SERUM LEVELS OF CALCIUM AND MAGNESIUM IN PATIENTS INFECTED WITH *SCHISTOSOMA HAEMATOBIUM* AND THOSE WITH BLADDER CARCINOMA

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Abstract

Background: Schistosomiasis is an ancient human disease with universal correlation between the endemicity of *S. haematobium*, genitourinary schistosomiasis and the frequency of bladder carcinoma. Calcium is the fifth most abundant mineral element in the human body and clearly correlated with T-cell activation. Magnesium is the fourth most abundant cation in the body with suggested a role of magnesium in the humoral antibody responses.

Objective: To correlate the serum levels of calcium and magnesium during S. haematobium infection and the immunosuppression state associated with this disease in addition to their possible role in the development of bladder carcinoma.

Methods: 200 individuals were included in this study (56 patients with acute schistosomiasis haematobium, 18 with chronic schistosomiasis, 20 with chronic schistosomiasis with bladder carcinoma, 50 with bladder carcinoma and 56 healthy controls). Venous blood was collected from each individual and the levels of calcium and magnesium were estimated in the serum of each individual.

Results: Calcium levels were found to be significantly lower in patients with acute schistosomiasis and significantly higher in patients with chronic schistosomiasis with bladder carcinoma when compared to the healthy controls. No significant difference was found between the levels in patients with chronic schistosomiasis and the healthy controls. Magnesium levels were found to be significantly lower in patients with acute schistosomiasis, chronic schistosomiasis with bladder carcinoma and bladder carcinoma, whereas no significant difference was found in those with chronic schistosomiasis, when compared to the healthy controls.

Conclusion: Because calcium and magnesium were found to be vital in the immune responses, the alteration in their levels might be one of the factors for the development of bladder carcinoma in patients with schistosomiasis.

Key words: *Schistosoma haematobium*, calcium, magnesium, bladder carcinoma.

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Introduction

Schistosomiasis is an ancient human disease, representing today a major public health problem. It is endemic in 76 countries, including Iraq, with an estimated total population of 200 million people affected. Still there are about 600 million people at risk[1,2]. In addition to the long survival of the parasite in humans, there is universal correlation between the endemicity of *S. haematobium*, genitourinary schistosomiasis and the frequency of bladder carcinoma[3].

Calcium is the fifth most abundant mineral element in the human body[4]. In addition to its obvious importance in skeletal mineralization, calcium plays a vital role in such basic physiologic processes as blood coagulation, platelet activation, neural transmission, enzyme activity, maintenance of normal tone and excitability of skeletal and cardiac muscle[5,6]. Moreover, a correlation was found between calcium levels and T-cell activation[7]. Hypocalcaemia has also been found to occur secondarily to magnesium deficiency and renal failure[8]. On the contrary, hypercalcaemia has been associated with various tumors, including epithelial ones[4,9,10].

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Magnesium is the fourth most abundant cation in the body and is essential to many physiologic processes. It is an activator of various enzymes[9,11]. Animal experiments suggest a role of magnesium in the humoral antibody responses[12].

This study was conducted to correlate the serum levels of calcium and magnesium during *S. haematobium* infection and the immunosuppression state associated with this disease in addition to their possible role in the development of bladder carcinoma.

Materials & Methods

Subject selection

The individuals studied were divided into 5 groups:

Group 1: Those with acute schistosomiasis haematobium (56 individuals). They were diagnosed as so by finding viable ova in their urine. Those individuals were inhabitants of Belad-Rouz in Diyala Governorate, about 50 kilometers northeast of Baghdad.

Group 2: Those with chronic schistosomiasis (18 individuals). They were diagnosed as so by finding calcified ova in the bladder wall during cystoscopic examination. Those individuals attended the Al-Kadhimiya teaching Hospital, Al-Karama Teaching Hospital and private clinics in Baghdad.

Group 3: Those with chronic schistosomiasis who had developed bladder carcinoma (20 individuals). They were diagnosed as so by finding calcified ova in the bladder wall and the presence of the tumor during cystoscopic examination and histopathological examination of biopsies obtained by transurethral resection of bladder tumor. Those individuals attended Al-Kadhimiya teaching Hospital, Al-Karama Teaching Hospital and private clinics in Baghdad.

Group 4: Those with bladder carcinoma (50 individuals). They were diagnosed as so by cystoscopic examination and the diagnosis being confirmed by the histopathological examination of biopsies obtained by transurethral resection of bladder tumor. Those individuals attended Al-Kadhimiya teaching Hospital, Al-Karama Teaching Hospital and private clinics in Baghdad.

Group 5: Healthy controls. 56 healthy individuals were selected for this study, 28 males and 28 females. Their ages ranged from 2-80 years.

Any individual who is a smoker, alcohol consumer, under any kind of therapy or with any other diseases (s) was excluded from the study.

Blood collection

2ml of venous blood was collected from each individual after disinfecting the anti-cubital fossa with 70% ethanol (Riedel-de Haen). Venipuncture was performed with a 2ml disposable syringe with a 23-gauge needle. Serum was obtained by centrifugation of the blood, after standing for 30 minutes at room temperature, at 2000rpm, 4^{o}C for 10 minutes.

