Assessment of dry eye in rural hospital setting, B.G. Nagara, Karnataka

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Abstract

Background: Dry eye is a common condition that is often under diagnosed. Normal vision requires moist healthy ocular surface. A sufficient quality of tears, normal composition of tears film, lid closure to maintain healthy ocular surface.

Due to lack of uniformity in definition and inability of any single diagnostic test or set of diagnostic test to confirm or rule out the condition. There has been a shift towards symptom based assessment as a key component in clinical diagnosis with grading of severity of dry eye.

Use of symptom based validated questionnaire might be beneficial as it allows grading of symptoms and is repeatable for comparative purpose before, during and after treatment. Recent advances in treatment suggests the use of lubricants, anti-inflammatory drugs, plugs to augment the tear film.

Objectives: A prospective study was conducted to assess the dry eye in rural hospital setting at B.G. Nagara Karnataka with the objective to study the frequency of occurrence of dry eye and identify risk factors, correlate dry eye status with clinical tests, demographic and disease profile and devise appropriate therapy.

Methods: A total of 63 cases were chosen from the outpatient department of Sri Adichunchanagiri Institute Of Medical Sciences and assessment of dry eye were made by tests like Tear breakup time, Schirmer's, Rose Bengal dye test with prior administered Ocular surface disease index (OSDI) questionnaire for subjective grading of dry eye.

Results: In our study majority 31.7% patients were in the group 41-50 years. Prevalence of overall dry eye in our study was 85.7%. Prevalence was more in females as compared to males. Risk factors associated with dry eye were identified with diabetes mellitus type II being more prevalent among them. In the study Osdi questionnaire had a good reliability and consistency (p<0.001). Pearson correlation with r value among various test like Tear breakup time, Schirmer's, Rose Bengal dye test and OSDI score showed a good correlation.

Conclusion: Dry eye is a chronic disease and increase in prevalence of dry eye increases with age. Subjective tests like OSDI correlated well with objective tests in our study. Grading of dry eye helps in better management of dry eye and its complications.

Keywords: Dry eye; OSDI; Rose Bengal dye test, Schirmer's test, Tear breakup time

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Introduction

Dry eye is a disorder characterised by either quantitative decrease or qualitative change in precorneal film resulting in spectrum of pathological changes that may adversely affect the ocular surface resulting in ocular surface disorders often leading to conjunctival squamous metaplasia and punctate epithelial erosion of cornea.¹

Dry eye results in discomfort and visual disturbance and tear film instability with potential damage to ocular epithelial surface and accompanied by increase in tear osmolarity and inflammation. Dry eye syndrome involves multiple risk factors that when disregarded can result in treatment failure and frustration both for the patients and the physician. Dry eye may lead to increase risk of infections, medications toxicity, contact lens intolerance, progressive ocular surface disease, scarring, cornea morbidity namely

keratinisation, corneal thinning, vascularisation, microbial and sterile corneal ulcer leading to perforation and severe visual loss. Hence correct diagnosis and appropriate management of dry eye is essential.²

Due to lack of uniformity in definition and inability of any single diagnostic test or set of diagnostic test to confirm or rule out the condition.³ There has been a shift towards symptom based assessment as a key component in clinical diagnosis with grading of severity of dry eye.

Use of symptom based validated questionnaire might be beneficial as it allows grading of symptoms and is repeatable for comparative purpose before, during and after treatment. Recent advances in treatment suggests the use of lubricants, anti-inflammatory drugs, plugs to augment the tear film.

Objectives

- 1. To assess the frequency of occurrence of dry eye in hospital setting.
- 2. Identify causes/risk factors of dry eye.
- 3. To correlate dry eye status with their clinical tests, demographic and disease profile.
- To describe the affect of appropriate therapy on dry eve

Materials and Methods

The study was conducted in the out patient department(OPD), Department of Ophthalmology, Adichunchanagiri Institute of Medical Sciences, B G Nagara, during the period December 2013-May 2015. Prospective interventional study consisting of cases coming with the complaints suggestive of dry eye in Department of Ophthalmology, AIMS, B G Nagar were recruited data was collected from 63 patients with the ODSI questionnaire and subsequent dry eye tests.

