Research Article

Effect of Antioxidant Supplementation in Cancer Patients on Chemotherapy

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Abstract

Background: Antioxidants protect cells from damage by inhibiting oxidation that produces free radicals that damage the DNA that leads to cancer. **Objective:** The aim of the current study was to determine the role of antioxidants in the cancer patients of Solapur, Maharashtra, India. **Materials and methods:** Various parameters in the present study were Serum nitric oxide, total lipid peroxide and Total Antioxidants. Enzymatic antioxidants were studied by the estimation of erythrocytic Superoxide Dismutase and Glutathione Peroxidase. Similarly, the levels of non-enzymatic antioxidants such as vitamin E and vitamin C were also estimated. These biochemical parameters were compared within the groups of Cancer patients and normal healthy control subjects. **Results:** The investigation shows that the factors responsible for increase in the oxidative stress are elevated in the cancer patients compared to that of control. These values were decreased upon administration of the antioxidant supplement. The serum levels of enzymatic and non enzymatic antioxidants were decreased in the cancer patients. **Conclusion:** Antioxidant supplement leads to replenish their levels. Thus antioxidant is involved in decreasing the oxidative stress and further damage.

***Keywords*:** Antioxidants, Cancer, Free radicals, Oxidative stress, Reactive oxygen species.

Introduction

Cancer is a disease in which the control of growth is lost in one or more cells, leading to a solid mass of cells known as a "Tumor" (Thurston David, 2007). Cancer is characterized by a shift in the control mechanisms that govern Cell Survival, Proliferation and Differentiation. Cancer in US is said to be the second leading cause of death and half of all men and one third of all women there develop cancer during their life time. About 6% of all deaths in India are reported due to cancers which contribute to 8% of global cancer mortality (Sarnath et al., 2014).

There are free radicals called Reactive Oxygen Species (ROS) (Commoner et al., 1954), produced regularly in our body as by-products of natural metabolic processes. These play a significant but paradoxical role acting as a "double-edged sword" to regulate cellular processes. By accepting electrons from DNA, they can cause damage to DNA. Their overproduction can be a major cause for cancer. The involvement of free radicals in the pathophysiology of many diseases including cancer is clearly evident from many reports. Body/cells develop variety of antioxidants to defend themselves from the ill-effects of free radicals.

Antioxidant is a substance that protects cells from damage by inhibiting oxidation, a chemical reaction which produces free radicals (highly reactive chemicals) that damage the DNA in cells (Said et al., 2014). Since damage to cells by free radicals can cause the damage that leads to cancer, antioxidants may reduce the risk of developing cancer (Lunawati et al., 2012). There are controversies in this regard as to whether these antioxidants help in the treatment preventing ill-effects on cancerous host cells or not. Hence it was planned to study the antioxidants in cancer patients undergoing chemotherapy.

Although this work has global implications, it was planned and aimed for the patients of one cancer hospital, Sri Siddheshwar Cancer Hospital and Research Centre,

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located in Solapur, Maharashtra, India. In light of the above facts this work was our sincere effort locally to evaluate the possibility of improving the life of cancer patients by reducing the ill effects of the disease and the anticancer drugs by the co-administration of antioxidants.

Materials and methods

Subjects Selection

Inclusion criteria

A) Healthy Human Controls

Age and sex matched thirty healthy human volunteers were selected. History was taken to make sure they had not suffered from any such disease that would lead to oxidative stress. Only those who proved to be in a good state of health and free from any sign(s) of chronic disease(s) or disorder(s) were included in the study design.

B) Study group subjects:

Patients clinically diagnosed to have been suffering from Cancer of any type were included.

Exclusion criteria:

A) Subjects who have had acute complications such as severe infections, major operations, hepatic or respiratory diseases, other chronic inflammatory conditions, trauma, GI disorder.

B) Subjects known to be previously on antioxidant vitamins or medications that could influence the oxidant and antioxidant status.

C) Smokers, alcoholics.

D) Diabetics.

