Dry Eye and its Relationship with Status of Serum Calcium in the Body at a Tertiary Care Institute: A Case Control Study

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Abstract

Background: Dry eye is a multifactorial disease of the tears and ocular surface that results in symptoms of dryness, grittiness, redness, burning sensation or any discomfort, visual disturbance and tear film instability leading to potential damage to ocular surface. The tear film consists of three layers starting from within outwards mucus, the aqueous layer and the lipid layer. The tear film and ocular surface form a complex and stable system that can lose its equilibrium through numerous disturbing factors. Studies which also involve tests of tear functions including Schirmer’s test, Tear break-up time, Fluorescein staining for determination of dry eye have found generally low prevalence rates. Hence the physiology of tear film and its binding with the eye shows that there is some involvement of serum calcium level with dry eye. The present study encourages us to assess the role of serum calcium level with patients of dry eye.

Aims and Objective: To assess the role of calcium with dry eye.

Material and Methods: Total 90 subjects (30 cases and 60 controls) who met the selection criteria were included in the study. Serum analysis has been done for calcium level in the body in the patients of dry eye. The study was conducted between August 2014 to November 2016.

Results: The lower serum level of calcium was significantly associated with dry eyes in the study.

Conclusion: Calcium plays an important role in the causative mechanism of dry eye in the patients of dry eye disease.

Keywords: Calcium, Dry Eye, Serum Level, Tear Film

1. Introduction

Dry eye is one of the most prevalent ocular surface disease in the world occurring from 4.4% to as high as 50% of middle aged and older people¹. The tear film consists of three layers starting from within outwards mucus, the aqueous layer and the lipid layer. The tear film and ocular surface form a complex and stable system that can lose its equilibrium through numerous disturbing factors². The earliest corneal manifestation of xerophthalmia is instability of the precorneal tear film which can lead to a dull and lustreless corneal appearance³. There are studies demonstrating that corneal epithelial cells contain VDR and 1 alpha hydroxylase mRNA and that there are significant Vitamin D metabolite concentrations in both the aqueous and vitreous humour. In addition, both 25(OH)D₃ and 1,25(OH)D₃ can enhance corneal epithelial barrier function and Vitamin D supplements enhance corneal occluding expression⁴. The role of vitamin D and calcium go hand in hand. Vitamin D is responsible for the calcium and phosphorus levels in the body.

Serum calcium status in the serum is suitable for studying its association with systemic conditions. However, it would be beneficial to obtain tissue specific Vitamin D status for localized conditions such as ocular surface disease. There is increasing evidence regarding extra-renal synthesis and tissue specific effects of vitamin D3 in other tissues⁵–⁷, including the eye⁸–¹⁰. The cells and
tissues in the eye are responsive to 1,25-dihydroxyvitamin D since VDR is present in the epithelium of the cornea, lens and ciliary body, corneal endothelium, retinal pigment epithelium, ganglion cell layer and photoreceptors of the human eye. The present study “Dry Eye and its Relationship with Status of Vitamins in the Body at a Tertiary Care Institute: A Case Control Study” was conducted to assess the role of serum level of calcium associated with dry eyes.

2. Aims and Objective

To assess the role of calcium with dry eye.

3. Material and Methods

Study was conducted in Department of Ophthalmology, Dr Vasantrao Pawar Medical College, and Nasik after Institutional review board approval. Total of 90 patients (30 cases and 60 controls) were taken in the study and their serum calcium level were measured.

Study Design and Study Population

- Study design: A case control study.
- Study settings: Department of Ophthalmology, Medical College and Hospital, Tertiary care centre.
- Duration of the study: Period of Two years from August 2014 to November 2016.
- Sample size: 90 (30 cases and 60 controls).
- Study Participants.

4. Eligibility Criteria

4.1 Inclusion Criteria

4.1.1 Inclusion Criteria for Cases

- Diagnosis of Dry Eye Disease based on following criteria:
  - Presence of dry eye symptoms.
  - Presence of qualitative and quantitative disturbance of the tear film in one or both eyes (Schirmer's test results<5mm or tear film break-up time<5 seconds).
  - Presence of conjunctival and corneal epithelial damage (total staining score, >3 points) in one or both eyes.
  - Adult Patients (>18 years of age) irrespective of gender satisfying the above criteria of dry eye disease.
  - Patient willing to take part in the study.

4.2.2 Inclusion Criteria for Controls

- Patients not diagnosed as Dry eye disease based on the above mentioned criteria.
- Adult Patients (>18 years of age) with group matching done for age and gender.
- Patient willing to take part in the study.

4.2 Exclusion Criteria for Both Cases and Controls

- Contact lens wearers- within 12 hours of any study visit.
- Patient who underwent LASIK surgery/cataract surgery.
- Patients diagnosed with Sjogren’s syndrome, Rheumatoid arthritis and Parkinson’s disease.
- Clinically significant eyelid deformity or eyelid movement disorder caused by conditions such as notch deformity, incomplete lid closure, entropion, ectropion, hordeola, or chalazion.
- Patients taking medications such as anti-histaminics, TCAs, OC pills, anti-hypertensives, diuretics or tetracyclines - within 3 weeks of any study visit.
- Punctal cautery or punctal plug placement within 60 days of screening.
- Abnormal nasolacrimal drainage.
- Any infective ocular diseases.
- Any allergies.
- Pregnancy.

5. Methodology

After satisfying inclusion and exclusion criteria, 30 cases of dry eye with age and gender matched 60 controls were enrolled in the study.

