BioMetals 1994, **7**, 45–48

Concentrations of some major and minor elements in larynx tissues with and without cancer

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Received 1 February 1993; accepted for publication 9 June 1993

In this study, concentrations of some major and minor elements were determined in the larynx tissues with and without cancer, and results obtained were statistically compared. No meaningful differences were found between sodium, potassium, calcium and copper concentrations in cancer tissues, corresponding cancer-free adjacent tissues and in control larynx tissues. Phosphate concentrations of the cancer tissues were higher compared with cancer-free adjacent tissues and control tissues. Iron, zinc and magnesium concentrations were found increased in both cancer and corresponding cancer-free adjacent tissues relative to control values. Intra- and inter-element correlations established within and between groups indicated that relations between elements were also disordered in the cancer tissues. We suggest that the changed element status of cancerous larynx tissues may arise from increased requirements of cancer tissues for some elements such as iron, zinc, magnesium and phosphate.

Keywords: cancer, larynx, metals

Introduction

In has long been known that some major and minor elements play an essential part in a number of biological processes. In this respect, it has been assumed that some elements may exert action, directly or indirectly, on the carcinogenic process (Tipton 1960, Schwartz 1975, Sunderman 1978, Sigel 1980). There are several reports indicating the existence of statistically meaningful differences between element concentrations of normal and cancerous tissues (Danielson & Stinnes 1970, Mulay *et al.* 1971, Valcovic 1980).

Relating to these subjects, many studies were performed in various kinds of cancer tissues such as breast (Murray *et al.* 1970, Santoliquido & Southwick 1976, Sherif & Howard 1984, Durak *et al.* 1991), colon and lung (Edgar & Howard 1989), cancelleous bone (Lappalainen *et al.* 1982), etc. Some researchers also investigated serum element concentrations of patients with various types of cancers (Fisher *et al.* 1976, Inutsuka & Araki 1978, Mellow *et al.* 1983) and found significant differences compared with normal subjects.

A few studies have been made to elucidate the element status of patients with and without larynx cancer. Among them, De Jeorge *et al.* (1966) found increased copper concentrations in the blood obtained from larynx cancer patients. In another study carried out by Drozdz *et al.* (1989), plasma zinc levels were found to be lower in the patients with larynx cancer. As far as we know, no attempt has been made to elucidate the element status of larynx tissues with cancer. For this reason, it has become the aim of the present study to establish the concentrations of some major and minor elements in larynx tissues with and without cancer.

Materials and methods

Samples

Fifteen squamous cell larynx cancer and 15 corresponding cancer-free adjacent larynx tissues from the same male patients ranging in age from 35 to 62 years (mean ± SD, 52.4 ± 16.4) were obtained by surgical operations from the Department of Otorhinolaryngology, Ankara University, Turkey. Seven control larynx specimens were obtained

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Table 1. Mean ± SD values (ppm) and Student's *t*-test results for elements

Groups	Zinc	Iron	Copper	Magnesium	Sodium ($\times 10^3$)	Potassium ($\times 10^3$)	Phosphorus ($\times 10^3$)	Calcium ($\times 10^3$)
A ($n = 15$)	25.64±10.94	59.25±20.73	9.56±8.60	202.5±151.3	11.51±2.76	0.76±0.29	1.04±0.59	0.44±0.11
B ($n = 15$)	24.70±12.16	70.00±20.98	7.14±7.10	181.4±109.9	12.60±0.85	0.79±0.26	0.48±0.26	0.39±0.12
C ($n = 7$)	10.20±8.00	12.00±5.79	10.00±4.53	90.00±20.50	11.87±0.60	1.00±0.26	0.40±0.22	0.48±0.08
P(A–B)	NS	NS	NS	NS	NS	NS	< 0.05	NS
P(A–C)	<0.025	<0.0005	NS	<0.05	NS	NS	<0.05	NS
P(B–C)	<0.025	<0.0005	NS	<0.05	NS	NS	NS	NS

A = cancer tissues.
B = corresponding cancer-free adjacent tissues.
C = control tissues.
NS = non-significant, $P > 0.05$.

from the Department of Forensic Medicine. Control specimens were immediately taken from dead male subjects, ranging in age from 30 to 55 years (mean ± SD, 48.2 ± 12.3). All the patients were smokers for about 15–30 years and one of them was alcoholic. Tissue element concentrations of this patient were not meaningfully different from the means of other patients, who only used alcohol in small doses. Unfortunately, we were not able to obtain information about the personal characteristics of the control subjects.

In the histopathological examinations, laryngeal tissue cells were found to be well-differentiated squamous cell cancer cells (Grade 1). The lesions of larynx tissues from two patients were ulcerative and others were proliferative. Since tissue element concentrations of two ulcerative patients were not meaningfully different from the means of general patient groups, we included these patients in the general proliferative cancer group.

After samples were cleaned, they were digested by heating in a nitric acid:perchloric acid mixture (5:1, v/v) and diluted by demineralized water to a defined volume. Analyses were carried out in the last clear solution.

Analyses

Sodium and potassium analyses were performed photometrically (Tietz *et al.* 1986). Phosphate concentration was determined according to Garber & Miller (1983). Iron, copper, zinc, calcium and magnesium concentrations were established by atomic absorption spectrophotometry (Varion Techtron Model AAS) and the standard addition technique (Kirkbright 1980).

Results

Results are given in tables. As shown in Table 1 there were no meaningful differences in sodium, potassium, calcium and copper concentrations between cancer tissues, corresponding cancer-free adjacent tissues and control ones. However, iron, zinc and magnesium concentrations were higher in both cancer and cancer-free adjacent tissues compared with control counterparts. Phosphate concentrations of cancer tissues were significantly higher than those of cancer-free adjacent tissues and control tissues.

