Studying the Concentrations of Some Trace Elements , Ceruloplasmin Enzymes and Blood Parameters in Cancer Cachexia patients

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Abstract

This study includes some trace elements Cu,Zn,Fe, Hemoglobin, White blood cell count and Ceruloplasmin concentrations in cancer cachexia patients, the non-infected patients by cachexia, and the control to know the effectiveness of these elements which affect on the disease .Blood sample were Collected from patients backing Al-Taleemy Sader hospital & cancer tumors center in south region from 1/5/2004 to 1/10/2005. Blood samples of 142 patients included{(75) samples of patients didn't take chemotherapy and suffered from cancer cachexia, and (47) samples of patients suffered from cancer and didn't infect by cachexia, (20) samples from healthy persons as a control group}. Results showed significant differences in concentrations of different groups; Maximum concentrations of hemoglobin(13.57± 1.22)gm/100ml,WBCs(6110±986.7)cell/m^3 were noted in control groups, also statistical analysis showed increasing in concentration of copper (277±22.44)µg/100ml and ceruloplasmin enzyme (87.93±16.6)mg/dl in cancer patients group compared with cachexia group cancer patients, while decreased concentration in control group. Also there was a decreasing in zinc concentration (61.8±10.99)µg/100ml,iron (51.9±10.58)µg/100ml in cachexia group cancer patients and showed high level in control groups.

Introduction

The word cachexia is derived from the Greek words kakos and hexis, meaning bad or poor condition, it occurs in some diseases such as Cancer, Acquired immune deficiency syndrome (AIDS), and Malabsorption. The cachexia can be divided into two categories, primary and secondary. Primary cachexia includes anorexia,decrease in nutrients,and changes in metabolic pathways. In secondary cachexia,weight loss is due to mechanical factors limiting intake(Fearon *et al.*,2001).Weight loss is seen most commonly in patients with Gastric & Pancreatic cancer as 83-87% comparing with other cancers (Wigmore *et.al.*,1997).Cachexia state occurs because of the changes in host tissues including loss of adipose tissue and skeletal muscle mass (Tisdale, 1998). Costa(1997) describes cachexia process which is complex process depends on anatomic site to tumor and tumor mass. Trace elements have important role in cancer disease especially copper which plays an important in the development of cancer and growth of cancer cell , the evidence for that is increase the level in cancer patients serum , and this increase that happen as a result of this link is part of the biological respons of the body to disease. In many studies with different types of cancer , proved increased copper level in serum , Copper levels in serum return to a normal level ,while patient who did not respond to treatment showed increased level of copper (Willingham & Sorenson,1986). And Sorenson,(1987) showed that most tumor cells have less effective Cu-ZnSOD compared with normal cells during the inflammatory process and most increase of copper in serum is a physiological response of the effectiveness of SOD or other copper enzyme to inhibit the growth of cancer cell. Copper concentration in plasma for cancer patients increase because the copper plays an important role in cancer development and growth of cancer cell by process called angiogenesis, it is considered an obligatory factor and activator key for this process to help inducing endothelial cell migration, proliferation, and invasion. The copper can also be supplied by the copper-containing molecule, ceruloplasmin, and produce angiogenesis (Brem & Wotoczek-obadia, 1998). The study of Mocchegiani *et.al*.(1994) on the laboratory mice showed that changes in the level of the zinc element have relationship with cancer disease. The iron element has an important role causing cancer disease. Therefore this element is useful as a food material for cancer cells which can increase growth and stimulate the vascularization process, repeated intramuscular injections of iron dextran complex in rats, showed, years later, sarcomas with rats in which iron preparations had been injected (Richmond ,1959).As for the zinc has been found that there is a relationship between this element decrease and cancer, Mocchegiani *et.al*., (1994). But WHO has confirmed in 2001 that there is no sufficient experience points to the carcinogenic effect of zinc on human. Also the iron urges cancer when injected in internal muscles of laboratory mice as iron dextran complex, and accumulation of iron in the liver may cause damage to these cell, leading eventually to fibrosis and cirrhosis of the liver,thus causing cancer (Bonkovsky, 1991) ,in the same way , accumulation of iron in colon causes ulcers eventually causing colonic carcinoma (Bird *et.al*., 1996)

Material and Methods

Dring the study 75 blood samples were collected from cancer infected patients and some of them suffer from cachexia, they where 47 blood samples from cancer infected patients non suffer from cachexia and 20 blood samples from healthy persons as control group.The study started from 1/4/2004 till 1/10/2005. Laboratary working

