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ALPHA -TOCOPHEROL IN CANCER

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ABSTRACT

Serum alpha-tocopherol of 98(62 male and 36 female) cancer patients and 30 (13 male and 17 female) control healthy subjects was investigated. The cancer patients showed a significantly low level of alpha-tocopherol as compared to control healthy subjects. Also, significantly higher levels of serum alpha-tocopherol were found in complete remission patients as compared to the partial response patients.

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INTRODUCTION

Free radical- related damage is thought to be involved in the cancer growth cooperative defence system. Vitamin A, beta-carotene, vitamin E and certain enzymes protect the body from free radical damage. Vitamin E is considered the first line of defence against cell membrane damage due to peroxidation. Vitamin E scavenges free radicals, terminating chain reactions and confining damage to limited areas of the membrane.[1] Vitamin E exercises its antitumoral effect as a free radical scavenger, protecting phospholipids of cell coats from peroxidation and DNA from attacks. It was suggested that daily supplementation with vitamin A and E reduced the rate of free radical chain reactions and related cell membrane injury.[2] Vitamin E and C acting as scavengers of nitrite compounds, prevent the formation of cancer-promoting nitrosamines.[3] Vitamin E appears to prevent tumour formation by stimulating a potent immune response to selectively destroy tumour cells as they begin to develop into recognizable foci of carcinoma.[4] Vitamin E at high level enhances the body's immune response, protects vitamin A from destruction in the body, and spares selenium. It also inhibits the conversion of nitrites present in smoked, pickled and cured food, to nitrosamines in the stomach. The nitrosamines are known as strong tumour promoters.[5] It was found that incubation of cells with vitamin E succinate altered the cell appearance to that of a normal cell and also inhibits growth of the mouse cancer cell.[6] In cell culture studies, vitamin E has been found effective in inhibiting transformation of normal cells to cancerous cells after exposure of isolated mouse embryo cells to radiation and chemicals.[7] A low vitamin E blood level may be a risk factor for cancer,[8] and subjects with low serum selenium and vitamin E levels had a significant ten-fold higher risk of breast cancer. According to one researcher, a low serum vitamin E concentration can predict cancer development in women.[9] High vitamin E intake was also associated with a significantly lower risk of cervical cancer.[10] Average plasma vitamin E and beta-carotene levels were significantly reduced in women with cervical cancer as compared with the control group.[11]

MATERIAL AND METHODS

The study includes 98 cancer patients (62 male and 36 female) with an average age of 54.9±1.3 years. The cancer patients were selected from the Outpatient Department of Radiotherapy, Jinnah Postgraduate Medical Centre, Karachi, Pakistan. The histopathology of all the patients was squamous cell carcinoma. The blood samples were collected from these patients at the time of diagnosis before giving any treatment. Thirty (13 male and 17 female) control healthy subjects having no signs of clinical malignancy were also included in this study. Their age varied from 21 to

50 years, and average age was 32.4±12.6 years.

The alpha-tocopherol was estimated in serum of cancer patients and healthy control subjects by high performance liquid chromatography by the method adapted from Leencher et al.[12] μBonda Pak C_{18} reversed phase column (waters) was used as stationary phase (size 2.1 mm × 300 mm steel column), pure methanol (Merck) was used as mobile phase. The mobile phase was filtered on "SCHOTT" Duran filter and degassed by an EYELA aspirator. The mobile phase was passed through the column at a flow rate of 1 mL/minute. Fractions were detected by UV-VIS spectrophotometric detector SPD-6AV at λ_{max} 254 nm.

RESULTS

The level of alpha-tocopherol was significantly decreased ($p<0.05$) in the serum of cancer patients as compared to control subjects (Table I). There was no significant difference in the level of alpha-tocopherol on the basis of sex, age, site of disease, nodes palpable and duration of disease (Tables II-V). A significantly low pre-treated level of alpha-tocopherol was found in patients who had shown partial response after one year of treatment as compared to the patients who had shown complete remission.

DISCUSSION

In the present study we have tried to find a correlation between serum alpha-tocopherol level and cancer in our population. The normal level of alpha-tocopherol in serum is 11 mg/L.[13] The normal level of alpha-tocopherol estimated in our population by the present work is 10.83±0.86 mg/L. A statistically significant difference was present in the level of this compound in a healthy population and cancer patients (Table I). The level of alpha-tocopherol was low in cancer patients. This finding is the same as was shown by a number of workers in western countries.[8,9,11,14-17]

Ibrahim et al. found low levels of vitamin A and its metabolites in cancer patients.[18] In our study, we tried to correlate alpha-tocopherol levels with the different important characteristics of cancer patients. Concerning the relation of alpha-tocopherol levels to different age groups, no significant difference was found, suggesting that the level of alpha-tocopherol is not influenced by the age of the patients (Table II). The level of alpha-tocopherol with respect to the site of malignancy has shown no significant difference. The level of serum alpha-tocopherol is low but not significant in those patients who had a longer period of disease rather than those who had a short period of disease symptoms. This is what we can expect and is helpful in deciding to provide supplementation of alpha-tocopherol during treatment of malignancy patients. The response was also evaluated in patients in relation to pre-treatment level after one year of treatment. The pre-treatment level of alpha tocopherol was statistically higher in those patients who had complete response (complete disappearance of all known disease symptoms in the absence of any new lesion appearing) than in patients who had partial response after treatment of one year (a reduction in size by at least 50% of the tumor

Table I. Variation of serum alpha-tocopherol in control and cancer patients.

Group	Alpha-tocopherol (mg/L)
Control	10.83±0.86 (30)
Patients	4.70±0.24* (98)

*Statistically significant ($p<0.05$) as compared to control.

Table II. Serum alpha-tocopherol in cancer patients on the basis of age group.

Age group	Alpha-tocopherol (mg/L)
Up to 45 years	4.8±0.41 (25)
Up to 60 years	4.51±0.34 (45)
Above 60 years	4.89±0.52 (28)

Table III. Serum alpha-tocopherol in cancer patients on the basis of site of cancer.

Site	Alpha-tocopherol (mg/L)
Head and neck	4.45±0.29 (61)
Lungs	4.99±0.65 (16)
Others (cervix, esophagus, etc.)	4.98±0.51 (21)

Table IV. Serum alpha-tocopherol in cancer patients on the basis of nodal involvement.

Nodes	Alpha-tocopherol. (mg/L)
Nodal involvement	4.38±0.35 (38)
No nodal involvement	4.91±0.31 (60)

Table V. Serum alpha-tocopherol in cancer patients on the basis of duration of disease.

Duration (from the date of diagnosis)	Alpha-tocopherol (mg/L)
Up to 3 months	5.19±0.43 (33)
3 to 6 months	4.56±0.54 (29)
More than 6 months	4.26±0.35 (36)

Table VI. Serum alpha-tocopherol in cancer patients on the basis of response.

Response after treatment of one year	Pre-treatment level of alpha-tocopherol (mg/L)
Complete remission	5.08±0.81 (14)
Partial response	3.13±0.49* (18)
Progressive disease	4.70±0.45 (22)

*Statistically significant ($p<0.05$) as compared to complete remission.

in the absence of any new lesion). This shows that a high pre-treatment level of alpha-tocopherol may produce a good response after treatment. This means as the disease progresses, alpha-tocopherol tries to confront it and its molecules scavenge the carcinogenesis which is induced by free radicals. This gives an idea to add supplement doses of alpha-tocopherol during cancer therapy.

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