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Full Length Research Paper

The status of trace elements in lymphoma and esophageal cancer patients: A case study

Bashir Ahmad[1]*, Humaira Ghani[1], Sadiq Azam[1], Shumaila Bashir[2] and Naseem Begum[3]

[1]Pharmabiotech Research Lab, Centre for Biotechnology and Microbiology University of Peshawar, KPK, Pakistan.
[2]Department of Pharmacy, University of Peshawar, KPK, Pakistan.
[3]Institute of Radioactive and Nuclear Medicines (IRNUM), Peshawar, KPK, Pakistan.

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Cancer is a life threatening disease. Many people die of cancer every year. Epidemiological studies suggest that alteration of trace elements in the body can contribute to the development of cancer. The aim of this study was to determine the concentration of zinc (Zn), copper (Cu), lead (Pb), Nickel (Ni), iron (Fe) and magnesium (Mg) in the blood, hair and nails of lymphoma and esophageal cancer (EC) patients in Khyber Pakhtunkhwa. The results reveal that the mean concentration of Cu, Pb and Ni increased significantly, while the concentration of Zn, Fe and Mg significantly decreased in the blood, hair and nails of lymphoma and EC patients. From this study it can be concluded that increased Pb, Cu, Ni and decreased Zn, Fe and Mg concentration in lymphoma and esophageal cancer patients suggest that these may play some role in carcinogenesis.

Key Words: Trace elements, lymphoma, esophageal cancer

INTRODUCTION

Esophageal cancer (EC) is the seventh most common cancer in the world. Every year about half a million people are diagnosed for EC and 83% people die of this disease worldwide (Parkin et al., 2005). In Pakistan, the incidence of EC is more common in Baluchistan and Khyber Pakhtunkhwa (Roohullah et al., 2005). Currently, no cancer registry exists in Pakistan and exact figures of cancer incidence are not available. According to the data collected by Institute of Radiotherapy and Nuclear Medicines (IRNUM) from different cancer centers, 80105 cancer patients visited these centers from 2004 to 2008. The number of patients registered in these centers increases each year. About 65243 patients were registered at IRNUM from 1994 to 2008. In these patients, lymphoma ranked 4th and EC ranked as 5th common cancer (Jafari and Safoora, 2009). Level of trace elements is altered in the body during certain diseases like cancer, diabetes, hypertension and coronary heart disease, defining their importance in diagnosing and predicting the chances of disease in normal individuals (Azin et al., 1998). Elemental concentration is not the same in all parts of the body. However, some parts of the body store them in significant amount. In hair, blood, serum, plasma, urine, saliva and nails, these elements are stored and have been therefore used as indicators for the estimation of trace elements in cancer patients (Mehra and Meenu, 2004; Guidotti et al., 2008). According to the United States (US) Environmental Protection Agency, milk, urine, saliva and sweat measure the component that is absorbed but excreted; the blood measures the component absorbed and temporarily in circulation before excretion and/or storage; the hair, nails and teeth are tissues in which trace minerals are sequestered and stored (Vaughan et al., 1991). Zinc (Zn) is an essential trace element; a mild deficiency in humans can adversely affect its clinical, biochemical and immunological functions. It protects against peroxidation and free radical formation as it is a constituent of the enzyme superoxide dismutase, which out competes damaging reactions of superoxide, thus protecting the cell from superoxide toxicity (Rogers et al., 1993). Copper (Cu) is an important trace element for normal functioning of the body but at very high concentration it becomes toxic. Cu plays an

*Corresponding author. E-mail: bashirdr2001@yahoo.com. Tel: +92-300-5881498.

important role in the angiogenesis of newly formed cancer cells. The function of Cu is to generate free radicals, damage tissues and replace Zn from many important enzymes, altering their function (Nasulewicz et al., 2004). Lead (Pb) can be toxic even at low concentrations. As a result of human activities, like vehicle exhaust (leaded gasoline), Pb smelters, battery plants, polluted drinking water from corroded pipes, ingesting soil or foods and food cans, it is widely present in our environment. High concentration of Pb causes cardiovascular problems, morphological renal and neurologic changes and embryo degeneration (Hayes, 1997; Pasha et al., 2010). Nickel (Ni) has been regarded as an important carcinogen. It is used to induce cancer in experimental animals and higher concentrations are responsible for high cancer rates. Ni can result in the formation of tumor through a variety of mechanisms. It prevents the intra-cellular communication and induces DNA deletions and inactivation of gene expression (Miki et al., 1987). Iron (Fe) is an integral part of many enzymes and proteins necessary for normal functions of the body. Its deficiency and excess, both are harmful to the body. At very high concentrations, it has the ability to favor the growth of cancer cells. It is carcinogenic due to its catalytic effect on the formation of hydroxyl radicals, which play an important role in oxidative damage of the body cells. It suppresses the activity of host defense cells and promotes the multiplication of cancer cells. In several studies, a positive correlation has been investigated between iron and cancer (Poljak, 2000; Reunanen et al., 1995; Zowczak et al., 2001; Wurzelman et al., 1996). Magnisium (Mg) has been classified as an anti-carcinogenic element, however it has both carcinogenic and anti-carcinogenic effects. It is involved in ATP production, DNA, protein synthesis and muscle contraction. Its deficiency can result in the formation of pre-cancerous cells. The process involved in the elimination of these cancerous cells also requires Mg (Son et al., 2007; Cortes and Mosses 2007). This study was aimed to find the concentration of Zn, Cu, Pb, Ni, Fe and Mg in the blood, hair and nail of lymphoma and EC patients and their healthy relatives visiting IRNUM, Peshawar, Khyber Pakhtunkhwa, Pakistan.

