

Determination Some Minerals in Cancer Tissue

Mona Al-Terehi^{1*}, Liwaa Hussein al-kilabi², Ayad M.J. AL –Mamoori³

Ali Hmood Al-Saadi³, Haider K. Zaidan³

1.University of Kufa, College of Scienc

2.University of Kufa college of medicine

3.University of Babylon, College of Science

Mona_diabetis@yahoo.com

Abstract

Study was aimed to detect some trace elements in human tumor tissue, Manganese, cobalt, cadmium and Zinc was measured in cancer and benign tissue using atomic absorption, results show that cancer tissue have higher concentration of cobalt and Zinc than benign tissue, it were 156.7 ± 6.5 and $205.79 \mu\text{g/g}$ respectively. Females had higher concentrations than males in cancer 211.41 ± 439.79 , 114.54 ± 0.05 , 157.05 ± 6.50 , $206.58 \pm 20.93 \mu\text{g/g}$ in Mn, Cd, Co and Zn respectively also in benign tissue Female 2373.37 ± 703.56 , 114.56 ± 0.06 , 154.50 ± 29.4 , $204.65 \pm 28.23 \mu\text{g/g}$ in the same minerals above.

Keywords: trace elements, atomic absorption, tumors tissue.

Introduction

As a result of contamination in Iraqi environment which increased after wars and used different weapons, trace elements were increased in different sites; soil, water, food and air, thus present study suggested to detect some trace elements in human tumors tissue. Different studies in Iraqi environment improved increasing in minerals concentration in different sites such as air, soil, river water and plants in another hand other studies suggested these minerals roles in carcinogenicity and cytotoxicity on human body. Taha et al., (2005) that the concentration of some minerals in the air of districts in Hilla city was abnormally high, the highest concentration in the air was recognized. Also many local studies explained the high concentrations of these metals in the local environment (air, water and food).

Cadmium (Cd) is a known toxic heavy metal that widely used in industry thus Cd is highly persistent in the environment, its effect on human health by occupational and environmental exposure. Cd exerts multiple toxic effects and has been classified as a human carcinogen by the International Agency for Research on Cancer (IARC). Cd is carcinogenic that causes some cytotoxic effect by disruption gene expression, inhibition of DNA repair systems, induction oxidative stress, and inhibition of apoptosis (Joseph, 2009).

Cobalt (Co) is an essential trace element being an integral part of vitamin B12 which is essential for folate and fatty acid metabolism. The carcinogenic potential of cobalt and its compounds was evaluated by IARC in 1991, which concluded that there was inadequate evidence for carcinogenicity in humans (lung cancer) (IARC, 1991).

Two different mechanisms of cobalt genotoxicity, DNA breakage induced by cobalt metal and especially hard metal particles, and inhibition of DNA repair by cobalt (II) ions contribute to the carcinogenic potential of cobalt compounds. There is evidence that soluble cobalt (II) cations exert a genotoxic and carcinogenic activity in vitro and in vivo in experimental systems but evidence in humans is lacking. Experimental data indicate some evidence of a genotoxic potential for cobalt metal in vitro in human lymphocytes but there is no evidence available of a carcinogenic potential. There is evidence that hard metal particles exert a genotoxic and carcinogenic activity in vitro and in human studies, respectively. There is insufficient information for cobalt oxides and other compounds (Lison et al., 2013).

Zinc (Zn) is a trace mineral which is vital for the functioning of numerous cellular processes, is critical for growth, and may play an important role in cancer etiology and outcome. The intracellular levels of this mineral are regulated through the coordinated expression of zinc transporters, which modulate both zinc influx as well as efflux. LIV-1 (ZIP6) was first described in 1988 as an estrogen regulated gene with later work suggesting a role for this transporter in cancer growth and metastasis (Grattan and Freake, 2012).

Manganese (Mn) is an essential element present in all living organisms and is naturally present in rocks, soil, water, and food. Exposure to high oral, parenteral, or ambient air concentrations of Mn can result in elevations in Mn tissue levels and neurological effects. However, current understanding of the impact of Mn exposure on the nervous system leads to the hypothesis that there should be no adverse effects at low exposures, because Mn is an essential element; therefore, there should be some threshold for exposure above which adverse effects may occur and adverse effects may increase in frequency with higher exposures beyond that threshold. Data gaps regarding Mn neurotoxicity include what the clinical significance is of the neurobehavioral, neuropsychological, or neurological endpoints measured in many of the occupational studies that have evaluated cohorts exposed to relatively low levels of Mn (Santamaria, 2008).

Mn toxicity has primarily been observed in occupational settings where there is the potential for chronic exposure to high levels or following the accidental ingestion of large quantities. John Couper was the first to report neurological effects associated with exposure to Mn in the scientific literature in 1837, when he described muscle weakness, limb tremor, whispering speech, salivation, and a bent posture in five men working in a Mn ore crushing plant in France²⁴.

