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Microelements levels of Iron, Manganese, Zinc, Copper, Lead, Cadmium, and Nickel in the serum samples of Iraq prostate cancer patients

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Abstract : Microelements are important components of biological activities,however; these elements can be toxic when it levels exceed the demand. In the present study, serum levels of microelements were measured in15 newly diagnosed patients with prostate cancer and 10 healthy subjects by using Flame Atomic Absorption Spectrophotometer (FAAS).resultswere showed that there was an elevation in serum levels of Mn ,Cu ,Ni ,Pb ,Fe ,Cd ,Zn($p< 0.05$) in prostate cancer patients , These changes may be important in the pathogenesis of prostate cancers, and these results have confirmed the relationships between prostate cancer and microelements in Iraq.
Keywords : Prostate cancer .Microelements. Serum levels.

Introduction

Prostate cancer is themore common type of cancer between males in Developed countries [1]. In Iraq, Iraqi Cancer Board 2011 registered that Prostate cancer affects 2.78 people per 100000 (Iraqi Cancer Board 2011). The causes of prostate cancer are not fully known[2]. Studies showed that exposure to heavy metals has toxic and carcinogenic effects on humans and animals[3].

Prostate cancer (PCa) is a general health problem and most common male cancer. Prostate cancer is the second cause of deaths in males of western peoples [4,5]. Prostate cancer rates different markedly with and within populations [6]. Understanding the hidden causes of the variations is important for cancer forbidding. Risk factors for prostate cancer have been specific. Age, race, and family history[7]. Diet is thought to be an emerging risk factor [8]. Microelements may implicate in various malignant neoplasms of different organs like liver cancer is mainly a common complication in thecase of access to the iron (Fe)[9]. The mechanisms of the hepatocarcinogenesis are thought to be that iron bound to low-molecular protein in the liver produces hydroxyl radicals via the Fenton reaction that damage DNA. Copper (Cu) and iron (Fe) accumulate in large quantities in the liver and spleen of the urinary tract, thorax, and respiratory tract, of cancers patients. Increased copper(Cu) exists in the form of copper-metallothionein) (Cu-MT) [9,] thought that hydroxyl radicals are created in the available of hydrogen peroxide as a result of a Fenton-like reaction and cause hepatitis and hepatocarcinogenesis due to of DNA damage[9]. Nickel (Ni) cause high rates of lung and nasal cavity cancer has been found in nickel refinery workers[10]. Lead (Pb) may cause lung, stomach and brain tumors has been Reported in workers in a lead refinery, and in lead poisoning. The carcinogenetic mechanism is assumed to be interference with the DNA repair process[11]. Cadmium (Cd) causes DNA fragmentation and chromosome

mutations and association with prostate cancer in a human. Abonrmal gene expression resulting in increased cell proliferation or prevetion of apoptosis may be the mechanisms for cadmium-mediated carcinogenesis[12]. Zinc (Zn)Second national Health and Nutrition Examination Survey (NHANES II) was concluded that the relation of serum zinc and Cancer mortality is nonlinear[13]. Manganese (Mn) works as protectors for mitochondria endothelial cells and red blood cells against damage caused by superoxide radicals throw superoxide dismutase and share free radical defense system. Changes in levels of (Mn) cause disturbance of antioxidant mechanism that can make target organs susceptible to carcinogens[14].

Material and methods

Blood samples were collected from fifteen (15) prostate cancer patients from AL-Amal general hospital in Iraq/Baghdad and ten (10) healthy subjects. Blood centrifuged 2000 rpm for 10 minutes. obtained serum was stored directly in ˉ20 C° until analysis. To digest the serum protein we add1.5 ml of concentrated nitric acid with 0.5 ml 30% H2O2 to 5ml of serum under 80 C° .after complete digestion the samples were diluted with deionized water to 25 ml and filtered by Whitman no.1filter paper before samples measurements by Flame Atomic Absorption Spectrophotometer (FAAS) type 7000A Shimadzu, Japan .The resultswere expressed as (ppm) [15].

Statistical analysis

Independent T-test was used by SPSS version 20 to analysis results for comparison between patient and control to show the significance differences.

Results

As shown in (Table- 1) and according to statistical analysis, there is very high level of manganese (Mn) in the serum of prostate cancer (PCa) patients compared with healthy subjects respectively (12.2±0.1, 1.2±0.01) with significance differences at $p \leq 0.05$.significance differences at $p \leq 0.05$ have been showed for (Cu) with the very high level in prostate cancer patients serum compared than healthy subjects respectively (13±0.1, 0.9 0.01). Nickel(Ni) results represented with high level in prostate cancer patients serum compared with healthy subjects respectively (3.1 ± 2.1, 2.5 ± 1.1). Lead (Pb) showed little raise in its levels in prostate cancer patients serum than healthy subjects respectively (1.6 ± 0.2, 1.3 ±0.1) with no significance differences.

Table 1: Heavy element Concentration in patients and Control (Mean ±S.E)

Control (Mean ±S.E)	Patient (Mean ±S.E)	Heavy Element (PPm)
1.2±0.01	**12.2±0.1**	**Mn**
2.5± 1.1	**3.1± 2.1**	**Ni**
0.9± 0.01	**13± 0.1**	**Cu**
1.3±0.1	**1.6±0.2**	**Pb**
2.3±0.01	**2.6±0.1**	**Fe**
3.8± 0.5	**7± 0.02**	**Cd**
2.2± 1.9	**25.1± 8.1**	**Zn**

In addition, Iron (Fe) appeared with a little increasing for the level in prostate cancer patients serum compared with healthy subjects respectively (2.6±0.1, 2.3±0.01) with no significance differences. Cadmium (Cd) showed a high level in the serum of PCa patients than healthy subjects respectively (7.0 ±0.02, 3.8 ±0.5) with significance differences. Zinc (Zn) has a very high level in prostate cancer patients serum compared with healthy subjects respectively (25±8.1, 2.2±1.9) with clear significance differences(Figure 1).

