

Altered Level of Serum Magnesium in Patients with Esophageal and Lung Carcinoma

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ABSTRACT- Background: Esophageal and Lung carcinoma are the leading cause of years of life lost because of cancer and is associated with the highest economic burden relative to other tumor types. Epidemiological studies identify magnesium deficiency as a risk factor for these types of human cancers. The present studies were performed to concerning the contribution of magnesium to tumorigenesis and investigate the concentration of magnesium in esophageal and lung carcinoma.

Aims and Objective: The aim of this study was to compare the serum magnesium levels of patients with carcinoma of lung and esophagus patients and apparently healthy people.

Material and methods: Study group consisted of 50 clinically diagnosed subjects (Biopsy confirmed 25 cases with Esophageal carcinoma and 25 cases with Lung carcinoma). The control group consisted of 50 healthy subjects were included in the study. Venous blood samples of each lung and esophagus cancer were obtained and serum magnesium level was measured by Atomic Absorption Spectrophotometer measurements.

Results: In the study group, we were found mean concentration of serum magnesium was decreased in esophageal (1.40±0.13 mg %) and lung carcinoma (1.23±0.12 mg %) in comparison to controls (2.08 ± 0.45 mg %).

Conclusions: Serum magnesium was found statistically significantly lower in study group when compared with control (P<0.0001).

Key-words- Lung and Esophagus Carcinoma, Magnesium, Atomic absorption spectrophotometer

INTRODUCTION

Lung Cancer is the second most common cancer in women after breast cancer and is also the second leading cause of cancer-related deaths in women worldwide.^[1] Uncontrolled cell growth in tissues of the lung, may lead to metastasis, which is the invasion of adjacent tissue and infiltration beyond the lungs. The vast majority of primary lung cancers are carcinoma of the lung, derived from epithelial cells. Esophageal cancer is the eighth most common cancer and sixth leading cause of cancer deaths in the world, with the majority of cases occurring in developing countries.^[1]

About 90% of esophageal cancers worldwide are Squamous Cell Carcinomas (SCC), mostly occurring in defined high-incidence areas of low and middle-resource countries. Historically, the highest incidences are reported in regions of Central Asia. One such region is Kashmir Valley in Northern India.

Some minerals and Trace-heavy elements play significant role in human health and disease. Trace elements at optimum levels are required for numerous metabolic and physiological processes in the human body.^[2] Studies have shown that 46% of all critically ill cancer patients admitted to an ICU (intensive care unit) in a tertiary cancer centre presented with hypomagnesemia and they concluded that the incidence of hypomagnesemia in critically ill cancer patients is high.^[3] The incidence rises to 60 to 65% in all patients admitted into the intensive care units in which nutrition, diuretics, hypoalbuminemia, and amino glycosides may play important roles.^[4] Normal magnesium levels in humans 1.5-2.5 mg/dl and maintained

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at a fairly constant level of serum magnesium to label Hypomagnesaemia is below (1.56 mg/dl).

Over 300 enzymes systems that influence the metabolism of carbohydrate, amino acids, nucleic acid, protein and ion transport, require magnesium.^[5] The role of magnesium in fatty acid and phospholipid metabolism, that affect permeability and stability of membrane, were elucidated.^[6]

It has been proposed that magnesium is central in the cell cycle, and that its deficiency is an important condition in pre-cancerous cell transformation.^[7] Magnesium deficiency would therefore lead to physiological decline in cells setting the stage for cancer. It is known that carcinogenesis induces magnesium distribution disturbance, which causes magnesium mobilization through blood cells and magnesium depletion in Non-neoplastic tissue.

Magnesium deficiency seems to be carcinogenic and in case of solid tumours a high level of supplemented magnesium inhibits carcinogenesis.^[8] Alouane L. *et al.*^[9] found that patients with lung cancer had serum magnesium levels lower than in normal controls. It suggested the hypothesis stipulating an increased magnesium uptake by the tumor cells. Ahmad et al studied that the concentrations of zinc and magnesium in blood were significantly decreased in esophageal cancer patients. This suggested that these might play some role in carcinogenesis.^[10]

However, role of serum level of magnesium in causing such types of carcinoma has not been studied to great extent. Therefore, the present study was undertaken to estimate the serum levels of magnesium & their role in causing lung and esophageal carcinoma patients with apparently healthy controls.