Materials and methods

Extract and determine heavy metals in soft tissue as following according to (Otc here, 2003).

1- Pulled out the soft tissue from samples by plastic forceps and put in polyethylene dishes with removing the excessive water by filter paper.

2- Tissue dried on 70 C° for 24 hr. with well grinding by Ceramic mortar.

3- (0.3) g has been taken from dried grinded samples and put it on Teflon Beaker, then added 10 ml from HNO₃ with heating on 85 C° for 1hr. After that, few drops of hydrogen peroxide added for completion of oxidation process within temperature increasing up to 135 C° for 30 min. until we have a clear solution and left it for a while to get a cooling and complete by D.D.W up to 50 ml, and centrifuge this sample to remove suspended lipid compounds in case of presence for 10 min. at 2500 r.p.m and sample transferred to polyethylene bottle to be ready for measurement by Atomic Absorption Spectrophotometer type 6300 (Shimadzu, Japan) and results expressed as µg/g. The Following equation was used to determine the concentration of heavy metals as µg/g.

$$\text{Conc} = \frac{A \times B \times D}{Df}$$

conc. = Metal concentration in sample (µg/g dry weight)

A= Metal concentration from standard curve (mg/L)

B= Final volume for filterable samples (ml)

Df= Dilution factor and used as follow ; Df = Volume of dilution sample solution ml / Volume of aliquot taken for dilution in ml D= dry weight (g).

Results

Sample characterization in present study show that Age mean was 41.66 years, samples consist of high percentage of different cancer tissue it was 72.41% and 27.58 % was benign tissue. According to gender samples consist of 55.55% female and 44.44% male table (1).

Table (1) Characterization of tumor samples used in present study.

Character of sample	Percentage
Age	41.66±22.68
Benign	27.58%
Cancer	72.41%
Female	55.55%
Mal	44.44%

In cancer tissue trace elements concentrations were higher than its concentrations in benign tissue, these elements were Co and Zn, while others elements were lower in cancer tissue, all variation was non-significant, table (2).

Table (2) Trace elements concentrations in human tumor tissue in µg/g.

Trace elements	Mn	Cd	Co	Zn
Cancer tissue	1999.87±421.18	114.54±0.05	156.7±6.50	205.79±19.75
Benign tissue	2110.73±557.00	114.57±0.065	153.59±6.33	196.89±22.34

mean±SD

According to gender, in cancer tissue females had higher concentration of Mn, CO and Zn, same results was showed in benign tissue; Mn, Co and Zn concentration were higher than male table (3).

Table (3) Trace elements concentration Ppm in human according to gender µg/g

Trace elements		Mn	cd	co	Zn
Cancer tissue	Male	1998.14±413.59	114.54±0.05	156.44±6.71	204.9±18.98
	Female	2011.41±439.79	114.54±0.05	157.05±6.50	206.58±20.93
Benign tissue	Male	1848.1±212.08	114.57±0.073	152.68±9.093	189.14±14.40
	Female	2373.37±703.56	114.56±0.06	154.50±29.4	204.65±28.23

mean±SD

Discussion

The Genotoxic effects of metals can be mediated either through metabolically activated electrophilic derivatives that interact with DNA and other macromolecules, or through direct binding of DNA (De Bont and van Larebeke 2004). Many metals have been shown to directly modify and/or damage DNA by forming DNA adducts that induce chromosomal breaks (Chakrabarti 2001).

Susceptibility to cancer is characterized by extensive DNA damage. This damage is thought to result from decreased repair capacity and/or by the direct carcinogenic interaction of metallic ions with DNA and DNA adducts (KLAUNIG, 2010)

Study show that even low doses and short term exposure to cadmium can cause specific DNA damage in breast tissue and may be a possible mechanism of action of cadmium on the cell cycle of human mammary cell lines (Roy et al. 2004). Cadmium significantly stimulated the growth of MCF-7 cells when compared with cells grown in estrogen-depleted medium, comparable with the degree of growth stimulated by estradiol (Roy et al., 2004). This study demonstrates that cadmium induces cell growth, and may have a possible role. Since zinc is essential for growth and cancer is characterized by uncontrolled growth, zinc accumulation suggests an involvement of zinc in breast tumor genesis. Zinc is important to cell proliferation; however, it accumulates in mammary tumors and supports tumor growth (Sukumar et al. 1983; Lee et al. 2003).

In one study twenty-one-day old female rats were assigned to a low-zinc, an adequate-zinc, or ad libitum control groups. On day 50, all rats were injected with 1-methyl-1-nitrosourea (MNU) to induce mammary tumors. MNU has been widely used in rodent models to induce diverse mammary tumors that differ in type and location of formation in the mammary gland for studying human breast cancer due to their similarities in hormone dependency. The carcinogenicity of MNU is due to its ability to induce a mutation in the H-ras oncogene (Lee et al. 2004). Results indicated low-zinc intake suppressed MNU-induced tumor incidence, tumor numbers and tumor multiplicity.

