IOSR Journal of Biotechnology and Biochemistry (IOSR-JBB)
ISSN: 2455-264X, Volume 1, Issue 6 (Sep. – Oct. 2015), PP 97-101
www.iosrjournals.org

Role of serum trace elements magnesium, copper and zinc, level in Libyan patients with bronchial asthma

Khaled S. Al-salhen(1),Sayed A. M. Mahmoud(2*),Salmah M.Omran(1), Safaa K. Mohammed(1)

(1)Department of Chemistry, Faculty of Science,(2)Medical Biochemistry Department, Faculty of Medicine,Omar Al-Mukhtar University, Al-Bayda, P.O. 919, Libya.

(*)Permanent address;Medical Biochemistry Department, Faculty of Medicine, Al-Azher University, Egypt

Abstract ;*The present study compared the levels of serum Mg, Cu and Zn between the adult with asthma and healthy volunteer in order to evaluate the associations of these nutrients with asthmatic patients.*
Thirty-three adults patients of both (19 males, 14 females) with the median age 39 years with bronchial asthma, who were admitted by the Department of Pulmonary Diseases of Shat and Alkyfaya Hospitals, were included in the study. Thirty-three adult patients of diagnosed bronchial asthma of both sexes (19 males and 14 females) attending Pulmonary Diseases Care Unit at Shat and Alkyfaya Teaching Hospital in El-Beida and Benghazi Cities and 31 healthy volunteers (17 males, 14 females) were studies. A serum elements level was measured using atomic absorption spectroscopy technique at calibration mode.The results indicated that serum of Cu, Zn and Mg levels in male and female adults with asthma were significantly lower (P<0.001) in compared to healthy controls.On the basis of this study finding and those of other reports, trace elements deficiency may contribute to diets and diseases through its significant effects on the antioxidant enzymes' functions, and decrease the antioxidant capacity in asthma. It seems that the estimation of serum or plasma trace elements may help in investigation of asthmatic disease in both males and females.
Keywords: *bronchial asthma, antioxidant, trace elements*

I. Introduction

In the last few years, nutrition has represented an important conditioning factor of many gastrointestinal, cardiovascular and pulmonary chronic diseases(Riccioni and D'Orazio, 2005). Trace elements such as zinc, copper and magnesium are essential micronutrients, whichplay a vital role in the body to perform its functions properly [1]. These elements and the minerals should present in the body in appropriate amounts and must be available for reacting with other elements to form critical molecules as well as to participate in various important chemical reactions [2].Deficiency of trace elements may be associated withproduction of free radicals with subsequent tissue damage and infectious diseases are often concomitantly observed and result in complex interactions[1]

In many studies reactive oxygen free radicals were indicted for the pathogenesis of bronchial asthma [3] (Jarjour and Calhoun, 1994), which is a chronic inflammatory disease of the respiratory tract [4]. There are some antioxidant enzymesto avoid the harmful effect of free radicals. These enzymes responsible for antioxidant defense have trace elements like zinc, copper,[5] and magnesium, within their structure and act as a cofactorfor these enzymes[5-7]. The antioxidant mechanisms that protect the lung against these oxidants include: three superoxide dismutases[2] and glutathione peroxidase [8]. Glutathione peroxidase has selenium and the superoxide dismutases have copper and zinc in their structure[8].Some studies have shown that the biological role of these elements in many physiological and pathological features as they play an important role in protection the body by inhibiting the generation of reactive oxygen free radicals.Changesin the level of these trace elements decrease the efficiency of antioxidant systems and this leads to hyper-reactivity and inflammation in the respiratory tract[9-12].There exists an imbalance between oxidants and antioxidants in allergic asthma causing inflammatory processes in the air ways [13]. The aim of the present study was conducted to evaluatethe relationship between serum levels of the trace elements zinc, copper and magnesium and the severity of asthma attacks in asthmatic adults.

II. Materials and methods

Chemicals

All glasswares were previously soaked in 5% nitric acid V/Vfor 24 hours, then allowed to stand 2 hours at room temperature and rinsed thoroughly with deionized water. This procedure was followed in order to exclude the possibility of contamination with trace elements. All chemicals were analytical grade and used without any purification. Stock solutions of Zn (II), Cu(II) and Mg(II) were prepared by dissolving appropriate amounts of ZnSO4.7H2O, CuSO4.5H2O and Mg(NO3)2.6H2O in 100 ml distilled water in volumetric flasks. Working solutions for each element were prepared by diluting its stock solution. Different concentrations (0.1-50ppm) stock solutions of trace elements were used for calibration of standard graphs.

