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Original Research Article

Comparison of tear function among newly diagnosed polycystic ovary syndrome (PCOS) and PCOS under treatment

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ABSTRACT

Purpose: To compare the tear function among newly diagnosed Polycystic Ovary Syndrome subjects and Polycystic Ovary syndrome under treatment.

Materials and Methods : Seventy Polycystic Ovary Syndrome (PCOS) subjects were included in the study with age ranging from 18 to 35 years, consisting of 35 subjects in group 1 as newly diagnosed PCOS and 35 in group 2 as PCOS under treatment. The subjects underwent comprehensive eye examination and slit lamp examination. Participants were asked to answer the ocular surface disease index (OSDI) questionnaire to know the symptoms of dry eye and the following tests such as Schirmer's 1 and 2, Tear film break-up test (TBUT) was performed to know the tear functions.

Results: No difference was found in OSDI scores when comparing two groups. Both Schirmer's test and TBUT test were significant. When both the groups are compared Schirmer's 1 p value for right eye is 0.001, left eye is 0.023.Schirmer's 2 p value for right eye is 0.002, left eye is 0.001.However TBUT p value for right eye and left eye is 0.00.

Conclusion: Through our findings we suggest that patients who are under treatment for PCOS, should take ophthalmic examination, especially for dry eye.

1. Introduction

Polycystic ovary syndrome is an endocrine disorder which causes anovulation, infertility in women during their reproductive age which is more common in women nowadays. It makes women more uncomfortable and causes frustrations. It causes either infrequent menstrual periods (oligomenorrhea) or absence of menstruation (amenorrhea).[1] The clinical characteristics of PCOS include hyper-androgenism, chronic anovulation, insulin resistance and infertility. This condition has both signs and symptoms like excessive production of androgens and ovarian dysfunction even if other specific diagnoses are not found. Hyperandrogenism is generally manifested as hirsutism, an excessive unwanted hair growth in face and acne.[2]

The prevalence of Polycystic ovary syndrome is about 60% - 80% worldwide[3,4] and incidence is 4% - 12%.[5] The term polycystic ovary syndrome means the ovaries are surrounded by numerous cysts which are caused by follicles. The aetiology of this condition is not known.[66].The diagnosis should be an evidence based one and long term measure. Ultrasonography,[7] blood test[8] are performed to confirm the disorder by the clinician. Treatment for Polycystic ovary syndrome is uncomplicated. Though, there is no universal treatment, few are executed according to the need and the symptoms of the patients. Some modifications in their regular exercises and oral-contraceptives can be

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planned as a mode of treatment,[9] as there is no specific drug available for the treatment of polycystic ovary syndrome.[10]

Sex hormones influence the anatomical and functional structures of the ocular surface like lacrimal glands, globlet cells, conjunctiva, meibomian glands, and cornea, including the tear film.[11] Main function of tear film is to make the ocular surface moist and lubricant. Tear film is made up of three layers, mucin, aqueous and lipid layer. Lipid layer is produced by meibomian gland that prevents the tear substance from quick evaporation. But, in PCOS condition due to the influence of sex hormone, dysfunction of the meibomian gland may result in tear film instability that causes evaporative dry eye which subsequently lead to vision impairment.[12–14] Hyper-androgenism in women results in tear film instability and dry eye.[15] Premature ovarian failure in women has more chance to get dry eye.[16]

"A multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles."[17] Though it is not very clear that how sex hormones affect the ocular surface in various diseases, many studies have reported the prevalence of dry eye in polycystic ovary syndrome but the status of treatment of PCOS that alters the sex hormone level was not taken into consideration for tear film imbalance improvement.

Therefore, for we aim to study the comparison of tear film function between the subjects who are diagnosed to have PCOS but not on treatment and subjects who are already under treatment for PCOS. The dry eye symptoms will be evaluated using Ocular Surface Disease Index (OSDI) questionnaire which is the only patient perspective instrument that has a formalized grading scheme.[18,19] And to investigate tear film stability and tear film quantity clinically TBUT and Schirmer's test will be performed.[20]

Several studies have been done on PCOS and the dry eye, but they all compared with the normal healthy individuals, and proved that the PCOS patients have dry eye .But in this study we aim to find whether patients taking treatment in PCOS has dry eye or they has to take ophthalmic medications along with the PCOS treatment.