MATERIALS AND METHODS

The study was carried out in the Department of Biochemistry in collaboration with the Department of Acharya Tulsi Regional Cancer Treatment and Research Institute in PBM Hospital, affiliated to Sardar Patel Medical College, Bikaner during 2013. The study was approved by ethics committee and informed consent was taken from all the patients. The study group consisted of 50 clinically diagnosed subjects (25 cases with Lung carcinoma and 25 cases with Esophageal carcinoma). The control group consisted of 50 Healthy subjects. Both study and control group were same socio-economic status with similar diet habits.

Inclusion Criteria

The criteria for the selection of patients were

- (i) Biopsy proved cases of Lung carcinoma and Esophageal carcinoma
- (ii) Who had not undergone any treatment i.e. chemotherapy or radio-therapy
- (iii) Who has not taken long course of any mineral supplement during last six months

Exclusion Criteria

The criteria for the selection of controls

- (i) Who were not suffering from any cancerous lesions
- (ii) Who has not taken any course of mineral supplement

Sample Collection and Storage

Blood samples were obtained by vein puncture and collected in a clean dry centrifuge tube. Standard precautions for trace element determination were taken, haemolysed samples were discarded. The blood was centrifuged at 3000rpm for 10 minutes and serum was stored at -4°C until the day of the test.

Biochemical Assessments

Serum magnesium concentration was determined by direct measurement method using Atomic absorption spectroscopy.^[11] Analytical reagent grade chemicals, standards were used. Water used for washing laboratory apparatus and for preparing solutions and standards was purified by deionization of redistilled water.

STATISTICAL ANALYSIS

The results were expressed as the mean \pm standard error (SE). One-way ANOVA was used for the comparison of mean values of the groups. Then, Student-t test was used to determine the difference between groups. In addition, Pearson's correlation analysis was carried out to determine the relationships among the variables.

RESULTS

The results as presented in the Table (1-2) show that the mean serum level of Serum Magnesium was altered in subjects having Esophageal (1.40 \pm 0.13) and Lung carcinoma (1.23 \pm 0.12). A statistically significantly lower ($p < 0.0001$) in serum magnesium levels was observed in patients with Esophageal and Lung carcinoma group than the healthy control group (Fig 1-2).

Table 1: Serum Magnesium Concentration (mg %) Comparison between Esophageal Carcinoma Patients (Case Group) with Normal Healthy Persons (Control Group)

Values	Normal Healthy Persons (Control Group) (n=50)	Esophageal Carcinoma Patients (Case Group) (n=25)
Mean	2.08	1.408
Range	1.31-3.00	1.18-1.66
SD	0.450	0.134
SE	0.063	0.026
t		7.335
p value		0.0001***

*** Highly significant

Table 2: Serum Magnesium Concentration (mg %) Comparison between Lung Carcinoma Patients (Case Group) with Normal Healthy Persons (Control Group)

Values	Normal Healthy Persons (Control Group) (n=50)	Lung Carcinoma Patients (Study Group) (n=25)
Mean	2.08	1.23
Range	1.31-3.00	1.06-1.53
SD	0.450	0.124
SE	0.063	0.024
t		9.252
p value		0.0001***

*** Highly significant

DISCUSSION

Trace elements and metals are known to play a vital role in metabolism. Magnesium is important for maintaining the integrity of DNA. Mg cations bind to DNA and reduce the negative charge density, thereby stabilizing the structure of DNA. It has been proposed that magnesium is central in the cell cycle, and that its deficiency is an important conditioner in precancerous cell transformation. In addition, immune competence (that eliminates transformed cells) is Mg dependent. Mg supplementation or deficiency was induced, relative to exposure to oncogens. Optimal Mg intake may be prophylactic against initiation of some neoplasm.

