The Role of Trace Elements in Retinal Diseases

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Abstract

Background: The role of serum zinc, and magnesium concentration activities in association with the Blood sugar level, and their link as biochemical marker risk for lens damage, inflammation, for the Retinal disease patients with diabetes beside lens replacement surgery, and in control individuals for both genders. Our purpose for the current study is to investigate serum concentration levels of blood sugar, zinc, and magnesium, as trace elements for patients with retinal diseases with diabetes in correlation with healthy subjects, and their effect on eye function, lens damage, inflammation, and bacterial or viral infections, or even undergo artificial intraocular lens surgery. Also to find a diagnostic prediction for blood sugar, magnesemia and zinc levels may induce causing diabetes retinopathy, cataract, or even glaucoma.

Materials and methods: Total of forty six diabetic retinopathy patients their mean is (53.36±16.3), and thirty four healthy controls with mean of (49.91±21.72) have been studied. The age has non-significantly ($P>0.05$) differ in diabetic retinopathy patients (53.36±16.31 year) from normal subjects (49.91±21.72 year). Retinal disease patients are diagnosed on the basis of pathological condition into diabetic retinopathy patients.

Results: Assessment, of serum zinc, and magnesium, and blood glucose levels were done for all groups. The concentricity of serum zinc levels are depressed, and non-significantly differ for diabetic retinopathy patients, higher in (33±19.48 ng/L with P= 0.122), from that of normal subjects. Whilst the level of magnesium was exhibited to be decreased for diabetic retinopathy patients, they showed (1.74±0.34 ng/L with P = 0.390) from that of normal subjects. Moreover, blood sugar levels are increased in diabetes than control (10.27±4.62 µmol/L versus 5.23±0.40 µmol/L with P = 0.0001). All parameters has are correlated non-significantly association with each other for diabetic retinopathy patients.

Key Words: Retinl Disorder Diseases, Blood Sugar Concentrations, Diabetes Retinopathy, Zinc Concentration, and Magnesium Concentration.

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Introduction

There are many trace elements with various activities either beneficial or toxic. A nutritional zinc (Zn^{+2}), and Magnesium (Mg^{+2}) ions are types of important and essential trace elements, for many metabolic, biological, physiological, immunological processes, and pathological conditions in human body. Also for chelation therapy it is the preferred medical treatment for reducing the toxic effects of metals (Flora, S.J. and V. Pachauri, 2010.). Zinc is essential cofactor required for life, and as such, mechanisms exist for its homeostatic maintenance in biological systems (Lonergan, Z.R. and E.P. Skaar, 2019).

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Zinc ion is dependent on both inside and outside of the cell regulatory function. From this point, deficiency of zinc ion is related to some metabolic processes impairment causing impaired of immune functions resulting in many disorders, consequently zinc ion is important for human being survival.

In developing countries, more than 25% of the population suffers from zinc deficiency due to inadequate zinc intake, while in industrialised countries the figure is as high as 15% (Wessels, I. and L. Rink 2020.).

Populations at greatest risk of inadequate zinc intake in industrialised countries are pre-school children, elderly people as well as vegetarians and vegans, who all eat lower amounts of meat-based foods (Gibson, R.S., et al., 2008.).

The fourth most plentiful, and crucial mineral is magnesium ion in humans. It is recognized as a regulator factor of blood pressure, important cardiac excitability, and recognized as an essential for many biochemical reactions especially in the protein, DNA and RNA synthesis, also for metabolism of insulin, and involved in energy unit production of adenosine triphosphate (ATP). The biological activities of ATP appear after binding with magnesium. Magnesium is the second most common cation in the intracellular fluid. Mg^{2+} plays a crucial role in regulating vascular functions and energy metabolism as well as maintaining water and electrolyte balance (Ajith, T.A., 2019.). Furthermore, magnesium ion, besides sodium, potassium and calcium ions are important electrolytes for human metabolism. About 99% of total body magnesium is located in bone, muscles and non-muscular soft tissue(Classen, H. and S. Nowitzki,1990, and Kisters, K.,1998).

