Detection of Fumonicin in Liver cancer cases in Al-Diwanyia city

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Abstract. The study aimed to investigate of mycotoxin (Fuminocin B1) in blood samples of patients suffers from liver cancer. Therefore 100 blood samples were collected randomly from patients in Al-diwanyia teaching hospitals, then detection of toxin by ELIZA method. The results showed 54 (54%) of patients were had Fumonicin in their blood in different concentrations varying from (2.801 to 10.041) ng/ml and these concentrations were high in patients aged from (61-70) years.

Key word: fumonicin B1. Mycotoxins, mycotoxicosis.

1. Introduction

Fumonicin are secondary metabolites, are the most prevalent member of a family of mycotoxins, produced by several species of Fusarium fungi such as Fusarium verticillioides, which occur mainly in maize (corn), wheat and other cereals. Fumonincin B1 contamination of maize has been reported worldwide at mg/kg levels. Human exposure occurs at levels of micrograms to milligrams per day and is greatest in regions where maize products are the dietary staple. (1).

In all animal species tested, fumonis in B1 has been associated with a wide range of adverse health effects, particularly on the liver and kidney. A particular concern is the cancer causing potential of the toxins, thought to arise following disruption of fat metabolism by the toxins, resulting in depletion of the fats known as complex sphingolipids and accumulation of the fats known as sphingoid bases and sphingoid base metabolites. Another concern is the potential immunotoxicity; depression of specific and nonspecific immune response has been observed in pigs and mice at low oral doses, but the data are inconclusive. Other concerns include possible indirect mutagenicity (DNA damage), although to date the weight of evidence indicates that fumonisins are neither directly mutagenic nor metabolized into DNA reactive compounds. (2).

Fumonisins have been observed to have effects on reproductive performance in pigs and rabbits, and birth defects – neural tube defects – have been induced in mice in a few studies. Concerning the potential neurotoxicity of fumonisins, while the toxins can induce leukoencephalomalacia (softening of brain tissue) in horses (equids), it is considered unlikely that fumonisins cross the blood–brain barrier and induce neurotoxic effects in the brain; rather, in equids, they are thought to act via disruption of vascular function. In pigs, the pulmonary edema caused by fumonisins has also been
linked to altered vascular function. The altered vascular function is likely to be caused by accumulation of sphingoid bases and their phosphorylated metabolites in the blood. (3).

The mechanisms responsible for cancer development should lie elsewhere. Important mechanisms for cancer development due to FB1 could be oxidative damage (ROS-production) and lipid peroxidation. Hepatic and renal tumors could also be due to apoptosis by FB1. As a response to this there could be continuous regeneration of cells, causing cancer. It seems to be that disrupted sphingolipid metabolism is the causative factor for FB1-induced carcinogenicity, as is the case with the toxic effects(4). Based on all these animal studies FB1 is classified by The International Agency for Research on Cancer (IARC) as possibly carcinogenic to humans (5).

Fumonics are found in a wide range of tropical or subtropical food commodities peanuts in particular. Other food commodities include, corn, figs, nuts and cereals. The contaminated foods reported to be associated with an in Asian region include maize, peanuts, rice, and other oil products. Fumoninic contamination of food is an ongoing global concern and considered an unavoidable and unpredictable problem, even where good agricultural, storage, and processing practices are implemented, posing a difficult challenge to food safety. Additionally, these mycotoxins are not easily eliminated, during food processing because of their stability against heat, physical, and chemical treatments (1). Furthermore, feed contamination can also pose an extra hazard for food safety due to the possible carry-over of mycotoxins to animal-derived products such as milk, meat, and egg leading to mycotoxin intake by humans. Fumonicin B1 can cause both acute and chronic toxicity in animals. Effects such as acute liver damage, liver cirrhosis, induction of tumors and teratogenic and other genetic effects are well documented. In modern days, acute toxicity of aflatoxin to humans has been encountered only rarely. Symptoms may include fever, vomiting and jaundice. Acute liver damage can occur which may be fatal in severe cases. (6). Human exposure to Fumonicin B1 is principally through ingestion of contaminated foods, inhalation of the toxins may also occur occasionally due to the occupational exposure, many strategies have been proposed for controlling the mycotoxin occurrence in different food commodities; however, no clear-cut solutions exist. Long term intake of Fumonicin B1 can be associated with hepatic cancer. Animal studies have showed that hepatocellular liver tumors may develop in animals like rats, hamsters and monkeys after prolonged oral administration. (3).

Due to the extreme concerns about Fumonicin contamination in food and feed and their negative public health and economic impacts, it has received greater attention compared to other mycotoxins. As it is realized that absolute safety is very difficult to be achieved, many developing countries have attempted to decrease the toxicity of Fumonicin by regulations that control exposure that restrict the limits of these toxins in food and animal feed (7).

Therefore, this study was designed to determine the levels of Fumonicin B1 in blood specimens of liver cancer cases.

2. Materials and Methods.

After having the Ethical agreement of the patients, we started blood specimens' collection form patients suffers from liver cancer whom attended to AL-Diwaniyah teaching hospitals throughout the period from June 2017 till December 2018.

