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Original Article

Plasma levels of α-tocopherol, γ-tocopherol and selenium in patients with prostate cancer in Nigeria

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ABSTRACT

Background: Evidence suggests that essential trace metals and vitamins play crucial roles in slowing down the initiation and progression stages of many cancers, but the plausible role of selenium and vitamin E, especially the gamma-tocopherol (γ-tocopherol), against prostate cancer is yet to be ascertained. **Aim:** To compare levels of selenium, alpha-tocopherol (α-tocopherol) and γ-tocopherol between prostate cancer (PCa) and benign prostatic hyperplasia (BPH) patients. **Methods:** Twenty (20) prostate cancer (PCa) patients and 25 patients with benign prostatic hyperplasia (BPH) recruited from Urology Clinic of the Department of Surgery, University College Hospital (UCH), Ibadan acted as case and control subjects, respectively. Informed consent was obtained from all participants. The plasma levels of selenium, α-tocopherol and γ-tocopherol were determined by Atomic Absorption Spectrophotometer (AAS) and High Performance Liquid Chromatography (HPLC), respectively. **Results:** γ-tocopherol levels were significantly higher in BPH patients (control) when compared with PCa patients. Selenium and α-tocopherol levels were lower in PCa patients, but not significant. **Conclusion:** Plasma low level of γ-tocopherol in PCa patients was statistically significant. This may be a risk factor among adult Nigerian men for the development of prostate cancer. Increased plasma level of γ-tocopherol through diet or supplementation may reduce the risk and progression of prostate cancer.

Key words: Prostate cancer, benign prostatic hyperplasia, α-tocopherol, γ-tocopherol, selenium, trace metals.

INTRODUCTION

Cancer is one of the dreaded degenerative diseases and a serious public health problem globally with its attendant clinical implications. In most industrialized countries, prostate cancer is the most common cancer among men after skin cancer.[1] One in 10 men in United States will have prostate cancer diagnosed in his lifetime.[1] Cancer of the prostate gland is unarguably the most common malignant tumor among men in most western communities of the world.[2,3] It has emerged to be the most common cancer among African-American men in the past few years.[4]

The increasing prevalence of prostate cancer has been ascribed primarily to an increase in the number of cases occurring in younger men with the advent of prostate specific antigen (PSA) screening programs and increased awareness of the disease in the last decade.[5] Prostate cancer is rarely diagnosed before the age of 50 years, but the incidence and mortality from the disease increase exponentially thereafter. There is a great variation in the geographic epidemiology of prostate cancer,[6,7] and the environmental factors such as lifestyle practices,[8] specific occupations,[9] and dietary insufficiency[10] appear to be significant contributors to this difference.

Prostate cancer was said to be uncommon among the West African blacks, specifically the Nigerian males.[11] This was confirmed in a report by Nkposong and Lawani,[12] that prostate cancer ranked 16th and constituted 2.2% of all malignancies in the cancer registry in Ibadan. Recent reports however, show that the incidence is on the increase. For instance, Ogunbiyi and Shittu have reported that prostate cancer has become number one cancer in Nigerian men and constitutes 11% of all male cancers.[4]

In many cancer prevention studies, the pathology of cancer has been linked to nutritional elements/micronutrients-antioxidant vitamins and trace elements. Dietary factors have been suggested to be associated with the risk of developing prostate cancer.[13] Few human and animal studies have indicated association between gamma-tocopherol and prostate cancer even though some reported otherwise. It is therefore the resolution of the present authors to determine the concentrations of selenium, alpha- and gamma-tocopherols in patients with prostate cancer.

METHODOLOGY

Study population

Twenty (20) patients newly diagnosed of prostate cancer, confirmed by prostate biopsy were selected as case subjects from the Urology Clinic, Department of Surgery, University College Hospital, Ibadan. Twenty-five (25) individuals newly diagnosed of benign prostatic hyperplasia (BPH) were selected as control subjects from the same clinic. This study excluded vegetarians, and subjects on vitamin supplements. This exclusion was possible based on participants' responses to questionnaires and clinical findings. The study was approved by Ethical Committee of the institution. The subjects were informed of the risks and benefits of the study after which their consents were obtained. Study was in accordance with ethical standards.

