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Original Research Article

Serum zinc and copper levels: a marker of disease activity in senile cataract patients

Pooja S. K. Rai[1]*, Smita A. Deokar[2], Ravi R. Yadav[3], Sudarshan Shelke[4], Shimi Sundharan[1]

[1]Department of Biochemistry, LTMMC and LTMGH, Sion, Mumbai, Maharashtra, India
[2]Department of Biochemistry, HBT Medical College and Dr. R N Cooper Municipal General Hospital Juhu, Mumbai, Maharashtra, India
[3]Department of Biochemistry, Sukhsagar Medical College and Hospital, Jabalpur, Madhya Pradesh, India
[4]Department of Biochemistry, Krishna Institute of medical Sciences, Karad, Maharashtra, India

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***Correspondence:**
Dr. Pooja S. K. Rai,
E-mail: poojaonline21@gmail.com

ABSTRACT

Background: The present study was aimed to study alterations in levels of zinc and copper in senile cataract patients.
Methods: 25 senile cataract patients in age group of 50 to 80 years and 25 control group were included in the study. Serum zinc and copper levels were determined by colorimetric method.
Results: Significantly increased levels of serum zinc in cataract patients (199.8±24.32 µg/dl) were found as compared to controls (85.80±3.6 µg/dl) ($p<0.0001$). Serum copper concentration in cataract patients (249.5±34.59 µg/dl) were significantly (<0.0001) increased when compared to controls (125.7±4.66 µg/dl).
Conclusions: Copper and zinc are involved in the pathogenesis of cataracts by different mechanisms such as damaging lipid membranes and lens capsule, crosslinking and in solubilization of lens proteins, leakage of beta and gamma crystalline into the aqueous humour through the production of hydroxyl radicals and peroxyl radicals. So, abnormal elevation of serum copper and zinc can be used as a marker in the opacification of the lens cortex in age-related human cataract.

Keywords: Copper, Senile cataract, Zinc

INTRODUCTION

Zinc is an essential trace element for humans, animals, plants and microorganisms. Zinc is stored and transferred in metallothioneins. It serves as structural ions in transcription factors. Zinc is found in approximately 300 specific enzymes and is "typically the second most abundant transition metal in organisms" after iron and the only metal which appears in all enzyme classes.[1]

In proteins, Zinc ions are often coordinated to the amino acid side chains of aspartic acid, glutamic acid, cysteine and histidine. Between 2 and 4 grams of zinc are distributed throughout the human body. Most zinc is in the brain, muscle, bone, kidney and liver, with the highest concentrations in the prostate and parts of the eye. Semen is particularly rich in zinc, a key factor in prostate gland function and reproductive organ growth.[2]

Copper is an essential trace element that is required for plant, animal, human health and normal functioning of aerobic microorganisms.[3] Copper is incorporated into a variety of proteins and metalloenzymes for essential metabolic functions. This micronutrient is necessary for the proper growth, development, maintenance of bone, connective tissue, brain, heart, and many other body organs. It is involved in the formation of red blood cells, absorption and utilization of iron, metabolism of

cholesterol and glucose, and synthesis and release of life-sustaining proteins and enzymes. These enzymes in turn produce cellular energy and regulate nerve transmission, blood clotting and oxygen transport. Copper stimulates the immune system to fight infections, to repair injured tissues, and to promote healing. It also helps to neutralize "free-radicals", which can cause severe damage to cells. Copper's essentiality was first discovered in 1928, when it was demonstrated that rats fed with copper-deficient milk diet were unable to produce sufficient red blood cells.[4]

Cataract is clouding of the lens in the eye leading to a decrease in vision. It can affect one or both eyes. Often it develops slowly and symptoms may include faded color, blurry vision, halos around light, trouble with bright lights, and trouble seeing at night. This may result in trouble in driving, reading, or recognizing faces.[5] Cataracts are the cause of half of blindness and 33% of visual impairment worldwide.[6,7]

METHODS

The present study was carried out in the department of biochemistry at central clinical laboratory, Dr. Vasantrao Pawar medical college and hospital, Adgaon, Nasik. Patients were selected from those who were admitted for cataract extraction in the department of ophthalmology, Dr. Vasantrao Pawar medical college and hospital, Adgaon, Nasik.

The study was conducted on the serum of 25 individuals between age group of 50 to 80 years who were distributed in two groups. Study group included senile cataract patients. Control group comprised of 25 persons aged 50-80 years with visual acuity of 6/6 or better in both eye and no lens opacities in either eye on slit lamp or ophthalmoscopic examination and to whom antioxidant medicines were not given.

