

Lipid Peroxidation and Antioxidant Status in Post-Operative Patients with Cancer Treated with Chemotherapy

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ABSTRACT

Background and Objectives: The aim of this study was to assess the effect of surgical interference and chemotherapy on lipid peroxidation and antioxidant status in patients with cancer disease.

Methods: Twenty one male patients with gastric, colonic, and prostate cancer; and 26 apparently healthy male subjects as a control group, were included in this study. Blood samples (5 ml) were taken from patients and controls and analysed for serum malondialdehyde (MDA) and total antioxidant status (TAS). Blood samples were taken from patients one week before and after the surgery and other blood samples were taken two weeks after the first dose of chemotherapy.

Results: In the cancer patients, serum MDA was significantly higher ($P < 0.001$), while serum TAS was significantly lower ($P < 0.001$) compared with the controls. After surgical removal of cancer, serum MDA was decreased significantly ($P < 0.001$), but serum TAS was increased significantly ($P < 0.001$) compared with the patients before surgery. Chemotherapy treatment further increased serum MDA significantly ($P < 0.001$), with a significant ($P < 0.001$) decrease in serum TAS compared with the measurements after operation.

Conclusions: Surgical removal of cancer decreased lipid peroxidation, and increased antioxidant status. Chemotherapy of cancer increased lipid peroxidation and depressed antioxidant defense system. Oxidative stress might be a consequence and not a cause of cancer.

Key words: lipid peroxidation, total antioxidants status, chemotherapy, cancer.

INTRODUCTION:

Oxidative stress is considered to be implicated in carcinogenesis. Lipid peroxidation in plasma or tissue presented by malondialdehyde (MDA) concentration was increased in different types of cancer including prostate¹, gastric², and colorectal cancer³. However, few studies found either no significant change or decrease in lipid peroxidation in cancer patients^{4,5}. The levels of individual antioxidants in prostate, gastric and colonic cancer patients were controversial^{1-3,5-8}. Lipid peroxidation in plasma of patients with cancer was higher than controls, and was further increased after chemotherapy⁹, whereas plasma total

antioxidants were decreased significantly in patients treated by antineoplastic drugs¹⁰. Most studies were focused on the individual antioxidants in cancer patients. In addition, few studies were found on the effect of surgical removal of cancer on oxidative stress and antioxidant defense system. Therefore, this study was conducted to evaluate the effect of surgical removal of the tumor and the use of chemotherapy on lipid peroxidation and total antioxidant status (TAS).

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PATIENTS AND METHODS:

The study included 21 male patients with cancer stage ΠI (9 gastric, 7 colonic, and 5 prostate cancer) were seen in Al-Jamhori Hospital, Mosul, Iraq, during the period from February to November 2007. Their ages ranged from 45 to 71 years (mean±SD: 63±7.3 years). The control group included 26 apparently healthy males, their ages ranged from 38 to 70 years (mean±SD: 58.5±8 years).

Fasting blood samples (5 ml) were obtained from patient and control groups and analysed for serum MDA and TAS at the Department of Pharmacology, Mosul college of Medicine, University of Mosul, Iraq.

Serum MDA was measured by Buege and Aust method¹¹. One ml of the reagent (0.375 thiobarbaturic acid, and 15 g trichloroacetic acid dissolved in 0.25 N HCl to make 100 ml) was added to 0.5 ml of serum. The mixture was mixed and heated in a water bath at 70 C° for 15 minutes and MDA was measured in the supernatant solution by spectrophotometer at 532 nm. MDA concentration was calculated by the following equation:

$$\text{MDA concentration } (\mu\text{mol/L}) = \frac{(\text{Absorbance of test} - \text{Absorbance of blank})}{\epsilon_{\text{MDA}}}$$

* 10⁶

S MDA is equal to molar extinction

coefficient of MDA = 1.56 * 10⁵ μmol/cm

Serum TAS was estimated by Miller et al. method¹² by using TAS kits (Randox, England). Samples, standard and blank (20 μl each) were added in plastic cuvettes separately, followed by one ml of chromogen and incubated to bring temperature to 37 C° and initial absorbance (A₁) was recorded by spectrophotometer at 600 nm. Then 200 μl of the substrate was added and mixed. The absorbance (A₂) was recorded after exactly 3 minutes at 600 nm.