Plan for data analysis: Statistical tests used are Percentages, Fischer Exact tests, Chi square test, pearson correlation with r value among test like Tear breakup time, Schirmers test, Rose Bengal test(Bjisterveld's score), OSDI score

Selection Criteria

Method of collection of data: Researcher examined the general, ophthalmic history and systemic disease history and complete the ocular examination of all the cases attending the outpatient department (OPD) pertaining to dry eye. A pretested/semi structural questionnaire was used for the assessment of dry eye including identification of risk factors.

Information about age, gender, current occupation, exposure to air, presence of allergic problems or concomitant systemic diseases, topical and systemic medications, contact lens usage, oral contraceptives, significant history of trauma, chemical burn, drug reaction, history of using any kind of tear substitute and any history of ocular surgery was obtained. History of any previously confirmed diagnosis (based on history and documents provided by the patients) of rheumatoid arthritis or other connective tissue disorder was also recorded.

Diagnosis and confirmation of dry eye was done by series of test, which in standard order of eye examination are as follows: Tear film break up time (TBUT), slit lamp examination of the anterior segment, assessment of the meibomian glands and schirmer-1 test and lastly the Rose Bengal staining.

TBUT was done first because manipulation of the eyelid may affect the result. The test was repeated 3 times in each eye and the average time was recorded. It was considered positive if the average TBUT is<10 seconds in 1 or both the eyes.

After a minimum gap of 30 minutes, Schirmer-1 test was performed. The result was considered positive if the amount of wetting of the paper is <5mm. Rose Bengal staining was done again after 30 minutes, taking care to avoid touching the ocular surface. A van Bjisterveld"s score of 4 or more was considered positive for dry eye diseases.

All dry eye cases were given appropriate treatment and the follow up was done upto 3 months so as to describe the affects of the treatment in terms of reduction of symptoms of dry eye.

Inclusion Criteria:

Both male and female patients equal to and above 20 years presenting with following symptoms

- 1. Burning sensation
- 2. Blurring of vision
- 3. Foreign body sensation
- 4. Ocular fatigue
- 5. Itching
- 6. Stinging
- 7. Redness
- 8. Intolerance to light

Exclusion Criteria:

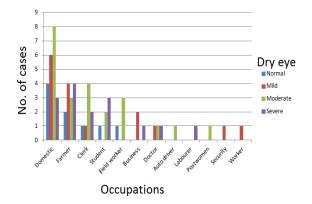
- 1. Patients less than 20yrs of age.
- 2. Patients with history of allergic conjunctivitis.
- 3. Patients with history of systemic disease.
- 4. Patients with history of acute ocular infections.
- Patients with history of extra and intra Ocular surgery within last 6 months.
- 6. Contact lens users.
- 7. Gross lid abnormalities

Results

A prospective interventional study was conducted to assess dry eye among 62 patients attending outpatient department of ophthalmology.

The gender distribution in our study was 55.6% females and 44.4% males. Mean age in our study was 40.8 years with prevalence of dry eye highest seen in 41-50 age group. In the present study majority of the study subjects 20(57.1%) were females doing domestic work with the 1 (3.6%) being male, with both comprising 21(33.3%) of the total with significant p value (p<0.001) on **Fischer Exact test.**[Table 1]

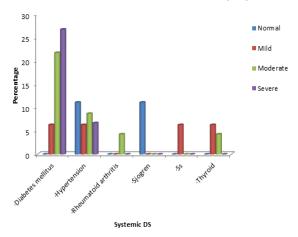
Table 1: Occupations of Patients Studied in Association with Prevalence of Dry Eye



In the present study the prevalence of dry eye among rural patients showed 12(75%) in the mild dry eye group, 15(65.2%) in the moderate dry eye group, 9(60%) in the severe dry eye group. Systemic diseases studies with the prevalence of dry eye was found in

21(33.3%) had systemic disease among which 10(15.9%) had Diabetes mellitus in the majority group with 1(6.3%) had mild dry eye droup, 5(21.7%) had moderate dry eye group, 4(26.7%) severe dry eye group. [Table 2]

Table 2: Systemic DS of Patients Studied in Association with Prevalence of Dry Eye



In the study prevalence of dry eye in association with risk factors present showed majority that is 54(85.7%) having significant risk factors namely diabetes mellitus, hypertension menopause, smoking,

low humidity, drug induced among others. Meibomian gland dysfunction which was diagnosed by the presence of the vascularisation, collarette and discharge was absent in majority 54(85.7%) and present in 9(14.3%) patients. (P=0.036* Significant, Chi-Square test).[Table 3]