Estimation of calcium and magnesium levels

The serum calcium and magnesium levels were determined using flame atomic absorption spectrophotometer (Perkin-Elmer 400) using acetylene as a fuel gas. The wavelengths used were 422.7 nm and 285.2 nm for calcium and magnesium respectively. Calculations were made using the best-fit line of regression equation of standard concentration curve.

Statistical analysis

The data were analyzed statistically using Student's t-test[13].

Results

Table 1 shows the levels of calcium and magnesium in the serum of individuals in the five groups. The levels of calcium in patients with acute schistosomiasis were found to be significantly lower ($P \leq 0.01$) than those in the healthy controls. On the

contrary, the levels in those with chronic schistosomiasis with bladder carcinoma and bladder carcinoma were found to be significantly higher (P ≤0.01) than those in the healthy controls. However, no significant difference was found between the levels of calcium in patients with chronic schistosomiasis and the healthy controls.

Magnesium levels were found to be significantly lower (P ≤0.01) in patients with acute schistosomiasis, chronic schistosomiasis with bladder carcinoma and bladder carcinoma, when compared to the healthy controls. No significant difference was found in the levels of magnesium when comparing the patients with chronic schistosomiasis and the healthy controls.

Table 1: Serum levels of calcium and magnesium (mg/dl ± standard error) in the serum of patients infected with *Schistosoma haematobium* and those with bladder carcinoma in comparison to the healthy controls.

Group / Elements	H.C.	A.S.	C.S.	C.S & B.C.	B.C.
Calcium (mg/dl)±S.E.	10.0±0.08	5.5±0.13	9.5±0.17	14.0±0.49	14.6±0.23
Magnesium (mg/dl)±S.E	1.50±0.04	0.60±0.04	1.35±0.10	0.62±0.10	0.59±0.05

H.C.= Healthy controls, A.S.=Acute schistosomiasis, C.S.=Chronic schistosomiasis,
C.S. & B.C.= Chronic schistosomiasis with bladder carcinoma, B.C.=Bladder carcinoma
S.E.=Standard error

Discussion

The significant decrease in the calcium levels in patients with acute schistosomiasis might be related to the immunosuppression state associated with this disease as proved by the decrease in the lymphocyte kinetics and adenosine deaminase activity of these patients[14]. A correlation was found between calcium levels and T-cell activation[7]. Hypocalcaemia can also occur secondarily to magnesium deficiency, renal failure and alkaline phosphatase increase[8]. Magnesium deficiency is revealed in our results and renal abnormalities might be a possibility in those patients[15], whereas alkaline phosphatase was found to be increased in such patients[14]. Moreover, calcium levels have long been associated with zinc bioavailability[16]. Zinc was found to be decreased in such patients[17].

The decrease in the immune responses in patients with acute schistosomiasis might also be due to a defect in certain hormones like 1, 25-dihydroxychlecalciferol hormone, which is responsible for calcium homeostasis. This hormone is derived from renal metabolism of vitamin D3 that is known to activate macrophages[18]. Abnormal renal metabolism has been associated with schistosomiasis[15], hence the defect in the immune responses. In addition, the relative distribution of calcium is altered as a result of changes in the protein concentrations[4,6,19]. Altered protein concentrations might result from renal function abnormalities.

The significant difference between the levels of calcium in patients with chronic schistosomiasis and the healthy controls might be due to the decrease in the antigen shedding during the chronic phase of the disease and so the physiologic activities become unaffected by the parasite.

The significant increase in calcium levels in patients with bladder carcinoma with or without schistosomiasis might be due to the malignancy-associated hypercalcaemia that occurs in various

tumors including epithelial tumors of the genitourinary tract. The parathyroid hormone related protein, secreted mainly from solid tumors, was found to be responsible for the hypercalcaemia mediated primarily via an increased renal re-absorption of calcium and secondarily by bone resorption[4,9,10].

The significant decrease in magnesium levels in patients with acute schistosomiasis chronic schistosomiasis with bladder carcinoma and bladder carcinoma might be one of the causes of immunosuppression recorded in these patients for magnesium is essential for the preservation of the macromolecular structure of DNA, RNA and ribosomes[4,20]. Therefore, the decrease in magnesium might lead to the destruction of the immune cells responsible for the host defense against schistosomiasis and tumor development. Animal experiments have suggested the role of magnesium in humoral antibody responses. It is unclear whether this is actually at the level of the B-cells or secondarily to a T-cell defect[12]. Moreover, the magnesium decrease might be due abnormal renal excretion, known in schistosomiasis[15]. Renal excretion is responsible for magnesium homeostasis[4]. Hypomagnesaemia is also a cause of early chronic renal disease[4,5,8] and certain malignancies like acute lymphoblastic leukemia[10].

The return of magnesium levels to the levels of the healthy controls in patients with chronic schistosomiasis might again be due to the decreased antigen shedding and so exerting no effect on the physiologic activities of the body.

The alteration in the calcium and magnesium levels in patients with schistosomiasis might play a role in the development of bladder carcinoma in such patients

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