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Original Article

Measurement of Activity of Serum Enzyme Glutathione-S-Transferase as a Tumor Marker in Stomach Cancer

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ABSTRACT

Glutathione-s-transferase (GSTs) is a family of enzymes involved in detoxification of foreign compounds. They participate in antioxidant defenses through several mechanisms including reactive oxygen species. GSTs catalyze the binding of large variety of electrophiles to the sulfydryl group of glutathione yielding less harmful and more water soluble molecules, which can be excreted via bile or urine. Since most reactive, ultimate carcinogenic forms of chemicals are generally electrophiles, GST takes considerable importance as a mechanism for carcinogen detoxification. Efforts for early diagnosis of stomach cancer have been spread over the past two decades with limited success and tumor markers are appealing tools for this purpose. Keeping this in view the present study was undertaken to determine the activity of serum GSTs in different stages of stomach cancer.

KEYWORDS: GST, Stomach Cancer, Tumor marker, Chemotherapy.

INTRODUCTION

Several modifiable environmental, dietary and habitual risk factors have been associated with development of gastrointestinal cancers, causal relationship between tobacco usage and gastrointestinal malignancies have been demonstrated for several decades. Dietary factors that have been closely associated with stomach cancer are western style breakfast, diets high in antioxidants and diets low in salt. The incidence rate of stomach cancer is 5.7 per 100,000 men and 2.8 per 100,000 women. Tobacco, which is widely used in India, is major cause of the cancer of the upper digestive and respiratory tract.[1,2] Upper gastrointestinal cancers are highly lethal diseases unless diagnosed early.

In the recent year's glutathione-S-transferase (GSTs) has attracted interest in the field of cancer because their activity is readily increased in chemically induced tumors.[3,4] They have a considerably important role in detoxification of carcinogens. GSTs are present in many species and tissues of the human gastrointestinal tract. Likewise, the human GSTs were found to be over expressed in most of the tumors.[4,5] GSTs expression in response to tumor formation is probably a resistance mechanism by which cells can survive, and the source of plasma enzyme is mainly transformed cells with over expression of GSTs. Indeed GSTs are one of the enzyme systems induces by anticarcinogens and thus can prevent tumor formation .GSTs have also been suggested to play an important role in multiple drug resistance in cancer chemotherapy.[6] In view of this present study was under taken to assess, the clinical utility of GST enzymes in stomach cancer.

MATERIALS & METHODS

A. Selection of Patients

Total 42 cases of carcinoma of stomach were selected for this study. They were divided in three groups as normal control, stage II stage III. In normal control consist of 40, stage II group consist of 21and stage III group consist of 21. All patients were clinically and histological diagnosed. All patients with stage-III received chemotherapy including cisplastin, cyclophosphamide and doxorubicin. Out of 42 patients 28 were males & 14 were female of stomach carcinoma were selected for this study. For normal control total 40 normal healthy age and sex matched persons were selected. GSTs, activity was measured in the serum of control group (n=40) and in patients with stomach cancer (n=42).Subjects with stomach cancer and those without any evidence of any type of cancer participated in this study as listed in table.

B.Collection of samples

5ml of fasting blood sample were collected in plain bulb. Serum was separated and used for determination of activity of glutathione-s-transferase. Serum GSTs

activity was measured by, using 1-chloro-2, 4 dinitrobenzene as substrate (purchased from Sigma company), according to the procedure described by Habig et al.[7]

Data were expressed as mean ±SD. Mean values were assessed for significance by unpaired student t test. Probability values p < 0.05were considered statistically significant.

RESULTS

Mean GSTs activity in serum was significantly higher in patients with stomach cancer as compared to control group (p<0.001). The patients of stomach cancer after chemotherapy had significantly elevated activity of serum GSTs than before chemotherapy.

As shown in table3 mean serum GSTs activity (mean±SD) in control using CDNB as substrate was 5.36±0.59 IU/L. Serum GSTs activity of stomach cancerous patients was 10.30 + 2.35IU/L. GSTs activity was significantly higher in stomach cancer patients than control (p<0.001).The 39 of 42 patients of stomach cancer had increased activity of serum GSTs.

Table1: Distribution for control and patients of stomach cancer

	Number of subjects (male/female)	Age-range (years)
Normal control	40 (24/16)	40-55
Stomach cancer	42 (28/14)	25-75
Stage II	21 (15/06)	25-69
Stage III	21 (13/08)	47-75

Table 2: Comparison of serum GST, activity in control with stomach cancer

	No. Of cases	Mean ± SD	No. of cases (Value> normal)
GST Control	40	5.36±0.59	40 (100%)
GST	42	10.30 + 2.35	39 (93%)

All Values are expressed in IU/L, P Value <0.001

Table 3: Serum GST activity in stomach cancer patients before and after chemotherapy.

	No. Of Cases	Mean ±SD	p-value
Control	**40**	**5.36 ± 0.59**	**-**
Before Chemotherapy (Stage II)	**21**	**8.43 + 1.95**	**< 0.001**
After Chemotherapy (Stage III)	**21**	**12.02 + 1.09**	**< 0.001***

DISCUSSION

Glutathione-s-transferase (GSTs) is a family of enzymes involved in detoxification of foreign compounds. They participate in antioxidant defenses through several mechanisms including reactive oxygen species.[7] GSTs catalyze the binding of large variety of electrophiles to the sulfydryl group of glutathione yielding less harmful and more water soluble molecules, which can be excreted via bile or urine. Science most reactive, ultimate carcinogenic forms of chemicals are generally electrophiles, GST takes considerable importance as a mechanism for carcinogen detoxification.[8]

The ability of the GSTs to provide cellular protection against a wide variety of xenobiotics makes this enzyme family an attractive candidate biomarker of both cancer susceptibility and chemopreventive activity.[3,6]

In the present study serum GST was significantly higher (p<0.001) in patients with stomach cancer as compared to those obtained from normal healthy control group (TABLE 2). Similar findings reported by G.S.Mohammadzadeh et al.[4] The increased activity of total GSTs in serum can be due to over expression of isoenzymes of GST in tumor tissues. GST-π class was found to be over expressed in most of tumor.[9,10] However, there are doubts over the use of total GSTs activity as a marker for all types of tissues .The GSTs activity of plasma represents a non invasive biomarker of the cellular protection. The strong correlation between the GST- π activities of plasma and stomach tumor tissues has been reported.[11]

Our result showed a significant increased(p<0.001) activity of GSTs in stage-III (received chemotherapy) than stage-II patients (TABLE 3).Many studies also showed progressive increase of GSTs with advancing cancer and has been associated with poor prognosis and development of drug resistance.[9-12]

K.Johansson et al.[12] reported GSTs protect the cells from lipid peroxidation and H_2O_2which is increased by cisplastin, a chemotherapeutic drug .Our results show the association of serum GST and chemotherapy in stomach cancer. Elevation of serum GST activity in stomach cancer is probably resistance mechanism by which cells can survive and sources of plasma enzyme is mainly

transformed cell with over expression of GST.

Thus progressive increases of enzyme GST with advancing cancer have been associated with poor prognosis. Elevated level of GST may be associated with development of drugs resistance in both oesophagus and stomach cancer.

CONCLUSION

Serum GSTs measurement in plasma maybe useful tumor marker in stomach cancer and serum GSTs activity might be helpful to predict the response of chemotherapy in advance stages of cancer. GST values are helpful in predicting the radiation response.

Overexpression of GST in neoplasia may be causal, allowing replicative advantage, or casual, accompanying clonal expansion. The major limitation to its widespread use is the length of time needed for performance of the assay and until this is overcome it will remain primarily a research tool.

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