2. Aim of this study

This study was to compare the tear function among newly diagnosed polycystic ovary syndrome (PCOS).

3. Objective

1. To understand the dry eye symptoms of the subjects through Ocular Surface Disease Index Questionnaire.
2. To determine the tear film stability and tear film quantity using Tear film break-up time and Schirmer's test.

4. Materials and Methods

4.1. Site of the study

Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai – 600 116.

4.2. Study design

Prospective study.

4.3. Period of the study

June to May 2020.

4.4. Sample size

Sample size was calculated by using SPSS statistics software 16.0 with a reference article : Coksuer H, Ozcura F, Oghan F,Haliloglu B, Karatas S. Effects of hyperandrogenism on tear function and tear drainage in patients with polycystic ovary syndrome. Journal of Reproductive Medicine. 2011 Jan1;56(1):65. The required sample size is 70. (35 as group 1 and 35 as group 2 as in inclusion criteria)

Formula:

$$n = \frac{2S_p^2[Z_{1-\alpha/2} + Z_{1-\beta}]^2}{\mu_d^2}$$

$$S_p^2 = \frac{S_1^2 + S_2}{2}$$

Where,

S_1^2: Standard deviation in the first group

S_2^2: Standard deviation in the second group

μ_d^2: Mean difference between the samples

α: Significance level

1-β: Power

The sample size was calculated with SPSS statistics software 16.0 version by applying following details in the above formula

Two Means	
Standard deviation in group I	20.1
Standard deviation in group II	18.5
Mean difference	1.3
Effect size	0.673575
Alpha error (%)	5
Power (1- beta) %	80
1 or 2 sided	2
Required sample size per group	**35**

4.5. Inclusion criteria

Age between 18 to 35 yrs., Newly diagnosed PCOS were included in group 1, PCOS under treatment for one or more years were included in group 2.

4.6. Exclusion criteria

Other systemic conditions that affect ocular surface (e.g. Thyroid dysfunction, rheumatic arthritis), Under medications that affect the ocular surface, Any ocular surface surgery, other ocular infections that disrupts the ocular surface, Contact lens users, long term computer users.

Study tools: Comprehensive eye examination, Refraction, Slit lamp examination, Ocular Surface Disease Index questionnaire (OSDI), Schirmer's test, Schirmer's 1 (without anaesthesia) Schirmer's 2 (with anaesthesia), Tear film break-up time (TBUT)

4.7. Procedures

Subjects with PCOS who meet the inclusion criteria are recruited in the study. Patients in the group 1 are newly diagnosed and the group 2 patients are under treatment for polycystic ovary syndrome. Patients were recruited from the Department of Obstetrics and Gynecology, SRIHER (IEC.No223). The subjects underwent a comprehensive eye evaluation which includes refraction; slit lamp evaluation, followed by tests for tear film function and a questionnaire to assess the symptoms of dry eye.

4.8. Methods

4.8.1. Questionnaire

The ocular surface disease index questionnaire consists of 12 questions which is used to assess dry eye symptoms and the effects it has on vision-related function in the past week of the patient's life.

1. The questionnaire has 3 subscales: ocular symptoms, vision-related function, and environmental triggers. Patients rate their responses on a 0 to 4 scale with 0 corresponding to "none of the time" and 4 corresponding to "all of the time."
2. A final score is calculated which ranges from 0 to 100 with scores 0 to 12 representing normal, 13 to 22 representing mild dry eye disease, 23 to 32 representing moderate dry eye disease, and greater than 33 representing severe dry eye disease.