The distribution of subjects in the present study was as shown in table 2

Table 1. Distribution of subjects in study groups

S. No.	Group	Types	No. of Subjects
1.	Group I	Control- Healthy Subjects	30
2.	Group II	Cancer Patients before chemotherapy	30
3.	Group III	Cancer Patients during Chemotherapy without Antioxidants	30
4.	Group IV	Cancer Patients during Chemotherapy supplemented with Antioxidants	30

The present study was approved by institutional ethical committee (IEC Letter no. IEC/COPS/01 Dt. 15.08.2011) and all such patients who gave written informed consent were only included.

Study procedure

All subjects were screened for inclusion and exclusion criterion and those who consented for the proposed study were included in the study. All the biochemical parameters listed below were evaluated in all the four groups listed in Table 1.

Sample collection

Venous blood samples were collected from the subjects under aseptic condition by venipuncture using a 20 ml sterile disposable syringe and needle. About 15 ml blood was collected and about 2-3 ml was taken for the routine investigations as required by the hospital. 7-8 ml of the blood was poured into sterile heparinised bulb and rest of the blood was taken in a sterile bulb and allowed to clot. Plasma and serum were separated from respective bulbs by centrifugation at 3000 rpm for 10-15 minutes at room temperature. Then all samples were stored at 4°C before the analysis and were analyzed on the same day. The above samples were subjected to investigation of the following biochemical parameters:

1. Serum Total Lipid Peroxide by the method of Kei Satoh (Satoh et al., 1978).
2. Serum Nitric Oxide (as nitrite) by a kinetic cadmium reduction method by Najwa Cortas and Nabil Wakid (Cortas et al., 1990).
3. Serum Total Antioxidant level using FRAP method (Benzie et al., 1996).
4. Erythrocytic Superoxide dismutase (RBC-SOD) by Randox (RANSOD) kits (Randox et al., 1994).
5. Serum Glutathione peroxidase activity using Randox kits (Randox et al., 1994).
6. Serum vitamin E by colorimetric method of Baker Frank (Frank et al., 1968).
7. Plasma vitamin C by DNPH method (Zloch et al., 1971).

The results were subjected to statistical analysis using Student's t-test. The biochemical parameters were compared between Healthy Control and Cancer Patients to determine the changes in these values due to carcinogenesis. Whereas comparison between the group III (cancer patients during chemotherapy without antioxidants) and group IV (cancer patients during chemotherapy with antioxidants) was carried out by t-test for understanding of effect of antioxidants on the serum levels of predetermined parameters and role of antioxidants on oxidative stress.

Results and discussion

The results of biochemical investigations in normal

Table 2. Effect of antioxidant on Biochemical parameters for Cancer patients on chemotherapy

Sr. No.	Parameter	Control	Cancer Patients		
			Before therapy	After Chemotherapy	With antioxidant treatment
1	Malondialdehyde (nM/dl)	510.47 ± 87.21	1798.51 ± 152.24	1509.28 ± 182.03	1200.88 ± 125.78
2	Nitric Oxide (μM/L)	41.59 ± 7.28	32.71 ± 6.31	96.69 ± 36.85	72.27 ± 4.09
3	Total Antioxidant Concentration (μM/L)	5.32 ± 0.28	2.95 ± 0.26	3.85 ± 0.21	4.78 ± 0.36
4	Superoxide Dismutase (U/ml)	6.41 ± 0.74	3.15 ± 0.36	4.19 ± 0.35	5.01 ± 0.59
5	Glutathione peroxidase (mg/gm of Hb)	678.26 ± 104.18	397.81 ± 18.60	484.21 ± 21.42	506.72 ± 60.23
6	VIT C (mg/dl)	1.08 ± 0.16	0.37 ± 0.38	0.48 ± 0.11	0.84 ± 0.11
7	VIT E (mg/dl)	1.02 ± 0.05	0.63 ± 0.07	0.92 ± 0.14	0.97 ± 0.05

Values expressed as mean ± standard deviation.

individuals and cancer patients are depicted in Table 2.

