

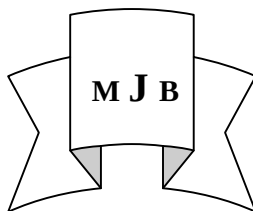
Correlation of Catalase with Trace Elements Zinc and Copper in Urinary Bladder Cancer Patients

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Abstract

This study was applied on patients having urinary bladder cancer fifty patients were choosing for this study complaining of haematuria, and proved to have bladder cancer by histopathological study for the biopsy taken from the bladder by cystoscopy performed under general anesthesia.

In this study the type of cancer was transitional cell carcinoma of urinary bladder of different stages.

In this work changes in activity of catalase as enzymatic antioxidant defense mechanism we studied in patients and control groups, the result revealed significant decrease in patient groups compared with control.

The changes in level of trace elements copper and zinc are studied in this work, the result revealed an increase level of copper and reduced level of zinc in patients groups in comparison with control groups.

الخلاصة

هذه الدراسة تمت على مرضى سرطان المثانة. خمسون مريضاً تم اختيارهم لهذه الدراسة، يعانون من التبول الدموي وثبتت إصابتهم بسرطان المثانة من خلال الدراسة النسيجية للعينات التي تم أخذها من بطانة المثانة من خلال نأظور المثانة الذي تم إجراؤه تحت التخدير العام.

من هذه الدراسة كان نوع السرطان هو سرطان النسيج الطلائي الانتقالي للمثانة في مراحل مختلفة.

في هذا العمل تم دراسة التغيرات التي حصلت على فعالية إنزيم الكاتلاز وهو أحد إنزيمات الفعالة ضد التأكسد حيث أظهرت النتائج انخفاض ملحوظ في فعالية هذا الإنزيم عند المرضى مقارنة بمجموعة السيطرة.

في هذا العمل تمت دراسة التغيرات في مستوى بعض العناصر حصراً وهي النحاس والكارصين وكانت النتيجة ارتفاع في مستوى النحاس وانخفاض في مستوى الكارصين عند مرضى سرطان المثانة مقارنة بمجموعة السيطرة.

Introduction

Urinary bladder cancer is one of the most common cancer worldwide, with high incidence in the industrial countries. Bladder cancer is more common in male than female, the mean age's about fifty, and few cases are under the age of forty [1].

Two main histological types of bladder cancer, transitional cell carcinoma main types in industrial area

,segoumose cell carcinoma mainly in area of high incidence of schistosomiasis[2]. Development and progression of bladder cancer is derived by the malfunction of specific gene i.e. due to over expression of oncogen or inactivation of tumor suppressor genes [3]. The oncogen that have been associated with bladder cancer are (ras) gene family mainly, including p₂₁ ras oncogen. The most important suppressor gene is P₅₃ [4].

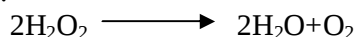
Staging is done to obtain prognostic information and to guide treatment selection, stage1 tumor confined to epithelium, stage2

tumor invasive to muscularis propria, stage3 tumor involvement of perivesical fat, stage4 tumor involved of adjacent organ as prostate pelvic wall lymph nodes and distal metastasis[5].

.Tobacco smoking is the most established modifiable risk factor for bladder cancer [6].Cigarette smoking induced oxidative stress and involved in DNA damage, and impaired anti oxidative defense mechanism [7].

.Variety of industrial exposure risk for developing bladder cancer ,primarily aromatic amines present in product of dyes and benzidine derivative ,other occupational hazard including painter , drivers truck , aluminums worker , mechanistic chemical worker printers , metal workers , hair dresser[8].

Catalase is an enzyme found in blood, bone marrow, mucous membrane, kidney and liver. Its function assumed to be the destruction of hydrogen peroxide formed by the action of oxidative stress .Mainly catalase are found in peroxisomes (cytoplasmic organelles involved in oxidation reaction by using oxygen molecules), peroxisomes are rich in oxidase and catalase which suggest that there may be a biological advantage in grouping the enzyme that produce H_2O_2 with enzyme that destroy it .other sources of H_2O_2 which is substrate for catalase is mitochondrial and microsomal electron transport system, as well as xanthene oxidase must be conceders as source of H_2O .