4.9. Schirmer's test

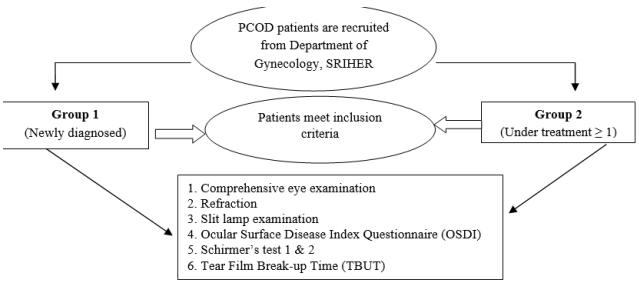
The Schirmer's test evaluates aqueous tear production. It is helpful in the assessment of patients with signs and/or symptoms of dry eye. To perform a Schirmer's test a special (no. 41 Whatman) filter paper is used which are 5mm wide and 35mm long. The test is performed with anesthetic (Schirmer's 2) for baseline secretion.

1. Topical anesthetic is used and then excess drop is removed from the eye before the test is started.
2. The filter paper is folded 5 mm from one end – usually there is a notch in the filter paper 5 mm from one end, which indicates the point the paper is to be folded.
3. The folded tip is inserted into the lower lid – at the junction of the middle and outer thirds of the lower lid – taking care not to touch the cornea or lashes.
4. The patient is asked to keep their eyes closed for the duration of the test.
5. After 5 minutes, the filter paper is removed and the amount of wetting from the fold is measured.

A reading of 10 mm or greater is generally considered the cut-off for a normal value for both tests. An abnormal finding is highly suggestive of aqueous deficient dry eye. This test suffers from variable repeatability and a wide range of sensitivity and specificity values but the accuracy seems to increase as the severity of the disease increases.

4.10. Tear film break-up time

1. Tear breakup time (TBUT) is a clinical test used to assess for evaporative dry eye disease. To measure TBUT, A single drop of 2% fluorescein drop is instilled in tear film of the lower conjunctival sac while the patients were looking upwards. The patient is asked not to blink while the tear film is observed under a broad beam of cobalt blue illumination.
2. The TBUT is recorded as the number of seconds that elapse between the last blink and the appearance of the first dry spot in the tear film, as seen in this progression of these slit lamps examination over time. A TBUT under 10 seconds is considered abnormal. The test should be repeated three times and the average is used to obtain the most reliable result. Ten seconds or greater is considered normal. Measurements were repeated for three times. These steps were also applied to the left eye.



4.11. Statistical analysis

Statistical package for social sciences (SPSS version 16.0) were used for statistical analysis. For the continuous data independent t test has been used for newly diagnosed PCOS and under treatment PCOS subjects.

5. Results

Totally seventy subjects were involved in the study of age 18 to 35 and they were divided into two groups as equally numbered. Group one has thirty five subjects who are newly diagnosed PCOS and group two has thirty five subjects who are under treatment of PCOS for past one year or more. In group two we have also noted the duration of the treatment. The mean, standard deviation has been found for the age in both the groups. According to age category both the groups were not significant. (p value 0.77) and we also found the mean and standard deviation for the duration of the treatment in group two this has been shown in the Table 1.

Table 1: Mean, SD and significant value of age and treatment of two groups

Category	Group 1(n=35) Mean±SD	Group 2 (n=35) Mean±SD	p value
Age	25.4±3.9	25.7±5.0	0.77
Duration of the treatment (≥1 year)	-	2.16±1.1	-

To find whether the dry eye reduces after treatment in PCOS we compared both groups with the following tests such as Ocular Surface Disease Index questionnaire, Schirmer's 1 & 2, Tear film Breakup time and found their mean, standard deviation and significant value (p value) and showed that there is no significant difference in OSDI scoring, and in Schirmer's test 1 (without anaesthesia), Schirmer's test 2(with anaesthesia) we compared right and left eye from both the groups, their mean, standard deviation has been found and they are clinically significant. Similarly TBUT is also clinically significant. The tests mean, standard deviation, p value are shown in Table 2.