Patients

They were randomly selected from patients followed up by the Department of Pulmonary Diseases of Shat and Alkyfaya Teaching Hospital in El-Beida and Benghazi Cities in Libya. All patients were previously diagnosed as asthmatics. None of the patients had diabetes mellitus, liver or kidney diseases, and infection or thyroid dysfunction.Thirty-three patients (19 males, 14 females) with bronchial asthma (aged 18 ± 65 yrs, median age 39yrs) were examined at the Hospital Shat Clinic. Thirty-one healthy non-asthmatic nonsmoking subjects (17 males, 14 females) aged 18±56 yrs (median age 37yrs) from the same population served as a control group. Laboratory tests were performed at the department of chemistry, El-beida, Libya.About five milliliters of venous blood samples of two groups were collected into plastic disposable syringes and serum was separated by centrifugation at 4000 rpm for 5 minutes at room temperature in the laboratory and transferred the clean serum to the -20 freezer in the biochemistry laboratory of Chemistry department in Eppendorf vials in order to measure the serum levels of zinc, magnesium and copper byFlame atomic absorption spectroscopy. The source of energy for atomization was air/C2H2. Absorbances were recorded at 4 22.8 nm, 324.7 nm and 213.9 nm for magnesium, copper and zinc respectively in the atomic absorption spectrometer. The study was conducted over a period of 1 year on the Omar Al-Mukhtar University, College of Sciences at Chemistry Department in Libya.

III. Statistical Analysis

The results were expressed as mean ± SD of all parameters in serum were calculated. The measurements were replicated 3 times for each sample. Student t-test was used for comparison of means and the significance level was set at $P<0.05$.If P value was less than 0.05, it was considered statistically significant.

IV. Results and discussion

This study was carried out to express the quantities of serum micronutrients in rural healthy couples of El-bieda city in Libya. Their ages range of females and males rural couples were between 16-34 years. Thirty-three patients (19 males, 14 females) volunteers were selected for this study. The Department of Pulmonary Diseases of Shat and Alkyfae Teaching Hospitals diagnosed all patients as asthmatics. They all had a history of intermittent wheezing, shortness of breath, chest tightness and were taking different asthma medications.

Level of serum elements was calculated after application of absorbance on suitable calibration curve from standard solutions (Fig. 1, 2 and 3).Figures 1, 2 and 3 represent calibration graphs for determination of Mg, Cu and Zn standard solutions were prepared in range of (5.00 to 50ppm), (0.8 to 1.5ppm) and (1 to 15ppm) respectively. The range for standard solutions were prepared accorded to normal ranges of Mg, Cu and Zn (18.0-30.0, 0.70-1.40 and 5.0-15.0 ppm) respectively[14,15].

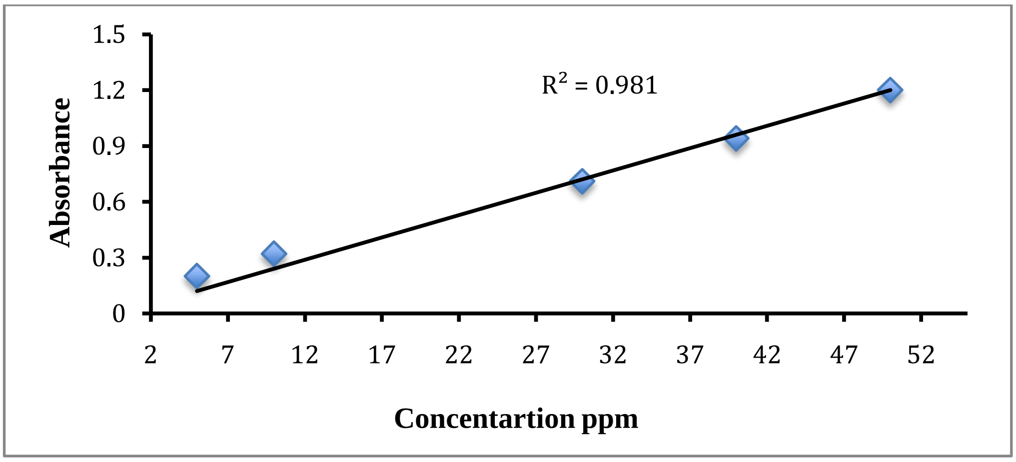

Fig. (1): Calibration curve of Mg in aqueous solution.

