

## Effect of Oral Contraceptive Pills on Tear Film in Women of Reproductive Age

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### Abstract

**Purpose:** To determine the effect of oral contraceptive pills on tear film of women of reproductive age group.

**Study Design:** Case control study.

**Place and Duration of Study:** Department of Ophthalmology & Department of Obstetrics & Gynecology, Govt. medical college, Kota from February 2020 to January 2021.

**Methods:** 100 females between the 20 to 45 years of age were recruited for this study. They were divided into two groups of fifty each. Group A included females using oral contraceptive pills for at least last eight months. Whereas, group B included control group of age matched females not using any contraceptive pills. The study dynamics was explained to all participants and informed consent was obtained. All cases underwent full gynecological and ophthalmological examinations including Schirmer test and tear film break – up time (BUT) and followed up for at least 3 months. Tear film status was assessed on the basis of tear film breakup time (TBUT) on slitlamp examination and Schirmer strip test<sup>2</sup> (without anesthesia). Study was approved from ethical committee of the hospital.

**Results:** Mean age was  $28.7 \pm 4.46$  years. We found that serum androgen levels were significantly reduced in women who were on oral contraceptives, similarly the tear secretion was also reduced in these women. We got linear correlation of Schirmer's test and TBUT-test with androgens profile (Serum DHEA level). As serum androgen levels decreased, Schirmer's test and TBUT-test results reduced.

**Conclusion:** Use of oral contraceptive pills has an adverse effect on the tear film status.

**Keywords:** Oral contraceptive pills, Tear film, TBUT, Schirmer's test,

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### I. Introduction

According to WHO 2009, 60-70% women use one of the method of contraception. 8.8% to 15.4 % women use oral contraceptives.

Estimated 100 million women use oral contraceptive pills world-wide.<sup>1</sup> These hormonal pills have combination of estrogen and progesterone. Oral contraceptives have many side effects such as nausea, vomiting, headache, mood changes, abdominal pain, increased risk of cardiovascular side effects and venous thrombosis. Ocular side effects of OCPs are blurring of vision and rarely retinal vascular occlusions. Many women on oral contraceptive have ocular complaints such as dry eye syndrome.<sup>2</sup> Many study on dry eye after menopause have been done but few studies were done on effect of oral contraceptive in reproductive age group. Dry eye syndrome (DES or keratoconjunctivitis sicca) is a common multifactorial disease of the tears and the ocular surface. Dry eye occurs when there is deficiency in aqueous tear production or excessive tear evaporation. Tear film along with ocular surface constitute lacrimal functional unit which is maintained through regulation by neuronal and hormonal mechanisms. Disruption of this functional unit by various causes can lead to dry eye syndrome. It is one of the leading causes of patient visits to ophthalmologists and optometrists in the United States and many parts of the world.<sup>3</sup> Dry eye syndrome (DES) is traditionally considered the disease of old age, female gender and postmenopause. Sex steroids hormones (Androgens, Progestin and Estrogens) have been identified in tear film and their levels correlated with serum level. Influence of not only estrogen but also of androgen and other sex hormones in the pathophysiology of DES has been correlated.<sup>4,5</sup> Many studies had suggested that androgens play a significant role on the structural characteristics, functional, and pathologic features of the lacrimal gland. There have been some suggestions that oral contraceptives (OC) might lead to qualitative and quantitative changes in tear film.<sup>3</sup> Various animal studies how that androgen receptors are present on various ocular tissues. These hormones regulate the secretory functions of lacrimal and meibomian glands.<sup>6</sup> Several studies suggested that sex hormones had role in structural functional characteristics of ocular

tissues and had aetiological role in pathogenesis of dry eye syndrome.<sup>7</sup> Tear physiology is affected by hormones from the hypothalamic pituitary gonadal axis, mainly as a result of the influence of sex steroids (androgens, estrogens, and progestins) as well as pituitary hormones. Somewhat dependent on species, the effect of androgen administration is to increase the volume of tears produced by the lacrimal gland and to increase tear protein levels. Estrogen has been shown to diminish tear output whereas progestins have been found to both increase and decrease Schirmer test values and tear film break-up time (BUT) in patients with dry eye.<sup>8</sup> Androgen, estrogen and progesterone receptors mRNAs were reported to be present in the epithelial cells of the lacrimal gland, meibomian gland, lid, palpebral and bulbar conjunctivae, cornea, uveal body, lens, and retina of humans.<sup>9</sup> There are few studies those done in reproductive age group of women regarding effect of OCPs on dry eye. Oral contraceptives may be an important cause of androgen deficiency in child bearing age group. It was also suggested that oral contraceptive might decrease mucus production, increase foreign body sensation, reduce contact lens tolerance and increases the risk of dry eye in women using oral contraceptive.<sup>7</sup>

