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ORIGINAL ARTICLE

Investigation of Ochratoxin A in blood and it's relationship with Cancer diseases

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ABSTRACT

Objective: This study aim to investigation of Ochratoxin A in blood and it's relationship with cancer diseases for tenderers and sleepers patients in AL-Hussein hospital - Department of Blood diseases and malignant tumors.
Methods: Twenty five blood samples (5ml) collected from 25 patient's male, female infected with cancer diseases .Age of the patients to range between 8-77 year. Also twenty five blood samples (5ml) from 25 person uninfected with cancer diseases (control treatment) each sample putting in gel tube and transported to the clinical laboratory.
Results: The result showed 15 out of 25 samples(60%) of blood collected from patient infected with cancer diseases were found to contain Ochratoxin A while 3 out of 25 samples(12%) were contain Ochratoxin A in control treatment(Healthy Person), The highest percentage blood samples contamination with Ochratoxin A that collected from patients at age groups (50 – 63)year and (64-77)year was (33.3%)for two groups. The percentage of blood samples that contamination with OTA that collected from male patients was 60%.
Conclusion: correlation coefficient (r=0.8703) demonstrate that excite relationship between Ochratoxin A and cancer diseases.

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INTRODUCTION

Mycotoxins are secondary metabolites produced by different fungal species that can be found in many agricultural commodities and processed food .Aflatoxin B1 (AFB1) and ochratoxin A (OTA) are some of the most relevant mycotoxins due to their toxic effects and demonstrated human exposure[1]. OTA is the toxic metabolite, produced by several fungal species such as genera *Aspergillus* and *Penicillium*, is present in food and feed products due to the thermo- stability of its derivatives[2].

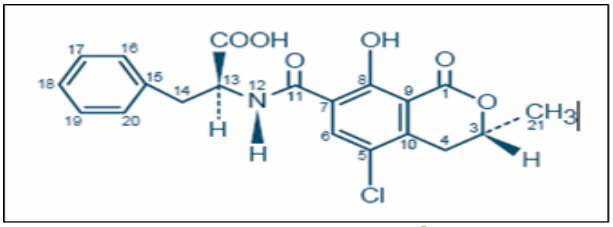

Figure 1. **Chemical structure of Ochratoxin A** [3]

Specifically, it has been detected in dairy products is generally negligible even though occurrence in cocoa ,cereal , bear and wine, pork products and chickpea[4-9]. OTA binds strongly to human serum albumin and shares a common binding site with other known anionic compounds, including warfarin, naproxen and phenylbutazone.Transfer of OTA to milk has been demonstrated in rats, rabbits and humans[10].
Micco *et al* (1995)[11] showed that OTA is also transferred to human milk, 22 out of 111 breast milk samples were contaminated with OTA in the range 0.1–12 ng/ml. Breitholtz-Emanuelsson *et al*. (1993)[12] showed that the concentration of OTA in human milk was approximately 10-fold lower than that in human blood (concentrations ranged from 10–40 ng/L and 90–940 ng/L in milk and blood respectively).

OTA is a nephrotoxic, hepatotoxic, embryotoxic, teratogenic, neurotoxic, immunotoxic, genotoxic and carcinogenic mycotoxin[13].

OTA has been implicated in the development of cancers of the human urinary tract because of the higher incidence of urinary tract tumors in humans in regions where BEN is endemic. The incidence rates of testicular cancer were significantly correlated with the per capita consumption of coffee and pig meat, two commodities known to contribute to the exposure to OTA in the diet[14].

OTA is absorbed initially at the stomach level because of its acid properties. The hydroxyl and carboxyl groups plan an important role insofar as for an acid pH, the non-ionized form favors OTA absorption. OTA is absorbed in the small intestine at the proximal jejunum[15].

The distribution of OTA in the tissues of the different animal species and human follows the subsequent pattern kidney > liver > muscle > adipose tissue. In humans, OTA crosses the placental barrier. The strong affinity bond between OTA and plasma proteins delays its elimination increasing thus the half life period. OTA as di-anion has two binding sites of serum albumin, one of them having very high affinity. There is a great difference between OTA half life period in plasma according to the species. After oral administration, the half life period is 35.5 days in humans; 3-5 days in pigs; 2-5 days in rats; 1-1.6 days in mouse; 8.2 h in rabbit; 4.1 h in chicken and 0.8 h in carp[3].

Aim of study: Investigation of ochratoxin A in blood of cancer patients. Also, study of relationship between ochratoxin A and cancer diseases.

MATERIALS AND METHDS

Extraction and diagnosis of OTA in blood of patients

This study was conducted according to AL-Musoui method (2015)[16] as the following steps:

A. Collection of samples

Twenty five blood samples (5ml) collected from 25 patient's male, female infected with cancer diseases. Age of the patients to range between 8-77 year. Also twenty five blood samples (5ml) from 25 person uninfected with cancer diseases (control treatment) each sample putting in gel tube and transported to the clinical laboratory.

