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Original Research Article

A Study of Oxidative Stress in Cancer Patient before and after Supplementation of Vitamin C and Vitamin E

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ABSTRACT

Cancer is the second leading cause of death behind heart disease. Increased lipid peroxidation is due to the altered ratio between free radicals and antioxidant status. This study is carried out in a group of 25 cancerous patients and 25 control subjects to analyze and evaluate the relationship between antioxidant vitamin C & E supplementation and its effect on the lipid peroxidation. Malondialdehyde (MDA), lipid peroxidation marker is estimated colorimetrically by Thiobarbituric acids reactive Substances (TBARS) and uric acid is estimated by Uricase method. Statistical analysis is done by Student't' test. MDA values in both the control & study groups decreased significantly after 7 days of vitamin supplementation. However no significant change in the uric acid concentration is noted in the control and cancer subjects. The study suggests that MDA value reduced in cancer patients within one week of antioxidant vitamin supplementation but for reduction of uric acid levels longer period of vitamin supplementation is required in both the population.

Keywords: Malondialdehyde (MDA), TBARS, Uric acid.

INTRODUCTION

Increased lipid peroxidation is due altered intracellular ratio between free radicals and antioxidant systems have been related to cancer. [1] Free radicals are formed in the body under normal conditions. They cause damage to nucleic acids, proteins, and lipids in cell membranes and plasma lipoproteins which can cause cancer, atherosclerosis, coronary artery disease, and auto-immune diseases. [2] Oxidative Stress (OS) is a general term used to describe the steady state level of oxidative damage in a cell, tissue, or organ, caused by the reactive oxygen species (ROS). This damage can affect a specific molecule or the entire organism. Reactive oxygen species, such as free radicals and peroxides, represent a class of molecules that are derived from the metabolism of oxygen and exist inherently in all aerobic organisms. There are many different sources by which the reactive oxygen species are generated. The free radicals originate endogenously from normal

metabolic reactions or exogenously as component of tobacco smoke and air pollutants and indirectly through the metabolism of certain dietary factors, drugs, solvents and pesticides as well as through exposure to environmental electromagnetic radiation. The univalent reduction of oxygen to ($O_2^{\bullet-}$) is a common event in mammalian metabolism and contrary to common belief, is essentially a useful reaction in aerobic systems, provided that it is restricted by antioxidant mechanisms. There are various pathophysiological processes which utilize oxygen and are thought to be important in promoting disease. [3]

Malondialdehyde (MDA) is a highly reactive three carbon dialdehyde produced as a byproduct of polyunsaturated fatty acid peroxidation and also during arachidonic acid metabolism for the synthesis of prostaglandins. MDA can combine with several functional groups of molecules including proteins, lipoproteins, RNA and DNA. The monitoring of MDA levels in biological materials can be used as an important indicator of lipid peroxidation in vitro and in vivo for various diseases like Cancer. [4]

The present study is undertaken in an effort to analyze, evaluate and compare the oxidative stress by measuring lipid peroxidation in between the cancerous and non-cancerous subjects.

MATERIALS AND METHODS

The present study is carried out at Gauhati Medical College and Hospital (GMCH), Guwahati, Assam. The study protocol was approved by the Research and Ethical committee of GMC, Guwahati. Oral informed consent is obtained from the patients and their attendants prior to study. This cross sectional study is conducted in a group of 25 cancerous patients with age & sex matched 25 healthy control group and to whom vitamin C (500mg) & E (400IU) supplementation was administered for one week.

The Cancer patients or test group consisted of patients with diagnosed malignancy based on clinical findings and histopathology examination. Subjects for the control group were selected randomly among persons from different sectors of the society belonging to diverse socio economic status. All individuals of the control group co-operated voluntarily. Factors producing free radical activity such as rheumatic arthritis, coronary artery diseases, Diabetes Mellitus, congestive heart failure, renal disease, hypertension & tuberculosis either in the past or present were excluded from the study and a careful screening was done in selecting test group subjects thorough detailed history, physical examination and laboratory diagnosis.

