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Research Article

Analysis of lipid peroxidation status in Prostate cancer patients receiving radiotherapy in Pakistani hospitals: an in-vivo human study

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ABSTRACT

Introduction: Prostate cancer is the fourth most common male malignancy worldwide and is the commonest malignancy of older age. The prevalence of prostate cancer increases with rise in age. It is the major cause of morbidity and mortality in male older than 65 years of age worldwide. **Objectives:** This study is aim to analyze the lipid peroxidation status in prostate cancer patients who are receiving radiotherapy in Pakistani hospitals.

Methodology of the study: The whole experimental work was conducted at DHQ hospital Gujranwala. Those prostate cancer patients who receiving radiotherapy were selected to study the lipid peroxidation status in the diseased condition.

Results: The data pertaining in the table explained that radiotherapy and chemotherapy both effect on the MDA levels of cancer patients. The statistical analysis shows that levels of MDA become increasing in prostate cancer patients who received adjuvant radiotherapy or simple radiotherapy. The level of MDA before radiotherapy is 3.48±0.65and it become increases in post radiotherapy. As the value of MDA post radiotherapy is 5.66±0.95. But in case of adjuvant radiotherapy it becomes 3.27±0.16 (pre-treatment) and 6.79±0.40 (post-treatment). The levels of MDA become increased because cell membrane is damaged due to therapies.

Conclusion: It is concluded that MDA is one of the important marker of body for protecting the body against the diverse effects of radiotherapy. Although many anti-neoplastic agents have clearly established mechanisms of action that are not dependent upon the generation of ROS/RNS, these drugs can only mediate their anticancer effects on cancer cells that are exhibiting unrestricted progression through the cell cycle.

Keywords: Cancer, Radiotherapy, patients, MDA

INTRODUCTION

Prostate cancer is the fourth most common male malignancy worldwide and is the commonest malignancy of older age[1]. The prevalence of prostate cancer increases with rise in age. It is the major cause of morbidity and mortality in male older than 65 years of age worldwide[2]. Autopsy studies have shown that every man at age of 90 almost have prostate cancer. Prostate cancer has the lowest number of life year's loss of all major cancers in men and women. It is the leading cancer diagnosed and is the second most common causes of cancer related death in men in United States[3]. African-American men have the highest incidence of prostate cancer in the United States and also Asian-American men have lower prostate cancer incidence than white or African-American men[4]. Prostate Cancer is the most ubiquitous form of cancer found in men above the

age of fifty years. Prostate cancer is the second most frequently diagnosed cancer and the sixth leading cause of cancer death in males, accounting for 14% (903,500) of the total new cancer cases and 6% (258,400) of the total cancer deaths in males in 2008. Incidence rates vary by more than 25-fold worldwide, with the highest rates recorded primarily in the developed countries of Oceania, Europe, and North America , largely because of the wide utilization of prostate- specific antigen (PSA) testing that detects clinically important tumors as well as other slow-growing cancers that might otherwise escape diagnosis[5].Prostate cancer incidence rates are strongly affected by diagnostic practices and therefore difficult to interpret, but mortality rates show that death from prostate cancer is about 10 times more common in North America and Europe than in Asia[6]. Oxidative stress is caused by an unfavorable balance between reactive oxygen species (ROS) and antioxidant defenses. ROS are generated during normal cellular metabolism, as a result of the influence of various environmental factors, as well as during pathological processes[7]. Reactive oxygen species play an important role in the pathogenesis of cancer. Oxidative stress caused by increased free radical generation and/or decreased antioxidant level in the target cells and tissues has been suggested to play an important role in carcinogenesis. Free radicals are capable of altering all major classes of biomolecules, such as lipids, nucleic acids and proteins, with changes in their structure and function. Prime targets of free radicals are the polyunsaturated fatty acids in cell membranes and their interaction results in lipid peroxidation. The levels of free radical molecules are controlled by various cellular defense mechanisms, consisting of enzymatic (catalase, glutathione peroxidase, superoxide dismutase) and non-enzymatic (vit. E, vit.C, glutathione) components[8].

Objectives of the study: This study is aim to analyze the lipid peroxidation status in prostate cancer patients who are receiving radiotherapy in Pakistani hospitals.

METHODOLOGY OF THE STUDY

The whole experimental work was conducted at DHQ hospital Gujranwala. Those prostate cancer patients who receiving radiotherapy were selected to study the lipid peroxidation status in the diseased condition.

Blood collection

5.0 ml blood sample was taken from vein. Blood was further processed for the estimation of lipid peroxidation. Commercially available enzymatic kits of Randox were used. Blood was centrifuged at 4000 rpm for 10 minutes and serum was separated. Blood samples will be collected into EDTA tubes from fasting proteins. The blood will be centrifuged and indomethacin and butylated hydroxytoluene will be added into the plasma samples before they will be stored at -80°C until analysis.