Table 3: MGD Incidence in Patients Studied

| MGD | Gen | Total | |
|---------|-------------|-----------|-----------|
| | Female Male | | |
| Absent | 27(77.1%) | 27(96.4%) | 54(85.7%) |
| Present | 8(22.9%) | 1(3.6%) | 9(14.3%) |
| Total | 35(100%) | 28(100%) | 63(100%) |

In the present study TBUT test of patient studied in association of dry eye showed right eye mean of 9.5 ± 2 standard deviation in mild dry eye group, mean of 6.39 ± 2.35 standard deviation in moderate dry eye group, mean of 3.20 ± 1.15 standard deviation in the severe dry eye group showing a significant p value of less than 0.001. Whereas in the left eye mean of 10.38 ± 2.42 standard deviation in the mild dry eye group, mean of 7.09 ± 2.48 standard deviation in the moderate dry eye group, mean of 3.67 ± 1.05 standard deviation of in severe dry eye group showing a **p value** of less than 0.001.[Table 4]

Table 4: TBUT Test of Patients Studied in Association with Prevalence of Dry eye

| TBUT Test | | Dry | Total | P value | | |
|-----------|------------|------------|---------------|-----------|-----------|----------|
| | Normal | Mild | Moderate | Severe | | |
| Right Eye | 11.00±2.45 | 9.50±2.00 | 6.39±2.35 | 3.20±1.15 | 7.08±3.40 | <0.001** |
| Left Eye | 12.00±2.96 | 10.38±2.42 | 7.09 ± 2.48 | 3.67±1.05 | 7.81±3.68 | <0.001** |

In the present study Schirmer's test of patient were studied with the prevalence of in right eye mean of 10.19 \pm 2.81 of standard deviation in the mild dry eye group, mean 8.26 with \pm 3.40 of standard deviation in the moderate dry eye group, mean of 4.47 with \pm 0.83 standard deviation in the severe dry eye group.

For left eye mean of 10.88 with ± 3.16 of standard deviation in the mild dry eye group, mean of 8.91 with ± 3.59 of standard deviation in the moderate dry eye group, mean of 4.47 ± 1.30 of standard deviation in the severe dry eye group with **p value** for both eyes being highly significant p<0.001.{Table 5}

Table 5: Schirmer's Test of Patients Studied in Association with Prevalence of Dry Eye

| Schirmer's | | Dry | Total | P value | | |
|------------|------------|------------|-----------|-----------|-----------|----------|
| test | Normal | Mild | Moderate | Severe | | |
| Right Eye | 12.33±3.00 | 10.19±2.81 | 8.26±3.40 | 4.47±0.83 | 8.43±3.76 | <0.001** |
| Left Eye | 13.33±4.36 | 10.88±3.16 | 8.91±3.59 | 4.87±1.30 | 9.08±4.19 | <0.001** |

In the study Rose Bengal test of patient studied with the prevalence of in right eye mean of 4.19 ± 1.52 standard deviation in the mild dry eye group, mean of 5.22 with ±1.31 standard deviation in the moderate dry eye group, mean of 7.47 with ±0.83 standard deviation in the severe dry eye group.

For left eye mean of 4.12 with ± 1.59 standard deviation in the mild dry eye group, mean of 5.22 with ± 1.53 of standard deviation in the moderate dry eye group, mean of 7.67 with ± 0.82 standard deviation in the severe dry eye group with **p value** for both eyes being highly significant p<0.001.(**ANNOVA TEST**).[Table 6]

Table 6: Rose Bengal Test (Bjisterveld's Score) of Patients Studied in Association with Prevalence of Dry Eye

| Rose Bengal | | Dry | Total | P value | | |
|-------------|-----------|-----------|-----------|-----------|-----------|----------|
| Test | Normal | Mild | Moderate | Severe | | |
| Right Eye | 2.89±1.05 | 4.19±1.52 | 5.22±1.31 | 7.47±0.83 | 5.15±1.94 | <0.001** |
| Left Eye | 2.89±1.16 | 4.12±1.59 | 5.22±1.53 | 7.67±0.82 | 5.19±2.07 | <0.001** |

In the study OSDI score on scale of 0-100 revealed greatest debility score >80, before treatment 4(6.3%) and after treatment 1(1.6%) showing percentage change of -4.7%. Whereas in the <40 group, OSDI before treatment was 30(47.6%), after treatment was 47(74.6%) representing the 27 % Change.

