoke, DNA damage, Oxidative burst, cellular modulations

I. INTRODUCTION

After birth and starting life junctures are the important periods and characterized by severe alterations of the redox balance and by physiological genetic changes in lung cells, which may leads to cancer and other diseases in maturity. Oxidative trauma is a major mechanism accounting for the carcinogenicity of cigarette smoke (CS), which becomes more significant carcinogenic, when exposure starts at birth and continues early in life. Data provide evidence that enhanced oxidative stress and the resulting DNA damage and airway inflammation provide a major contribution to the high susceptibility to CS early in life.

Tobacco smoke is a multifarious mixture of more than five thousand compounds including about 200 hazardous chemicals. These chemicals have the capability of persuade various progressive human

diseases. Oxidative stress induced by these hazardous compounds in smoke results in pulmonary disease and apoptosis of human airway epithelial (HAE) cells. One of the hazardous chemical of nicotine induces physical addiction to tobacco and also causes pulmonary diseases, cardiovascular diseases or cancers to smokers. Ishii (2013) provides evidence that lung is a directly affected organ by cigarette smoking, various respiratory diseases including lung cancer, chronic obstructive pulmonary disease, interstitial lung diseases, bronchial asthma, are caused and worsen by cigarette smoking not only in case of active smoking but also in case of passive smoking. A lot of carcinogen in cigarette smoke causes lung cancer through the DNA damage. Oxidants in cigarette smoke induce airway inflammation and tissue injury.

II. CELLULAR OXIDATIVE DAMAGE

Cigarette smoking is a well-known inducer of oxidative stress and observed as a main source of production of exogenous pro-oxidants, reactive oxygen species (ROS) and free radical generators. Smoking increased the ROS production and responsible for the depletion of its cleaners in the circulating blood, this contributing to initiation of oxidative stress. Further, this oxidative stress may direct to cell injure and breakdown through the free radical-mediated decomposition of vital molecules, such as DNA, proteins and lipids. On the other end, DNA is also a major target of constant oxidative damage from endogenous oxidants. Although numerous protecting systems defense cellular macromolecules against oxidation, there is a high rate of damage to DNA .

It is investigated that biological damage caused by reactive oxygen species, such as superoxide radical, singlet oxygen, hydrogen peroxide, and the hydroxyl radical, contributes getting older and various diseases, such as cancer and heart disease. These oxygen species are formed in vivo as byproducts and intermediates of aerobic metabolism and during oxidative stress. Numerous defense systems protect cellular macromolecules against oxidation; nevertheless, there is a high rate of damage to DNA. The oxidized DNA is continuously repaired, and the oxidized bases are excreted into the blood serum and then the urine. It has been observed that chronic cigarette smoking enhanced oxidative DNA damage.

The latest study on deleterious effects of cigarette and non-cigarette discharge exposure on acute and chronic modulation of the sympathetic nervous system provide that tobacco smoke lead to increased sympathetic nerve activity, which becomes persistent via a positive feedback loop between sympathetic nerve activity and reactive oxidative species. It is now obvious that cigarette smoking is one of the most injurious and preventable risk factors. However, because of the large composition of cigarette smoke, the complete details of generation of various diseases are not fully understood and explained. The studies show that cigarette smoke potently induces DNA crack of genetic cells, immune modulation, Immune apoptosis and oxidative damage. The common view is that cigarette smoke acts as a mutagen and DNA damaging agent in normal epithelial cells, driving tumor initiation. More specifically, study show that cigarette smoke exposure is indeed sufficient to drive the onset of the cancer-associated fibroblast phenotype via the induction of DNA damage, autophagy and mitophagy in the tumor stroma.

DNA damage happens almost all the times in cells, but is repaired also continuously done. Occurrence of all these mutations and their growth in one cell which finally becomes tumorigenic appears possible, if the DNA repair mechanism is vulnerable. Cigarette smoke's substances like NNK and NNAL are well established carcinogens. 72 enzymes involved in the DNA repair Mechanisms for their interactions with ligands (NNK and NNAL) were analyzed. Study indicated the loss of functions of these enzymes, which probably could be a cause for fettering of DNA repair pathways resulting in damage accumulation and finally cancer formation.

