Assessment of magnesium and calcium status in oral cancer patients

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ABSTRACT

Background: Tumor markers assist in the field of oral cancer. The aim of this study is to determine whether Mg and Ca ions could serve as tumor markers.

Materials and methods: A total sample of 53 individuals was studied that includes 33 patients with oral cancer and 20 well-matching control. Estimation of Mg and Ca levels in the lymphocytes of healthy individuals and patients, in the normal and diseased tissues of patients were performed using atomic absorption spectrophotometer.

Results: The values of both elements in the lymphocytes of patients were exchangeable according to the histopathological diagnosis. They were generally elevated in comparison to the control. (Ca = (3.983±3.214mean ±SD), Mg = (2.598±2.364 mean ±SD). Decrease levels of either elements in the diseased tissues observed in comparison to normal tissues in both sexes but it was more obvious in females than males (P<0.001 for Ca, P<0.002 for Mg).

Conclusion: Patients with oral cancer are immune suppressed and immune disturbance could be the cause of the results found in this work.

Keywords: Magnesium, Calcium, Lymphocytes, oral cancer.

INTRODUCTION

Magnesium is associated with so many different biological processes like its importance in oxidative-phosphorylation reactions (1) and for the mobilization of Ca in the bone (2). In addition Mg is a necessary cofactor of DNA, RNA and ribosomes, it is needed in binding mRNA to polysomal subunits and for the activation of aminoacetyl RNA complexes during protein synthesis (3,4).

Since sections of the chromosomes in the nucleus are held together by Ca & Mg, therefore, changes in the concentration of these metals might determine the degree of chromosomal aberrations (1). Mg is central in the cell cycle and its deficiency is an important conditioner in precancerous cell transformation and immunocompetence is Mg dependent too, Mg deficiency can paradoxically increase the risk of, or protect against oncogenesis (5).

Hypocalcaemia associated with cancer has been reported to be resulted from the production of circulating hormone like factors by the tumor or from elaboration of osteolytic factors by these tumors (6, 7).

There are several studies concerning the levels of Mg and Ca in the serum of patients with various human diseases and cancer (8, 9, 10, 11) in the serum, red cells and lymphocytes of patients with broncheal asthma (12), in the erythrocytes of leukaemic patients (13). Since there is no such study in oral cancer patients, therefore, this study was conducted to examine the alterations in the concentration of them in the tissue and lymphocytes of these patients.

MATERIALS AND METHODS

Fifty three individuals were included in this study. 33 of them were proven to have oral cancer (clinically and histopathologically), age range (18 months – 80 years) and 20 healthy individuals that served as control.

Patients were evaluated by full medical history for any existing systemic disease that may affect the parameters to be measured. Patients were collected from three major hospitals and the histopathological diagnosis was proved by three laboratories (Oral Pathology laboratory/ College of Dentistry and the laboratory of the hospitals the patients were from and/or a private laboratory).

The levels of both elements in the lymphocytes of patients and controls, as well as in cancerous and normal tissues of patients were estimated as follows:- venous blood was aspirated after an over night fasting by a stainless steel needle and collected in metal free tubes (haemolysed samples were always discarded). The sample was transformed in EDTA containing tube for lymphocyte
separation following the ficoll paque in vitro isolation procedure. 

Tissue biopsy was taken from the lesion and normal sites of the mucosa at the day of surgery, weighed by an electrical sensitive balance (sartorious 2432, maximum 200g), then digested by 4ml conc. Nitric acid and heated without boiling until the volume was reduced to about one drop lastly 4ml HNO₃ (1%) was added. Estimation of Mg and Ca was performed by direct aspiration of the prepared samples using (Perkin – Elmer 4000) atomic absorption spectrophotometer. 

Students (t) test and correlation test were used for statistical analysis, results were considered significant when P<0.05.

RESULTS
Out of the 33 patients, 14 were males and 19 were females’ age range (18 months – 80 years). The histopathological presentation of them is shown in table (1). Twenty cases out of 33 were diagnosed for the 1st time, the other 13 were recurrent tumors (six of them presented with recurrence of the primary lesion, the other seven presented with palpable, mobile lymph node only, which are proved histopathologically to be invaded by malignancy).

According to the TNM system; 12 cases were classified as stage III, 7 stage II, 6 stage I, one case stage IV, 7 cases the primary lesion has been resected and the patient presented with palpable, mobile lymph node.

