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Original Article

Study of blood levels of antioxidant enzymes and erythrocyte Malondialdehyde (MDA) in ovarian, cervical and uterine cancer at stage I

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Abstract

Objectives : To evaluate the status of antioxidant enzymes and lipid peroxidation in women with genital cancer at stage I. *Methods :* Erythrocyte malondialdehyde and antioxidant enzymes levels were estimated in the blood of women with stage I genital cancer (n=94) and the results were compared with the levels in age and socioeconomic status matched healthy women (n=50). *Results :* There was significant increase in erythrocyte malondialdehyde level ($p<0.001$) and decrease in antioxidant enzymes ($p<0.001$) in women with genital cancer. *Conclusion :* Female genital cancer at stage I is associated with disturbed levels of antioxidant enzymes and lipid peroxide. This could be demonstrating oxidative damage /injury.

Key words: female genital cancers, erythrocyte malondialdehyde, antioxidant enzymes.

Introduction

Amongst the uterine, cervical and ovarian cancer, cervical cancer is very common in women of the low socioeconomic group in the society. The causes of these cancers may be chemical carcinogens, radiation and virus infections and oxidative stress. In the normal aerobic cell, there exists a balance between oxidative damage and protection by antioxidants[1]. Inadequate antioxidant protection or excess production of reactive oxygen species (ROS) create a condition known as oxidative stress, which is known to play an important role in various diseases like cancer[2]. Enzymes including super oxide dismutase, glutathione peroxidase, catalase and reduced glutathione along with a variety of dietary antioxidants such as tocopherol and ascorbic acid constitute major defense against oxidative damage in the cell[3]. The deficiency of these enzymes may lead to structural and functional disorganization of cell membrane, which is rich in polyunsaturated fatty acids. The auto oxidation of polyunsaturated fatty acid (nonenzymatic) leads to formation of malondialdehyde. In various female genital cancers the activity of these enzymes are decreased[4]. Increased production of free radical (due to decreased level of antioxidant system) cause lipid peroxidation, which is identified as one of the basic reactions involved in oxygen free radical induced cellular damage[5]. Very few studies are available on the status of these enzymes at stage I of female genital cancer patients. Therefore the present study is aimed to determine the status of antioxidant enzymes at stage I of female genital cancer. The erythrocyte malondialdehyde is taken as the product of lipid peroxidation.

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Material & Methods

The study was carried out in different female genital cancer cases. We have selected subjects between the age groups of 30-58 years suffering from ovarian, cervical and uterine cancer (n=94). These patients were histopathologically confirmed stage I, and admitted for the first time in the Cancer Hospital and Research Institute (CHRI) Gwalior (M.P.). The histopathological studies were carried out in histopathology lab of CHRI. Cancer patients with other diseases like diabetes, cardiovascular diseases, liver diseases, kidney diseases and other types of tumors etc. were excluded from the study. Biochemical studies – The blood samples were collected under aseptic conditions for the analysis of various antioxidant enzymes, erythrocyte malondialdehyde and reduced glutathione on the first day of admission in the female ward of CHRI. The glutathione was estimated in whole blood while glutathione peroxidase, superoxide dismutase, catalase and erythrocyte malondialdehyde were estimated from hemolysate. The erythrocyte malondialdehyde was estimated by the method of Bidder and Jaeger [6]. The Antioxidants enzymes, glutathione peroxidase, superoxide dismutase and catalase were estimated by the method of Hafeman et al [7], Mishra et al [8] and Sinha et al [9]. The reduced glutathione was estimated by the method of Beutler [10]. The hemoglobin percentage was estimated in hemolysate by the cyanmethaemoglobin method of Drabkin and Austin[11]. Protein contents of the hemolysate was estimated by the method of Lowry et al[12] using Bovine albumin as the standard. For statistical analysis, the data was compared with normal healthy control subjects of the same age group and socioeconomic status.

The socioeconomic status was calculated by the method of Kumar [13]. The student 't' test was calculated by using software Xact. The written consent and all ethical measures were taken during the studies.

Table 1. Characteristics of women with genital cancer (n=94).

Type of	Number of cases	Years	Socio economic status (Percentage of women)				
			Low	Lower middle	Middle	Upper middle	High
Cervical	41	32-55	60.97	24.39	7.31	4.87	2.43
Ovarian	35	37-58	51.42	23.07	5.71	8.57	8.57
Uterine	18	47-55	44.44	22.22	11.11	11.11	11.11

Table 2. Blood levels of antioxidant enzymes E.MDA in different female genital cancers at stage I.