In the present study of patients before treatment in association with the prevalence of dry eye shows OSDI score of 41.10 mean with ± 23.84 standard deviation, on osdi scale 41.90 with ± 23.51 standard deviation both showing **p** value less than (p<0.001) highly significant. [Table 7]

Table 7: OSDI score and Scale before Treatment of patients studied in association with prevalence of dry eye

| Before | | Total | P value | | | |
|------------|------------|------------|-------------|-------------|-------------|----------|
| Treatment | Normal | Mild | Moderate | Severe | | |
| OSDI Score | 11.32±4.49 | 23.79±5.37 | 42.15±9.63 | 75.81±11.14 | 41.10±23.84 | <0.001** |
| OSDI Scale | 12.97±1.55 | 25.04±7.65 | 42.81±10.46 | 75.85±10.63 | 41.90±23.51 | <0.001** |

In the present study prevalence of dry eye patients after treatment was associated with OSDI score mean of 29.08 with ± 18.78 standard deviation and scale showed mean 0f 29 with ± 18.55 standard deviation both showing p value less than(p<0.0001)highly significant.[Table 8]

Table 8: OSDI score and Scale after Treatment (end of 3 months follow up) of patients studied in association with prevalence of dry eye

| After | | Dry | Total | P value | | |
|------------|------------|------------|------------|-------------|-------------|----------|
| Treatment | Normal | Mild | Moderate | Severe | | |
| OSDI Score | 10.86±4.57 | 14.61±4.07 | 28.24±7.07 | 56.71±13.49 | 29.08±18.78 | <0.001** |
| OSDI Scale | 12.97±1.55 | 13.73±5.66 | 28.17±5.63 | 56.81±13.31 | 29.15±18.55 | <0.001** |

In our study group grading of dry eye before treatment and after treatment mild dry eye was present in patients 16(25.4%) before treatment 24(38.1%) after treatment reflecting a percentage change of 12.7%. Moderate dry eye was present in 23 (36.5%) before treatment 13 (20.6%) after treatment reflecting a percentage change of -15.9%. Severe dry eyes was present in 15(23.8%) before treatment 2 (3.2%) after treatment reflecting percentage change of -20.6%. Of the 63 patients 9(14.35) were normal before treatment which showing percentage change 23.8% to normal in 24(38.1%) patients after treatment at the end of 3 months.

In our study group medical management of dry eye showed 55(87.3%) patients requiring treatment of which eye drops namely polyvinyl alcohol 16(25.4%), carboxymethyl cellulose 24(38.1%), cyclosporine 15(23.8%) were prescribed, whereas 2 patients required punctal plugs.

In our study prevalence of dry eye was noted as follows mild dry eye 16(25.4%), moderate dry eye 23(36.5%), severe dry eye 15(23.8%).

In our study among the 63 patients studied occurrence of risk factors in dry eye majority that is 35(55.6%) were females, low humidity 15(23.8%), diabetes mellitus 10(15.9%), cigarette smoking 12(19%), alcohol 10(15.9%) computer 9(14.3%), post-menopausal 7(11.1%)

In our study correlation among the various test like TBUT, Schirmer's, Rose Bengal test, Osdi showed good correlation with significant p value among all p<0.001 highly significant.[Table 9]

Table 9: Pearson Correlation

| Pair | Pearson correlation | | |
|------------------------------------|---------------------|----------|--|
| | r value | p value | |
| OSDI Score vs TBUT | -0.801 | <0.001** | |
| OSDI Score vs Schirmers test | -0.695 | <0.001** | |
| OSDI Score vs Rose bengal test | 0.772 | <0.001** | |
| TBUT vs Schirmers test | 0.833 | <0.001** | |
| TBUT vs Rose bengal test | -0.817 | <0.001** | |
| Schirmers test vs Rose bengal test | -0.757 | <0.001** | |