2.1. Specimens Collection

Blood samples were collected from patients, Serum samples were prepared from the blood and kept at –20 °C for Fumonicin B1 detection.
2.2. ELISA assay of Fumonicin B1.

The presence of Fumonicin was confirmed using an immuno-enzymatic commercial kit according to company instructions based on monoclonal antibodies specific for each of them (Transia, Lyon France). Briefly, the extract was evaporated to dryness and taken up in the sample buffer provided in the kit; 50 μL of the sample was then pipetted into duplicate wells of an ELISA plate sensitized with the monoclonal antibody specific for Fumonicin B1. Following incubation and washing, 50 μL of the specific monoclonal antibody conjugated to horseradish peroxidase dissolved in the conjugate buffer provided in the kit was added, incubated and washed again before the substrate was added and incubated for color development as recommended by the suppliers. Color intensity was read off an ELISA reader provided with the kit. Standards included in the kit allowed the calculation of Fumonicin B1 concentration in the extract assayed (8).

2.3. Statistical analysis of the data

The data were tabulated in a data sheet, and they were analyzed using the computer programme SPSS (Statistical Package for Social Sciences) version 20.0. by Chi-Square. The difference was considered significant when the probability (P) value was ≤ 0.01 (9).

3. Results and discussion

The results showed 54(54%) out of 100 blood specimens collected from patients were contaminated with FB1. Table (1). So, this study clarified that highest percentage (55.5%) of blood specimens contamination with FB1 was recorded in age group (61-70) years Table (2). Regarding to concentration of FB1 in blood specimens we show in Table (3) concentration of FB1 in patients were ranged between (2.801 to 10.041) ng/ml and high concentration (6.212 -10.041) ng/ml were recorded in age group (61-70) years.

| Case study                  | No .of specimens | No. of specimens have FB1 | Percentage |
|-----------------------------|-------------------|---------------------------|------------|
| Patients with cancer liver  | 100               | 54                        | 54%        |

Table (2): Distribution of FB1 positive specimens according to age groups.

| Age group (year) | No. of specimens | No. of specimens contain FB1 | Percentage (%) |
|------------------|------------------|------------------------------|----------------|
| 30-40            | 13               | 6                            | 11             |
| 41-50            | 19               | 8                            | 14             |
| 51-60            | 23               | 10                           | 18.5           |
| 61-70            | 45               | 30                           | 55.5           |
| Total            | 100              | 54                           | 54            |

\[ X^{2\text{cal.}} = 1.3 \]
\[ p \leq 0.01 \]

Table (3) Concentration of FB1 in positive specimens

| Age group (year) | No .of specimens | Concentration of FB1 (ng/ml) | Mean ±standard error |
|------------------|------------------|-----------------------------|----------------------|
| 30-40            | 13               | 2.801 -4.500                | 5 ±3.4               |
| 41-50            | 19               | 2.980 -5.550                | 3 ± 2.6              |
From above results that summarized in tables 2 and 3 we showed the percentage of contamination and concentration of FB1 in blood specimens was arise with increased age of patients, this may be belong to the fact that mention the effect of this toxin accumulates due to exposure to it during life style by eating or drinking the contaminated product and chronic exposure of FB1 has been linked to development of cancer. Where evidence to date indicates that fumonisins are not acutely toxic (10).

Fumonicin B1 contamination in various foods is a major threat to the health of exposed people, this emphasizes the importance of monitoring FB1 and its metabolites in food products, the presence of FB1 in body fluids of patients is a potential risk of impairment of growth during their development, since it is well known that it inhibits protein synthesis , Further, it has been suggested that FB1 reduces the nutritional capacity of food by interfering with metabolic processes (11). Exposure to FB1 from early age could be a predisposing factor for primary liver cancer. Indeed, it is well known that mycotoxins, viral hepatitis, alcohol, and cigarette are high risk factors for cancer development (10).

This toxin is considered to have the potential to induce regenerative cell proliferation in the liver and kidney, leading to cancer in animal models (11). But there is few reports on the effects of fumonisin in humans, one study found no significant association between fumonisin exposure and the risk of hepatocellular cancer (12) while another study indicated FB1 contamination in rice was associated with increased risk of esophageal cancer(13). A study in women conducted in Guatemala showed that fumonisin intake from maize-based foods was correlated with evidence indicative of disruption of fat metabolism as seen in carcinogenicity studies conducted with animal models. (12)

In conclusion, FB1 seem to be present in intake foods like eggs, meat, meat products and milk, indicating that transfer into consumer is negligible. A high prevalence of contamination was found in the blood patients, exposure to fumonisins needs to be kept as low as possible to protect the consumer. Many countries have regulations governing fumonisins in food with prescribed acceptable limits, and most have maximum permitted or acceptable levels for different foodstuffs. Fumonisins damage health and business opportunities, and importing countries are imposing increasingly more stringent regulations.

4. References

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|      | 51-60 | 61-70 | Total |
|------|-------|-------|-------|
|      | 23    | 45    | 100   |
| 5.010 - 6.011 | 6.212 -10.041 | 5 ±4.7 | 6 ±3.21 |
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