MATERIALS AND METHODS

The research work was carried out at Centre of Biotechnology and Microbiology (COBAM), Centralized Resource Laboratory (CRL), University of Peshawar and IRNUM, Peshawar.

Selection of patients and controls

Research subjects were selected under two broad categories of patients and controls. Patients of lymphoma and EC from IRNUM were selected to determine the level of trace elements. EC patients were of two types; Adenocarcinoma (AC) and Squamous cell carcinoma (SCC). Lymphoma patients were also of two types; Hodgkin Lymphoma (HL) and Non-Hodgkin Lymphoma (NHL). A consent form was signed from the patients prior to sampling and filling record sheets.

Criteria for including patients in the research study were; age (18 to 80 years), gender (both male and female), biopsy proved cancer patients, no history of chemotherapy or radiotherapy and those who had not used any mineral supplement for the last four months. Record sheets for esophageal and lymphoma cancer was designed separately. Samples were collected from lymphoma and EC patients for analysis. Close relatives of the patients were selected as controls, matched for socio-economic history and dietary habits with the same procedure adapted for patients.

Sample collection

Whole blood, hair and nails were collected from each patient and the control. About 5ml of blood was taken intravenously using sterile syringes. Blood was then immediately transferred to EDTA coated vacutainers to prevent blood clotting. Needle was removed while transferring blood from syringes to avoid hemolysis.

Dyed hairs were not sampled. Elemental concentration of hair vary along its length so, hair were collected by cutting hair near the scalp with the help of sterilized scissors. They were stored in a zip mouthed plastic bag and given proper number for identification. Subjects were asked to wash their hands and nails with a medicated soap followed by drying with a clean tissue paper. Nails were collected from fingers using sterilized scissors. They were transferred to the zip mouthed plastic bag and given proper number for identification.

Most sampling was carried out in summer, so blood collected was stored in IRNUM at 4°C until further treatment. Storage of hair and nails however pose no such problems and were stored in plastic bags in separate cartons.

Acid digestion of samples

The acid digestion of samples was carried out following the methods of Azin et al. (1998), Mohsen et al. (2008) and Tariq et al. (1995) with certain modifications. 0.5 ml of blood was taken in a conical flask. 10 ml of concentrated nitric acid (65%) was added to it and left overnight at room temperature. Digestion was completed by evaporating the solution completely from the samples. Final volume of the sample was brought to 100 ml by using 0.1% nitric acid.

The hair specimens were cut into small pieces and rinsed with alcohol followed by double distilled water. For digestion, 10 ml of 65% nitric acid was added to a conical flask containing 50 mg of hair and was left for 24 h at room temperature. Digestion was completed by complete evaporation of the solution. The final volume of the sample was brought to 100 ml using 0.1% nitric acid. Nail samples were weighed. Same steps for washing and digestion were carried out as described for hair.

Sample analysis by atomic absorption spectroscopy

Samples were finally analyzed by atomic absorption spectrometer (Perkin Elmer A Analyst 800) for Zn, Cu, Pb, Ni, Fe and Mg.

RESULTS AND DISCUSSION

The concentration of trace elements in blood, hair and nails of lymphoma and EC patients are presented in Tables 1 and 2. The mean Zn concentration in the blood,

Table 1. Concentration of trace elements in blood, hair and nails of Lymphoma patients and controls.

Type of cancer	Sample analyzed (µg/ml)		Zn	Cu	Pb	Ni	Fe	Mg
Lymphoma	Blood	Control	7.97±0.99	0.53±0.01	0.81±0.04	1.05±0.00	0.65±0.09	32.47±0.90
		Patients	4.23±0.42	1.65±0.14	1.17±0.08	1.63±0.13	0.61±0.10	29.42±1.88
	Hair	Control	174.99±9.57	18.00±0.08	15.91±0.73	5.37±0.23	22.85±1.30	120.34±3.4
		Patients	167.80±13.86	21.64±1.63	26.31±2.33	5.92±0.58	120.34±3.41	67.46±22.02
	Nails	Control	141.67±4.20	5.52±0.23	15.63±0.44	5.82±0.58	14.46±0.24	31.08±0.18
		Patients	120.37±12.62	7.78±0.57	21.31±1.65	9.03±1.46	12.63±1.44	15.84±4.30

Table 2. Concentration of trace elements in blood, hair and nails of Esophageal cancer patients and controls.