Hydrogen peroxide which is substrate of catalase is reactive species but production of H_2O_2 in the body are used for synthesis and detoxification process ,as well as for immune defense Hydrogen peroxide is generating in the

peroxisomes to aid in the degradation of fatty acid and other molecules , H_2O_2 use for detoxification reaction involved in liver by cytochrome p_{450} , also H_2O_2 use in the phagocytic process of leukocytes in defense process against bacterial infection in this inflammatory cells NADPH oxidase associated with plasma membrane reduce O_2 to generate super oxide radicals and this produce H_2O_2 by action of super oxide dismutase , and this H_2O_2 is substrate of catalase and when accumulate to toxic level cause oxidative stress[9].

The disturbance between prooxidant and antioxidant balance result in oxidative stress which is defined as imbalance between the production of various reactive oxygen species(ROS) and the ability of antioxidant protective mechanism to cope with these ROS component and prevent its adverse effect on biological system [10].

These ROS are defined as molecules or atoms that have one or more unpaired electron in there's outer shells. it is consequence has tendency to accepted an electron from other substance and make it highly reactive[11].

The ROS including mainly following species [12].

- $O_2^{\cdot -}$ super oxide anion radical
- $HO^{\cdot}$ Hydroxyl radical
- H_2O_2 Hydrogen peroxide
- $Roo^{\cdot}$ Lipid peroxide radical
- 1O_2 singlet oxygen
- HOCL Hypochlorous
- O_3 Ozone

Zinc is essential trace element for all forms of life. It is absorbed from duodenum, zinc is mostly transported bound to albumen, alpha-2-macroglobulin and transferene, zinc sequestration in enterocytes with metalothionein, some of this transfer to the plasma, the rest is lost when the enterocytes are sloughed[13]. Zinc plays important roles in growth and development, the immune response,

neurological function, and reproduction [14].

Zinc has an antioxidant action [15]. and anticancer action[16]. and has role in vitamin A action Zinc is a component of retinol binding protein, which is necessary for transporting vitamin A in the blood[17].

Copper in the body shifts between the cuprous(Cu^{++}) and cupric (Cu^{+}), the ability of copper to easily accept and donate electron explains its important role in oxidation- reduction (redox) effect about 90% of copper bound to ceruloplasmin which is copper containing protein the copper containing enzyme, while when copper first absorbed by intestine it is transported to liver bound to albumen. Ceruloplasmin (ferroxidase I) and (ferroxidase II), which have the capacity to oxidize ferrous ion (Fe^{+2}) to ferric ion (Fe^{+3}) the form of iron that can be loaded onto the protein transferrin for transport to the site of red blood cell formation [18]. The copper is one of the metals that have the ability to catalyze the formation of $\text{OH}^{\cdot}$ and other radicals from H_2O_2 and $\text{O}_2^{\cdot}$ through Fenton reaction so has oxidative power [19].

Aims of study

1. Studying the activity of catalase enzyme in urinary bladder cancer patients and compared the activity with control group.
2. Study the changes occurring in serum level of trace elements zinc and copper in bladder cancer patients and control

Materials and Methods

1-Samples

Two groups of samples were included in this study, patients group fifty patients (forty six males and four females) proved to

Have urinary bladder cancer admitted to Al-Hilla teaching hospital, and twenty five healthy persons considered as control groups. Five ml of blood was obtained from each subject, and was pushed slowly into plain disposable tubes without anticoagulant. Serum was obtained by centrifuging 2500 rpm for approximately 10-15 minutes.

Methods:-

Determination activity of Catalase by decrease in absorption in H_2O_2 by spectrophotometer [20].