Basic information was taken from all study participants as per proforma. All participants underwent clinical as well as ophthalmic examination as follows:

- History.
- Visual Acuity (with Log MAR chart).
- Anterior Segment Examination.
- Schirmer’s Test.
- TFBUT (Tear Film Break Up Time).
- Ocular Surface Staining.
- Tonometry.
- Fundus Examination.

After examination, patients’ serum level of calcium have been measured.
5.1 History
A thorough and detailed history of all selected patients was taken as per proforma of the study. Patient’s age, sex and associated ocular complaint was noted.

5.2 Ocular Examination
- A one-time examination of the cases and controls was done and no follow-ups were included in the study.
- Best corrected visual acuity (BCVA) was recorded in both the eyes with the use of LogMAR chart in the OPD.
- Intraocular Pressure was measured using Goldmann Applanation tonometer.
- A thorough and detailed examination of the anterior segment was performed on the slit lamp.
- Both direct and consensual papillary reactions were checked.
- Following which pupils were dilated using 0.8% w/v tropicamide with 5.0% w/v phenylephrine drops 2 to 3 times for 20 to 30 mins.
- (Phenylephrine was avoided in hypertensive patients).
- A detailed fundus examination was done by direct ophthalmoscope, indirect ophthalmoscope 20D lens and Slit-lamp biomicroscopy with +90D lens (conventional ophthalmoscopy) in fully dilated pupil.
- Schirmer’s test has been done in both eyes using 41 no. Whattmann filter paper and readings has to be taken after 5mins.
- After fluorescenestaining, Tear Film Break Up Time (TF-BUT) and Ocular surface Staining score was measured with the help of cobalt blue filter of slit lamp.

5.3 Serum Analysis
Blood samples were collected for serum level of calcium and role of calcium will be compared among cases and controls.

Serum calcium level is analysed with the help of chemi and bioluminescence principle and with the use of instrument LUMAX MODEL 4101 CLIA strip reader.

5.4 Statistical Analysis
Appropriate statistical analysis will be done for interpretation of given objectives. Independent t test was applied to mean serum level of calcium in cases and controls. A probability value (p value) ≤ 0.05 was considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel 2007 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 17.

6. Results
In the present study, there were 30 cases and 60 controls. The case to control ratio was 1:2. Out of 90 patients, 33.33% i.e., 30 patients were cases and 66.67% i.e., 60 patients were controls which were enrolled in the study (Table 1).

Table 1. Distribution of cases and controls
<table>
<thead>
<tr>
<th></th>
<th>No. of Patient</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case</td>
<td>30</td>
<td>33.33%</td>
</tr>
<tr>
<td>Control</td>
<td>60</td>
<td>66.67%</td>
</tr>
<tr>
<td>Total</td>
<td>90</td>
<td>100.00%</td>
</tr>
</tbody>
</table>

In the present study, out of 30 cases of dryness 11 (36.67%) were males and 19 (63.33%) were females. The male to female ratio (0.58:1) showing significant female preponderance in cases of dry eye. Out of 60 controls in the study, 31 (51.67%) were males and 29 (48.33%) were females showing nearly equal distribution amongst them (Table 2).

Table 2. Gender wise distribution of cases and controls
<table>
<thead>
<tr>
<th></th>
<th>Case (Dryness)</th>
<th>Control (No Dryness)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>No %</td>
<td>No %</td>
</tr>
<tr>
<td>Male</td>
<td>11 36.67%</td>
<td>31 51.67%</td>
</tr>
<tr>
<td>Female</td>
<td>19 63.33%</td>
<td>29 48.33%</td>
</tr>
<tr>
<td>Total</td>
<td>30 100.00%</td>
<td>60 100.00%</td>
</tr>
</tbody>
</table>

In the present study, out of 30 cases of dryness, 17 (56.67%) were vegetarian and 13 (43.33%) were taking mixed diet. Out of 60 controls, 28 (46.67%) were vegetarian and 32 (53.33%) were taking mixed diet. Among 30 cases, those taking vegetarian diet were more prone to dryness rather than those taking mixed diet. It is observed in the present study that those taking vegetarian diet were 1.30 times more prone to dryness than those taking mixed diet (Table 3).

Table 4. Mean difference of serum calcium levels in cases and controls
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>t</th>
<th>df</th>
<th>p-value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sr. Calcium</td>
<td>Case</td>
<td>30</td>
<td>8.52</td>
<td>0.67</td>
<td>-4.509</td>
<td>88</td>
<td>&lt;0.0001</td>
<td>Highly Significant</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>60</td>
<td>9.01</td>
<td>0.36</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
epithelial profile, Bowman layer damage, recruitment of dendritic cells, and altered sub-basal nerve plexus features in patients with chronic dry eye disease\textsuperscript{22}.

8. Conclusion

- Serum calcium is mainly seen affected by significantly decreased levels and having role in the association of dry eye.
- Hence the patients with dry eyes should be approached with a holistic view of assessing the serum calcium levels and managing them with holistic approach.

9. References

11. Yin Z, Pintea V, Lin Y, Hammock BD, Watsky MA. Vitamin...
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Cite this article as: Patil M, Balwir D, Khune A, Dhewale S. Dry Eye and its Relationship with Status of Serum Calcium in the Body at a Tertiary Care Institute: A Case Control Study. MVP Journal of Medical Sciences 2018; 5(1):82-86.