Trace Elements: Can They Have A Role in Diagnosis of Bladder Cancer?

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ABSTRACT

This study included 60 patients with different urinary bladder troubles and their ages ranged from 18 to 65 years. Our patients were divided into 3 groups. Group A included 40 patients with different types and grades of urinary bladder carcinoma, group B included 10 cases with urine analysis showing pyuria and group C included 10 patients with urine analysis showing hematuria. Urine changes in the last two groups were non-malignant and non-calcular in origin. Ten persons aged from 20 to 60 years were included as a control group. Twenty four hours urine samples were collected from the patients and controls. They were centrifugated and ashing was done by heating the residue at 600 degree in an oven for 48 hours. The ash was subjected to atomic emission spectroscopic study to detect the trace elements. The results showed specific pattern for each group of patients. Also, in the malignant group the level of trace elements was variable according to the type and grade of the malignancy. So trace elements could be used as a diagnostic tool for bladder carcinoma but further studies and follow up are recommended.

Key words: Bladder tumors, trace elements

INTRODUCTION

Trace elements are required in small concentrations as essential components of biological enzyme system, or structural portions of biologically active constituents. They constitute, in toto, less than 0.01% of the total body weight. Urine analysis of trace metals forms a significant role in clinical chemistry, but the optimal preparation and analysis of urine samples has not been investigated. Trace elements exist in the human body in free or combined form which have electrochemical, catalytic and structural functions.

In some reports, urinary excretion of trace elements changed in some diseases. The role of trace elements in malignancy has been the subject of interest and reports of many authors are often conflicting and contradictory.

The purpose of this study was to evaluate the trace elements level in urine of patients with urinary bladder carcinoma as a diagnostic tool; also, evaluation of trace elements in urine of patients with pyuria and hematuria of non-malignant, and non-calcular origin.

MATERIALS & METHODS

This work was performed on 60 patients with different urinary bladder troubles. Their ages ranged from 18 to 65 years. Patients were subjected to complete clinical and urological examination. They were divided into:

• Group A: including 40 patients with cancer bladder of different types and grades where cystoscopy and biopsy were done to prove the histological type and the grade of the bladder carcinoma.

• Group B: including 10 cases with urine analysis showing pus cells over 100 per high power field.

• Group C: including 10 patients with urine analysis showing red blood cells over 100 per high power field. Urine changes of group B and C were of non-malignant and non-calcular origin.

• Ten persons aged from 20 to 60 years were included as a control group.

Twenty four hours urine samples were collected from all the patients and controls; They were kept in refrigerator till the whole samples were collected. All samples were studied in the National Research Center where they were
centrifuged by centrifuge 50,000 cycles/minutes for 10 minutes. The residue was freeze dried. Drying was done by heating the residue at 600 degree in an oven for 48 hours till fixation of the weight (i.e. only inorganic component were left). The ash was subjected to atomic emission study to establish whether an element was detected or not in the sample. Also it gave the concentration level of the element in the sample. The spectrograph used was a medium quartz ultraviolet (Zeiss Q24).

RESULTS

According to the histopathological findings of the urinary bladder, there were 27, 10 and 3 cases which were transitional, squamous and adenocarcinoma respectively (table 1).

Table (1) : Number distribution of the pathological types and grading of the urinary bladder carcinoma

<table>
<thead>
<tr>
<th>Grade</th>
<th>Transitional cell carcinoma</th>
<th>Squamous cell carcinoma</th>
<th>Adenocarcina of the urinary bladder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>8</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Grade II</td>
<td>11</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Grade III</td>
<td>8</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
<td>10</td>
<td>3</td>
</tr>
</tbody>
</table>

The level of the trace elements in the cancerous urine samples was recorded and tabulated (Table 2)

The results were variable according to the type and the grade of the urinary bladder carcinoma but in general there was a decrease in the sodium level.

