Status of Antioxidant Enzymes in Female Genital Cancer

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OBJECTIVE - To know the degree of lipid peroxidation and status of antioxidant enzyme as a marker in female genital cancer patients. **METHOD** - Erythrocyte lipid peroxidation, status of antioxidant enzymes and lipid profile level were estimated in blood from patients of gynecological cancer (n =100) and compared with those of socioeconomic and age matched healthy controls (n=50). **RESULTS** - There was significant increase in erythrocyte MDA level and marked decrease in antioxidant enzymes in ovarian, cervical and uterine cancer patients. Lipid profile was not significantly changed. **CONCLUSION** - Biochemically, female genital cancer onset is associated with nonsignificant change in lipid profile, decrease in antioxidant enzyme especially GSH – Px and increase in erythrocyte malondialdehyde (MDA). Glutathione peroxides (GSH Px) could be taken as a marker to know the early stage of female genital cancer, if periodic estimation of this enzyme is done after the age of 32

Key words : antioxidant enzymes, erythrocyte MDA

Introduction

Oxidative stress refers to a disturbance in pro - and antioxidant balance in favour of pro– oxidant. Oxidative stress issues come up when reactive oxygen species of free radicals like H_2O_2, hydroxides and epoxide evade or overwhelm the antioxidant protective mechanism of the cell[1]. Free radicals are capable of independent existence and contain one or more unpaired electron. They directly attack critical target molecules or attack poly-unsaturated fatty acid (PUFA). Malondialdehyde (MDA), a product of lipid per - oxidation which is reported to be higher in carcinomatous tissues than non - diseased organs[2,3].

Antioxidants like vitamin E also play an important role in protection against lipid peroxidation. The cell develops several lines of defence against the oxidative attack. The most important defence systems are of two types. One is scavenger enzymes of free radicals i.e. catalase (CAT), super oxide dismutase (SOD) and glutathione peroxides (GESH – PX) and the other is reducing substances such as reduced glutathione, cystein, vitamin C, tocopherol, carotene etc[4]. The function of these enzymes is to keep free radicals at the physiological level. In various female genital carcinoma, the activity of these enzymes were found to be reduced[5].

Material and Method

The study was carried out in different gynecological cancer cases. For the study, we have selected women in the age group of 30 to 58 years, suffering from ovarian, cervical, uterine and vulval cancer (n 100). These women had histopathological confirmation and were undergoing treatment in the Cancer Hospital and Research Institute, Gwalior. The blood samples were taken for analysis of various antioxidant enzymes EMDA and lipid profile. Simultaneously, the record of other physiological parameters like B.P., and Hb% was made. The vulval cancer patients being small in number were ignored from the study (n 6).

All blood samples were analyzed for erythrocyte lipid peroxidation[5], reduced gluthione[6] and antioxidant enzymes like glutathione peroxidase[7], catalse , super oxide dismutase[9] while lipid profile was done by standard kit method (span diagnostic ltd).

For statistical analysis, the data was compared to normal healthy control subjects of the same age group and socio-economic status. The written consent of the women and all ethical measures were taken prior to the study.

Result

The levels of erythrocyte MDA, reduced glutathione and antioxidant enzymes such as glutathione peroxidase, super oxide dismutase and catalase and the lipid profile in different female genial cancer patients were compared with age-matched controls. Table I give the types of cancer and number of cases with their age group and socioeconomic status. Erythrocyte MDA is significantly increased as compared to the control group ($p< 001$) and the level of antioxidant enzymes were significantly decreased in all the types of cancer ($p< 001$) (Table II). The lipid profile was not significantly changed as compared to that in the controls (Table III).

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Table - I: Characteristics Of Female Genital Cancer Subjects.

Types of cancer	No of cases	Age (years)	Socio economic status				
			Low	Lower Middle	Middle	Upper Middle	High
Cervical	41	32-55	25	10	3	2	1
Ovarian	35	37-58	18	9	2	3	3
Uterine	18	47-55	8	4	2	2	2

Table – II Status of Antioxidant Enzymes and Erythrocyte MDA in Different Female Genital Cancer Subjects

Types of Subjects	GSH Unit/dl	GSH Px Unit/gm Hb	SOD Unit/mg/Hb	CAT Unit/mg protein	Erythrocyte MDA incubation gm Hb for 2 hour incubation
Control	48.2 - 62.0	17 - 19.4	2.1 - 4.6	4.34 - 5.8	100 - 140.00
(n=50)	54.69 ± 3.59	18.19 ± 0.583	15 ± 0.59	4.84 ± 0.84	125.32 ± 14.01
	6.46%	3.23%	19.02%	9.93%	11.18%
Cervical	5.85 - 45.41	17.11 - 19.52	1.18 - 2.8	1.8 - 5.2	126 - 369
Cancer	22.68 ± 10.63[a]	13.15 ± 3.09[b]	2.22 ± 0.31[b]	3.09 ± 0.77[b]	187.76 ± 48.66[b]
(n=41)	46.88%	23.51%	14.25%	21.79%	25.91%
Ovarian	6.05 - 43.7	6.1 - 17.0	1.18 - 2.54	1.0 - 4.2	119 - 639
Cancer	19.55 ± 8.75[a]	12.65 ± 2.87[b]	2.22 ± 0.34[b]	3.13 ± 0.82[b]	96.57 ± 89.3[b]
(n=35)	23.73%	7.77%	0.84%	0.84%	225.19%
Utrine	10.93 - 40.09	6.73 - 19.9	1.14 - 2.46	2.0 - 4.33	140 - 288
Cancer	22.09 ± 7.80[a]	12.5 ± 3.46[b]	2.06 ± 0.34[b]	3.38 ± 0.79[b]	188.38 ± 35.2[b]
(n=18)	35.30%	72.50%	16.80%	23.4%	18.69%

values are- Min. – Max., Mean ± S.D., C.V.% [a] P<.001 Highly Significant, [b] P< .01 Significant

Table – III Status of Lipid Profile in Female Genital Cancer Subjects.