In our study comparison of variable according to the prevalence of dry eye with regards to the Osdi, TBUT, Schirmer's, rose Bengal test reveals strongly significant p value. Osdi mean 41.10±23.84 standard deviation, TBUT mean 7.44±3.51 standard deviation, schirmer's test mean 8.75±3.92 standard deviation, Rose Bengal mean 5.17±1.98 standard deviation overall validated the tests done.[Table 10]

| Table 10: Comparison of | Variables A | According to | Prevalence o | f Dry E | ye and Total |
|-------------------------|-------------|--------------|--------------|---------|--------------|
| | | | | | |

| Variables | Dry Eye | | Total | P value |
|-----------------|--------------------|-------------|-------------|----------|
| | No Dry Eye Dry Eye | | | |
| Age in years | 41.44±13.88 | 40.74±11.17 | 40.84±11.47 | 0.866 |
| OSDI | 11.32±4.49 | 46.06±22.05 | 41.10±23.84 | <0.001** |
| TBUT | 11.50±2.65 | 6.77±3.18 | 7.44±3.51 | <0.001** |
| Schirmer's test | 12.83±3.61 | 8.07±3.57 | 8.75±3.92 | <0.001** |
| Rose Bengal | 2.89±1.05 | 5.56±1.84 | 5.17±1.98 | <0.001** |

In our study prevalence of dry eye was 85.7%.

Discussion

Rural based clinical studies on dry eye prevalence are few. Symptom based dry eye was found to be common among dry eye studies subjects. Dry eye was common in women than men. The present study demonstrated that dry eye was more prevalent with increasing age in age group (41-50) years. Prevalence varied according to diagnostic criteria. Population studies and distribution therefore comparison with clinical studies is difficult.

Overall prevalence in Asian studies is as follows:

Jaipur study 2005 by Sahai found prevalence of 18.4%. Leh study 2008 by Gupta found prevalence of 54%. Beijing eye study 2009 by Jie found prevalence of 21%. Saudi Arabia study 2009 by Bukhari found prevalence of 93.2%. Delhi study 2010 by Gupta found prevalence of 29.3%.

Past studies suggest dry eye prevalence ranges from 10.8% to 57.1%. The vast disparity in dry eye prevalence stems mainly from the different dry eye diagnostic criteria employed and different cut off value for objective dry eye test. In our study dry eye prevalence of 85.7%. In our study dry eye prevalence increased progressively with age which is consistent with the findings in other dry eye studies. With the peak in the age group 41-50 years which relates to their predominantly outdoor activities in dry hot environment at B G Nagara.

Most studies report higher prevalence of dry eye in females than males. Our study is no exception. With 55.6% of study patients who were females had dry eye compared to 44.6% males but this was not statistically significant. Menopause causes estrogen deficiency and alters the milieu of the lacrimal gland leading to less secretion and dry eye.

We noted a higher dry eye prevalence in rural residence than urban dwellings. In our opinion rural prevalence in our population were a direct consequence of exposure of rural residents to dry dusty winds and high temperature in B G Nagara.

Most of the patients with occupation had outdoor activity exposing them to dry environmental conditions, which on Fischers Exact test gave a p value(p<0.001) which was significant. Exposure seems to be more in domestic workers exposed to outdoor activity, farmers, labourers, security etc. Much of the case was seen in rural area with the prevalence being 68.3% compared to urban.

Most of the systemic diseases mention in the study like diabetes mellitus, hypertension, rheumatoid arthritis, Sjogren's, thyroid which comprises 33.3% of patients having dry eye, with prevalence being high in cases of Diabetes mellitus. Among the medications used by the patients prior to the study like antihypertensive, antihistamines, anticholinergics, antidepressants used could affect the outcome in diagnosis of dry eye.

The correlation between subjective and objective findings was good but not in all cases and could be caused by multifactorial nature of dry eye syndrome. There are indications that dry eye condition is associated with chronic meibomian gland disease. However in our study only 14.3% had MGD (meibomian gland disease) which was statistically significant (p=0.036) on chi square test.

In our study 50 (79.4%) of patients have some symptoms such as foreign body sensation, burning, grittiness related to dry eye. there was good association between subjective symptoms of dry eye and its validation with objective test like, Tbut, Schirmer's, Rose Bengal test. Objective studies of dry eye commonly involved TBUT, Schirmer's, Rose Bengal test (bjisterveld's score) and when used in our study showed significant p value of less than 0.001.8

Also in the present study the OSDI demonstrated consistency and good test reliability. The OSDI also demonstrated excellent validity effectively discriminating between normal, mild, moderate and severe dry eye diseases as defined by both the physician assessment of severity and composite disease severity score. Pearson correlation with r value shows perfect correlation between test and significant p value

(p=0.001). OSDI score/scale showed strongly significant value with dry eye before and after treatment (p less than 0.001).