The finding of the present study indicates statistically significant decrease in serum Magnesium was recorded in Lung and Esophageal Carcinoma as compared to that of control subjects. It might be possible that due to general additional mechanisms by which magnesium might have protected against Cancer. Wolf et al reported that the decrease concentration level of serum magnesium was statistically significant in Lung carcinoma as compared to that of normal subjects was conducted a study and observed that the low magnesium induced immune-inflammatory response, which triggers cytokine production, oxidative stress and endothelial dysfunction which all participate to low magnesium related effects.^[12] Gurreo-Romero et al supported the hypothesis that serum magnesium in Lung carcinoma patients has very important role in maintain genoming stability and proposed several additional mechanisms by which magnesium might have protected against lung cancer.^[13]

As reported by siems et al the statistically significant decrease in serum magnesium level in Esophageal carcinoma might be due to low magnesium level induced to oxidative stress is at present the best candidate for triggering such an anti-proliferative signal, hormone, different pathways may be involved depend on whether the cells are diploid, immortalized or transformed.^[14] Zhi-Gang Sun et al. observed that the content of magnesium in esophagus cancerous tissues was significantly lower than that in the normal tissues ($p < 0.01$).^[15] Although, the mechanism underlying the deviation of serum magnesium in malignancy is not clear but however the decrease in serum magnesium level might be due to stress induced by the malignancy.

CONCLUSIONS

The serum magnesium concentration was found to be decreased significantly in esophageal and lung carcinoma as compared to that of control group might be due to low magnesium level induced to oxidative stress. So, magnesium deficiency can lead directly to cancer. Magnesium deficiency is carcinogenic, and in the case of solid tumors, a high level of supplemented magnesium inhibits carcinogenesis. Both carcinogenesis and magnesium deficiency increase the plasma membrane permeability and fluidity and modifications of cell

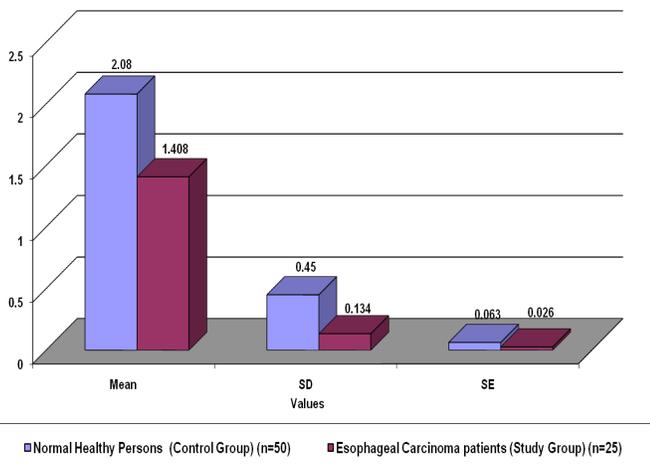


Fig: 1 Serum Magnesium Concentration (mg %) Comparison between Esophageal Carcinoma patients (Case Group) with Normal Healthy Persons (Control Group)

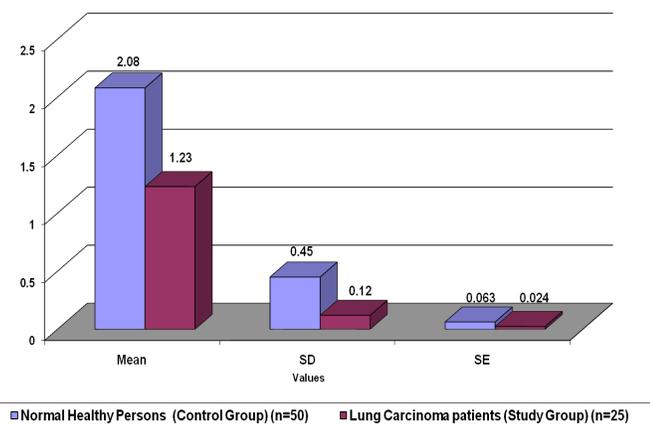


Fig: 2 Serum Magnesium Concentration (mg %) Comparison between Lung Carcinoma Patients (Case Group) with Normal Healthy Persons (Control Group)

membranes are principal triggering factors in cell transformation leading to cancer. Using cells from induced cancers, they found that there is much less magnesium binding to membrane phospholipids of cancer cells compared to normal cell membranes. It has been suggested that magnesium deficiency may trigger carcinogenesis by increasing membrane permeability. The membranes of magnesium-deficient cells seem to have a smoother surface than normal and decreased membrane viscosity, analogous to changes in human leukaemia cells. The result may be significant in understanding the possible contribution of serum magnesium in the patho-physiological process of developing cancer and may help in developing the strategies for prevention and early diagnosis.

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