The body content of magnesium ion decreases in association with age, and age disorder diseases developments as in diabetic retinopathy where the stored magnesium in content of bone decreases with age, and magnesium ion that is stored in this way is not completely bioavailable during magnesium ion deprivation. Intracellular magnesium ion is divided into bounded to proteins, and ionized. Extracellular magnesium principally present, in both red blood cells or serum. The main concentration of serum magnesium ion is filtered by the kidney, and the remainder of magnesium bound to protein is pH dependent. Mg^{2+} can maintain the lens sodium pump activity and antioxidant status and block the calcium channels and release of glutamate in nerve endings. Furthermore, it can prevent the apoptosis of retinal ganglion cells (Ajith, T.A., 2019.).

Hypomagnesemia has been shown to precipitate hyperglycemia and has, therefore, been implicated in insulin resistance and its microvascular complications. Poor glycemic control has been associated with retinopathy (Kumar, P., et al., 2019).

Also, several complications of diabetes may be related to increased intracellular oxidants and free radicals associated to decreases in intracellular Zn and Zn-dependent antioxidant enzymes (Miao, X., et al., 2013.)

This article aims to investigate the role of serum Mg and Zn association with diabetic retinopathy disease.

Materials and Methods

Study Design

The subjected patients examined by common tests for retina disorder conditions, by Diagnostic A-Scan, Fluorescein angiography is test used to diagnose and monitor the impact of diabetic retinopathy and macular degeneration, Fundus photos. Nerve fiber layer analyzer, also Visual field test by a ophthalomegalist according to Patients diagnosed according to Fundus Auto Fluorescence (FAF) and Amsler grid test**.** the doctor checked that whether they have the symptoms for diabetic retinopathy patients. Chemical Analysis done for totally eighty, of both genders, at morning fasting at least for eight hours for blood specimens and data were collected directly in Ibn Al Haytham Hospital, and directly analyzed, all the measured individual ages are between (0.5-82 year), 34 subjects are diagnosed as normal controls, and 46 subjects diabetic retinopathy.

Sample Collection

All subjects were donated 5 mL of blood form vein, and the blood then was centrifuged at 1500g for 10 minutes. The serum was analyzed directly without storing.

Methods

Biochemical determinations include serum zinc, and magnesium ions concentration activities by a colorimetric determination of Zinc ion in serum, plasma, from Gesan the Ref. 490510. While magnesium a colorimetric determination is also from Gesan, and the Ref E4400330 respectively using Semi-Automated Colorimetry, Chem-100 depend on the correlation between the colour density with the concentration of coloured substance. When monochromatic light of a specific wavelength, of light passes through colored sample solution to be determined light will be absorbed in relation to colour density. Fasting Blood Sugar (FBS) we used Cobas c 111 Analyzer for estimation assay at Ibn Al Haytham Hospital Baghdad Iraq.

Statistically Analysis

This study carried out by using SPSS-26 (Statistics Packages for Social Sciences-Version 26). ANOVA was used for comparing parameters according to age groups. Independent student t-test was used for comparing the parameters between patients and controls. The difference in importance of the various percentages (qualitative data) was checked by using Pearson Chi-square test with the implementation of Yate correction, or Fisher Exact test whenever appropriate. The statistical meaning P was found to be equal to or less than 0.05.

Results

The results are expressed as mean ± SD (range). In general, concentrations were associated with sample collection of Iraqi volunteers, so a direct collection for blood specimens done after data were collected, and directly analyzed. Results are isolated and characterized the concentrations of serum zinc and magnesium, and sugar for cohort of retinal diseases with diabetic retinopathy patients and normal controls in Baghdad, Iraq. The first group of diabetic retinopathy consist of twenty three patients for each gender the distribution of these subjects according to gender was non-significant (P>0.05) at both groups, and eleven of male and twenty three for controls, of 0.5-82 years old. The age has non-significantly (P>0.05) differ in diabetic retinopathy patients (53.36±16.31 year) from normal subjects (49.91±21.72 year). The distribution of subjects according to age has shown that the majority of the normal subjects (20) and diabetic retinopathy patients (21) were at the ≥60 year's old category all these results are indicated in Table 1.

Table 2 shows the level of blood sugar for diabetic retinopathy patients, and normal subjects, it has elevated significantly (P<0.01) in diabetic retinopathy patients (10.27±4.62 μmol/L) compared to normal subjects (5.23±0.40 μmol/L). Whereas, glucose level has shown non-significant differences (P= 0.737) at age comparisons for both normal and patients groups (P= 0.384).

