Original Research Article

Evaluation of Dry Eye in Female Androgenic Alopecia Patients

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Abstract

Materials and methods: Twenty five left eyes of 25 female androgenetic alopecia patients (Group 1) and 25 left eyes of 25 age matched healthy female volunteers (Group 2) were enrolled in the study. The presence of dry eye was evaluated with the invasive tear film break-up time (T-BUT) & Schirmer 1 test. **Results:** The mean ages of Group 1 and Group 2 were 49.3 ± 7.6 (range, 39-59) and 50.8± 6.4(range, 39-60) years, respectively (P = 0.4). Mean T-BUT was statistically significantly lower in Group 1 (P = 0.01). Mean Schirmer 1 score was lower , but the differences were not statistically significant (P = 0.2). **Conclusion:** Female androgenic alopecia and Meibomian gland dysfunction & dry eye have common pathogenesis in the form of alterations in sex hormones. Significant differences were detected in the results of dry eye tests between subjects with female androgenic alopecia and healthy control. Hence female androgenic alopecia patients should be examined for dry eye and should be treated to prevent serious consequences.

Keywords: Androgenic alopecia; Dry eye; Schirmer test; T BUT

Introduction

Androgenetic alopecia is a non-scarring version of diffuse alopecia which can affect genetically predisposed men and women [1]. When androgenetic alopecia occurs in women, it is called 'female pattern hair loss' which is the most common cause of hair loss in women [2]. The frequency of female androgenetic alopecia is known to increase with aging and menopause [3]. The diagnosis is usually made by clinical and dermoscopic features, which are characterized by the retainment of the frontal hairline together with hair follicle miniaturization on the central hair line [4]. Hair follicle miniaturization results in progressive reduction in hair's diameter, length and pigmentation which means the transformation of terminal hair into vellus hair in affected locations. A main reason for hair thinning is the testosterone metabolite dihydrotestosterone's effect on androgen-sensitive hair follicles [5,6].

Dry eye is a very common disease that is more prevalent in females, especially during menopause and postmenopause [7]. Estrogens and androgens play a role in the production and regulation of the layers of the tear film (ocular surface homeostasis) [8], and changes to these in the postmenopausal period can result in dry eye [9, 10].

The purpose of this study is to determine whether female androgenetic alopecia patients are more likely to suffer from dry eye in comparison to normal healthy individuals. To our knowledge, not many studies to date has evaluated the relationship between dry eye and female androgenetic alopecia.

Materials and Methods

25 left eyes of 25 female androgenetic alopecia patients (Group 1) and 25 left eyes of 25 age matched healthy female volunteers (Group 2) were enrolled in the study. All female androgenetic alopecia patients included in the study were diagnosed by a specialized dermatologist receive any prior treatment. Since there is no specific laboratory tests for the severity of the disease was categorized according to diagnosis of female androgenetic alopecia, the patients were diagnosed by clinical and dermoscopic features showing features of hair follicle miniaturization. The Ludwig's scale, including three degrees, from a mild thinning, to a complete loss of hair in the central scalp[11]. Among 25 female androgenic alopecia patients, 9 were considered mild, 13 were moderate and 3 were serious in terms of severity of the disease.Patients with other dermatologic, ocular and systemic diseases or using systemic medications which can promote dry eye such as isotretinoin, antidepressants or diuretics, etc., patients who already were using artificial tears and patients using contact lens were excluded from the study. In Group 1 and Group 2, women in postmenopausal period and non-menopausal women were also recorded.All subjects included in the study underwent a detailed ophthalmological examination. For detecting dry eye presence, invasive tear film break up time (T-BUT) with fluorescein instillation and Schirmer 1 test were performed, respectively.Each subject provided written informed consent. The institutional review board approved the study. The Statistical Package for the Social Sciences version 11.5.0 was used for statistical analysis. Data are presented as mean ± SD, with ranges provided, where appropriate. For each continuous variable included in the study, normality was checked by the Shapiro-Wilk test. To compare continuous variables the Student's t test or Mann-Whitney U test was used. P values of less than 0.05 were considered statistically significant.As minimum sample size was not conducted prior to subject recruitment, a post hoc power test was conducted using alpha = 0.05, sample size (n1:20, n2:20) and effect size = 1.059, to ensure sufficient power for statistical validity of data results and the software was GPower3. Post hoc power tests were conducted for each measurement. Power > 0.80 was considered sufficient for statistical validity.