All the subjects with chronic liver diseases, kidney diseases, cardiovascular disorders, rheumatoid arthritis, carcinomas or patients affected by other local or systemic pathologies or drug treatments that may influence the redox state of the lens and oxidative stress were not included in the scope of present study.

Patients with ocular surgery, trauma, infection, inflammation of eye were also excluded from the study. Fasting blood samples were obtained from both case and control groups and sent to the laboratory. Serum copper and zinc levels were measured by Colorimetric method.

RESULTS

All results were expressed in mean±SD. One-way analysis of variance (ANOVA) was used to test the significance of difference and "t" test was used to test significance of difference between two groups.

Significantly increased levels of Serum Zn in cataract patients (199.8±24.32 µg/dl) were found as compared to controls (85.80±3.69 µg/dl) ($p<0.0001$). Serum Cu concentration in cataract patients (249.5±34.59 µg/dl) were significantly increased ($p<0.0001$) when compared to controls (125.7±4.66 µg/dl).

Table 1: Levels of plasma copper and zinc in study and control groups.

Parameter	Control group, (n=25)	Cataract group, (n=25)	p-value
Serum Zn (µg/dl)	85.80 ± 3.69	199.8 ± 24.32	<0.0001
Serum Cu (µg/dl)	125.7 ± 4.66	249.5 ± 34.59	<0.0001

DISCUSSION

Anderson et al studied that zinc content of aqueous humour was found to be considerably lower than the corresponding serum values. From this finding, it was suggested that aqueous humour does not serve as a likely route of delivery of zinc to the cornea.[8]

Akyol et al showed that serum zinc and copper concentrations of patients with cataract were determined. There was a significant negative correlation between the aqueous humour levels of zinc and copper in patients with cataract. It was concluded that an increased copper value together with a low zinc value might be of importance in patients with cataract.[9]

Yildirim et al found that Oxidative stress is one of the major factors which may lead to the early cataract formation. Oxidative events are of immense importance in senile cataract in the lens, and may have a role in the pathogenesis of cataract as exhibited in this study.[10]

Gunduz et al were studied that the increased concentration of zinc in the lens of senile cataract patients suggests that zinc might play a role in developmental mechanism of the senile cataract.[11]

Yang et al found that the activity of superoxide dismutase in patients with senile cataract decrease dramatically in comparison with normal control, and there was no statistical difference about trace elements of Cu and Zn between senile cataract and control group. The results

support the hypothesis that the formation of senile cataract is due to decrease in antioxidative scavenger system of lens with age.[12]

Goralska et al investigated serum zinc (Zn), and copper (Cu) levels in cataract patients. These results demonstrate that increased Cu content of the lens presumably has a greater association with the development of lens opacification in senile cataract than Zn content.[13]

Cook, Balaji, Goralska et al found that Zinc and copper is implicated in the pathogenesis of cataracts by

- damaging lipid membranes and lens capsule
- crosslinking and in solubilization of lens proteins
- leakage of beta and gamma crystalline into the aqueous humour through the production of hydroxyl radicals and peroxyl radicals.[14-16]

Quintanar et al studied that aggregation of eye lens proteins into high-molecular-weight complexes which causes light scattering and lens opacity. Copper and zinc concentrations in cataractous lens were increased significantly as compared to a healthy lens which shows that metals as potential etiological agents for cataract. The natively monomeric, β-sheet rich human γD (HγD) crystalline was one of the more abundant proteins in the core of the lens (most thermodynamically stable proteins in the human body). Both Cu and Zn ions induced rapid, nonamyloid aggregation of HγD, forming high-molecular-weight light-scattering aggregates, decreased the thermal stability of HγD and promoted the formation of disulphide-bridged dimers, suggesting distinct aggregation mechanisms.[17]

CONCLUSION

There are numerous factors acting over many years for causation of cataract. The major reason lies behind the formation of cataract is the damage induced by free radicals, reactive oxygen/ nitrogen species to the crystalline lens. In this review, we have discussed the different events and mechanism in the lens due to accumulation of Zinc and Copper that gives rise to cataract genesis. Thus, Zn and Cu induces membrane damage, protein modification and accumulation, inflammation, lenticular apoptosis, etc, and all these alter the refractive properties of the lens resulting in the opacity and cataract.

So, raised level of serum copper and zinc can be used as a marker for the development of age-related human cataract. Further studies are required on copper and zinc levels on senile cataract.

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