*Hb concentration:-we depanded on

cyanometheamoglobin methods (Coles,1980).
*White Blood Counts (WBCs): -we depended on Hemocytometer (Coles,1980).
*Ceruloplasmin test:-we used radial immunodiffusion plate (Berne,1974).
*Copper test :-we depended on coloirmetric test (Stookey,1970).
* Zinc test:- we depended on coloirmetric test (Deadre,1977).
* Iron test:- we depended on TPTZ- coloirmetric test (Itano,1978).
Static analysis :-
Using analysis of Variance test (Anova test)by using statistical package of Social Science (SPSS) and Biovariate correlation (AL-Rawi&Khalaf allah,1980)

Results and Disscution

The study showed as in table (1) that there were significance differences in hemoglobin concentration, the WBCs count ,increase copper and ceruloplasmin concentration as well as decrease in iron and zinc concentations for cancer cachexia patients compared with the non- infected cachexia cancer patients and control group.

Table(1):-Hemoglobin conc.(gm/100 ml),white blood cell count (cell/mm3),Ceruloplasmin conc. (mg/dl) & Trace elements concentration in cachexia cancer patients and non cachexia cancer patients and control group.

	Hemoglobin gm/100 ml Mean± S.D	White blood cell cell/mm3 Mean± S.D	ceruloplasmin enzyme conc. mg/dl Mean±S.D	Zinc concentration 100ml/ µg Mean±S.D	Copper concentration 100ml/ µg Mean±S.D	Iron concentration 100ml/ µg Mean±S.D
Cachexia cancer Patients n=75	10.55±0.7 **	4718±662.8 **	80.21± 14.91 **	61.8 ±10.99 **	257± 28.08 **	51.9± 10.58 **
Non cachexia cancer Patints n =47	10.62±0.8 **	5276±649.8 **	87.93±16.6 **	67.93±11.78 **	277±22.44 **	56.9±19.09 **
Control groups n =20	13.57±1.2	6110±986.7	43.61±8.32	87.73±7.61	106.6±15.14	107±14.39

**** There is a significant difference at level (p<0.01) between cancer cachexia patients compared with non cancer cachexia patients and control group.**

Table(2):-Describes hemoglobin conc.(gm/100ml),WBCs (cell/mm3),Copper conc. (µg /100 ml) , Zinc conc.(µg /100 ml),Iron conc. (µg /100 ml)and Ceruloplasmin conc. (mg/dl) in cancer cachexia patients group.different letters describe found significant difference(p< 0.05) between species.

Cancer cachexia group	Female	Male	hemoglobin conc. (gm/100ml)	white blood cell count (cell/mm3)	Copper conc. (µg/100 ml)	Zinc conc. (µg /100 ml)	iron conc. (µg/100ml)	Ceruloplasmin conc. (mg/dl)
Stomach cancer patients n=17	11	6	10.4±1.01 b	4876±707.5 ab	270.5±61.0 b	61.0± 13.22 b	49.01 ±8.96 b	85.1±11.2 b
Pancrease cancer patients n=10	5	5	11.5±1.32 a	5085±829.8 b	175.8±66.1 a	76.9± 13.55 a	76.2 ±33.33 a	60.8±20.9 a
Metastatic cancer patients n=29	20	9	10.5±0.06 a	4641±654.9 a	260±28.0 b	60.0± 13.0 a	56.4 ±11.96 a	83.2±18.0 a
Breast cancer patients n=19	19	_	12±2.02 b	5410±1187.2 b	201.5±80.5 b	70.9 ±13.05 b	70.5± 29.66 b	62.3±16.5 b
Control n= 20	10	10	13.5± 1.2	6110 ± 986.7	106.6± 15.14	87.7± 7.6	107 ± 14.3	43.6 ± 8.3

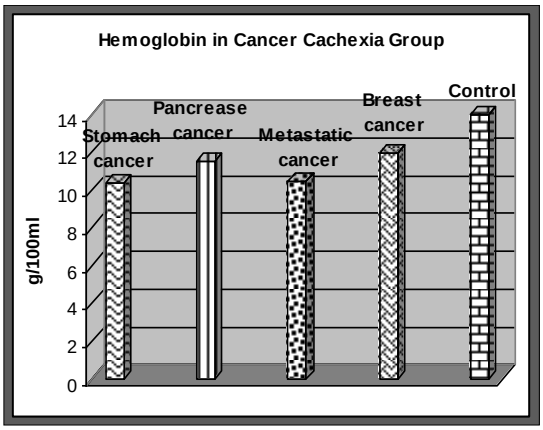

Figure (1): Describe hemoglobin concentration(gm/100 ml) in cancer cachexia group.