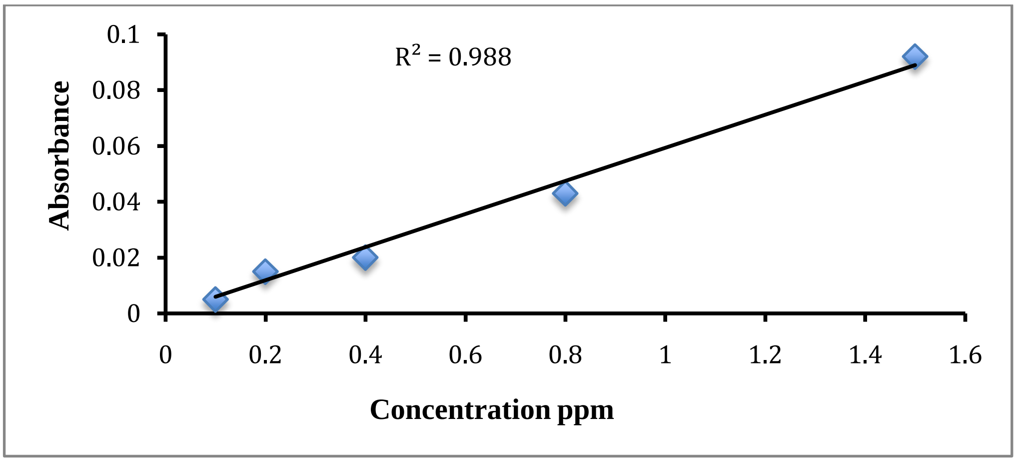

Fig. (2): Calibration curve of Cu in aqueous solution.

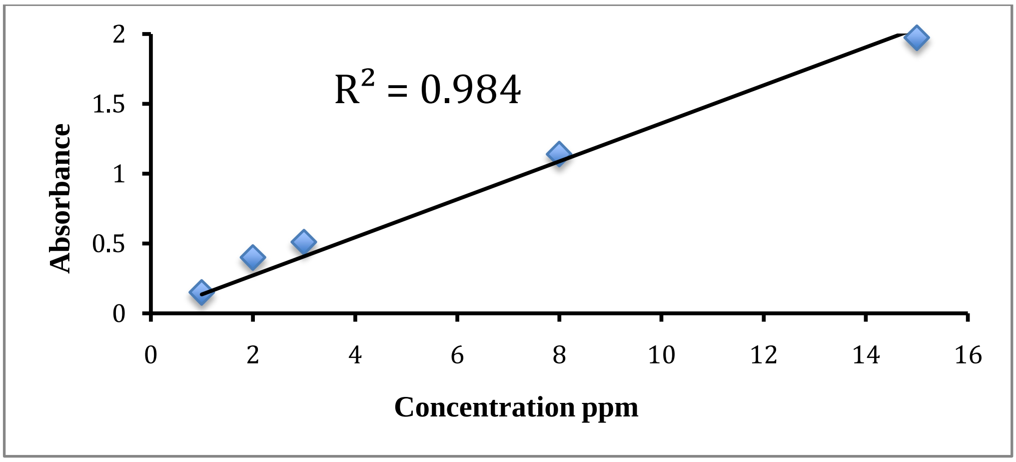

Fig. (3): Calibration curve of Zn in aqueous solution.

Mg, Zn and Cu serum levels were examined in all groups. Serum Mg, Zn and Cu levels were found to be significantly decreased ($p<0.05$) in male and female asthmatic patients compared to their controls (Table 1 and 2).

Table (1): Comparisonof traces elements concentration (ppm) in blood serum of adult male asthmatic patients and healthy volunteers.