Oxidative stress plays an important role in the pathogenesis, neoangiogenesis, and dissemination of cancer, as it induces phenotypic modifications of tumor cells. The free radicals increase the oxidative stress which plays a fundamental role in the carcinogenesis. Antioxidants are known to neutralize the free radicals which will be helpful in reducing the oxidative stress. In the present work, attempt was made to correlate the level of free radicals in cancer patients with or without antioxidant supplementation.

i. Serum Malondialdehyde

It is observed from Table 2 and Fig. 1 that, serum Lipid peroxide (MDA) is considerably increased in the cancer patients compared to healthy control group. The value is further increased in the cancer patients after chemotherapy which is evident of increased oxidative stress in these subjects ($P < 0.001$). From the values of serum total lipid peroxide after antioxidant treatment, it can be understood that the value in cancer patient is significantly decreased ($P < 0.001$) suggesting decrease in the oxidative stress due to antioxidant effects.

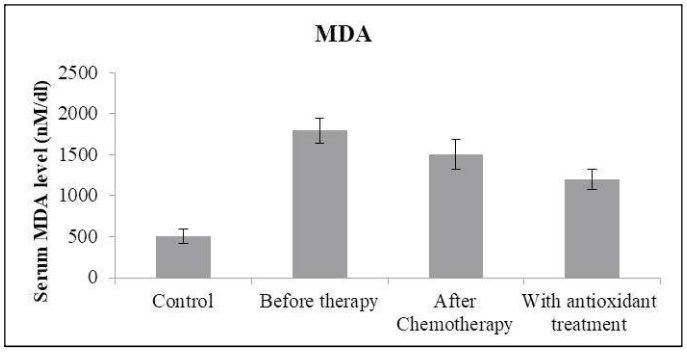

Figure 1. Effect of antioxidant MDA levels in control and cancer patients in Chemotherapy

ii. Serum Nitric Oxide (as nitrite)

Nitric Oxide plays an important role in animal carcinogenesis. NO can participate in the complicated process of carcinogenesis by mediating DNA damage in early phases of tumorigenesis, as well as support tumor progression through the induction of angiogenesis and suppression of the immune response. From Table 2 and Fig. 2, it can be observed that the level of NO in cancer patients is decreased compared to the normal individuals. But after chemotherapy, the level of nitric oxide is significantly elevated which create an oxidative stress on the physiological functions in cancer patient ($P < 0.001$). The role of antioxidant is clearly evident in decreasing the serum Nitric oxide concentration.

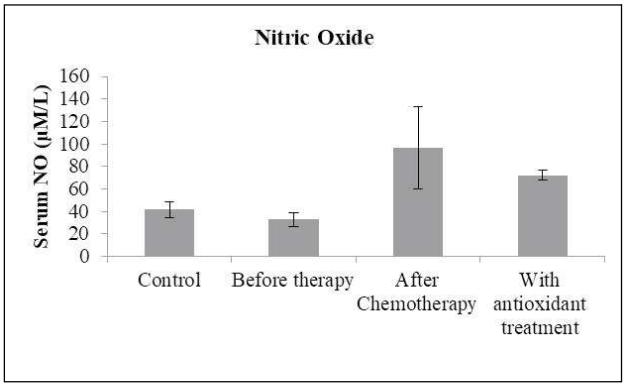

Figure 2. Effect of antioxidant NO levels in control and cancer patients in Chemotherapy

iii. Serum Total Antioxidant level

Table 2 and Fig. 3 reveal that the total antioxidant concentration in the normal control was found to be 5.32 ±

0.28 µM/L. The level of antioxidant in cancer patients is certainly decreased by 45% ($P < 0.001$) which is indicative of lack of free radical scavenging mechanism leading to increased generation of reactive oxygen species. Administration of antioxidants in the form of A to Z tablet formulation, leads to maintain the total antioxidant concentration.

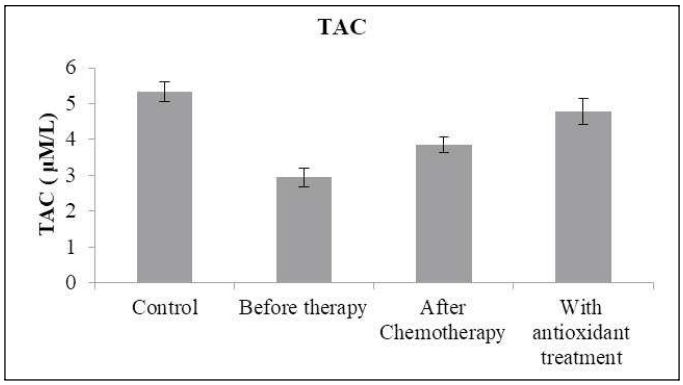

Figure 3. Effect of antioxidant TAC levels in control and cancer patients in Chemotherapy