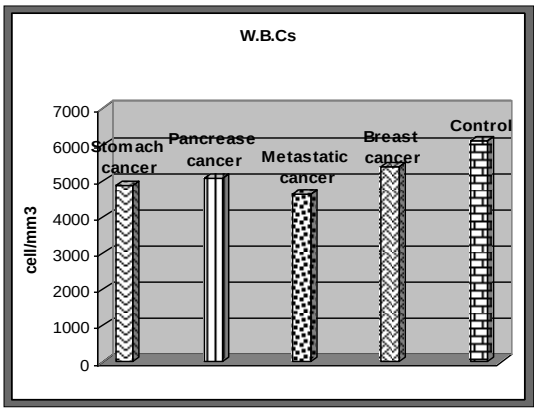

Figure (2): Describe white blood cell count (cell/mm3) in cancer cachexia group.

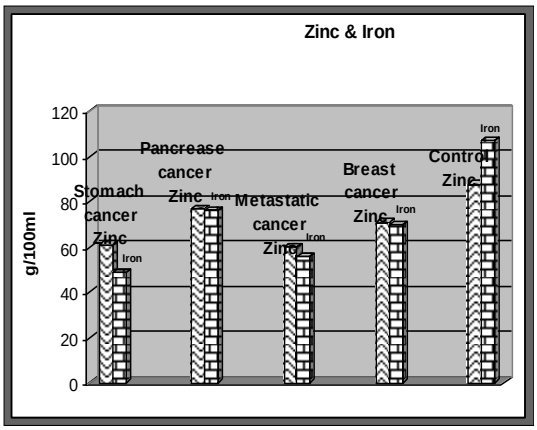

Figure (3): Describe iron and zinc concentration (µg/100ml) in cancer cachexia patients group.

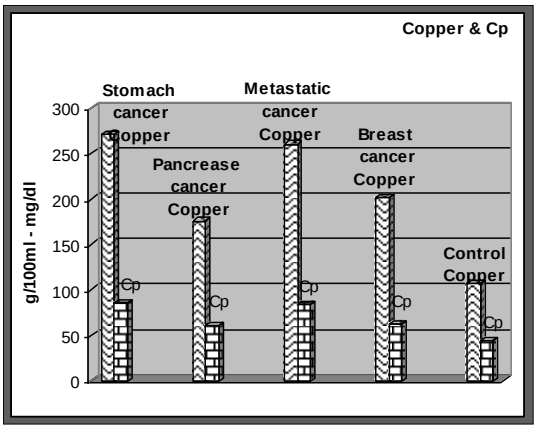

Figure (4): Describe copper concentration(µg/100ml) and ceruloplasmin concentration(mg/dl) in cancer cachexia patients group.

In addition the results revealed significant differences in cachexia cancer types ,so we noticed hemoglobin concentration and WBCs count decrease, increase copper and ceruloplasmin concentrations also decrease zinc and iron concentration in stomach & metastatic cancer patients compared with pancreatic and breast cancer patients (table 2) (figure 1,2,3,4). We thought that the decrease of hemoglobin , iron, and WBCs may be caused by un controled division of tumor as poly layers , of tumour masses these tumour masses need blood supply which gaind by new vascularization inside the soild tumour causing decrease in hemoglobin concentration (Benjamin *et al*.and Schmidt *et al*.,1999).Also the cancer cells affected on erythropoietin hormone production from kidney , decrease of this hormone level leads to decrease of blood cells (Ludwig *et al*.,2002). The reason of copper and ceruloplasmin increase may due to cytokines production which are cofactors to cancer cells and give the cancer cells nutrition and oxygen and helpe them to grow and diffuse to other organs , so the copper was an activator material and the key to the operation or act as a cofactor for these processes and this according with (Parke *et.al*.,1988).The reason for decreased zinc levels in cachexia cancer patients may be due to zinc loss from plasma during immunity and inflammatory response against cancer cells (Prasad,2000) ,as well as zinc loss caused atrophied thymus gland which ia an important gland for blood cells maturation .The zinc is an important cofactor in the activation of thymulin hormone which is responsible for the cellular immunity and differentiation of T- lymphocyte (Mocchagiani *et.al*.,1995)as well as to its important function in cellular membranes ,function of many enzymes and the immune response and inflammatory cells of the tumor so its important in the metabolism of lipids,proteins,carbohydrates and nucleic acids, so it's deficiency is a result of the oxidative metabolism of proteins, lipids and nucleic acids for patients with cancer cachexia .The reason for decreased level of iron and hemoglobin in stomach and metastatic