Trace elements	no. of detection	Group	Upper limit	Lower limit	Mean ± SD	P value
Mg	57 51	Patients Control	12.40 27.45	6.70 25.22	8.10 ± 4.03 26.33 ± 1.63	p<0.001
Cu	57 51	Patients Control	0.91 1.41	0.14 1.36	0.53 ± 0.49 1.36 ± 0.06	p<0.001
Zn	57 51	Patients Control	4.18 13.56	1.83 12.79	3.04 ± 1.66 13.26 ± 0.60	p<0.001

Values are presented as mean ± SD with 95% confidence. p-value: $p<0.001$ for asthmatic versus healthy volunteers.

Table (2): Comparison of traces elements concentration (ppm) in blood serum of adult female asthmatic patients and healthy volunteers.

Trace elements	no. of detection	Group	Upper limit	Lower limit	Mean ± SD	P value
Mg	42 42	Patients Control	15.0 28.10	5.50 27.67	27.88 ± 0.30 10.50 ± 7.61	p<0.001
Cu	42 42	Patients Control	1.01 1.47	0.15 1.42	0.58 ± 0.60 1.44 ± 0.04	p<0.001
Zn	42 42	Patients Control	4.11 14.10	1.69 12.99	2.90 ± 1.71 13.55 ± 0.78	p<0.001

Values are presented as mean±SD with 95% confidence. p-value: $p<0.001$ for asthmatic versus healthy volunteers.

The results of the study have been showed in Tables 1 and 2 indicate that the mean concentrations for magnesium, copper and zinc in blood serum of both sexes' adult healthy volunteers in comparison with normal ranges; magnesium, copper and zinc are in normal range [14,15] and no significant difference between the both sexes. These results agree with previous studies showed that normally the difference of trace elements between the sexes was no significant[16,17].In the current study, serum zinc concentrations were decreased for adult asthmatic patients in both sexes (Table 1 and 2). The result observed that adult asthmatic patients in both sexes have deficiency in zinc level which below 3.0ppm.The results obtained for Zn concentration in control and patient groups, which are shown in the Tables (1 and 2) for both sexes, show significantlydecreased ($p<0.001$). The results were so similar to those published in other literature[11,18].Zinc is regarded one of the main components of antioxidant enzymes leading to decreased harmful effects of oxygen free radicals. Reduction of zinc may cause diminishing the antioxidants system effects and as a result leads to inflammation and hyper activity in air ways [19,20].Zinc deficiency disturbs oxidant and antioxidant balance, which is named oxidative stress. This stress makes pulmonary damage directly and increase of oxidative stress in patients with asthma is mentioned in many studies[21].According to the study of Dey Toro et al, zinc deficiency leads to change in immune response from TH1 to TH2 that is effective in the pathophysiology of asthma [22].Following a study by El-Kholy et al at the Department of Pediatric diseases in Ain Shams University, Cairo, Egypt, it was concluded that zinc play vital roles in protein synthesis and enzymes activity and serum levels of zinc was lower in children with asthma than normal people [23].

The mean serum of Cu for male and female patients were 0.53 ± 0.49 ppm and 0.58 ± 0.60 ppm respectively while that for controls were 1.36 ± 0.06 ppm and 1.44 ± 0.60 respectively. This significantly decreased level ($p<0.001$) of Cu element was also found by other studies (Nevin et al., 2001; 2004; Bahri et al., 2004). Free oxygen radicals including hydrogen peroxide, superoxide and hydroxyl radicals are involved in the pathogenesis of asthma[24,25]. There exist some defense mechanisms under the title of antioxidants agents various harmful agents causing inhibition of free radicals production, reducing their activity and degradation of them. The most important antioxidants include glutathione peroxide and dismutase superoxide[26,27].Copper deficiency is a significant risk factor for asthma [28,29], as it has been linked to inability to produce the important antioxidant enzyme, superoxide dismutase that contains Cu and Zn. This enzyme is extremely important in defense, so decreasing these trace elements causes the effects of antioxidant system to be lower and this leads to hyperactivity and inflammation in the respiratory tract[30].