The level of zinc was non-significantly (P>0.05) differ in that of diabetic retinopathy (P=0.317), from that of normal subjects with significantly (P= 0.017), but this surprisingly, for normal subjects have shown significant differences (P<0.05) of zinc ion level at age comparisons, in which people at older ages have possessed the lower levels of zinc.

The level of Mg was non-significantly (P>0.05) differ in that of diabetic retinopathy (1.74±0.34) from that of normal subjects (1.82±0.24), whereas, Mg level has shown non-significant differences (P>0.05) at age comparisons for both normal and patients groups, see Table 4.

Table 1. Distribution of age, and gender for retinal diseases with diabetic retinopathy patients and normal controls in Baghdad, Iraqi.

Parameter		Normal, N=34	Diabetic retinopathy, N=46	p-value
Age (year)	Mean±SD (range)	49.91±21.72 (0.50-82)	53.36±16.31 (15-76)	0.596
	< 30	6	4	0.121
	30-39	6	2	
	40-49	0	11	
	50-59	2	8	
	≥ 60	20	21	
Gender	Male	11	23	0.326
	Female	23	23	

Table 2. Blood glucose level (μmol/L) for diabetic retinopathy patients in comparison with normal subjects

Groups		Normal, N=34	Diabetic retinopathy, N=46
Age (year)	< 30	5.13±0.58	6.75±0.07
	30-39	5.60±0.62	7.10±0.04
	40-49	-	9.86±3.45
	50-59	5.30±0.01	11.47±5.82
	≥ 60	5.13±0.37	11.02±5.30
	p-value	0.384	0.737

Table 3. Serum zinc ion (ng/L) level for diabetic retinopathy patients in comparison with normal subjects

Groups		Normal, N=34	Diabetic retinopathy, N=46
Age (year)	< 30	73.67±7.02	13.50±3.54
	30-39	51.67±33.56	12.0±0.10
	40-49	-	37.80±16.54
	50-59	30.0±0.06	26.75±18.63
	≥ 60	33.11±10.58	39.10±21.02
	p-value	0.017#	0.317
Gender	Male	39.60±20.23	39.27±18.37
	Female	46.0±23.55	26.73±19.31
	p-value	0.591	0.134

Table 4. Magnesium level (ng/L) for diabetic retinopathy patients in comparison with normal subjects.

Groups		Normal, N=34	Diabetic retinopathy, N=46
Age (year)	< 30	1.93±0.42	1.65±0.21
	30-39	1.57±0.12	1.70±0.04
	40-49	-	1.80±0.32
	50-59	1.80±0.03	1.55±0.31
	≥ 60	1.87±0.17	1.80±0.41
	p-value	0.233	0.801
Gender	Male	2.02±0.30	1.72±0.42
	Female	1.73±0.14	1.76±0.27
	p-value	0.097	0.810

Table 5. The level of parameters in normal and patients subjects.

Parameter	Normal, N=34	Diabetic retinopathy, N=46	p-value
Glucose (μmol/L)	5.23±0.40 (4.8-6.10)	10.27±4.62 (6-21.9)	<0.0001 *
Zinc ion (ng/L)	44±22.10 (16-89)	33±19.48 (9-69)	0.122
Magnesium ion (ng/L)	1.82±0.24 (1.50-2.40)	1.74±0.34 (1.20-2.70)	0.390
The comparisons carried out by using Independent-student t-test *significant at p≤0.05			

All parameters has shown non-significant (P>0.05) association with each other in diabetic retinopathy patients.

Discussion

The results of glucose are agreed with (Yuqi Liu et al. 2020).

We are all at risk to inhalation, or our eyes, too of zinc ion -containing fumes originates from environmental pollution such as industrial processes or environmental smoke are the main causing to affect. However, zinc's physiological role in humans was unknown until 1961 when zinc deficiency in humans was discovered (Roohani, N., et al., 2013). Zinc ion is associated with growth, gonad development, immune function and pregnancy outcome improvement, and hair loss prevention (Prasad, A.S., 1995, Fukada, T., et al. 2012, and Prasad, A.S., 2009).