Types of subjects	GSH Mg%	GSH Px Unit/gm Hb	Superoxide dismutase Unit/gm/Hb	CAT Unit/mg protein	E.MDA nmol MDA/ gm Hb for 2 hr incubation
Control (n=50)					
Range	48.2-62.0	17-19.4	2.1-4.64.34-5.8	100-140.00	
Mean	54.69±3.59	18.19±0.58	3.15±0.59	4.84±0.84	125.32±14.01
Cervical cancer (n=41)					
Range	5.87-45.41	2.18-20.66	1.5-4.2	1.8-5.2	138.6-369
Mean	17.25±7.80[b]	11.06±2.52[a]	2.23±0.26[a]	2.8±0.7[a]	225.88±58.70[a]
Ovarian cancer (n=35)					
Range	6.05-27.26	6.1-14.85	1.12-2.54	2.2-4.2	167-639
Mean	15.70±5.16[b]	10.93±2.66[a]	2.06±0.380[a]	3.17±0.77[a]	248.14±117.24[a]
Uterine cancer (n=18)					
Range	37.00-40.09	18.83-19.9	2.10-3.45	3.20-4.20	170.10-180.9
Mean	20.45±1.36[b]	13.49±0.98[a]	2.3±0.01[a]	3.40±0.2[a]	236.57±16.42[a]

Values are – Min.-Max., Mean±SD

[a] – P<0.01-Significant and [b] – P<0.001-Highly significant, when compared with the respective values in the controls.

Results

The levels of erythrocyte malondialdehyde, reduced glutathione and antioxidants enzymes such as glutathione peroxidase, superoxide dismutase and catalase in different female genital cancers were compared with age matched control subjects. Table 1 shows the type of cancer, number of cases and socioeconomic status of subjects. In our study we observed that the erythrocyte malondialdehyde was significantly increased, (p<.001) while the level of all antioxidant enzymes were significantly decreased (p<.001). The glutathione level was also decreased (p<.001) in all three female genital cancers (Table 2).

Discussion

It is evident from Table 1, that the incidences of female genital cancer are very high (40-61%) in low socioeconomic group as compared to the other groups. It may be due to their habitats, poor hygiene, early marriage, multiparity, virus infection etc. The increased level of erythrocyte malondialdehyde in all the three types of cancers observed in our study reflects increase lipid peroxidation at stage I, which is in agreement with that of Masotti etal [14] who reported that the increased lipid peroxides in proliferating cell lead to an increase in the serum lipid peroxide levels in cancer patients [15].

The antioxidant enzymes like superoxide dismutase and catalase, catalyses the cell defense reaction against the potential harmful effects of superoxide ion generated by wide variety of biological process. In our study, we found a significant decrease in erythrocyte superoxide dismutase and catalase (Table 2) activity in carcinoma of uterine and cervix. Thus the erythrocyte is always susceptible to damage and decrease of catalase activity in uterine cervical carcinoma, leading to accumulation of free radicals which may be one of the factors for genesis of cervical cancer. Lowered super oxide dismutase and elevated lipid peroxide in cervical cancer patients suggests that elevated lipid peroxidation is closely associated with decreased super oxide dismutase activity [2]. No supporting evidence in uterine cancer is reported regarding superoxide dismutase and catalase activity. The glutathione peroxidase is another metallozyme, the activity of which was found to be decreased (p<.001) in all the three cancers (Table 2). This observation coincides with the report of Thomson[16] and Sundstrom[17]. A decrease in glutathione peroxidase activity may be due to selenium deficiency[18,19], though we have not estimated trace metal level. Moreover, the integrity of red blood cells is partially maintained by the enzymes glutathione peroxidase[20]. The glutathione appears to be pivotal, made up of three amino acids viz. cysteine, glycine and glutamic acid. It is a part of its metabolizing enzymes i.e. glutathione peroxidase and reductase. The significant decrease (p<.001) (Table 2) in blood glutathione is another finding in our study. It is well known that NADPH is necessary for reducing GSSG (oxidized glutathione) to GSH by glutathione reductase in the red cell[21]. Therefore the reduced level of GSH may be due to either a decrease in availability substrate (amino acid) for glutathione synthesis [22], or decreased activity of glutathione reductase [21]. The reason for these acquired enzyme deficiency is not clear but it may be suggested that biochemical abnormalities in the red cell precursor in cancer conditions may reduce the production and action of these antiperoxidative enzymes thereby debilitating the system to an inefficient state to manage free radical damage. By assessing the status of these enzymes we could indicate the oxidative damage in the cell at stage I of the disease along with clinical manifestations.

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