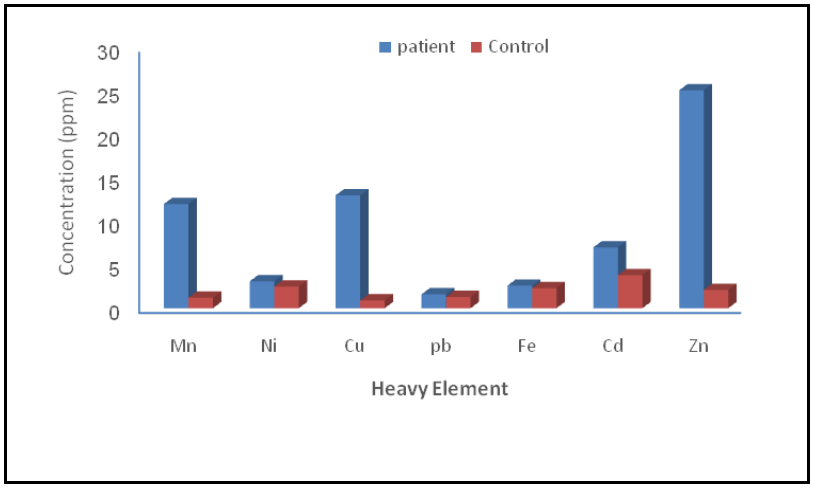

Fig. 1: Heavy Elements Concentration (ppm) in patient and Control.

Discussion

Low serum Manganese (Mn)level was reported in patients with bladder and renal cancers [16,17], due to Manganese influences the activity of transcription factor such as (HIF-1α, AP-1, NF-κB and p53) and affects DNA stability via Mn-SOD[14]. Advanced stages of prostate cancer (Gleason grade 3 or 4) are potentially associated with decreased activity of Manganese superoxide dismutase. In this study, there is a high level of Mn in the serum of prostate cancer patients it may be due to some alteration in the interaction of the equilibrium between microelements like Zn/ Fe ratio in the PCa patients. In addition to the patients has newly diagnosed with prostate cancer and not in advanced stages. These finding referred to by[18],[19].

Copper is considered as a vascular endothelial growth factor (VEGF). Copper can induce tumor cell growth by angiogenesis [20]. Studies have shown greatly elevated levels of Cu, Cu/Zn ratio in cancer, such as breast, prostate, and liver cancer.[21] .In this study, we find there is the high elevation of copper (Cu) level in the serum of prostate cancer patients (PCa) than healthy subjects because patients might cause an elevation in copper level due to intratumoral copper [22].

Little researches were undertook the role of nickel in the pathogenesis of prostate cancer despite it is a mutagen and associated with lung and nasal Cancer [23], and cancer of the prostate or bone have also been found in nickel workers, this study shows a high level of nickel in the serum of prostate cancer patients because the bioavailability of nickel and the presence of components induces oxygen-free radical reactions strongly influence the carcinogenicity. Nickel-induced accumulation of iron may be directly responsible for the formation of reactive oxygen species and the subsequent enhancement of lipid peroxidation[24]. Lead (Pb) is atoxic element and carcinogenic. [25] It has been supposing that Lead (Pb) has a role in the carcinogenesis via inhibition of DNA repair, induce oxidative damage to cells and tumor suppressor proteins in addition to the interaction with DNA-binding proteins[26].Our finding in this study found there is as light elevation in (Pb) serum level in PCa patient and this result coincide research that has same result [27].

Iron(Fe) is a fundamental element participate in events vividness in theproduction of heme and DNA synthesis [28,29].Our study record slight elevation in iron (Fe) serum level because it is possible that elevated iron can predispose to prostate cancer due to the ability of this element to reacts with hydrogen peroxide and stimulate the highly reactive hydroxyl radicals, leading to increasing oxidative stress and then increases free iron concentrations by Fenton reaction[30].

Cadmium (Cd) deposition mainly in the prostate and cause prostatic proliferative lesions, including adenocarcinomas,[31]. The mechanisms of cadmium in carcinogenesis through indirect genotoxic mechanisms, like oxidative stress, inhibition of DNA repair system, stimulation of the epidemiologic study, cell line and experimental study indicate that insoluble Cd compounds are carcinogen than Cd soluble compounds [32]

Cell proliferation, obstruction of apoptosis or through epigenetic mechanisms [33]In our study, data show there is high level of Cd in the serum of PCa patients and this result agrees with other research mentioned

elevation of Cd level in PCa patients like[23]. zinc (Zn) as protector against oxidative stress be an essential component of DNA-binding damage and share in differentiation, and apoptosis . low level of zinc (Zn) can contribute homeostasis that related to the diseases of the oxidative modifications to DNA which increase the incidence of prostate cancer [34]. Although some research refers to there is no association between serum zinc level and prostate cancer risk[35]. The result of this study show a high level of zinc in the serum in prostate cancer patients and that result agree with some researchers that high intraprostatic zinc level may be the main reasons acting in initiation and progression of prostate carcinogenesis [35-42].

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