Under aseptic & antiseptic precaution, 2 ml of the venous blood was collected by venipuncture after proper consent of participating subjects. In both the groups lipid peroxidation test (MDA level) and uric acid estimation were done colorimetrically. MDA was estimated by Thiobarbituric acid reactive substances (TBARS) at 530nm & resulting absorbance is referred to a standard curve prepared by 1,1,3,3, tetraethoxy propane (SIGMA) [5] and Uric acid is estimated by uricase method. [6]

After the biochemical estimations, the results obtained were statistically analyzed by using statistical software SPSS 16. The results were expressed as Mean± SD and were taken as significant when the probability (p value) is less than 0.05 as percentage of the observing values of 't' at a particular degree of freedom.

RESULTS & OBSERVATION

Our results from table 1 shows MDA & uric acid values in normal control and cancer patient group before and after supplementation of vitamin C & E. In both

the groups there is a statistical decrease in MDA value after 7 days of vitamin supplementation whereas Uric acid showed a non significant increase after supplementation of Vitamin C & E. Again correlation of Uric acid & MDA in Cancer patients were also seen before and after Vitamin supplementation as in Figure 1 and Figure 2 respectively. This correlation coefficient(r) was obtained by linear regression analysis and it showed a inverse correlation.

Table1: Showing the statistical analysis of MDA & uric acid values in normal control and cancer patients groups before and after supplementation of vitamin C & E

Parameters	Study Group	#Before supplementation of vitamin C & E (nmol/ml)	#After supplementation of Vitamin C & E (nmol/ml)
MDA value (nmol/ml)	Control(n = 25)	3.36 ± 1.00	2.49 ± 0.90**
	Cancer patients (n = 25)	4.42 ± 1.01	3.8 ± 0.96*
Uric acid (mg/dl)	Control(n = 25)	4.64 ± 0.72	4.74 ± 0.72^{NS}
	Cancer patients (n = 25)	3.70 ± 1.27	4.09 ± 1.29^{NS}

Legend #Values are given as mean ± S.D. (*p<0.05-Significant, **p<0.001-Highly Significant, NS-Not significant)

Figure 1:- Correlation of Uric acid & MDA in Cancer patients before Vitamin supplementation

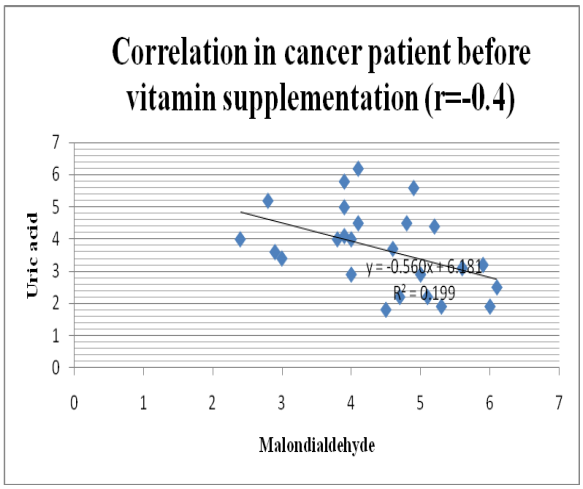
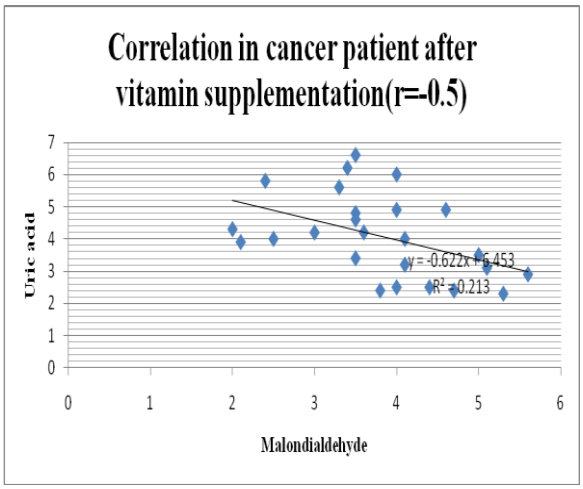


Figure 2:- Correlation of Uric acid & MDA in Cancer patients after Vitamin supplementation



