Assessment of Catalase Activity in Oesophageal Cancer- a Case Control Study

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ABSTRACT
Background: Oesophageal cancer has long been considered one of the deadliest malignancies, and the most common histological types are squamous cell carcinoma (SCC) and adenocarcinoma (AC), which together constitute more than 90% of oesophageal malignancies. It has been reported that oxidative stress plays a role in the pathogenesis of cancer. Catalase (CAT) is an endogenous antioxidant enzyme that neutralizes H2O2 into H2O and O2 and can be up regulated by oxidative stress. Objective: To assess oxidative stress by evaluating the activity of catalase in oesophageal cancer patients and to compare it with the healthy controls. Methods: Blood samples from oesophageal cancer patients (n=24) and healthy controls (n=24) were collected and plasma was separated and analysed for the catalase activity. Results: The BMI was found to be significantly lower in oesophageal cancer patients when compared to that of controls (p<0.001). The catalase activity was significantly high (p <0.001) in patients with oesophageal cancer when compared to the healthy controls. This may be due to the adaptive response to oxidative stress and indicative of dysfunction of the antioxidant defence system in oesophageal cancer patients.

INTRODUCTION

Antioxidant enzymes constitute one of the major cellular protective mechanisms against oxidative stress in the human body 1. Antioxidants are classified as enzymatic and non-enzymatic antioxidants. Enzymatic antioxidants include: glutathione peroxidase, glutathione reductase, catalase and superoxide dismutase. Non enzymatic antioxidants include vitamin E, vitamin C, carotenes and retinols and some transition metals such as zinc, copper and selenium 2. Anti-oxidants protect DNA from oxidative damage and thereby, protect cells against carcinogenesis 3.

Catalase (EC 1.11.1.6) is a hemoprotein containing four heme groups and exists as a dumbbell-shaped tetramer of four identical subunits. It is localized in the peroxisomes in blood, bone marrow, mucous membrane, kidney and liver 4.

Catalase, an endogenous antioxidant enzyme that neutralizes reactive oxygen species by decomposing H_2O_2 into H_2O and O_2 and therefore is up regulated by oxidative stress 5. Hence the present study was focussed to determine the activity of the antioxidant enzyme, catalase in patients with oesophageal cancer and in healthy controls.

RESEARCH DESIGNS AND METHODS:
STUDY SUBJECTS:

Blood samples of patients (n=24) with oesophageal Cancer were collected from the speciality Hospital, Madurai and from healthy volunteers (n=24) after getting their consent. The study was approved by the ethics committee of the hospital.

Plasma catalase activity was estimated by 6 and protein was estimated by 7. The activity of the enzyme was determined colorimetrically at 620nm and was expressed as μmol of hydrogen peroxide consumed / minute / mg protein. Hydrogen peroxide in the range of 2 to 10 μmoles/ml was used as standard. The data was represented as Mean±SEM. Mann-Whitney rank sum test was performed for catalase activity to find out whether there is any significant difference.

RESULTS:

It was observed in the study, the incidence of oesophageal cancer was high among males (75%) when compared to that of females (25%). The average age (years) in patients and controls was found to be about, 59.91±2.08 years and 42.25±1.86 years respectively.

In the present study, significant reduction in BMI was observed among the cases. [Table-1]. It was also noted that, the habit of smoking (38%) and combination of alcohol consumption and smoking (22%) was high when compared to the other combinations of risk factors like tobacco and smoking (6%) ; tobacco, alcohol and smoking (6%) in male patients, but was completely absent in female patients (Non smokers) (Figure 1).