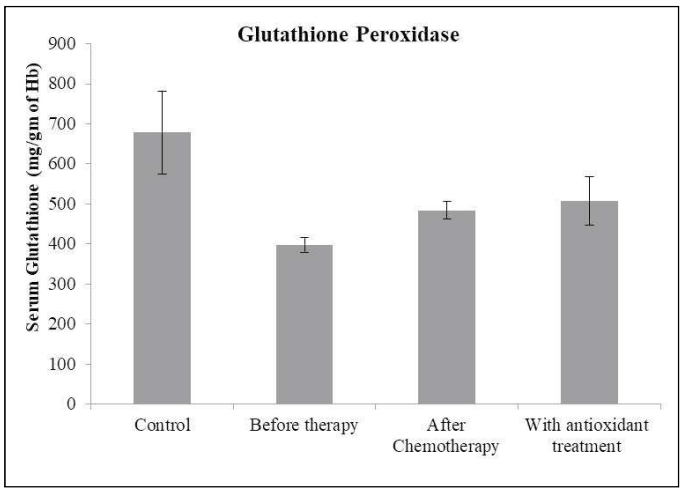

Figure 4. Effect of antioxidant GPx levels in control and cancer patients in Chemotherapy

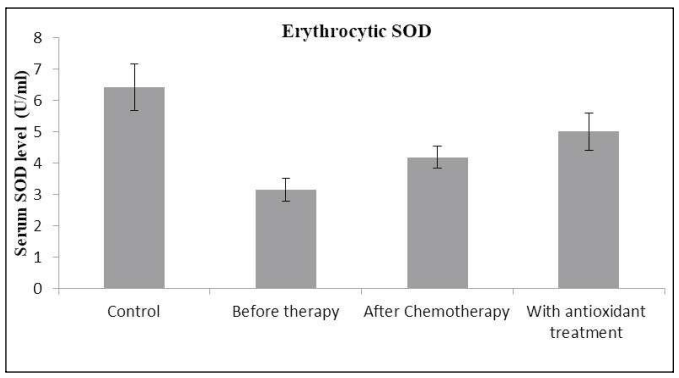

Figure . Effect of antioxidant SOD levels in control and cancer patients in Chemotherapy

Enzymatic antioxidants

Some primary enzymatic antioxidants such as superoxide dismutase (SOD), and glutathione peroxidase (GPx) protect against cellular and molecular damage caused by the ROMs. It can be observed from Table 2 and Fig. 4-5 that SOD and GPx levels are significantly decreased in the cancer patients compared to controls ($P < 0.001$). The values are increased after chemotherapy and further, remarkably restored after the antioxidant treatment.

Non-enzymatic antioxidants

In the present study two non-enzymatic antioxidants viz. Vitamin C and Vitamin E were studied. Antioxidants and carotenoids may be valuable chemopreventive agents. Table 2 shows the levels of non enzymatic antioxidants in various study groups. The results show that the levels of these nutritional components in serum are significantly decreased during carcinogenesis ($P < 0.001$). After chemotherapy, Vitamin C and Vitamin E concentrations are found to be elevated ($P < 0.001$) protecting against the harmful effects of free radicals. But the increased level of the non enzymatic antioxidants is higher due to supplemented antioxidant formulation.

Conclusion

Although a cursory glance over literature survey shows to a wide variety of opinions about the concomitant administration of antioxidants along with the chemotherapy, the present investigation finds the beneficial aspects of antioxidant supplement to cancer patients. After the study of seven biochemical parameters and correlating with the status of oxidative stress in the control and cancer patients, it can be concluded that it is advantageous to give the antioxidant supplement in cancer patients as it is responsible for reduction in the reactive oxygen radicals. At the same time, antioxidant supplements lead to replenish the decreased levels of body's own free radical scavenging mechanisms. Thus the effort can be said to be worthy even if it extends the life of an extremely small number of patients, even marginally or even if it serves in improving the quality of the 'life survived' by the patients undergoing chemotherapy.

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