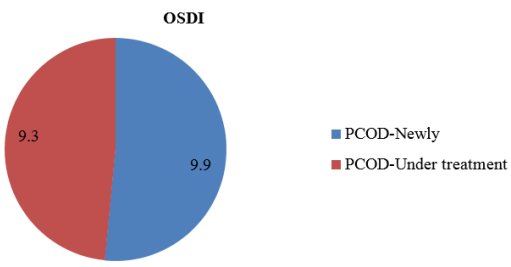


Fig. 1: Comparison of OSDI questionnaire among two groups:

Table 2: Mean±SD and significant values of all tests

Tests	Group 1(n=35) Mean ±SD	Group 2(n=35)Mean ± SD	p value
OSDI Score	9.96±5.3	9.39±5.3	0.494
Schirmer's 1(mm)	OD :20.6±7.9	OD:25.7±5.1	0.001*
	OS:21.6±8.3	OS:25.2±5.2	0.023*
Schirmer's 2(mm)	OD:17.6±7.9	OD:22.4±4.3	0.002*
	OS:17.3±8.3	OS:22.9±5.0	0.001*
TBUT(sec's)	OD:6.6±2.8	OD:11.4±2.2	0.00*
	OS:7.5±2.6	OS:11.5±2.2	0.00*

*statistically significant

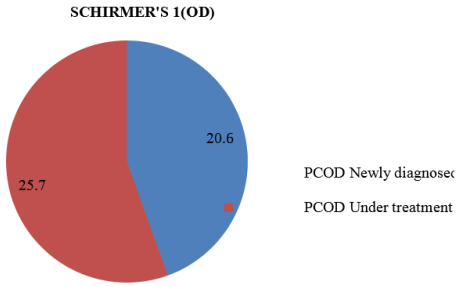


Fig. 2: Comparison of Schirmer's 1 test for right eye among two groups:

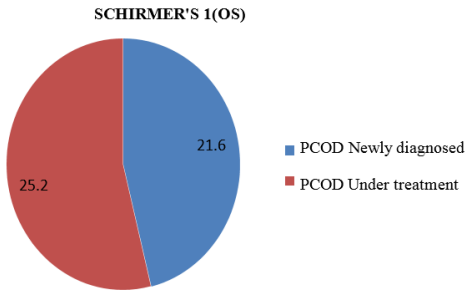


Fig. 3: Comparison of Schirmer's 1 test left eye among two groups:

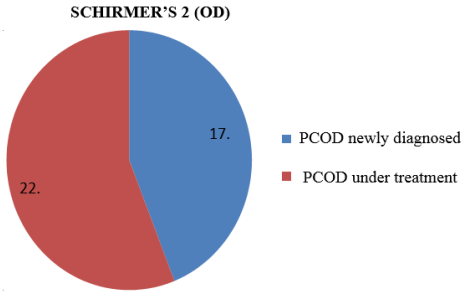


Fig. 4: Comparison of Schirmer's 2 test right eye among two groups:

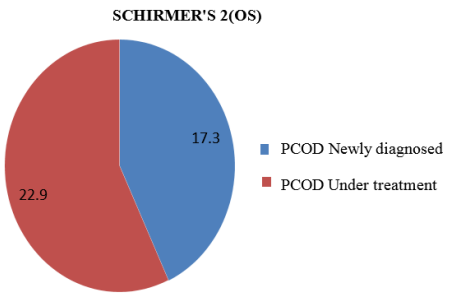


Fig. 5: Comparison of Schimer's2 test left eye among two groups

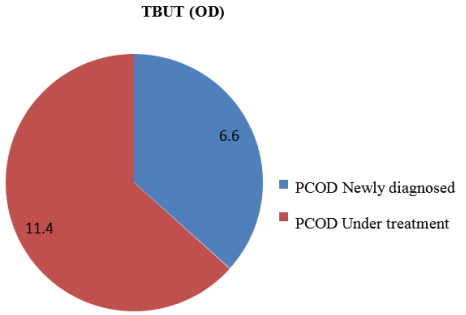


Fig. 6: Comparison of TBUT test right eye among two groups

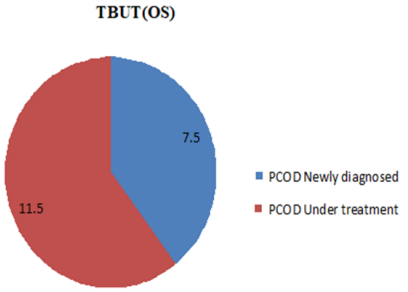


Fig. 7: Comparison of TBUT test left eye among twp groups

6. Discussion

In this study we have assessed tear function by comparing newly diagnosed polycystic ovary syndrome subjects and subjects who are under treatment for polycystic ovary syndrome and the duration of treatment is ≥ 1 year. Newly diagnosed subjects are taken as group 1(n=35) and under treatment subjects are taken as group 2(n=35) and the total subjects are 70. Our study objective is to understand the dry eye symptoms using questionnaire, and the another objective is to determine the tear film quantity and tear film stability in Polycystic ovary subjects.

We compared the tear film function using Ocular surface disease index (OSDI) questionnaire to know the symptoms of dry eye, Schirmer's 1(without anaesthesia), Schirmer's 2(with anaesthesia) to find the tear film quantity and Tear film break-up time (TBUT) to find the tear film stability.

Women with Polycystic ovary syndrome are associated with the signs and symptoms of dry eye,[13,21] Symptoms of dry eye in polycystic ovary syndrome are significant while testing in TBUT (p= 0.00) in TBUT and Schirmer's tests too. We found these significant differences by comparing the right eyes of both the groups using Schirmer's test 1 & 2 and TBUT test. But there was no significant difference in OSDI questionnaire. The study by Bonini et al. (2007)[22] had a significant difference in TBUT and Schirmer's when comparing PCOD with PCO subjects.

B.Yuksel et.al (2015)[23] had a significant difference in TBUT but there is no significant difference in Schirmer's and OSDI where as our study revealed a significant difference in Schirmer's test (with and without anesthesia) in both newly diagnosed PCOS and PCOS on treatment.

Karaca Adıyeke et.al (2017)[24] had significant difference in both TBUT and Schirmer's test.Yaran Koban et .al (2019)[25] compared the PCOS subjects with normal healthy group and had the significant difference in TBUT but no correlation in Schirmer's and OSDI score.

Several studies have difference in TBUT and Schirmer's test and many studies have done only with the Schirmer's 1(without anaesthesia); so it cannot be correlated (Schirmer's 1 will not give a accurate value). But in this study we have done both Schirmer's 1 and 2 with both the PCOS groups, unlike previous studies. Our first objective is to find the dry eye symptoms using OSDI questionnaire which showed insignificant value.

The second objective we had is to determine the tear film stability and tear film quantity in both groups. We already know that PCOS patients have dry eye and with this study we came to know that subjects who are under treatment for polycystic ovary syndrome also have problem with tear film stability and tear film quantity.

7. Limitation of the study

Though we found that patients under treatment of PCOS had no improvement in tear film production and stability, we should further investigate which mode of treatment is to be given for the patients in order to reduce dry eye.

8. Conclusion

As per our main objective dry eye symptom in newly diagnosed subjects and PCOS subject under treatment were analyzed using OSDI questionnaire were not statistically significant. But it showed significantly reduced TBUT values and Schirmer's value. This proves though PCOS patients don't have any significant symptoms for dry eye. There might be a change for poor lipid evaporation of tear film which might result in dry eye. PCOS patients have dry eye and they need ophthalmic examinations and medications, which is already known. Now from this study, patients who are taking treatment for Polycystic ovary

syndrome showed a greater duration of TBUT test and more production of aqueous tear layer in Schimer's 1& 2 test as compared to newly diagnosed subjects. Hence recommending the PCOS patients (who are in treatment) for ophthalmic examination becomes mandatory.

9. Acknowledgment

None.

10. Source of Funding

None.

11. Conflict of Interest

None.

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