cancer patients compared with other types of cancer is due to tumor cells diffusion to other places of the body through basal lamina crossing to lymph and blood vessels ,these cells need blood and iron for spread to organs and these cells secrete (especially to red marrow and compact bone) materials which cause decomposition of bone and destroy the predecessors of red blood corpuscles and destroy the stem cells which are responsible for blood cell formation and differentiation , one of these materials is prostaglandin E2 which causes a cachexia and weight loss in patients with cancer(Weinberg ,2000). The reason may be due to copper and ceruloplasmin levels in metastatic and stomach cancer patients caused by malabsorption and bleeding in intestinal tract because of presence of tumor cells this accord with (Nayak *et.al.*,2003),also the cancer cells accumulation in digestive tract causes nodules and sores this cause decrease absorption of iron and others elements and causes bleeding of affected organ like expistaxis or hemoptesis haematuria.The zinc seems to be important for integration of epithelial cells lining the blood vessels and gastrointestinal tract so the presence of tumor cell in these organs may causes sores, ulcers or bleeding and affects the enzymes and gastric acids which had principle effect in zinc absorption so it decreases zinc absorption or may be due to haemolysis so zinc is released to blood excreted in urine this accord with (Su & Birmingham,2002).

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دراسة تراكيز بعض العناصر النزرة وانزيم السيريولوبلازمين والمعايير الدموية وعلاقتها بمرض الهزال السرطاني

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الملخص

شملت الدراسة حساب قيم بعض العناصر النزرة Cu , Zn, Fe وخضاب الدم وعدد خلايا الدم البيض وتركيز انزيم السيريولوبلازمين في مجموعة مرضى الهزال السرطاني ومجموعة مرضى السرطان غير المصابين بالهزال ومجموعة السيطرة لمعرفة مدى أهمية هذه العناصر في حدوث المرض .تمت الدراسة بجمع عينات الدم من المرضى الذين راجعوا مستشفى الصدر التعليمي ومركز الاورام السرطانية في المنطقة الجنوبية للفترة من 1/5/2004 لغاية 1/10/2005فقد تم جمع عينات الدم من 142 مريضاً تضمنت: (75) عينة من أشخاص مرضى غير خاضعين للعلاج الكيمياوي ولديهم حالة هزال سرطاني و(47) عينة من أشخاص مصابين بمرض السرطان وليس لديهم حالة هزال و(20) عينة من أشخاص أصحاء أعتبرت كمجموعة سيطرة وبعد قياس بعض العناصر النزرة في مصل الدم وخضاب الدم وعدد كريات خلايا الدم البيض وعدد الصفائح الدموية وتركيز انزيم السيريولوبلازمين في المجاميع المدروسة أظهرت النتائج وجود فروقات معنوية مختلفة في تراكيز القياسات سابقة الذكر في المجاميع ، وقد تبين أن أعلى تركيز لخضاب الدم (1.22±13.57)غرام 100/مل وعدد كريات الدم البيضاء (986.7±6110) خلية /ملم 3 في مجموعة السيطرة مقارنة مع بقية المجاميع . كما أظهرت نتائج التحليل الأحصائي أرتفاع تركيز عنصر النحاس (22.44±277) مايكروغرام / 100 مل وانزيم السيريولوبلازمين (16.6±87.93) ملغرام / دالتون في مجموعة مرضى السرطان غيرالمصابين بالهزال مقارنة مع مجموعة مرضى الهزال السرطاني . وأظهرت مستويات منخفضة في مجموعة السيطرة .كما أظهرت نتائج التحليل الأحصائي أنخفاض تراكيز عنصر الزنك (10.99±61.8) مايكروغرام 100 / مل وعنصر الحديد (10.58±51.9) مايكروغرام 100 / مل في مجموعة مرضى الهزال السرطاني مقارنة مع مجموعة مرضى السرطان غير المصابين بالهزال بينما كانت مستويات عالية في مجموعة السيطرة.