STATISTICAL ANALYSIS

Student's t-test was performed to evaluate the differences in roughness between group P and S. Two-way ANOVA was performed to study the contributions. A chi-square test was used to examine the difference in the distribution of the fracture modes (SPSS 19.0 for Windows, SPSS Inc., USA).

RESULTS

The data pertaining in the table explained that radiotherapy and chemotherapy both effect on the MDA levels of cancer patients. The statistical analysis shows that levels of MDA become increasing in prostate cancer patients who received adjuvant radiotherapy or simple radiotherapy. The level of MDA before radiotherapy is 3.48±0.65and it become increases in post radiotherapy. As the value of MDA post radiotherapy is 5.66±0.95. But in case of adjuvant radiotherapy it becomes 3.27±0.16 (pre-treatment) and 6.79±0.40 (post-treatment). The levels of MDA become increased because cell membrane is damaged due to therapies.

Table 01: MDA levels in prostate cancer patients

PROSTATE	CONTROL	MDA(moles/ml)			
		MALES (n=13)		FEMALES (n=00)	
	2.35moles/ml	BEFORE	AFTER	BEFORE	AFTER
R1	0.00	3.5±0.74	5.22±0.85	0.00	0.00
R2	0.00	3.6±0.82	5.42±0.80	0.00	0.00
R1+C	0.00	0.00±0.00	0.00±0.00	0.00	0.00
R2+C	0.00	3.27±0.16	6.79±0.40	0.00	0.00
C	0.00	0.00±0.00	0.00±0.00	0.00	0.00
Total	2.35	3.48±0.65	5.66±0.95	0.00	0.00

Means±SD

R1=Received Radio Therapy Single Time

R2=Received Radio Therapy Two Times

R1+C=Received Radio Therapy Single Time + Chemotherapy

R2=Received Radio Therapy Two Times + Chemotherapy

C=Only Received Chemotherapy

DISCUSSION

Cancer therapy, such as chemotherapy, can result in the generation of excess ROS/RNS[7]. Thus cancer therapy and the resulting production of excess oxidative stress can damage biological systems other than tumors[8].

Thus, in the present study we have demonstrated the status of lipid peroxides and antioxidants in plasma and erythrocytes of prostate cancer patients in comparison with normal subjects. During chemotherapy the highest known levels of oxidative stress are generated by anthracycline antibiotics, followed in no particular order by alkylating agents, platinum-coordination complexes, epipodophyllotoxins, and camptothecins[9].

The primary site of ROS/RNS generation during cancer chemotherapy is the cytochrome P450 monooxygenase system within liver microsomes. Enzyme systems, such as the xanthine-xanthine oxidase system, and non-enzymatic mechanisms also play a role in creating excess oxidative stress during chemotherapy[10].The very high levels of oxidative stress caused by anthracyclines is also related to their ability to displace coenzyme Q10 (CoQ10) from the electron transport system of cardiac mitochondria, resulting in diversion of electrons directly to molecular oxygen with the formation of superoxide radicals[10].

Anthracyclines and other chemotherapeutic agents cause generation of high levels of ROS/RNS, but not all chemotherapeutic agents generate excess oxidative stress. Some agents generate only modest amounts of ROS/RNS. Examples of this are: platinum-coordination complexes and camptothecins, taxanes, vinca alkaloids, anti-metabolites, such as the anti-folates, and nucleoside and nucleotide analogues[11].

However, most chemotherapeutic agents generate some oxidative stress, as do all anti-neoplastic agents when they induce apoptosis in cancer cells. Drug-induced apoptosis is usually triggered by the release of cytochrome c from the mitochondrial electron transport chain. When this occurs, electrons are diverted from NADH dehydrogenase and reduced CoQ10 to oxygen, resulting in the formation of superoxide radicals[12].

Chemotherapeutic agents used to treat cancer cause oxidative stress, which produces side effects, and among the most common side effects is chronic fatigue. Chronic fatigue caused by cancer therapy can reduce therapeutic efficacy[13].

They must also have intact apoptotic pathways. Thus oxidative stress interferes with cell cycle progression by inhibiting the transition of cells from the G0 to G1 phase, slowing progression through S phase by inhibition of DNA synthesis. This results in inhibition of cell cycle progression of the G1 to S phase, and it also results in inhibition by checkpoint arrest[13-15].

CONCLUSION

It is concluded that MDA is one of the important marker of body for protecting the body against the diverse effects of radiotherapy. Although many anti-neoplastic agents have clearly established mechanisms of action that are not dependent upon the generation of ROS/RNS, these drugs can only mediate their anticancer effects on cancer cells that are exhibiting unrestricted progression through the cell cycle.

Contribution of author

All the authors contributed equally. Dr. Anamconceived of the presented idea and do all the lab work and carried out the experiment with other co-authors. Dr. Noreen developed the theory and performed the computations. Dr. Amna supervised the findings of this work and Dr. Anum and Dr. Noreen developed the theoretical formalism, performed the analytic calculations and performed the numerical simulations. All the authors contributed to the final version of the manuscript.

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