In Iraqi environment many studies improved increasing heavy metals in human body, in study on lactating mothers milk Ziadan et al (no published data) found that increasing in Mn, Co, Zn and Cd in mothers milk in Hilla city also Al-muhanna (2011) found increasing in heavy metals Pb, Fe and Ni. In environment researchers found that Iraqi river air and soil was polluted by different heavy metals (Salman et al., 2007; Hassan et al., 2009) this led us to conclude that increasing heavy metals in human especially in tumors tissue resulted from environment that may be responsible on carcinogenesis and causes cancer.

References

- 1- IARC (1993) Monographs on the Evaluation of Carcinogenic Risks to Humans. IARC, Lyon 119-237
- 2- Joseph P (2009) Mechanisms of cadmium carcinogenesis. *Toxicol Appl Pharmacol* 238:272-9. doi:10.1016/j.taap.2009.01.011
- 3- Taha N. D., Hashem K. A. and Abd-alameer S. I. (2005). Determination lead in Hilla city air. First Environmental research conference. Babylon University
- 4- Salman J.M., Hassan M.F. and Saleh M. M. (2007). Concentrations of nine heavy metals in muscles of fish *Barbus lutescheckel*, *Aspius vorax heckel*, *Barbus grybus heckel* and *hypophthalmichthys molitrix* Richardson collected from Euphrates river. *J. of Environmental*, 1, 5-19.
- 5- Hassan, M. F., Saleh M. M. and Salman J. M. (2010). A study of physicochemical parameters and nine heavy metals in the Euphrates river, Iraq, *E-J. of Chemistry* 7, 685-692.
- 6- Otchere, F.A. (2003). Heavy metals concentrations and burden in the bivalves (*Anadara* (*Senilia*) *senilis*, *Crassostrea* *tulipa* & *Perna* *perna*) from lagoons in Ghana: Model to describe mechanism of accumulation and excretion. *African Journal of Biotechnology*, 2 (9): 280-287.
- 7- IARC (1991). Cobalt and cobalt compounds. *IARC Monogr Eval Carcinog Risks Hum* 1991;52:363-472.
- 8- Lison D.; De Boeck M., Verougstraete V, Kirsch-Volders, M. (2013). Update on the genotoxicity and carcinogenicity of cobalt compounds. *Occup Environ Med* 2001;58:619-625.
- 9- Chakrabarti SK, Bai C, Subramanian KS. 2001. DNA-protein cross links induced by nickel compounds in isolated rat lymphocytes, role of reactive oxygen species and specific amino acids. *Toxicol Appl Pharmacol*. 170:153-165.
- 10- Roy S.S, Mukherjee S, Mukhopadhyay S, Das SK. (2004). Differential effect of cadmium on choline phosphotransferase activity in normal and cancerous human mammary epithelial cell lines. *Mol Cancer Ther* 3(2):199-204.
- 11- De Bont R, van Larebeke N. (2004). Endogenous DNA damage in humans: a review of quantitative data. *Mutagenesis* 19(3):169-85.
- 12- Grattan B, and Freake, C. (2012). Zinc and Cancer: Implications for LIV-1 in Breast Cancer, *Nutrients*, 4, 648-675.
- 13- Couper J. (1837) On the effects of black oxide of manganese when inhaled into the lungs. *Br Ann Med*

Pharm 1837; 1 : 41-2.

14- Santamaria, A.(2008).Manganese exposure, essentiality & toxicity, Indian J Med Res 128, October 2008, 484-500.

15- Lee,R., Woo,W., Wu,W.B., Kummer,A., Duminy,H. and Xu,Z. (2003) Zinc accumulation in N-methyl-N-nitrosourea-induced rat mammary tumors is accompanied by an altered expression of ZnT-1 and metallothionein. ExpBiol Med 228:689-696.

16- Lee S, Simpson M, Nimmo M and Xu Z.(2004). Low zinc intake suppressed N-methyl-N- nitrosourea-induced mammary tumorigenesis in Sprague- Dawley rats. Carcinogenesis 25(10):1879-1885.

17- KLAUNIGJ., KAMENDULIS M. , AND HOCEVAR B. (2010).Oxidative Stress and Oxidative Damage in Carcinogenesis, Toxicologic Pathology, 38: 96-109.

18- Sukumar S, Notario V, Martin-Zanca D, Barbacid M. 1983 Induction of mammary carcinomas in rats by nitroso-methylurea involves malignant activation of H-ras-1 locus by single point mutations. Nature 306(5944):658-61.

19- Al-Muhana, E. (2012) DETERMINATION OF SOME HEAVEY METALS (LEAD, CADIMUM, NICKEL AND IRON) IN BREST MILK OF LACTATING MOTHERS IN HILLA CITY-2012. Diplomathesis college of medicine.