Collection and preparation of blood samples

Ten (10) mls of random venous blood was collected between 08.00-10.00 hours and carefully dispensed into Lithium-heparin bottle. The blood samples were centrifuged in Centaur MSE centrifuge machine (Cantaur 2) at 3000g for 5 minutes. The plasma obtained was separated into plane serum bottles and stored frozen (-20^{0}C) until analysed.

Determination of selenium and tocopherols

Plasma selenium was determined with atomic absorption spectrophotometer (AAS) using a direct method described by Kaneko.[14] The method is based on the principle that atoms of the element aspirated into AAS absorb light of the same wavelength as that emitted by the element when in the excited state.[14] The tocopherols were analyzed by HPLC (Waters, USA. Model 626 HPLC Pump with IonPac® ASII-HC Anion-Exchange Column).

Statistical analysis

Data were analysed using the SPSS® for Windows® version 16.0 (SPSS Inc, Chicago, IL, USA). The data were expressed as mean ± standard deviation. Student's t test was used to compare the difference between the means. Pearson's Correlation was used for correlation analysis. Significant level was set at *P*-value < 0.05.

RESULTS

Table 1 shows the age, selenium and tocopherols levels in PCa and control subjects. There were no significant difference in the age, selenium and α-tocopherol between the PCa and controls subjects. Only the γ-tocopherol level differed significantly between the PCa and control subjects. The mean value of γ-tocopherol in control subjects was significantly higher compared with the PCa subjects (46.68 ± 6.62µg/dl against 42.66 ± 6.78µg/dl; *P* < 0.05).

Table 2 shows the correlation coefficients between the tocopherols and selenium in PCa subjects and in control subjects separately. There was a positive correlation between α-tocopherol and γ-tocopherol in each of the subject groups. Positive and statistically significant correlation was observed in control group only (*P* < 0.01). No correlation between γ-tocopherol and selenium in PCa subjects, but weak and positive correlation exists in controls.

Table 1: Comparison of plasma levels of selenium and tocopherols between prostate cancer patients and controls

Parameters	PCa (n=20)	Controls (n= 25)	*P*-values
Age (years)	71.35 ± 8.54	69.80 ± 10.08	0.089
α-tocopherol (µg/dl)	58.53 ± 7.73	62.29 ± 9.22	0.082
γ-tocopherol (µg/dl)	42.66 ± 6.78	46.68 ± 6.62	0.023
Selenium (µg/dl)	22.92 ± 3.30	25.31 ± 5.10	0.097

Table 2: Relationship between tocopherols and selenium between subjects (PCa) and controls

Parameters	Correlation coefficient		*P*-values	
	PCa	Control	PCa	Control
α- vs. γ-tocopherol	0.433	0.834	0.078	0.048*
α- vs. selenium	-0.012	0.329	0.134	0.071
γ- vs selenium	0.001	0.302	0.289	0.092

*$P < 0.05$

DISCUSSION

A chemo-preventive role of essential micronutrients against a variety of malignancies has been demonstrated in several cancer prevention and risk factor studies. Compelling evidences indicate that dietary factors can contribute to human cancer risk and as such many of the cancers common in the third world countries and western world, including liver, colon, prostate and breast cancers have been related to dietary behaviors.[15] It is often hypothesized

that essential micronutrients may play a general role in carcinogenesis through their functions as antioxidants,[16] induction of apoptosis, inhibition of cellular proliferation, preservation of genome integrity and being a key component of enzymes like glutathione peroxidase, which protect cells from free radical damage.[17,18] A protective effect of selenium and α-tocopherol, the major form of vitamin E in supplement, against prostate cancer has been observed in clinical[19,20] and randomized[21] trials to evaluate the efficacy of selenium and α-tocopherol in a crusade to prevent prostate cancer. The reduction of risk by γ-tocopherol, the main form of vitamin E in the US diet, is becoming increasingly pertinent in relation to prostate pathology, although results of studies on serum levels of α-tocopherol and γ-tocopherol have, hitherto, been inconsistent.[22-26]