From table 2 it was observed that:

a) Transitional type showed the following characters:
   - Decrease level of copper and sodium in all grades.
   - Increase level of aluminum, boron, calcium and phosphorus in all grades.

b) Squamous type showed the following characters:
   - Decrease level of sodium in all grades.
   - Decrease level of copper in grade I and II.
   - Increase level of magnesium, phosphorus and silicon in all grades.
   - Increase level of aluminum, boron and calcium in grade I and II.

c) Adenocarcinoma type showed the following characters:
   - Decrease level of copper and sodium.
   - Increase level of aluminum, boron, calcium, phosphorus and silicon.

Table (2): Shows the level of the elements in the different types and grades of urinary bladder carcinoma and control group.

<table>
<thead>
<tr>
<th>Element</th>
<th>Control</th>
<th>Sq G1</th>
<th>Sq G2</th>
<th>Sq G3</th>
<th>Tr G1</th>
<th>Tr G2</th>
<th>Tr G3</th>
<th>Ad. Ca</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aluminum</td>
<td>1%</td>
<td>3%</td>
<td>3%</td>
<td>1%</td>
<td>3%</td>
<td>2%</td>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>Boron</td>
<td>0</td>
<td>0.03%</td>
<td>0.002%</td>
<td>0</td>
<td>0.001%</td>
<td>0.003 %</td>
<td>0.001%</td>
<td>0.002%</td>
</tr>
<tr>
<td>Calcium</td>
<td>3%</td>
<td>5%</td>
<td>5%</td>
<td>3%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Copper</td>
<td>0.3%</td>
<td>0.1%</td>
<td>0.03%</td>
<td>0.3%</td>
<td>0.1%</td>
<td>0.1%</td>
<td>0.1%</td>
<td>0.03%</td>
</tr>
<tr>
<td>Magnesium</td>
<td>3%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
<td>4%</td>
<td>3%</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Sodium</td>
<td>&gt;10%</td>
<td>8%</td>
<td>3%</td>
<td>8%</td>
<td>8%</td>
<td>8%</td>
<td>5%</td>
<td>8%</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>1%</td>
<td>6%</td>
<td>10%</td>
<td>8%</td>
<td>7%</td>
<td>7%</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Silicon</td>
<td>0.1%</td>
<td>6%</td>
<td>2%</td>
<td>3%</td>
<td>3%</td>
<td>3%</td>
<td>1%</td>
<td>1%</td>
</tr>
</tbody>
</table>
Comparing with control and malignant groups, the level of trace elements was recorded in 20 cases of hematuria and pyuria divided equally into two groups (table 3). These patients presented with hematuria (> 100/HPF) or pyuria (> 100/HPF) due to urological diseases other than malignancy or stones.

The results of cases of hematuria and pyuria were compared with the results of malignancy in table 3.

Table (3): Changes of the trace elements in the different pathological and control groups

<table>
<thead>
<tr>
<th>Element</th>
<th>Control</th>
<th>Hematuria</th>
<th>Pyuria</th>
<th>Malignancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aluminum</td>
<td>1%</td>
<td>1%</td>
<td>3%</td>
<td>1-3%</td>
</tr>
<tr>
<td>Boron</td>
<td>0</td>
<td>0</td>
<td>0.01%</td>
<td>0</td>
</tr>
<tr>
<td>Barium</td>
<td>0.3%</td>
<td>0.1%</td>
<td>3%</td>
<td>0.01-1%</td>
</tr>
<tr>
<td>Calcium</td>
<td>3%</td>
<td>1%</td>
<td>5%</td>
<td>3-5%</td>
</tr>
<tr>
<td>Copper</td>
<td>0</td>
<td>0.1%</td>
<td>3%</td>
<td>0.01-1%</td>
</tr>
<tr>
<td>Iron</td>
<td>0</td>
<td>1%</td>
<td>0</td>
<td>0.001-0.01%</td>
</tr>
<tr>
<td>Magnesium</td>
<td>3%</td>
<td>0.1%</td>
<td>5%</td>
<td>3-5%</td>
</tr>
<tr>
<td>Sodium</td>
<td>&gt;10%</td>
<td>1%</td>
<td>&gt;10%</td>
<td>3-8%</td>
</tr>
<tr>
<td>Nickle</td>
<td>0.001%</td>
<td>0</td>
<td>1%</td>
<td>0-1.1%</td>
</tr>
<tr>
<td>Lithium</td>
<td>0.1%</td>
<td>0</td>
<td>1%</td>
<td>0.01-0.1%</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>1%</td>
<td>0.1%</td>
<td>3%</td>
<td>3-10%</td>
</tr>
<tr>
<td>Silicon</td>
<td>0.1%</td>
<td>3%</td>
<td>3%</td>
<td>1-6%</td>
</tr>
</tbody>
</table>