Serum magnesium levels were measured in all groups of volunteers, the results were observed that the levels of Mg were significantly decreased level ($p<0.001$) in adult asthmatic patients for both sexes about 37% less than healthy volunteers level(Tables 1 and 2). These results are in agreement with the data of other studies [11, 31,32] confirming the beneficial effect of this element on lung function.Magnesium is the second most prevalent intracellular cation, and it has an important role as a cofactor invarious enzymatic reactions and regulates physiological functions including protein synthesis, intracellular signal distribution and enzyme catalysis [33,34]. In addition, magnesium suppresses the excitability of muscle fibers by reduction of acetylcholine secretion from motor nerve terminals. Moreover, it inhibits production of inflammatory mediators by helping stabilization of T-cells and inhibiting mast cell degranulation[35]. Again, it reduces the severity of inflammation in asthma by stimulating nitric oxide and prostacyclin syntheses[35].

As is seen, all these studies on trace elements measurement have been done in a limited number of patients. As measurement tests are expensive, they are not easily available and difficult for clinical application. Therefore, generally serum Mg, Cu and Zn levels are used for the monitoring of changes in body Mg concentration during acute attack and stable phases of asthma. In the present study, serum Mg, Cu and Zn levels were measured because of the facts that these trace elements is not measured in our unit and there is yet no available study on this subject in Libya.

V. Conclusions

We conclude that quantitative determination of these elements in the serum of asthmatic patients assisting in the early detection of the disease and evaluation of therapeutic agents.Diet and nutrition may be important modifiable risk factors for the development, progression and management of obstructive lung diseases such as asthma.However, further multicenter studies with greater sample sizes are needed to warrant the results of this study.