In the intra-correlation analyses, we found that the relationships between calcium–phosphate, iron–copper, copper–zinc and copper–magnesium were disordered in cancer tissues, and the relationship between copper–magnesium was also disordered in cancer-free adjacent tissues relative to control larynx tissues. In the inter-correlations analyses, we found positive relationships between phosphate, magnesium and zinc concentrations of cancer tissues and of cancer-free adjacent tissues (Tables 2 and 3).

Table 2. Intra-correlation values within groups

Elements	Group ($n = 15$) A–A	Group ($n = 15$) B–B	Group ($n = 7$) C–C
Ca–P	0.50	−0.59	−0.75
Na–K	0.74	0.64	0.70
Fe–Cu	NC	0.50	0.72
Fe–Zn	0.50	0.52	0.70
Fe–Mg	NC	NC	NC
Cu–Zn	NC	0.50	0.70
Cu–Mg	NC	NC	0.72
Zn–Mg	0.67	0.86	0.80

A = cancerous larynx tissue.
B = cancer-free adjacent larynx tissue.
C = non-cancer larynx tissue.
NC = no correlation, $P > 0.05$.

Table 3. Inter-correlations values between groups

Elements	Groups ($n = 15$) A–B
Ca–Ca	NC
P–P	0.52
Na–Na	NC
K–K	NC
Mg–Mg	0.98
Zn–Zn	0.55
Fe–Fe	NC
Cu–Cu	NC

See Table 2 for details.

Discussion

Although there are several reports on the element concentrations of cancerous tissues, results obtained in the studies performed by different groups exhibit significant differences (Tipton 1960, Danielson & Stinnes 1970, Mulay *et al*. 1971, Schwartz *et al*. 1974, Sunderman 1978, Sigel 1980, Valcovic 1980). In general, different element concentrations were found in various kinds of cancer tissues (Tipton *et al*. 1960, Schwartz *et al*. 1975, Lappalainen *et al*. 1982, Edgar & Howard 1989). Therefore, we thought that establishment of major and minor element status of larynx tissues with and without cancer might contribute to the elucidation of element and cancer relations.

Looking at the results, high concentrations of iron, zinc, magnesium and phosphate in cancer tissues are of note. In fact, the concentrations of iron, zinc and magnesium were also higher in cancer-free adjacent tissues compared with controls. The phosphate concentration was highest in cancer tissues, which might demonstrate the high energy (ATP) requirement of cancer cells and tissues.

The relationships between elements indicate that element relations were also disordered in cancer tissues compared with non-cancer ones. In this regard, the calcium–phosphate relation was especially noteworthy. The calcium–phosphate relationship was negative in cancer-free adjacent tissues and control tissues, whereas it was positive in cancer tissues. Similarly there were positive relationships between iron–copper, copper–zinc and copper–magnesium concentrations in control tissues but no correlations were present between these elements in cancer tissues. Disordered intra-relations between the elements mentioned also demonstrated the changed element status of cancer tissues and cells. Accordingly, positive inter-correlations between phosphate, magnesium and zinc concentrations of cancer tissues and non-cancer adjacent tissues were in agreement with the high concentrations of these elements in cancer tissues and non-cancer adjacent tissues.

Our results indicated that concentrations of some elements in cancer, corresponding cancer-free adjacent larynx tissues and control tissues were different, and relations between elements were changed in the cancer tissues compared with non-cancer tissues. Although the results of this study show a good agreement with those of some studies, they are in contrast with others. Indeed, there is controversy in the literature about element concentrations in cancer tissues. In this respect, in a study carried out by Edgar & Howard (1989), it was found that trace element distribution in normal and malignant human tissues exhibits significant differences. Increases in some elements in breast tumors have also been reported in some other studies (Schwartz *et al*. 1974, Garber & Miller 1983). In the study carried out by Edgar & Howard (1989), copper and zinc concentrations were, however, found decreased in lung tumors and, similarly, calcium, copper and iron concentrations were found decreased in cancerous colon tissues, which were in agreement with some previous observations (Mulay *et al*. 1971, Renade & Panday 1984). In another study, Schwartz *et al*. (1974) found substantially higher potassium, phosphorus, copper, magnesium and zinc levels in malignant breast tissues. On the other hand, Wright & Dormandy (1972) found elevated zinc levels in cancerous liver tissue. In several studies, copper levels were found elevated in some types of cancer Tsilyunyk *et al*. 1965, Hrgovic *et al*. 1973, Inutsuka *et al*. 1973). As seen, there are great differences in the element concentrations of various kinds of cancerous tissues in the publications by several research groups.

How can we explain these results in terms of element and cancer relations. In our opinion, element imbalances observed in cancer tissues may arise from general changed cellular metabolism in the cancer process. It means that changed element status of the cancer tissues may not be a reason for, but in fact, a result of the disease itself. It seems quite possible that the requirement of cancer tissues for some elements such as zinc, iron, magnesium and phosphate is more than in non-cancer tissues, and this requirement leads to accumulation of some elements in some types of cancer tissues and partly in corresponding cancer-free adjacent tissues. This

event may also cause derangement of normal cellular relations among the elements in the tissues. This hypothesis was also proposed by Santoliquido & Southwick *et al.* (1976) in that malignant cells require more magnesium and zinc compared with normal cells. Differences established in metal concentrations may also reflect the known role of metalloenzymes in the anaerobic metabolism of malignancy.

Metals–cancer relationships need further study before reaching a definitive explanation.

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