In developing country like India, there is increasing trend of using OCPs by reproductive age group women as method of contraception, so they might be at the risk of dry eye syndrome. In this study we tried to investigate the correlation of OCP and androgen profile with dry eye in women taking oral contraceptives in child bearing age group. While the influence of androgens may account for most of the sex-related differences found in the lacrimal tissue, the effects of estrogen are still unclear and the evidence regarding its role is often conflicting.<sup>5</sup> Estrogen is known to cause a decrease in lipid production and size of sebaceous glands in general.<sup>3</sup> Thus, one could speculate that dry eye symptoms would be more severe during states of increased estrogen, such as in pregnancy or hormonal contraceptive use. Yet, despite the widely held clinical perception that the use of hormonal contraceptives may be associated with dry eye symptoms, there are surprisingly few studies examining this relationship.<sup>10-12</sup> Sex hormones act on their receptors present in the cornea, lacrimal gland, palpebral and bulbar conjunctiva meibomian gland.<sup>13</sup> As a result, fluctuation of serum hormone levels can promote a change in tear production, evaporation, drainage and homeostasis of the ocular surface.<sup>14</sup>

## II. Methods

This study was conducted at Department of Ophthalmology & Department of Obstetrics and Gynecology, Govt. medical college, Kota from February 2020 to January 2021 and recruited 100 females between 20 to 45 years of age. This study was prospective case control study. This study involves 100 healthy women of child bearing age group, were visiting the family planning clinic of Gynecology OPD. The 100 participants were equally divided into two groups. The case group consists of 50 females who were currently on oral contraceptives. The control group consists of 50 females who were not using any hormonal contraceptive. Inclusion criteria comprised of women between the ages of 20 to 45 years using oral contraceptive pills for at least since the last eight months, whereas the exclusion criteria included pregnant patients, menopausal women and those who previously underwent any surgery as well as those women having any presence of systemic disease or using systemic medication. Females with ocular surgery, contact lens use, chronic topical medication, laser treatment, chemical injury, blepharitis and any other obvious ocular disorder were also excluded. They were divided into two groups of fifty each. Group A included females using oral contraceptive pills for the last eight months, whereas, group B included control group of females not using any contraceptive pills. The patients of both groups were demographically matched. The study dynamics was explained to all patients and informed consent was obtained. Study approval was obtained from ethical review committee. A thorough history including personal information, gynecological history, medicine use and duration of hormonal contraceptive was taken from each patient along with presence of or complain of any ocular problem. Comprehensive ocular examination was performed in the OPD to rule out the presence of ocular surface and anterior segment abnormality. The tear film status was assessed in each patient on the basis of Tear film breakup time (TBUT) on slit lamp examination and Schirmer strip test 2 (without anesthesia). Schirmer's strip test 2 (without anesthesia) was performed using Whatmann filter paper 41 which was gently placed at the intersection of middle and outer two thirds of the lower lid taking care not to tap cornea or the eye lashes. Patients were advised to look up and blink normally or close the eyes as per their convenience. The paper was removed after five minutes and reading was documented from bent portion of the paper in millimeters. Readings less than 10 mm after 5 min was considered as abnormal. Tear film breakup time (TBUT) was measured using fluorescein dye drop into the cul-de-sac and tear film was observed on slit lamp with cobalt blue light. Patients were asked not to blink and the appearance of the first dry spot over the cornea was observed indicating a break in the continuity of the tearfilm. The time between the first complete blink and the appearance of the first dryspot was measured.

**Statistical analysis:** The data was analyzed with SPSS software. The effect of oral contraceptives on tear secretion and tear film stability in control and case group were determined by using student unpaired t test. P value <0.05 were taken as significant.

### III. Results:

*Table1: Mean serum levels of DHEA with standard deviation and p value between both groups.*

	Group	N	Mean(ng/dl)	Std.deviation	p-value
Serum DHEA levels	Control	50	9.46	0.60	0.0006
	Test	50	9.08	0.46	

Table 1 demonstrate mean serum levels of DHEA in both groups. The mean serum DHEA levels were significantly reduced in test group as compared with control group and difference was statistically significant.

Table2: Schirmer test.