This study showed that the mean age of the PCa subjects (71.35±8.45) was slightly higher than the controls (69.80±10.08) but not significant (*P<0.05*). Age, an independent variable, has long been implicated as a risk factor for PCa among men.[27] At about 45 to 50 years of age and above prostate undergoes age-related enlargement, which sometimes may be due to cancer. In the elderly, there is a decreased appetite for diets which invariably may lower the levels of micronutrients such as selenium and tocopherols. Consequent upon this, incidence of prostate cancer may increase as the age increases.

Selenium is an antioxidant with anticancer activity. The anticancer efficacy of selenium has been attributed to its role in inhibiting cellular proliferation, inducing apoptosis and as a cofactor in enzymes or proteins[28] and thus its biochemical function in glutathione peroxidase.[29] This study found a statistically non-significant difference in α-tocopherol levels between PCa subjects and control subjects. Decreased level of selenium in PCa subjects suggests biochemical depletion of this antioxidant. Selenium intake may be low or might have been used up in the biochemical activity of glutathione peroxidase (GPx), which keeps at bay the generated free radicals to prevent oxidative stress recently implicated in prostate carcinogenesis.[30] This finding is consistent with a recent study by Adedapo *et al*.,[31] on biochemical tie breaker between benign prostatic hyperplasia and prostate cancer subjects, selenium showed no significant difference between the two groups. Knekt *et al.*[32] indicated no association between selenium level and prostate cancer risk. In Carotene and Retinol Efficacy Trial (CARET),[33] there was no association between prostate cancer risk and selenium. In contrast however, several prospective and epidemiologic studies have reported inverse association between selenium and prostate cancer.[34-36]

In this study, α-tocopherol, although not statistically significant, was lower in PCa subjects. Biochemical reactions freely generate free radicals capable of causing damage to cell membrane but could be prevented by cellular antioxidant defense mechanism of which α-tocopherol is a prominent player. Our result was in consonance with the findings of Nomura *et al.* that there was no clear association between serum α-tocopherol level and prostate cancer risk in a nested case-control study of Japanese-American men.[22] This observation was also reported by Adedapo *et al.*[31] stating no significant variation between α-tocopherol and prostate cancer. However, it was noted from the literatures that significant difference was observed consistently among smokers where free radicals generated reduced antioxidant status in advanced prostate cancer. A report by Gan *et al.*[25] indicates inverse association for progressive cancer among current/ex-smokers than never-smokers. γ-tocopherol and its metabolites inhibit cyclooxygenase activity and thus possess anti-inflammatory properties. Lipophilic electrophiles, reactive nitrogen oxide species are trapped by γ-tocopherol.[13] This finding suggests a higher magnitude of risk reduction for prostate cancer if concentration of this form of vitamin is increased in plasma. A study by Helzlsouer *et al.* reported that men in the highest quintile of plasma γ-tocopherol concentration had a 5-fold reduction in the risk of prostate cancer compared with those

in the lowest quintile.[35] Significant positive correlation (*P<0.01*) exists only between α-tocopherol and γ-tocopherol in controls. There may be a synergistic biochemical relationship between these two tocopherols but less with selenium. But studies suggest that large doses of α-tocopherol decreases plasma and tissue γ-tocopherol concentrations while γ-tocopherol doses increase both.[35,37-40]

CONCLUSION

Plasma γ-tocopherol level in PCa subjects in this study was low and found to be statistically significant; an indication that dietary sources of gamma-tocopherol were not taken regularly by patients with PCa. This low level may be related to the risk and progression of prostate cancer among men. Supplementation with gamma-tocopherol and its adequate intake in food sources (soybean, corn oils and safflower oil) by Nigerian men is suggested.

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