Cigarette smoking is one of the most important and avoidable risk factors for atherosclerosis. Based on controversial reports on the pro-atherogenic activity of cigarette smoke condensate, also called tar fraction (CSC), study carried to analyze the effects of CSC on the viability of endothelial cells in vitro. The show that low concentrations of the hydrophobic tar fraction induces DNA damage resulting in a P53-dependent and BCL-XLinhibitable death cascade. Higher CSC concentrations also induce apoptotic-like signalling but the signalling cascade is then redirected to necrosis. Despite the fact that CSC induces a profound increase in cellular reactive oxygen species production, antioxidants exhibit only a minimal cell death protective effect.

According to the American Thoracic Society (ATS)/European Respiratory Society (ERS) Statement, chronic obstructive pulmonary disease (COPD) is

defined as a preventable and curable disease with a strong genetic component, characterized by airflow limitation that is not complete reversible, but is usually progressive and associated with an enhanced inflammatory response of the lung to noxious particles or gases. In predisposed individuals, cigarette smoke harms the airway epithelium creating the release of endogenous intracellular molecules or danger-associated molecular patterns from stressed or dying cells. These signals are captured by antigen presenting cells and are transferred to the lymphoid tissue, generating an adaptive immune response and enhancing chronic inflammation.

Previous studies in twins indicate that no shared environment, beyond genetic factors, contributes substantially to individual variation in mutagen sensitivity; however, the role of specific causative factors (e.g. tobacco smoke, diet) was not elucidated. In this investigation, a population of 22 couples of monozygotic twins with discordant smoking habits was selected with the aim of evaluating the influence of tobacco smoke on individual response to DNA damage. Overall, the results obtained indicate that differences in smoking habits do not contribute to a large extent to inter-individual variability in the response to radiation-induced DNA damage observed in healthy human populations.

Cigarette smoke contains numerous compounds that cause oxidative stress and alter gene expression in many tissues, and cigarette smoking is correlated with male infertility. When a person continuously have this habit of smoking, it leads him as a impotent. To identify mechanisms by which this occurs, we evaluated expression of antioxidant genes in mouse spermatocytes in response to cigarette smoke condensate (CSC). CSC exposure led to oxidative stress and dose-dependent upregulation of Hsp90aa1, Ahr, Arnt, Sod1, Sod2, and Cyp1a1 expression in a mouse spermatocyte cell line. An antagonist of the aryl hydrocarbon receptor (AHR).abrogated several CSC-mediated changes in mRNA and protein levels. Consistent with these results, spermatocytes isolated by laser-capture microdissection from CSC-treated mice showed increased expression of several antioxidant genes.

In vivo exposure to CSC was genotoxic to spermatocytes, resulting in apoptosis and disruptions to the seminiferous tubules. Our in vivo and in vitro data indicate that CSC-mediated damage to murine spermatocytes is AHR-dependent and is mediated by oxidative stress. Cheah et al. (2013) investing recently that a major class of chemicals found in tobacco smoke is formed by aldehydes, in particular formaldehyde,

acetaldehyde and acrolein. Responses compared of the individual aldehydes with that of the non-aldehydes. Also the response of the aldehydes when present in a mixture at relative concentrations which are present in cigarette smoke studied. Overall, aldehyde responses are primarily indicative for genotoxicity and oxidative stress [21]

Cigarette smoke (CS) is convincingly carcinogenic in mice when exposure starts at birth. It has been investigated the induction and modulation of alterations in the kidney and urinary bladder of CSexposed mice. Also alter the re-productive system via a significant increase in abnormalities affecting epididymal spermatozoa. Induction of oxidative stress and increase in DNA single- and double-strand breaks in CS-exposed mice, findings suggest that involuntary smoking is potentially able to impair fertility in subjects exposed early in life.

III. CONCLUSION

In this literature surveyed the present review will be the eye-opener for social benefit as it would be helpful in interpreting the unidentified mechanism of oxidative burst by tobacco exposure for the researchers on one hand and new healing techniques for the affected individuals on the other. A vast script pertaining to the toxicological effect of cigarette smoke and other such type of carcinogens has been focused on the metabolic activation; DNA breaks leading to transmutation and transformations but, mechanisms behind the predisposition and development of immune-oxidative damage by tobacco is still mysterious and insufficient. Moving ahead, it may also provide substantial help to understand the molecular pathogenesis of disease caused due to chewing tobacco as well as cigarette smoke. Furthermore, it may help in the design the new idea concern about new anti-toxic remedial approach for effective prevention and advance medi-care for long lasting chronic individuals.

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