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LETTER TO THE EDITOR

LIPID PEROXIDATION LEVELS IN PEPTIC ULCER AND GASTRIC CARCINOMA

Sir,

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Peptic ulcers and carcinomas are two major pathological conditions of the gastrointestinal tract. Malignancies of the G.I tract are relatively resistant to radiation therapy and benefit from chemotherapy remains modest, whereas an effective rational therapy still remains elusive in cases of gastro duodenal ulceration. One of the common denominators proposed in genesis of these diseases is free radical stress. Free radicals are highly reactive molecules, which are produced as a by-product of metabolism (1). A reactive free radical generated in the body reacts with non-radical and results in free radical chain reaction leading to formation of new free radicals. If the defence mechanism of body fails to combat them, these free radicals pose a threat of injuring tissues by reacting with cell lipids. Lipids in the cell membrane undergo degradation to form hydroperoxides. Polyunsaturated fatty acids, PUFA, are especially liable to lipid peroxidation. Lipid hydroperoxides decompose to form a variety of products including malondialdehyde (MDA). MDA was used as an indicator to assess oxidative damage of cells and tissues (2) and profile of antioxidant defence was studied as superoxide dismutase and catalase activities in the above stated studies.

Thirty cases of peptic ulcer proved by endoscopy (both duodenal and gastric ulcer) and an equal number of gastric carcinoma were selected from the out patient Department of Medicine and Gastroenterology, University Hospital, Banaras Hindu University, Varanasi. Gastric carcinoma patients were also confirmed by histopathological examination of the biopsy. Fifteen healthy age and sex-matched subjects were included following their informed consent to provide as control cases. Blood samples were collected form the antecubital vein and serum was separated. Levels of malondialdehyde (MDA) in the serum were examined in patients of peptic ulcer and gastric carcinoma and referred to those in healthy control subjects. All the patients included in the study underwent endoscopic examination. Biopsy from the patients of gastric carcinoma, in addition, was taken for histopathological examination.

The assay of malondialdehyde level (MDA) in the serum was performed by the technique of Philpot (3) with the suggested modification (4). A fresh stock reagent of TCA-TBA-HCI was prepared at the time of assay. 0.01% butylated hydroxytoluene was added to the stock reagent to abolish the metal catalysed auto oxidation of lipids (5).

Standard MDA solution was prepared from malondialdehyde bis (dimethyl) acetal solution obtained from Aldrich Chemical Co., USA. Two ml of stock reagent was added separately to 1 ml test sample, standard and blank respectively. All the samples were extracted with 4 ml of n-butanol and the optical absorbance was recorded at 530 nm in SICO spectrophotometer.

Antioxidant enzyme superoxide dismutase was assayed by the measurement of the ability of the enzyme to inhibit the auto oxidation of pyrogallol (6). Change in optical absorbance of sample with respect to blank per minute was recorded at 420 nm in the spectrophotometer. The enzyme inhibition caused by the serum was expressed in mg protein/ml of serum. Catalase activity was assayed by the decomposition of hydrogen peroxide (7). The activity was expressed as µM of H_2O_2 decomposed per mg protein/mt. Statistical analysis was done by paired t-test.

Lipid peroxide levels were assessed as malondialdehyde (MDA) levels in mMol/L in 75 individuals – comprising of 30 cases of peptic ulcer and equal number of gastric carcinoma cases. The results of both the groups were compared with age and sex matched 15 healthy individuals. Peptic ulcer patients were in the age group of 41.0 ± 12.7 years whereas the mean age of gastric carcinoma patients was 53.3 ± 8.7 years.

The patients of peptic ulcers and gastric carcinoma showed a significant increase in lipid peroxidation levels and parallel decline in superoxide dismutase and catalase activities in comparison to their control cases (Table I). The increase in lipid peroxidation level in peptic ulcer, with even greater increase in carcinoma is consistent to propose free radicals inflicting permanent alteration in genetic material, which may serve as an initial step in the process of carcinogenesis. The patients are further prone to oxidative damage as observed from the decline in antioxidant enzyme levels of super oxide dismutase and catalase activity. Severity of ulcer is known to increase with significant decrease in antioxidant status (8, 9).

Free radicals are produced in the

TABLE I: Status of lipid peroxidation (LPO), Superoxide dismutase (SOD) and Catalase (CAT) in peptic ulcer and gastric carcinoma patients.

Groups	*Number*	*Gender M/F*	*Age (Years)*	*LPO mMol/L*	*SOD mg Protein/ ml of serum*	*CAT µM of H_2O_2 decomposed/mg of protein/mt*
Control	15	10/5	33.5±0.02	0.32±0.034*	25.6±2.7	9.13±1.53
Gastric Ulcer	10	8/2	53.2±8.8	0.655±0.04*	20.2±2.7*	6.18±1.27*
Duodenal Ulcer	20	13/7	35.0±9.6	0.684±0.06*	22.8±3.1*	6.71±1.01*
Gastric Carcinoma	30	21/9	53.3±8.7	0.923±0.079*	19.1±1.9*	5.80±1.80*

Data is expressed as Mean±SEM.
*P value <0.001 when compared with respective control.

mitochondria of cell during biological oxidation and if not quenched rapidly, they damage the lipid membrane by peroxidation. Lipid peroxidation can be measured as diene conjugates and thiobarbituric acid- reactive substances (TBARS) assays of human tissues and body fluids. Oxidation occurs when high levels of oxygen react with exposed surfaces during respiration. It happens every time we take in a breath of air. Oxygen is required for energy generating combustion involving endogenous substrates and to detoxify xenobiotics. Oxidation reaction ensures that the molecular oxygen is completely reduced to water. During this process, oxygen acts as a terminal 4-electron acceptor and is eventually converted to stable chemical compound, water. However the reduction of oxygen is frequently incomplete, even under normal conditions or some time, univalent reduction occurs with electrons added one at a time and a series of chemical intermediates are produced which are highly reactive and obnoxious to living systems (10). Various antioxidant enzymes like super oxide dismutase, catalase and glutathione peroxidase control the accumulation of free radicals (11). Any imbalance in the activity of these enzymes normally leads to faulty disposal of free radicals and its accumulation. These reactive oxygen species besides lipid peroxidation are also responsible for oxidation of bases in cellular DNA and consequent mutagenic, cytotoxic and crosslinking outcomes. Resulting net uncontrolled expression of certain genes effects multiplication of cells leading to malignancy (1, 10, 11).

Reactive oxygen species has been implicated in gastrointestinal disorders, related to gastric hyper secretion and gastro intestinal mucosal damage (12). High free radical activity in patients of peptic ulcer and gastric carcinoma and a decline in the enzymatic activity of superoxide dismutase alongwith catalase observed in the present study supports oxidative damage of mucosa alongwith fall in antioxidant defence in development of gastric ulcers and carcinoma. Larger confirmation of the observations may help contemplating rational preventative and corrective strategies.

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