The values of both elements in the lymphocytes of patients were exchangeable according to the histopathological diagnosis; however, they were generally elevated in total cases when compared to the normal. The mean value (2.598±2.364 for Mg; 3.983±3.214 for Ca), as shown in table (2).

Females had more lymphocyte Ca level than males (1.75 vs 5.2). While lymphocyte Mg level and range were nearly similar in both sexes table (2).

Regarding the changes in the level of either element in the tissues. There was a reduction in the diseased tissues when compared with the normal almost in all cases table (3). The alterations appeared more predominant in females, they showed significantly less Ca and Mg levels (P<0.001 and P<0.002 respectively) in cancerous tissues than normal, and there was a strong +ve correlation between the normal and diseased areas (r=0.75 for Ca, r=0.72 for Mg) tables (4 and 5). Although the same differences may be true for males but they did not reach significant level and there is no correlation between diseased and normal tissues in any of these elements. The levels of both elements in females' tissues (normal and diseased) were greater than those in males table (3).

On the other hand, when the mean values of these elements in lymphocytes were correlated with those of tissues both normal and diseased areas, only males showed a strong +ve correlation in Mg values (r=0.8); lymphocytes Mg level versus healthy tissues and a −ve correlation (r=−0.6), lymphocyte Mg level versus diseased tissue table (4), while females showed good unchanged correlation between lymphocytes Ca level and tissue in both diseased and normal sites table (5).

DISCUSSION
There are no available data concerning the values of those elements in the lymphocytes and tissues of patients with oral cancer or cancer of other sites in the body, therefore, our explanations for the changes of these minerals in the present work will be mainly speculations and suggestions.

According to the present study the values of Ca and Mg were exchangeable in the lymphocytes of cancer patients in relation to the histopathological diagnosis, thus, they can not be used as marker of the tumor activity whereas the elevation of either elements in the lymphocytes shown in table (2) could be explained on the basis that it is accumulative increase since lymphocytes reported to be inactive in cancer patients. 

Regarding the values of Ca and Mg in the tissues of patients, there is reduction in the levels of both minerals in diseased tissues in comparison with normal tissues (in all cases) table (3), this reflects that these tissues are unable to maintain minerals any more.

No significant correlation found between healthy and diseased tissues in males for both elements so that their values changed independently where as females showed a high correlation between healthy and diseased tissues for either elements these differences probably are related to certain hormonal differences between both sexes. This

* normal tissue was taken from the normal tissue surrounding the lesion
explanation could be also true for the results found regarding the correlation between lymphocytes and diseased tissues as well as lymphocytes and healthy tissues in either element for both sexes.

The negative correlation seen in tables (4, 5) may be as a result of small number of patients included in this correlation particularly males, n=5.

All the findings observed in this work leads to one direction that patients with oral cancer are immune suppressed and the condition correlates positively with the severity of the case, patients with stage I and stage II tumors have been shown to have relatively normal levels of cellular immunity (16). Since our patients were mostly referred to stage III, thus the hypothesis that immune disturbance could be the cause of these results may be considered true but further explorations are needed to confirm this hypothesis.

**Table (4): The relationship between lymphocytes \( (\mu g/mm^3) \) and tissue \( (\mu g/mg) \)
Mg in patients with oral cancer.**

<table>
<thead>
<tr>
<th></th>
<th>Sex</th>
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<th>t</th>
<th>p</th>
<th>df</th>
<th>n</th>
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<td>Healthy vs diseased tissue</td>
<td>Male</td>
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<td>0.5141</td>
<td>0.620</td>
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<td>11</td>
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<td>0.721</td>
<td>3.759</td>
<td>0.002*</td>
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<td>15</td>
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<td>Lymphocyte vs healthy tissue</td>
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<td>2.361</td>
<td>0.099</td>
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<td>5</td>
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<td>0.165</td>
<td>0.873</td>
<td>7</td>
<td>9</td>
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<td>1.304</td>
<td>0.283</td>
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<td>5</td>
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<td>-0.114</td>
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<td>0.769</td>
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**Table (5): The relationship between lymphocytes \( (\mu g/mm^3) \) and tissue \( (\mu g/mg) \)
Ca in patients with oral cancer.**

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**REFERENCES**

7) Tsao SW, Burman JF, Caster RL. Hypercalcemia and in vitro osteolysis associated with xenografts of