Type of cancer	Sample analyzed (µg/ml)		Zn	Cu	Pb	Ni	Fe	Mg
Esophageal cancer	Blood	Control	7.92±0.55	0.54±0.03	0.81±0.05	1.05±0.03	0.65±0.07	32.62±0.80
		Patients	4.80±0.65	0.80±0.07	1.01±0.05	2.09±0.35	0.59±0.07	25.68±1.48
	Hair	Control	175.32±11.48	18.03±0.55	15.91±0.99	5.40±0.45	22.82±1.81	120.98±10.32
		Patients	144.85±11.33	27.30±0.95	26.70±5.97	9.85±0.60	22.07±1.70	74.25±10.01
	Nails	Control	141.41±6.66	5.57±0.48	15.64±0.97	5.83±0.56	14.42±2.34	31.12±3.24
		Patients	120.41±9.54	7.88±0.56	24.58±4.78	9.70±0.82	13.62±2.15	18.82±7.11

hair and nails of the controls was higher than those for lymphoma and EC patients. In lymphoma and EC patients, the Zn concentration in blood was significantly different from the controls and was comparable to the study of Memon et al. (2007). The mean Zn concentration determined in the hair of lymphoma and EC controls was lower than the concentration determined in the hair of people in other parts of the country like Thar and Chakwal (Khalique et al., 2006; Afridi et al., 2005). Lower Zn concentration was found in the hair of lymphoma and EC cancer patients than in the controls. The mean concentration of Zn in the nails of the controls was much lower than the concentration found in the nails of the normal people (Sukmar and Subramanian, 2007). It was reported that Zn concentration in nails was significantly lower in patients compared to their healthy relatives and is in agreement with our results (Mohsen et al., 2008). Cu concentration was found significantly low in the blood, hair and nails of lymphoma and EC patients than for the controls ($p<0.05$). In the blood, hair and nails of normal people, Cu concentration can vary from 0.82 to 1.22, and 22 and 20.8 µg/mg respectively (Pasha et al., 2010; Sukmar and Subramanian, 2007; Rehman et al., 2004). Our determined Cu concentration was lower than this range. The findings of this study are consistent with those of Pasha et al. (2010) are consistent with those of Pasha et al. (2010) and (Tariq et al. (1995), in that the Cu concentration increased in blood and hair of cancer patients than in controls. Increased Cu concentration in the body can be attributed to the intake of Cu rich foods or to the use of Cu made cooking utensils (Tariq et al., 1995). This increased intake of Cu makes it carcinogenic by the formation of free radicals.

The study reveals that Pb concentration in the blood, hair and nails of lymphoma and EC patients was significantly increased as compared to the controls ($p<0.05$).The determined Pb concentration was higher than the concentration determined by Tariqet al. (1995) and Mehra and

and Meenu (2004), in the blood, hair and nails of normal people. Our observation of increased Pb concentration in the blood, hair and nails of lymphoma and EC patients appears to be in agreement with the results of Tariq et al. (1995), Azin et al. (1998), and Mehra and Meenu (2004). In all these studies, increased Pb concentration was associated with increased cancer risk. Increased Pb concentration in the blood, hair and nails can be due to environmental exposure. The subjects may have gotten increased Pb from the vehicle exhaust or by consumption of food contaminated with Pb. This increased Pb concentration results in the accumulation of the free radical in the body and thus causes cancer (Tariq et al., 1995).

There was a significant difference in the mean Ni concentration in lymphoma and EC patients and controls ($p<0.05$). Its blood, hair and nails concentration was higher in patients. Concentration of Ni in the blood, hair and nails of normal people has been reported as 1.11, 0.6 to 6.5 and 4.3 to 5.1 µg/mg, respectively (Tariq et al., 1995; Sukmar and Subramanian, 2007; Lyengar et al, 1998; Olabanji et al, 2005). The determined Ni concentration of hair falls within this range. However, in hair and nails, we found higher Ni concentration. This study indicates high Ni concentration in the blood, hair and nails of lymphoma and EC patients than in the controls. This is in support with the previous studies of Azin et al. (1998) and Tariq et al. (1995) indicating important role of Ni in carcinogenesis. In our country, untreated sewage is used for the purpose of irrigation. Food derived from such resources can be the source of higher Ni concentration in the blood, hair and nails of the people. The resulting increased Ni concentration favors the formation of tumors through inhibition of intracellular communication and DNA mutations (Stephanie et al., 2007). Fe was significantly lowered in the blood, hair and nails of lymphoma and EC patients as compared to its level in the normal control group of individuals. This is in contrast to the findings of Pasha et al. (2010) and Rogers et al. (1993). They reported higher concentration of Fe in the hair and nails of cancer patients. Mg concentration of blood, hair and nails was lower in patients as compared to their healthy relatives. This result appears to be in contrast to the previous study of Pasha et al. (2010) and Azin et al. (1998) who reported high Mg concentration in the hair of cancer patients. Increased Pb, Cu, Ni and decreased Zn, Fe and Mg concentration in lymphoma and EC patients suggest that they may play some role in carcinogenesis. The major difference between our study and other studies is that we found low Fe and Mg concentration in the blood, hair and nails of lymphoma and EC patients. Further studies are required to find out the reasons for the alteration of these elements in the cancer patients of Khyber Pakhtunkhwa.

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