Figure-1: Comparison of modifiable risk factors among cases.
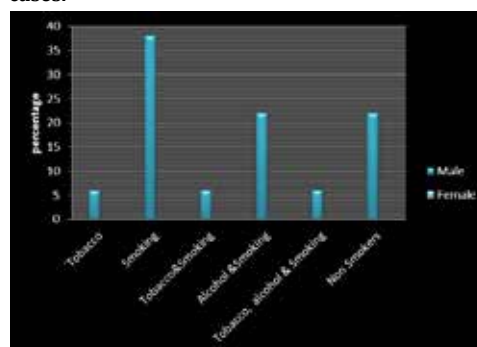
The catalase activity in oesophageal cancer patients highly significant than those of the healthy subjects (median 20000.0 inter quartile range [2500.0-70000.0]) μmols/min/mg protein compared with 499.5 [138.5-1818.0]) μmols/min/mg protein; p<0.001; Mann-Whitney rank sum test. (Table-1)

TABLE 1: Demographic data and catalase activity among oesophageal cancer patients and controls:

Demographic data	Cases (N=24)	Controls (N=24)
Male (%)	18(75%)	18(75%)
Female (%)	6(25%)	6(25%)

Age(years) Mean±SEM	60±2	42±1.8
BMI Mean±SEM	18.64±0.80	20.91±0.31
Catalase activity (µM/min/mg protein)	22316.66±4073.15[a]	681.91±108.13

[a] **Statistically significant (p<0.001)**

DISCUSSION:

Catalase has one of the highest turnover numbers of all enzymes; one catalase enzyme can convert 40 million molecules of hydrogen peroxide to water and oxygen each second 8. Catalase is a tetramer of four polypeptide chains, each over 500 amino acids long. The optimum pH was approximately 7 for human catalase activity 9.

In the present study the incidence of oesophageal cancer was predominant in males. Similar finding was also reported in a study conducted for the incidence of oesophageal cancer within the United States, with an overall 3:1 male-to-female ratio 10.

Common presenting symptoms of esophageal cancer are dysphagia, odynophagia, and progressive weight loss. 11. In the present study the reduction in body weight and lower BMI among the cancer patients can be attributed to the obstruction of the food passage due to the progression of the oesophageal cancer by which the individuals were deprived of solid foods and survived through liquid diet. People seek for medical support only when they develop symptoms like difficulty in swallowing and are diagnosed of oesophageal cancer at their advanced stages.

Several modifiable environmental, dietary, and habitual risk factors have been associated with the development of oesophageal carcinoma. Studies have provided reliable evidence that heavy alcohol consumption and cigarette smoking were the two personal habits that often coexists as important risk factors for oesophageal carcinoma 12. Earlier studies have demonstrated the relationships between tobacco usage and gastrointestinal malignancies 13, emphasizing the importance of smoking cessation strategies with appropriate treatment of pre malignant conditions and aggressive monitoring may significantly improve morbidity and mortality associated with late diagnosis.

In the present study the catalase activity was found to be high in patients with oesophageal cancer when compared with controls. It suggests that there is an increased oxidative stress accompanied by an adaptive increase of catalase activity. A study conducted in different cancer types have 14 also reported that catalase activity of patients with early cancer was found to be significantly higher than that of the controls. However, another study 15, conducted among the breast cancer patients have reported that the rate of catalase activity in cancer patients was significantly lower than controls.

Exposure to environmental factors, such as UV light, cigarette smoke, environmental pollutants and gamma radiation, accelerates the generation of ROS 16. Oxidative damage to cellular macromolecules can arise through overproduction of ROS and faulty antioxidant and/or DNA repair mechanisms. The resultant altered gene expression patterns evoked by ROS contribute to the carcinogenesis process. Recent evidence demonstrates an association between a number of single nucleotide polymorphisms (SNPs) in oxidative DNA repair genes and antioxidant enzyme genes with human cancer susceptibility 17, 18.

Dietary modifications seem to play a role in the reduction of cancers of the upper aerodigestive tract, suggesting a benefit from a diet high in fruits and vegetables. Scientists believe that fruits and vegetables contain high levels of phyto chemicals that may modify carcinogenesis through their antioxidant properties, suppressing the abnormal proliferation of early, preneoplastic lesions 19.

Though catalase is not essential for some cell types under normal conditions, it plays an important role in the acquisition of tolerance to oxidative stress in the adaptive response of cells 20. However, genetic variations in the antioxidant gene coding for enzyme may lead to decreased or impaired regulation of the enzymatic activity and alter ROS detoxification which in turn may modulate disease condition and reflects directly on the oxidative DNA damage and subsequently the individual's risk of developing cancer. Hence genetic polymorphism in catalase gene, associated with altered expression and its activity in cancer patients need to be investigated.

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