From Table (3), it was observed the following:

a) Patients presented with pyuria (group B) showed:
   1. Increase level of lithium, Nickle and copper in comparison with malignant and control groups.
   2. Presence of Barium.
   3. Increase Aluminum, calcium, magnesium, phosphorus and silicone levels compared with control group.
   4. Boron and iron were not detected.

b) Patients presented with hematuria (group C) showed
   1. Increase iron level compared with malignant and control groups.
   2. Decrease calcium, magnesium, sodium and phosphorus levels.
   3. Disappearance of Nickle and lithium.
   4. Increase silicon level compared with control group.
   5. Boron and barium were not detected.

DISCUSSION

In the last few years there were trials to detect the changes of the trace elements which may occur in pathological and nonpathological conditions(3,4,7,8). Both ethanol and protein malnutrition cause zinc depletion and increase urinary zinc and manganese excretion, whereas ethanol also increases urinary iron excretion and liver manganese(8). These changes may be observed in the tissues and body fluids as blood and urine(3,4,7,8).

It is well known that malignancy is not a simple process as malignant cells are rapidly multiplying cells so they show an increase in the basic requirements for their division. Study of this point showed that the increase of such basic requirements could be considered as a diagnostic spot light for urothelial malignancy. In some literature, there was a relation between malignancy and trace elements(5-6).

Silverbeig (1984) studied the trace elements in breast cancerous tissues and body fluids (serum and urine) and he found that trace elements level in serum and urine did not reflect the state of malignancy(6). But he revealed that malignancy affected the tissue levels of calcium, nickel, zinc, selenium and rubidium(6).

In another study, prostatic zinc and magnesium levels showed marked increase in hyperplastic prostate, while in cancer prostate the zinc level decreased(6). Men who work with batteries and are chronically exposed to cadmium, a known antagonist of zinc, have been
shown to have a higher incidence of prostatic carcinoma\(^9\).

In this study, using the spectroscopic techniques for detection of trace elements gave us an idea about the minute levels in the urinary sediment (part per million per mg dry sample) so any changes which could not be detected by other techniques (mg/dl) could be easily and early detected by this technique. This was proved in the other reports\(^{4,10}\). In this work, urine trace elements defined by spectroscopy was measured in patients who had different types and grades of urinary bladder carcinoma.

From our data it was observed a definite and specific relation could be obtained to diagnose or suspect the cell of the tumour as in the urine samples of squamous carcinoma and grade I transitional cell carcinoma, the magnesium level increased while it did not increase in adenocarcinoma. Also it was very evident from the above tables that there is a strong relation between some trace elements and grading of the tumor irrespective of its histopathological type. This was observed in the squamous cell carcinoma as the aluminum, boron and calcium levels increased in grade I and II only. Also, copper level decreased in grade I and II squamous cell carcinoma while in the grade III it was as the control level. Patients who had transitional cell carcinoma, magnesium level increased in grade I only.

Our work was extended to study the trace elements changes in cases of pyuria and hematuria of non-malignant and non-calcular origin. The results revealed, that there were specific pattern for each group. Comparing our data with another study of trace elements in urine of calcular patients, there were decreased levels of aluminum and sodium and increased levels of boron, calcium and magnesium\(^{11}\). This confirmed that benign lesions had specific pattern of trace elements. From the previous data we concluded that trace elements level in urine of bladder carcinoma had its specific patterns, which differ from the non-malignant diseases of the urinary tract. These findings need further evaluation and follow up to be used as a diagnostic tool for bladder carcinoma.

**REFERENCES**

Appleton and Lange, California, 1988, P 330 - 334.