Results

The mean ages of Group 1 and Group 2 were 49.3 ± 7.6 (range, 39-59) and 50.8± 6.4(range, 39-60) years, respectively (P = 0.4)(Table 1).Schirmer 1 measurements of Group 1 and Group 2 were 16.2±7.4 (range,6-30) mm, and 18.3 ±6.7 (range,6-30) mm, respectively (P =0.2) fig 1. T-BUT measurements of Group 1 and Group 2 were 9.9±

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5.4(range,5-19), and 14.1±6.1 (range, 6-23) seconds, respectively (P =0.01).

Figure 1: Schirmer test

Among dry eye tests mean T-BUT was significantly lower in Group 1 (P =0.01), and mean Schirmer 1 score was lower in Group 1, but the difference was not statistically significant (P =0.2).

Table 1: The demographics, dry eye test results of the groups

Parameters	Group 1	Group 2	P value
Age (years)	49.3 ± 7.6	50.8 ± 6.4	0.4
Schirmer-1	16.2 ± 7.4	18.3 ± 6.7	0.2
T-BUT (sec)	9.9 ± 5.4	14.1 ± 6.1	0.01

Among Group 1, there were 12 women in post menopause. Schirmer 1 measurements of post menopausal and non-menopausal women 15.2±5.6(range, 5-20) mm, and 16.3 ± 5.7 (range, 5-30) mm, respectively (P = 0.7)(Table 2). T-BUT measurements of postmenopausal and non-menopausal women were 9.6±4.9 (range,5-15), and 10±6.6(range, 5-19) seconds, respectively (P = 0.86). Among dry eye tests there was no statistically significant difference between postmenopausal androgenetic alopecia patients and non-menopausal androgenetic alopecia patients.

Table 2: The Dry eye tests of the post menopausal and non menopausal women in group 1

Parameters	Post-menopausal (Mean, SD, Range)	Non menopausal (Mean, SD, Range)	P value
Schirmer-1	15.2 ± 5.6	16.3 ± 5.7	0.7
T-BUT (sec)	9.6 ± 4.9	10.0 ± 6.6	0.8

In the post hoc analysis, the power of the statistics for T-BUT measurements was > 0.9; however the power of the statistics for Schirmer I measurements was 80.6%.

Among Group 2, there were 13 women with postmenopause. Schirmer 1 measurements of post menopausal and non-menopausal women in Group 2 were 14.7 ± 7.1 (range, 5-25) mm, and 20.6 ± 4.1 (range,10-30) mm, respectively (P = 0.02) (Table 3) . T-BUT measurements of postmenopausal and non-menopausal women were 12.7 ± 6.4 (range, 4-18), and 15.0 ± 4.9(range, 5-20) seconds, respectively (P = 0.34). Among dry eye tests there was statistically significant difference between postmenopausal healthy volunteers and non-menopausal healthy volunteers in terms of dry eye tests such as Schirmer 1(P=0.025)

In the post hoc analysis, the power of the statistics for Schirmer 1, T-BUT measurements was >0.80.

Table 3: The Dry eye tests of the post menopausal and non menopausal women in group 2

Parameters	Post-menopausal (Mean, SD, Range)	Non menopausal (Mean, SD, Range)	P value
Schirmer-1	14.7 ± 7.1	20.6 ± 4.1	0.02
T-BUT (sec)	12.7 ± 6.4	15.0 ± 4.9	0.3

Among Group 1, 10 patients were considered 'mild', 12 were considered 'moderate' and 3 were considered 'serious' according to Ludwig scale, in terms of severity of the disease. The moderate and severe cases were combined for statistical purposes and compared with mild cases.