	Group for Schirmer's test	N	Mean(mm/5min)	Std.deviation	P alue
Schirmer's Test	Control	50	30	6	0.00
	Test	50	14	3	

Table 2 demonstrate the tear secretion (Schirmer's Test values) in both groups. The mean of Schirmer's test was 30mm/5minutes in control group while in test group it was 14mm/5minutes. Tear secretion was significantly reduced in test group as compared with control group and difference was statistically significant (p= 0.00). These findings suggest that tear secretion was significantly reduced in women who were on oral contraceptives.

Table3: TBUT test

	Group for TBUT	N	Mean(sec)	Std.deviation	pvalue
TBUT	Control	50	14.7	1.4	0.06
	Test	50	14.2	1.3	

Table 3 demonstrate mean TBUT test in both groups. The mean of TBUT test was 14.7 seconds in control group while in test group it was 14.2seconds. The TBUT values were reduced in test group but the difference was not significantly as compared with control group (p=0.06). In present study we found that serum androgen levels were significantly reduced in women who were on oral contraceptives, similarly the tear secretion was also reduced in these women. We got linear correlation of Schirmer's test and TBUT-test with androgens profile (Serum DHEA level). As serum androgen levels decreased, Schirmer's test and TBUT-test results reduced.

### IV. Discussion:

Production of tears in the eyes act as a natural lubrication, nourishment provider and protection against the environmental dust particles, irritants and infections along with the maintenance of a smooth ocular surface. Any imbalance in the tear film status, either due to composition changes, production abnormality or increased evaporation may lead to dry eyes.<sup>15</sup> Endocrine system has a significant effect on the lacrimal gland, as proved by the presence of receptors for androgens, estrogen and progesterone in the ocular tissues.<sup>16,17</sup> Contraceptive pills most commonly work by inhibiting ovulation.<sup>18</sup> The results of this study revealed that there was significant difference in tear secretion (P<0.05) but not in tear stability between women on oral contraceptives and women not using hormonal contraceptives. The results were consistent with the observation various studies who carried out a similar study on the correlation in androgen profile in pre-menopausal women with dry eye syndrome.<sup>18-21</sup> They reported that the oral contraceptives in pre-menopausal women may contribute to dry eye syndrome. They also inferred that oral contraceptives may be an important cause of androgen deficiency in this age group.

Our results were similar to the observations made by previous studies which reported that oral contraceptive pills in the reproductive age group lead to dry eye syndrome owing to the androgen deficiency caused by the use of oral contraceptive pills.<sup>19,20,22</sup> The presence of estrogen and progesterone receptors in the meibomian glands of human and various animal species suggests that this tissue is predisposed to the influence of female sex hormones.<sup>23</sup> The influence of estrogen on the meibomian gland appears to antagonise the actions of androgen, with resultant effects on suppression of lipid synthesis and promotion of meibomian gland dysfunction and thus evaporative dry eye.<sup>24</sup> Some studies support observations that dry eye may be associated with estrogen supplementation. In one report, asymptomatic post - menopausal women developed dry eye symptoms after three months of estrogen / progesterone replacement therapy, while symptomatic women were not relieved of dry eye by hormone replacement therapy.<sup>25</sup> Hormonal influences on tear physiology maybe manifested with the use of oral contraceptives, or during menopause when significant changes from the normal hormonal state occur. There are some reports of dry eye symptomatology and intolerance to contact lens wear by women using oral contraceptives.<sup>26</sup> Oral contraceptives containing estrogen might decrease tear volume and reduce BUT. It was also suspected that estrogen oral contraceptives might attenuate mucous production, increase foreign body sensation, decrease visual acuity and increase the risk of dry eyes in women using the

drugs.<sup>8</sup> A study by Sullivan had a similar observation that androgen insufficiency could be an imperative etiological aspect in the pathogenesis of evaporative dry eye in reproductive age women. Despite such findings, the effects of oral contraceptives in pathogenesis of dry eye remain controversial.<sup>27</sup> A minority of studies has found no association between the androgen levels and tear film status in women.<sup>28,29,30</sup> This was contradictory to this study since this study did observe a difference in the tear film status of the women of both groups i.e. those using oral contraceptives had a reduced TBUT and Schirmer strip test result as compared to non oral contraceptive pill users.

## V. Conclusion:-

This study concluded that using oral contraceptive pills has an adverse effect on the tear film status as compared to the non users. Present study suggest that androgen profile decrease in women taking oral contraceptives. Use of oral contraceptives may be an important etiological factor in pathogenesis of dry eye disease reproductive age group women.

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