Original Research Article

Serum calcium and phosphorus levels: a marker of disease activity in senile cataract patients

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ABSTRACT

Background: The present study was aimed to study alterations in serum levels of calcium and phosphorus levels 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 Calcium and Phosphorus levels were determined by Orthocresolphthalein, Fiske SubbaRow method respectively

Results: Significantly increased levels of serum calcium in cataract patients (11.58±1.65 mg/dl) were found as compared to controls (8.53±1.45mg/dl) (p<0.0001). Serum phosphorus concentration in cataract patients (5.28±0.46 mg/dl) were significantly increased when compared to controls (3.02±1.23mg/dl) (p<0.0001).

Conclusions: Presence of G-protein receptors in lens leads to the release of intracellular calcium. As total calcium in the lens increases, we hypothesize that higher intercellular calcium concentrations, coupled with decreased Ca²⁺-ATPase activity and greater membrane permeability could lead to elevated free intracellular calcium levels causing cataract. So, abnormal elevation of serum calcium and phosphorus can be used as a marker for prevention of age-related human cataract.

Keywords: Calcium, Phosphorus, Senile cataract

INTRODUCTION

The lens is a biconvex suspended in the anterior segment of the eye by suspensory ligaments.¹ The transparency of the lens is essential for its normal physiological functions, and this is primarily attributed to a number of factors:

- avascular nature of the lens,
- as tight packing of cytosolic proteins, the crystallins,
- pyknotic nuclei that are located in the equator of the lens away from the optic axis and loss of cell organelles,
- lamellar arrangements of the lens fibre cell in the cortex and nucleus.²³
While the lens confers one third of the refractive power of the eye, it is able to alter the focussing range (i.e. to accommodate) in a number of species. This ability decreases with age and is effectively lost in the sixth decade of life in the human eye.4-5

The capsule within which the lens sits is a thin, transparent and semi-elastic basement membrane. The lens capsule has structural, biomechanical and protective functions.4-7 The capsular elasticity allows the lens to adapt to a specific shape to change its shape or accommodate for near and distant vision.8

The lens epithelium is the major site of metabolic activity in the lens; it plays a basic role in homeostasis of the lens: the passage of nutrients, ions and antioxidants into the lens is regulated by aquaporins (water channels) and \( \text{Na}^+/\text{K}^+ \) ATPase pumps of the lens epithelium. The lens epithelium is involved in the synthesis of the antioxidant glutathione (GSH) and is linked with biosynthesis of ultraviolet (UV) filters such as the tryptophan metabolite 3-hydroxykynurenine.9,10 These UV filters diffuse into the cortex and nucleus and offer a photo-protective function against the photo-oxidative damage short UV radiation.11

The major cytosolic proteins, the crystallins (\( \alpha-, \beta-\) and \( \gamma-\)), are distributed in varying proportions across the cortex contributing to the gradient index.12

Nuclear hardening with age may be caused by post-translational modifications (PTMs) of the crystallin proteins.13 Hardening of the lens nucleus and low concentrations of endogenous antioxidants with age may be causal factors in age-related nuclear cataract.14,15

The lens relies on an effective apparatus of water and ion channels (aquaporins and connexins) to maintain nutrition and homeostasis located in the lens epithelium and cortex. The other major antioxidant GSH is biosynthesised in the lens cortex and diffuses into the nucleus.16,17 It has, however, been shown that the rates of water and water-soluble transport via the lens epithelium and cortex declines with age. The decrease in antioxidant transport might contribute to the oxidative damage in the lens with age and ultimately to the formation of age-related cataract and.18

In the lens an increase in internal calcium can be induced by a very large number of processes: by oxidation, either of external or internal sulphhydryl groups by removal of external glucose perversely, by reducing external calcium and, in a gradual manner, by age itself.19-22 The end result of the calcium increase by whatever means is an increase in light scatter in the lens and, in those systems in which it has been investigated, a concomitant loss of lens proteins.23 This loss appears to be due to activation by calcium of an enzyme cascade where one possible participant is calpain although others may play a role. Light scatter is also greatly reduced, even in lenses that have become grossly swollen due to an uptake of sodium and water. It has been recognised for some time that, in human cortical cataracts and in experimental model systems, total and free calcium rise in tandem. Interestingly, calcium electrode studies carried out on human lenses have shown that in localised cataracts, free calcium rises only in the opaque areas as compared to normal individuals.