.Determination of serum level of zinc through reaction of zinc with chromagen reagent and the color intensity is proportion with zinc concentration which determination by spectrophotometer [21].

.Determination of serum level of copper through reaction of copper with chromagen reagent and the color intensity is proportion with copper concentration which determination by spectrophotometry [22].

Statistical analysis

The statistical analysis was done using t-test.

Results and Discussion

In this work the result represented the measurement of serum activity of Catalase in urinary bladder cancer patients and control groups. The results are as follow:-

Table 1 The mean serum level of catalase activity in UBC patients and control.

Groups	CAT. activity K/ml	SD	P value
Patients	0.09	0.025	<0.01
Control	0.35	0.09	significant

In this work the mean activity of catalase in UBC patients is significantly lower than that activity in control group, p value <0.01 , the activity of catalase enzyme in UBC patients is approximately 25% as an activity in control groups.

Catalase enzyme is an antioxidant enzyme, present in aerobic cells . It catalyzed the decomposition of hydrogen peroxide H_2O_2 to water and oxygen , H_2O_2 is produced in cell by controlled pathway , H_2O_2 elicits a broad spectrum of cellular response ranging from mutagenic growth stimulation, to apoptosis to necrosis at different concentration level . Hydrogen peroxide at high concentration is deleterious to cells, and it is accumulation causes oxidation in cellular targets such as DNA , proteins , and lipid, lead to mutagenesis and cancer developing With elevation of reactive oxygen species and repression antioxidant

enzyme as catalase lead to progression of malignant cell . Catalase message protein level and activity level were found to be down regulated in the malignantly progressed cells, so level of catalase activity decreased in malignancy state, and causes accumulation of hydrogen peroxide to toxic level and causes injury to the cell, and stimulate progression of tumor cell. In vitro study of molecular mechanisms of tumor progression by ionizing radiation to produce malignant in mouse the study show with elevation of reactive oxygen species and reduction of antioxidant defense mechanism including catalase and, this reduction and attenuation activity of catalase play a functional role in the malignant progression of mouse cancer[23].

The serum level of zinc in UBC patients and control are shown in table 2

Table 2 The mean serum level of zinc in UBC patients and control groups.

groups	Mean of zn $\mu\text{g/dl}$	SD	P value
Patients	64.14	4.2	0.01
control	99.6	8.6	significant

The mean serum level of copper in UBC patients and control are 167 and

101 $\mu\text{g/dl}$ respectively, the result in the following table

Table 3 The mean serum level of copper in UBC patients and control.

groups	CU $\mu\text{g/dl}$	SD	P value
Patients	167	20	<0.01
control	101	10.4	significant

In this study there is a significant difference in zinc level between patients and control groups in UBC patients the serum level of zinc is significantly lowered than that in control , p value <0.01 , in contrasted to this result the serum level of copper is significantly elevated in UBC patients in relation to control, p value <0.01 .

Copper is one of the metal has ability to catalyzed formation of $OH^\cdot$ And other radicals from H_2O_2 and O_2 through Fenton reaction [24].

Zinc has antioxidant property through antagonism of redox active transition metal such as copper [25].

Zinc and copper are antagonized each other by competition between these metals in intestinal mucosal cell [26].

The correlation between catalase versus copper, zinc in bladder cancer

patients are represented in the following table

Table 4 Represented the correlation between the catalase via copper ,zinc level in bladder cancer patients.

The correlation of cat.K/ml vs.	Correlation coefficient (r)	P value
Copper Cu µg/dl	-0.07	NS
Zinc Zn µg/dl	-0.09	NS

According to this result there is negative non significant correlation between catalase via copper ,zinc trace elements pvalue< 0.05

Conclusion

1. There is decrease in enzymatic antioxidant defenses mechanism in bladder cancer state mainly catalase
2. Copper and zinc level are disturbed in bladder cancer state copper level has oxidative property is elevated in cancer state while zinc level is decrease in bladder cancer

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