Zinc ion is one of the most abundant nutritionally essential elements in the human body, it is found in all body tissues with 85% of the whole body zinc in muscle and bone, 11% in the skin and the liver and the remaining in all the other tissues, in multicellular organisms, virtually all zinc ion is intracellular, 30-40% is located in the nucleus, 50% in the cytoplasm, organelles and specialized vesicles (for digestive enzymes or hormone storage) and the remainder in the cell membrane (Tapiero, H. and K.D. Tew, 2003).

Zinc ion is dependent on both inside and outside cell regulatory function. The effects of zinc are based on the intra- and extracellular regulatory function of the zinc ion and its interactions with proteins (Grüngreiff, K., T. Gottstein, and D. Reinhold, 2020). From this point, the deficiency of Zinc is related to some metabolic processes impairment causing impaired of immune functions. The reduced resistance to infections due to impaired immune functions, changes in skin and its appendages and disorders of wound healing and haemostasis (Kambe, T., et al., 2015).

Moreover, Zinc ion is a cofactor for many metalloenzymes required for cell membrane repair, cell proliferation, growth and immune system function, also in the regulation of carbohydrate, fat and protein metabolism and plays an important role as a second messenger, as a signal ion, it has an antioxidant effect and influences the redox metabolism, although the zinc ion (Zn^{2+}) is redox inert (Maret, W.,2019, and Lin, P.-H., et al., 2018).

Our findings of zinc are similar to (Ruiz-Ocaña et al. 2018). Also in the bone levels of Zn^{2+}, were significantly decreased showing limited proliferation and differentiation of the osteoblasts (Gurban, C.V. and O. Mederle, 2011).

Magnesium ion also plays a role in the active transport of calcium and potassium ions across cell membranes, a process that is important to nerve impulse conduction, muscle contraction, and normal heart rhythm (Ross, A.C., et al., 2012). An adult body contains approximately 25 g magnesium ion, with 50% to 60% present in the bones and most of the rest in soft tissues (Erdman Jr, J.W., I.A. Macdonald, and S.H. Zeisel, 2012). The widespread of this element level in insulin metabolism may result in unwanted type-2 diabetes mellitus. Low levels of magnesium ion are indicated according to the results in Table 4 with non-significant P value for age correlation with magnesium ion in diabetic retinopathy, and control subjects. These results are similar, and agree with (Gröber et al. 2015, and

Ramadass et al. 2015). Low levels of magnesium have been associated with a number of chronic diseases, such as Alzheimer's disease, insulin resistance and type-2 diabetes mellitus (Gröber et al. 2015).

Magnesium role in glucose and insulin metabolism, mainly through its impact on tyrosine kinase activity of the insulin receptor, by transferring the phosphate from ATP to protein. Magnesium may also affect phosphorylase b kinase activity by releasing glucose-1-phosphate from glycogen. In addition, magnesium may directly affect glucose transporter protein activity 4 (GLUT4), and help to regulate glucose translocation into the cell (Guerrero-Romero, F., et al.,2015, Song, Y., et al.,2005, Forouhi, N., et al., 2007, and Barragán-Rodríguez, L., M. Rodríguez-Morán, and F. Guerrero-Romero, 2008.). Finally the finding results indicate prediction of hypomagnesemia and reduced zinc levels may induce causing diabetes retinopathy, cataract, and glaucoma or induce ocular surgery for advance stages. Historically incisional surgery has been used in cases of advanced disease (Li, X.-J., et al., 2018.).

Conclusions

We notice the ages of diabetic retinopathy or advanced lens damage or blindness and correlate with the increased blood sugar, and reduced magnesium and zinc concentrations in comparison with controls for that these level are a good diagnostic investigator for diabetic retinopathy, or even advanced stages for this disorder. The intensive glucose therapy or lens surgery may be protect the retina, but regarding that one of the most important ways is to take adequate magnesium and zinc supplement for overall health, and the life style beside therapy provides the same protection to these patients in response to different effect severity in the ocular of diabetic retinopathy patients. Also, a registered dietitian nutritionist specializing in each hospital for management of chronic diseases especially the silent disease of diabetic retinopathy. Finally, the finding results indicate a diagnostic prediction for increased blood sugar, hypomagnesemia and reduced zinc levels may induce causing diabetes retinopathy, cataract, and even glaucoma.

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