Inorganic phosphorus is critical for numerous normal physiologic functions including skeletal development, mineral metabolism, energy transfer through mitochondrial metabolism, cell membrane phospholipid content and function, cell signaling, and even platelet aggregation.24

### 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. The patients were selected from those who were admitted for cataract extraction in the ophthalmology department, 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 includes senile cataract patients. Control group comprised of 25 persons aged 50-80 years with visual activity 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 the eye were also excluded from the study. Then a fasting-state blood sample was obtained from both case and control group and sent to the laboratory. Serum Calcium and Phosphorus levels were determined by Orthocresolphthalein and Fiske Subbarow method respectively.25,26

### Statistical analysis

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

### RESULTS

Table 1 shows significantly increased levels of serum Calcium in cataract patients (11.58±1.65mg/dl) were
found as compared to controls (8.53±1.45 mg/dl) (p<0.0001). Serum Phosphorus concentration in cataract patients (5.28±0.46 mg/dl) were significantly increased when compared to controls (3.02±1.23 mg/dl) (p<0.0001).

Table 1: Levels of Serum Calcium and Phosphorus in study and control groups.

<table>
<thead>
<tr>
<th>Parameter (mg/dl)</th>
<th>Control group (n=25)</th>
<th>Cataract group (n=25)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Calcium</td>
<td>8.53±1.45</td>
<td>11.58±1.65</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Serum Phosphorus</td>
<td>3.02±1.23</td>
<td>5.28±0.46</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

DISCUSSION

The lens possesses an impressive array of G-protein receptors that are coupled to the release of intracellular calcium. Duncan et al hypothesized that higher intercellular calcium concentrations, coupled with decreased Ca\(^{2+}\)-ATPase activity and greater membrane permeability could lead to elevated free intracellular calcium levels. This could, in turn, induce the formation of calcium oxalate crystals and contribute to trigger a cascade of events that culminate in increased light-scattering from proteins and, to a lesser extent, from lipids.27

Clark et al found that ion balance is also an important functional factor for maintaining lens transparency. Studies have shown distribution of Ca\(^{2+}\) and Na\(^{+}\) was high and that of K\(^{+}\) was low in the cataract lens, possibly because calcium could influence cell membrane permeability and reduce Na\(^{+}\)/K\(^{+}\) ATPase enzyme activity.28 As a result, potassium and sodium ion channel open secondarily, which causes sodium retention and increases light scattering, eventually resulting in lens opacity.29

Maintenance of calcium homeostasis is critical to the clarity of the lens. Zeng, Duncan, Bial, et al studied the inward passive diffusion of calcium, perhaps through a nonspecific cation channel, is countered by the actions of the plasma and sarco- and endoplasmic reticular Calcium-adenosine triphosphatase (ATPase) pumps.30-32 With age, the increased entry of calcium into clear lenses is offset by an increase in the activity of Calcium-ATPase pumps. Gandolfi, Paterson, Delamere et al determined that due to cataract, however, lens membrane permeability increases further, total lens calcium is elevated and Calcium-ATPase activity is decreased by 50%.33-35 The Calcium-ATPase pump is sensitive to lipid order, which changes with age and cataract. Accordingly, the decrease of Calcium ATPase activity with cataract may be a consequence of lipid structural changes, an increase in Ca\(^{2+}\)-ATPase oxidation, or both. Elevated calcium levels are related to numerous processes: activation of proteases, inhibition of Na, K-ATPase activity, cell growth, protein synthesis, disintegrative globulization calcium influx, cell death, increased membrane permeability, and aggregation of proteins and lipids. All these factors could contribute to alterations in lens molecular structure and increased light-scattering by the lens which causes increase in calcium and phosphorus that correlates with opacity in cataractous human lenses.36

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 calcium and Phosphorus that gives rise to cataract genesis. Thus, Calcium and Phosphorus induces membrane damage, protein, lipid 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 Calcium and Phosphorus can be used as a marker for the development of age-related human cataract. Further studies are required on Calcium and Phosphorus levels on senile cataract.

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REFERENCES