B. Extraction of OTA

i. Add 3ml of chloroform to each tube and mixing well by hand.
ii. Save the sample in closed tube in refrigeration.
iii. After that isolating clear layer in clean glass tube and keep tube open and put in oven at (40 C°) for day.

C. Detection of OTA

i. Thin layer chromatography (TLC) technique used in detection of OTA in serum of patients.
ii. Thin layer chromatography plates put in oven (120 C°) for one hour to activate it.
iii. Make straight line on TLC plate in distance of about 1.5 cm from the base plate.
iv. OTA stander prepared by dissolving one mg in 4ml chloroform so that (concentration it was 250 µg/ml).
v. OTA stander (15µl) put as spot on TLC plate by capillary tube and put 15µl on plate from each extracted samples with a distance 2 cm between sample and another then let the spots to dry in laboratory condition.
vi. And then put the plate in separation tank containing 100ml from mixture 90 ml methanol and 10ml D.W (mobile phase) let the TLC in tank until the mobile phase reach to 2cm from upper edge of plate.
vii. TLC plate exit from the tank and let it to dry under the laboratory condition.
viii. Then plate examined under UV light (360nm) and compare the color and relative flow (RF) of extracted samples with the standard toxin.

RESULTS

Investigation of ochratoxin A in blood of cancer patient

The result showed 15 out of 25 samples of blood collected from patients infected with cancer were found to contain OTA with significant difference of number blood samples contamination with OTA (3only) that collected from healthy person,also this study clarified that highest percentage blood samples contamination with OTA that collected from patients at age 50 and 77 year (33.333%) while group (22-35) year had the least percentage (6.666%) Table 2. This study showed the percentage of blood samples contamination with OTA that collected from male patients and female patients was 60% and 40% respectively Table 3.

Table 1. **Calculated of chi-square of the number of blood samples that contain OTA for the patients infected with cancer and healthy person.**

Case	Number of patients With OTA	Number of patients Without OTA	Total
Cancer patient	15	10	25
Control	3	22	25
Total	18	32	50

X^2 Cal. =12.5 ; X^2 table (0.05, 1) =3.841

The presence of ochratoxin A is related with cancer.

Table 2. **Effect of age on percentage of blood contamination with Ochratoxin A for healthy peoples and cancer patients.**

Range of age	Healthy person with toxin	Percentage (%)	Patient with toxin	Percentage (%)
8-21	0	0	2	13.333
22-35	1	33.333	1	6.666
36-49	0	0	2	13.333
50-63	2	66.666	5	33.333
64-77	0	0	5	33.333

Table 3. **Effect of gender on percentage of blood contamination with Ochratoxin A for cancer patients.**

Gender	patient with toxin	Percentage (%)	X^2
Female	6	40	Cal.=0.6
Male	9	60	Table=3.841

therefore ,the number of male and female with toxin is equal and with out any significance difference ,and this difference belong to chance factor.

Relationship between OTA and cancer diseases

Estimation of correlation coefficient (r=0.8703) show that excite relationship between OTA and cancer disease occurrence.

DISCUSSION

Results of this study agree with many studies [16] showed 23.07% from patients blood specimen had ochratoxin A, So healthy persons were had ochratoxin A in their blood 10% and showed the males highly infected 87.5% with ochratoxin A while in female 70% and 71-80 year age had highly infected 92.85% with ochratoxin A. Micco *et al* (1995)[11] showed that 22 out of III breast milk samples were contaminated with OTA in the range 0.1-12 ng/ml.

Breithoitz-Emanuelsson *et al* (1999)[12] showed that the concentration of OTA in human milk was approximately 10 fold lower than in human blood.

This result agrees with many studies, that showed that OTA is carcinogenic mycotoxin[17,18]. OTA has been implicated in the development of cancers of the human urinary tract because of the higher incidence of the urinary tract tumors in humans in regions where BEN is endemic in Croatia's BEN endemic region, the prevalence of the tumors of the pylon and ureter is 11 times greater than in the non-endemic region[19].

Results from a study of 766 patients in Serbia showed that women and young people are more commonly affected in endemic regions and the usual site of tumors is the renal pelvis and the urethra, whist in non- endemic region, tumor are most frequently seen in the urinary bladder at a lower incidence[20].

Shwartz 2002[14] showed that incidence rates of testicular cancer were significantly correlated with the per capita consumption of coffee and pig meat, two commodities known to contribute to the exposure to OTA in the diet. This study consider the first study that demonstrated that exist relationship between Ochratoxin A and many types of cancer diseases as lung cancer, lymphatic node cancer, Breast cancer, Ovaries cancer, Pancreas cancer, Stomach cancer, Brain cancer, Prostate cancer and Leukemia

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