History of risk factors like old age, female gender, postmenopausal, Lasik surgery, connective tissue disorders, low humidity, cigarette smoking, alcohol consumption, ovarian dysfunction were elicitated associated with dry eye. Other risk factors which were inquired but not found like history of radiation therapy, hepatitis C infection, retinoids, botulinum toxin, hematopoetic stem cell transplantation, low dietary intake of omega 3 fatty acids, hiv infection, systemic chemotherapy. ¹⁰

Among the severe 2 patients underwent silicon punctal plug implantation at the end of three months follow up in both eyes. Affordability being the limiting factor in rural patients, late intervention at the end of the follow up of the dry eye study was done.

One patient underwent tarsorrhaphy.

Mild, moderate, severe cases were managed with polyvinyl alcohol eye drops in 16 patients, carboxymethyl cellulose in 24 patients and cyclosporine in 15 patients respectively.¹¹

Systemic diseases though absent in 42(66.7%) patients, was present in 21(33.3%) cases. In the study diabetes mellitus (one case had chemical alkali injury of one eye), hypertension, rheumatoid arthritis, Sjogren, syndrome, scleroderma and thyroid disease, with 15.9% having diabetes mellitus being the leading cause. Hence dry eye evaluation must be done in these diseases.

Conclusion

Prevalence of dry eye disease in the indigenous people was found to be 85.7% which was more than other studies quoted. Attributable to this fact is that BG Nagara hardly sees any rain fall and throughout the year the climate is hot, dusty with dry winds blowing throughout the year and most of the population and others having predominantly outdoor activity in sunny conditions. Consensus regarding protocol in dealing with dry eye clinical diagnosis and standardisation of objective test is lacking. With new methods of diagnosing, monitoring and treatment on the horizon future management of this condition is promising. More research on effect of tropical climate on dry eye is required.

It is recommended that establishment of dry eye clinics at rural health centres should be done. Dry eye disease evaluation should be part of eye examination routinely. OSDI questionnaire should be part of working protocol in evaluating dry eye TBUT, Schirmer's, Rose Bengal test which are objective test when done correctly correlates well with Osdi subjective test. Silicon punctal plugs are very effective in severe dry eyes as also tear substitutes in various grades of dry eye. Role of risk factors and environmental conditions influencing dry eye should be studied into future.

References

- Begley C G et al. The Relationship between habitual patient reports symptoms and clinical signs among patients with dry eye of varying severity. Invest Ophthalmol Vi Sci 2003;44:4753-61.
- Elmer Y et al. Dry Eye. Yanoff and Duker Ophthalmology 3rd edition. Mosby Elsevier Publishers 2009;3:324-9.
- International Dry Eye Workshop Subcommittee. The Definition and Classification of Dry Eye Disease Workshop DEWS. Ocul Surf 2007;5:75-97.
- Gupta N, Prasad I, Himashree G, D'Souza P. Prevalence of dry eye at high altitude: A case controlled comparative study. High Alt Med Biol 2008;9(4):327-34.
- Jie Y, Xu L, Wu YY, Jonas JB. Prevalence of dry eye among adult Chinese in the Beijing Eye Study. Eye (Lond). 2009 Mar;23(3):688-93.
- Bukhari A, Ajlan R, Alsaggaf H. Prevalence of dry eye in the normal population in Jeddah, Saudi Arabia. Orbit. 2009;28(6):392-7.
- Tabbara KF, Wagoner MD. Diagnosis and Management of dry eye syndromes. In: Smolin G, Editor. New drugs in ophthalmology. Massachusettes. Boston: Little Brown and Company, 1996;36(2):61-75 (International Ophthalmology Clinics).
- Mizuno Y et al. Association between clinical diagnostic tests and health-related quality of life surveys in patients with dry eye syndrome. Jpn J Ophthalmol. 2010; 54(4):259-65.
- Grubbs JR, Tolleson-Rinehart S, Huynh K, Davis Rm. A review of quality of life measures in dry eye questionnaires. Cornea. 2014 Feb; 33(2):215-8.
- Uchino M et al. Prevalence and risk factors of dry eye disease in Japan: Koumi study. Ophthalmology. 2011 Dec;118(12):2361-7.
- Henry D et al. Evaluation of topical cyclosporine for the treatment of dry eye disease. Arch Ophthalmol 2008;126(8):1046-50.