$$\text{Factor} = \frac{\text{concentration of standard}}{(\Delta_{\text{blank}} - \Delta_{\text{sample}})}$$

The blood samples were taken from the patients one week before and after surgical removal of cancer, and other blood samples were taken two weeks after starting the first dose of chemotherapy. The patients with gastric cancer were given 5-fluorouracil 500 mg/m², adriamycin 50 mg/m², and mitomycin 15 mg/m². The colonic cancer patients received oxaliplatin 85 mg/m², 5-fluorouracil 500 mg/m² and folinic acid 200 mg/m². The prostate cancer patients received prednisolone 10 mg/day, mitozantrone 12 mg/m². The chemotherapy was started two weeks after the surgery. Patients and controls with any other disease, drug treatment or even smoking or alcohol intake were excluded from this study. Data are presented as mean±SD. Unpaired t-test was used to compare patients with the controls. Paired t-test was used to test the effect of surgery and chemotherapy in the

RESULT:

patient group.

Serum MDA in the cancer patients was significantly higher (P<0.001) than controls. After surgery, serum MDA decreased significantly (P<0.001) compared with the parameter before surgery. Chemotherapy increased serum MDA compared with that after surgery (Table 1).

Serum TAS in the patients with cancer was significantly lower (P<0.001) than controls. However, serum TAS was increase significantly (P<0.001) after surgery compared with that before surgery. Chemotherapy depressed serum TAS significantly (P<0.001) compared with the parameter after surgery (Table 1).

Table 1: Serum MDA and TAS from controls and patients with cancer.

	Serum MDA ($\mu\text{mol/L}$)	Serum TAS (mmol/L)
Controls (n=26)	1.00 \pm 0.19	2.12 \pm 0.3
Patients (n=21)		
Before surgery	2.84 \pm 0.20 ^a	1.22 \pm 0.15 ^a
After surgery	2.70 \pm 0.26 ^b	1.30 \pm 0.15 ^b
After chemotherapy	3.08 \pm 0.2 ^c	1.00 \pm 0.12 ^c

^a P<0.001 VS controls, ^b P<0.001 VS before surgery, ^c P<0.001 VS after treatment.

DISCUSSION :

Lipid peroxidation was significantly higher in the present patients with cancer than controls. These results are consistent with many studies^{7,13,14}. The increase in lipid peroxidation is not known whether a cause or a consequence of carcinogenesis. The improper balance between reactive oxygen species (ROS) production and antioxidant defense results in oxidation stress which deregulates the cellular functions leading to various pathogenic conditions including cancer¹⁵. The oxidative stress hypothesis of carcinogenesis asserts that many carcinogens can generate free radicals that damage cells, predisposing these cells to malignant conversions¹⁶. Furthermore, MDA is highly toxic and should be considered as more than just a marker of lipid peroxidation. Its interaction with DNA and proteins has often been referred to as potentially mutagenic and atherogenic¹⁷. Serum MDA was decreased significantly after surgical removal of cancer in the present patients, but it was higher than controls. The decrease in lipid peroxidation was not noticed after surgery of gastric and colorectal cancer^{8,18}. Surgery by itself can produce oxidative stress. Further experimental study of the effect of surgery on oxidative stress in animals is suggested.

Serum TAS includes all enzymatic and non-enzymatic antioxidants¹². Serum

study to represent all individual antioxidants, because different changes occurred in the individual antioxidants in patients with cancer^{1,13,19}. The decrease in serum TAS in the present patients with cancer was also consistent with the increase in lipid peroxidation. In the present study, serum TAS was increased significantly after surgical removal of cancer. These results are consistent with the reduction of lipid peroxidation in such patients, since cancer disease produced oxidative stress⁷. The drugs of many classes of antineoplastic agents are known to generate oxidative stress in biological systems²⁰. The generation of reactive oxygen species by a cancer chemotherapeutic agent or free radical intermediates of the drug might play a role in its cytotoxicity or adverse effects²¹. Therefore, antioxidant supplementation for cancer patients treated with chemotherapy might reduce the activity of the drug or decreases its adverse effects²¹. In conclusion, lipid peroxidation was increased with depression of serum TAS in patients with cancer. Surgical removal of cancer decreased lipid peroxidation and improved serum TAS. Chemotherapy further increased lipid peroxidation in cancer patients with significant decrease in serum TAS. Oxidative stress might be a consequence of cancer.

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