

Cigarette Smoking Increases Oxidative Stress in Prostate Cancer Patients – A Preliminary Study

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Summary

Cigarette smoke is an oxidant, creating free radicals that are involved in carcinogenesis namely in Prostate Cancer (PC). However, a correlation between cigarette smoking and PC progression remains unclear.

This study was directed to evaluate the correlation between cigarette smoking, Oxidative Stress (OS) and PC development and progression. The Total Antioxidant Status (TAS), Glutathione (GSH) and Malondialdehyde (MDA) were analysed in the plasma and/or in the erythrocytes of PC patients, 5 smokers and 9 non-smokers and in controls, 2 smokers and 4 non-smokers.

Our results show a significantly decrease in TAS and GSH, and an increase in MDA levels, in PC smoker group. These results suggest that cigarette smoking may be involved in prostate carcinogenesis.

Introduction

PC is the most frequently diagnosed neoplasm and the second leading cause of cancer-related mortality in men (1). OS, resulting from the imbalance between the Reactive Oxygen Species (ROS) and the anti-oxidants system, in favour of the oxidants, has been linked to PC development and progression

(2). ROS play an essential role in the regulation of cell signalling. However, an increase of ROS requires an adaptation in the antioxidant system, otherwise, may cause damage on biomolecules such as DNA, lipids and proteins that are implicated in a several number of diseases including cancer. The antioxidant system comprises enzymes such as superoxide dismutase, catalase, glutathione peroxidase and glutathione S-transferase (GST), and also other molecules, such as vitamins E and C and GSH. ROS may result from intracellular generation or from external factors as cigarette smoke (3). Smoking has been linked to an increase of PC risk, in individuals with P1 Ile105val polymorphism in GST gene, that codifies an enzyme involved in the detoxification of carcinogens. These compounds comprises Polyaromatic Hydrocarbons (PAHs) derived from several combustions including cigarette smoke (4). On the other hand, PAHs induce thyroid cancer cells proliferation (5) and increase metalloproteinase expression in PC cells (6). However, a correlation between smoking and PC development remains unclear.

Taking these results together, it seems plausible that smoking may be implicated in OS modulation and in prostate carcinogenesis.

We are interested to investigate the correlation between cigarette smoking, OS and PC development and progression. To approach our goal we provided this preliminary study, based in the determination of TAS, GSH levels, and lipid peroxidation in PC patients.

Materials and Methods

Blood samples: All samples were obtained from the Portuguese Institute Oncology of Coimbra and patients had consented to participate in the study. This work was performed in the plasma and/or in the erythrocytes of 14 PC patients, 5 smokers and 9 non-smokers and in 6 controls, 2 smokers and 4 non-smokers.

GSH quantification: Plasmatic levels of GSH were determined by spectrophotometry using the assay kit from OxisResearch, according to manufacturer's instruction based on the formation of a chromophoric thione directly proportional to GSH.

TAS evaluation: TAS was evaluated by a chromogenic method using a commercially available kit from Randox Laboratories Crumham's.

Lipid peroxidation measurements: Levels of lipid peroxidation were measured by the formation of a thiobarbituric acid (TBA) adduct of malodialdehyde (MDA), separated by HPLC according to Draper & Hadley (7).

Results

We found a significant increase in lipid peroxidation indicated by MDA levels and a decrease in TAS and GSH in the PC smoker group compared

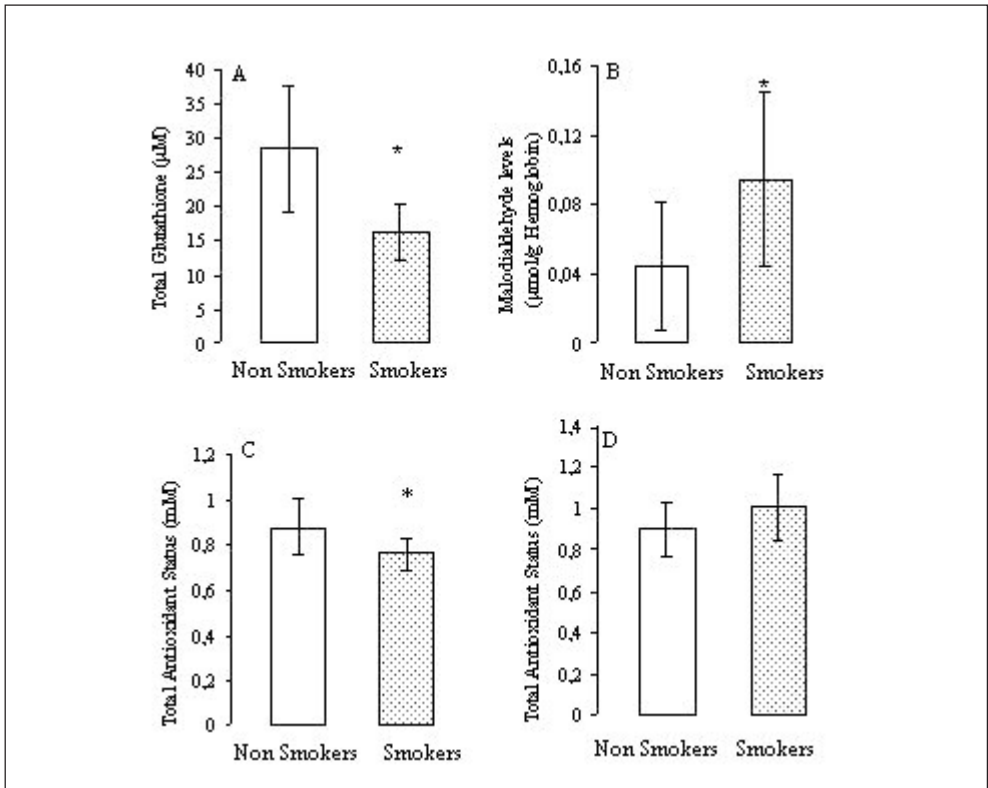


Figure 1: Effect of cigarette smoking on OS parameters in PC patients and controls. The OS parameters are analysed in peripheral blood of prostate cancer patients, PC, (A, B, C) and in healthy controls (D), smokers and non smokers. Values represent the arithmetic means \pm SD of separate experiments. Significant differences between smokers and non smokers are according to student's t-test at least $p < 0,05$ (*). PC smoker group show a significant decrease of glutathione and TAS in serum (A and C, respectively), and an increase of MDA in erythrocytes (B).

with non-smokers (Fig. 1-A, B, C). The alteration in these parameters are more pronounced in patients with metastasis (data not shown), which are in agreement with those obtain by Yossepowitch (8). However, in healthy control group, non significant differences between smokers and non smokers are detected (Fig 1-D).

Our results suggest that cigarette smoking an OS may be both implicated in PC development and progression. However, these results must be confirmed with an enlarged sample size.

Conclusions

PC patients, and in particular PC smoker individuals, are subject to higher OS, resulting in oxidative damage as determined by serum lipids peroxidation. This evidence may be related with the decrease of GSH and TAS. Our results suggest that cigarette smoking and OS may be involved in PC development and progression. However, these observations need to be confirmed by large-scale studies.

This work is supported by the Investigation Center of Environment, Genetics and Oncobiology (CIMAGO).

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