References

[1] N. Lukác, P. Massányi, Effects of trace elements on the immune system. Epidemiol. Mikrobiol. Imunol. 56, 2007, 3-9.
[2] Q. Shazia, Z. Mohammad, I. Taibur Rahman, U. Hossain, Correlation of oxidative stress with serum trace element levels and antioxidant enzyme status in beta thalassemia major patients: A review of the literature. Hindawi publishing corporation, anemia, 7, 2012, 20-23.
[3] N.N. Jarjour, W.J. Calhoun, Enhanced production of oxygen radicals in asthma. . J. Lab. Clin. Med. 123, 1994, 131-137.
[4] D.J. Fraenkel, S.T. Holgate, Etiology of asthma: Pathology and mediators , In: C.W. Biermann, D.S. Pearlman, G.G. Shpiro, W.W. Busse. Allergy, Asthma and Immunology from Infancy to Adulthood. WB Sauners Company., Philadelphia, 1996.
[5] A. Kocyigit, F. Armutcu, A. Gurel, B. Ermis, Alterations in plasma essential trace elements selenium, manganese, zinc, copper, and iron concentrations and the possible role of these elements on oxidative status in patients with childhood asthma. Trace Elem Res 97, 2004, 31-41.
[6] F. Kelly, I. Mudway, A. Blomberg, A. Frew, T. Sandstrom, Altered lung antioxidant status in patients with asthma. Lancet. 354, 1999, 482.
[7] G. Riccioni, N. D'Orazio, The role of selenium, zinc, and antioxidant vitamin supplementation in the treatment of bronchial asthma: adjuvant therapy or not? . Expert opinion on investigational drugs. 14, 2005, 1145-1155.
[8] L. Vuokko, J. Kinnula, Superoxide dismutase. American journal of respiration and critical care medicine. 167, 2003, 1600-1161.
[9] A. Emelyanov, P. Fedoseev, P.J. Barnes, Reduced intracellular magnesium concentrations in asthmatic patients. Eur. Respir. J. 13,1990, 38-40.
[10] T.T. Aiq, C. Joanne, R. Richard, D.Z. Peter, New insights into the role of zinc in the respiratory epithelium. Immunology and Cell Biology 79, 2001, 170 -177.
[11] E. Bahri, A. Ferah, A. Ahmet, K. Levent, D. Nejat, A. Remzi, D. Fatma, Trace elements status in children with bronchial asthma. European Journal of General Medicine 1,2004, 4-8.
[12] L. Jayaram, S. Chunilal, S. Pickering, R. Ruffin, P. Zalewski, Sputum zinc concentration and clinical outcome in older asthmatics. Respirology. 16, 2011, 459-466.
[13] I. Rahman, W. MacNee, Role of oxidants/antioxidants in smokinginduced lung diseases. . Free Radic. Biol. Med. 21, 1996, 669-681.
[14] C. Burtis, E. Ashwood, D. Burns, Tietz textbook of clinical chemistry and molecular diagnostics. Washington DC, 2011.
[15] J.B. Hennry, Clinical and Management by Laboratory Method. WB. Saunders, 2009.
[16] S.C. Buxadadearas, Farre-Rovira, Whole blood and serum zinc levels in relation to sex and age. Rev. Esp. de Fisiol. 41,1985, 463-469.
[17] L.S. Chawla, P.N. Verma, V.K. Puri, Study of trace elements Zn, Fe, Cu, Mg in normal healthy population. J. Assoc. Phys. India 3,1982, 41-47.
[18] U. Nevin, K. Ozkan, C. Kanan, T. Sule, U. Huseyin, O. Banu, Serum trace element levels in bronchial asthma. . Turk. Respir. 2, 2001, 10-15.
[19] S. Pucheu, C. Coudray, N. Tresallet, A. Favier, J. de-leiris, Effect of dietary antioxidant trace elements supply on cardiac tolerance to ischemia-reperfusion in the rat. J. Mol. Cell. Cardiol. 27, 1995, 2303-2314.
[20] S. Comhair, K. Ricc, M. Arroliga, A. Lara, R. Dweik, W. Song, Correlation of systemic superoxide dismutase deficiency to Air flow obstruction in Asthma. Am. J. Respir. Crit. Med. 172, 2005, 300 -313.
[22] R. Di Toro, C. Galdo, G. Gialanella, Zinc and copper status of allergic children. Acta. Paediatr. Scand. 76, 1987, 612 - 617.
[23] M. El-Kholy, M. Gas Allah, S. El-Shimi, F. El-Baz, H. El-Tayeb, M. Abdel-Hamid, Zinc and copper status in children with bronchial asthma and atopic dermatitis. J. Egypt Public. Health Assoc. 65,1990, 657-668.
[24] R. Dworsk, Oxidant stress in asthma. Thorax. 55,2000, 551-553.
[25] N. Jarjoun, W. Calhoun, Enhanced production of oxygen radicals in asthma. J. Lab. Clin. Med. 123, 1994, 131-136.
[26] B. Halliwell, Free radicals, antioxidant and human disease:Curiosity,cause or consequence? . Lancet. 344, 1994, 721-724.
[27] K. Shanmugasundaram, S. Kumar, S. Rajajee, Excessive free radical generation in the blood of children suffering from asthma. Clin. Chim. Acta. 305, 2001, 107-114.
[28] Soutar, A., Seaton, A., Brown, K., 1997. Bronchial reactivity and dietary antioxidants. . Thorax. 52, 166-170.
[29] C. Bodner, D.K. Jodden, K. Brown, J. Little, A. Rose, Seaton, Antioxidant intake and adult-onset wheeze: Acasecontrol study , Aberdeen WHEASE Study Group. . Eur. Respi. J. 13, 1999.
[30] H.R. Raeve, F.J. Thunnisen, F.T. Kaneko, F.H. Guo, M. Lewis, Decreased Cu-Zn-SOD activity in asthmatic airway epithelium: correction by inhaled corticosteroid invivo. . Am. J. Physiol. 272, 1997, 148-154.
[31] Y. Hashimoto, Y. Nishimura, H. Maeda, M. Uokoyama, Assessment of magnesium status in patients with bronchial asthma. . J. Asthma. 6,2000, 489-496.
[32] A.G. Kazaks, J.Y. Uriu-Adams, T.E. Albertson, J.S. Stern, Multiple measures of magnesium status are comparable in mild asthma and control subjects. . J. Asthma. 43, 2006, 783-788.
[33] H. Huijgen, H. Van Ingen, W. Kok, Magnesium fractions in serum of healthy individuals and CAPD patients, measured by an ion-selective electrode and ultra filtration. Clinical Biochemistry. 29, 1996, 261-266.
[34] L. Dominguez, M. Barbagallo, G. Di Lorenzo, A. Drago, S. Scola, G. Morici, Bronchial reactivity and intracellular magnesium: a possible mechanism for the bronchodilating effects of magnesium in asthma. Clin. Sci. (Lond). 95, 1998, 137-142.
[35] H. Nevin, H. Hüsem, T. Özden, A. Çiğdem, E. Nuri, F. Serdar, S. Rengin, Serum magnesium concentration in children with asthma. . Eurasian. J. Pulmonol. 16, 2014, 36-39.