DISCUSSION

In control group MDA (malaondialdehyde) value on day 1 was 3.36 ± 1.00 nmol/ml & after 7 days of vitamin supplementation there was highly significant decrease in serum MDA values with a mean value of 2.49 ± 0.90. Again, in the cancer patients groups there was significant ($p<0.05$) reduction of malaondialdehyde value from the day 1 (4.42 ± 1.01 nmol/ml) to Day 7 (3.8 ± 0.96 nmol/ml) following antioxidant vitamin supplementation. However the malondialdehyde concentration in the cancer patients was also higher in day 1 and day 7 in comparison to the control patients indicating increased production of free radicals in cancer and thereby causing free radical mediated tissue damage in the cancer.

Previous studies by Iris Benzie et al, [7] Ray G. et al [8] had showed that there was significant increase in serum MDA values of cancer patients ($p<0.05$) than the normal control group. Choi SW et al [9] in their study showed that there was no evident of protective or deleterious effect of vitamins

on single day supplementation on MDA. However, Huang et al [10] supplementing vitamin for 2 months showed that there was significant decrease in lipid peroxidation.

Iris Benzie et al [7] in their study observed that a combination of a vitamin C-'sparing effect improved redox cycling of vitamin E in vivo and a lipid lowering effect, increased intake of vitamin C could increase plasma vitamin E levels and possible vitamin E status. Again Simone et al [11] suggests that vitamin supplementation does not interfere with the efficacy of chemotherapy and radiation therapy in cancer patients; rather it may increases the survival of the patient.

Heather C, Kuiper et al in their study found that HPNE *(*4-hydroperoxy-2-nonenal metabolites*)* in urine metabolites are biomarkers of oxidative stress or biomarkers of the physiological response to oxidative stress. Decrease in the levels of urinary HPNE metabolites, thus supporting the notion that vitamin C supplementation reduces oxidative stress and Lipid peroxidation. [12]

The present study showed a non significant elevation in the uric acid level in both the control & test subjects after supplementation of Vitamin C & E. In the control group the uric acid concentration increased from 4.64 ± 0.72 mg/dl in day 1 to 4.74 ± 0.72 mg/dl in Day 7 whereas the value of serum uric acid in Cancer patients group in day is 3.70 ± 1.27 mg/dl which increased to 4.09 ± 1.29 mg/dl in day 7. This elevated uric acid level appears to compensate with increased oxidative stress production. [13] However the limited time period may be a constraint to establish the significant antioxidant role of the uric acid in our study. A study with longer duration may help in establishing the exact role of uric acid as an antioxidant.

Low levels of lipid peroxidation products are essential to many normal cellular processes because small amount of lipid peroxides and semi stable breakdown products act as intracellular and extra cellular messengers. Any excessive amounts of lipid peroxides are kept in control by the antioxidant system. Conditions that can stimulate lipid peroxides are numerous and include hyperoxia, hypoxia, copper or iron toxicity and lack of antioxidant defenses. Although a variety of antioxidant mechanisms serve to control lipid peroxidation, under certain conditions the protective mechanisms can be overwhelmed, leading to elevated levels of peroxidation products. [14.15] Therefore any imbalance between prooxidant and antioxidant defenses in which the former dominates may be broadly defined as "oxidative stress" of which lipid peroxidation is one important manifestation. As from Figure 1, our study showed an inverse correlation of malondialdehyde & Uric acid in cancer patient indicating the role of malondialdehyde as oxidant & uric acid as antioxidant. This is more evident following the supplementation of antioxidant vitamins as in figure 2. This finding is in accordance with the above mentioned study that there exists a delicate balance between the oxidants & antioxidants in our body. Any alteration in this delicate defense leads to the generation of pathology in the body.

CONCLUSION

The present study suggests that there is a significant decrease of serum Malondialdehyde values after antioxidant vitamins supplementation for a minimum of 1 week period. It may be concluded that, though the mechanism is not fully understood, the antioxidant vitamins- C and E supplementation for a minimum of 1 week period can improve the oxidative stress in cancer patients. Thus it could be included in

the regime for the prevention and/ or treatment of this awful disease. But longer duration of vitamin supplementation for more than one week may be required for uric acid. Further investigation in this context may prove fruitful in future.

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