Types of subject	TC mmol	TG mmol	HDL mmol	VLDL mmol	LDL mmol
Control	3.8 - 6.2	0.85 - 1.7	0.7 - 1.7	0.39 - 0.78	2.05 - 4.00
(n=50)	5.30 ± 0.58	1.27 ± 0.19	1.31 ± 0.29	0.58 ± 0.86	3.41 ± 0.58
	11.04%	15.43%	22.58%	14.96%	17.24%
Cervical	3.10 - 6.88	0.7 - 2.82	0.5 - 3.60	0.62 - 1.31	2.13 - 4.91
Cancer	4.90 ± 1.06[a]	1.67 ± 0.76[a]	1.31 - 0.70[a]	0.79 ± 0.32[a]	4.08 ± 1.07[a]
	21.79%	45.74%	53.37%	40.90%	26.20%
Ovarian	3.59 - 7.64	0.22 - 3.35	0.28 - 2.04	0.5 - 1.43	2.16 - 5.99
Cancer	4.95 ± 1.01[a]	1.71 ± 0.74[a]	1.12 ± 0.52[a]	0.77 ± 0.35[a]	4.29 ± 1.09[a]
	20.45%	43.23%	46.93%	45.88%	25.39%
Uterine	2.30 - 6.33	0.7 - 3.08	0.45 ± 3.62	0.8 - 1.95	2.10 - 5.79
Cancer	4.46 ± 1.10[a]	1.63 ± 0.75[a]	1.24 ± 0.74[a]	0.95 ± 0.46[a]	3.80 ± 1.18[a]
	23.69%	46.15%	59.97%	62.24%	31.20%

Values are – Min. Max., Mean ± SD, CV% [a]NS – Non Significant as compared to control

Table – IV : Variation of Antioxidant Enzyme Status, Erythrocyte MDA and Lipid Profile in Female Genital Cancer Subjects.

Types of Cancer	GSH	GSH-Px	SOD	CAT	EMDA	TC	TG	HDL	VLDL	LDL
Uterine Vs Cervix	0.75	1.29	0.99	1.02	0.92	1.13	1.00	1.12	1.52	1.19
Uterine Vs Ovarian	0.87	1.28	0.79	1.02	0.56	1.15	1.06	2.22	1.35	1.22
Cervix Vs Ovarian	1.15	1.29	0.79	1.00	0.61	1.01	1.05	1.98	0.89	1.03

Values are in %

Discussion

Free radical mediated lipid peroxidation has been proposed to be critically involved in several diseases including cancer[10]. In uterine, cervical and ovarian carcinoma, we found increased lipid peroxide i.e. erythrocyte MDA level which is in agreement with the study of Christopher et al[11]. The increased lipid peroxide in proliferating cells leads to an increase in the serum lipid peroxide levels in cancer patients. The probable reason for the elevated level of serum lipid peroxide in cervical carcinoma may be due to poor antioxidant system (both enzymatic and nonenzymatic). This in turn leads to the accumulation of lipid peroxides in cancer tissues which are being released in to the blood stream. Dixit et al[12] have reported that the accumulation of hydrogen peroxide in combination with super oxide can generate hydroxyl radicals and singlet oxygen, which are potent initiators of lipid peroxidation in female genital carcinoma which may be due to its poor antioxidant defences. This is in agreement with the studies reported in lymphoma and hepatoma[13]. The enzymes SOD and catalase catalyze cells, defence reaction against the potential harmful effects of super oxide anion generated by a wide variety of biological process. We have found significant decrease ($P < 0.001$) in both super oxide dismutase and catalase activities (Table II) in carcinoma of female genital tract leading to a net increase in the level of super oxide free radicals. Thus the erythrocyte is always susceptible to damage and decrease in catalase activity in female genital carcinoma.

The reason for decreased level of GSH-PX is not clear but it may be suggested that bio-chemical abnormities in red cell precursors in cancer may reduce the production and function of these anti peroxidative enzymes there by debilitating the system to an inefficient state to manage free radical damages. On comparing three carcinomas it was observed in our study that significant variation was present in GSH and catalase. Further, we found significantly high level of EMDA ($P < 0.001$) (Table II). This may be related to damage of erythrocyte membrane due to decreased activity of antioxidative enzymes and increased level of lipid in serum. The increase of membrane lipid per - oxidation (EMDA) after loss of both structural integrity and biological properties of the membrane also increased the susceptibility of free radical damage[14]. In our study we did not find any significant correlation of lipid profiles with antioxidant enzymes.

Thus, at the onset of female genital carcinoma, overall deficiency of antioxidant enzyme takes place but the periodic investigation of GSH-PX and catalase could help in the management of early stages of female genital carcinoma.

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