Schirmer 1 measurements of mild and moderate and severe cases were 15.5 ± 5.9 (range,5-30) mm, and 14.3± 7.3 (range,5-20) mm, respectively (P=0.58). T-BUT measurements of mild and moderate and severe cases were 10 ± 4.8 (range, 4-18), and 9.7 ± 3.9(range, 4-14) seconds, respectively (P=_0.46).Among dry eye tests, statistically there was no significant difference between mild and moderate and severe androgenetic alopecia patients in Group 1.

In the post hoc analysis, the power of the statistics for T-BUT measurements was > >0.80; however the power of the statistics for Schirmer 1 measurements was 69.9%.

Discussion

Female androgenetic alopecia is a common cause of non-scarring alopecia in women [12]. Alterations in sex hormones play an important role in the pathogenesis of androgenetic alopecia. In androgenetic alopecia patients 5-alpha reductase enzyme is upregulated by both genetic and environmental factors which are not known for certain. The 5-alpha reductase converts testosterone to dihydrotestosterone, and dihydrotestosterone binds to the androgen receptors and this results in the transformation of healthy terminal follicles into vellus-like weak hairs in areas which are dependent on androgens such as central and parietal regions of the scalp [3]. For this reason, frontal hairline retainment is an important factor for differential diagnosis.

Another sex hormone, estrogen is also thought to play a role in hair growth. The increase in the prevalence of female androgenetic alopecia during menopause [13] and hair loss in women receiving tamoxifen for breast cancer [14] support this assumption. Some research has been carried out on estrogen's role in female androgenetic alopecia. Recently, sequence variations in the estrogen receptor 2 gene have been published suggesting linkages with female androgenetic alopecia [15].The ocular structures which are related to dry eye disease, ocular surface-cornea, conjunctiva, tear film and also lacrimal and Meibomian glands are affected by sex hormones significantly. Sex hormones-androgen and estrogen-show their impact by gene expression and alterations in gene expression are considered to lead dry eye disease [16].On ocular surface including the cornea, conjunctiva and the tear film, sex hormones are thought to have an important impact. In patients with polycystic ovary syndrome, which is a disease related with hyperan drogenism, it has been shown that abnormal mucous secretion and abnormal mucous filaments exist due to conjunctival goblet cell hyperplasia [17]. Further, it has been emphasized that patients with hyperandrogenism treated with antiandrogens showed signifi cantly longer T-BUTS. Also in a study reported by Mantelli et al. [18], it was found that in patients with complete androgen insensitivity and dry eye, there was a decrease in mucin expression in tear film related to the dysfunction in goblet cells dependent on androgens.Alteration in sex hormones is the main cause of androgenetic alopecia however, only one third of women who are diagnosed as androgenetic alopecia show increased androgen levels

[35]. This could be related to the androgen receptors' effect in peripheral tissues. It is already known that sex hormonal changes can trigger dry eye; however, changes in receptor receptivity can have a significant effect altering the ocular surface home ostasis [9, 10]. The abnormality in androgen receptors in both hair follicles and Meibomian glands could be a cause of the high prevalence of dry eye and Meibomian gland dysfunction in female androgenetic alopecia patients.In studies investigating androgenetic alopecia histopathologically, periocular inflammation around the hair follicle [19] and increased prostaglandin D2 [20] levels were found in effected scalp areas. In a histopathology study of androgenetic alopecia, peri ocular inflammation around the hair follicle is said to be related to chronic mild inflammation. As dry eye pathogenesis also includes inflammation, the coincidence of androgenetic alopecia and dry eye could both be based on chronic inflammation[21].

As shown in many studies, postmenopausal women tend to have higher incidence of dry eye [22]. However, the precise role of sex hormones in postmenopausal women and the relation to dry eye syndrome remains unclear. In postmenopause period, ovarian production of estrogen and androgen are reduced [10]. The decrease in ovarian androgen production and in adrenal androgens due to age related changes might be the factors contributing to dry eye disease [23].In the present study, we compared 25 women with and 25 without androgenetic alopecia, and assessed whether or not they had dry eye. We found a strong correlation between female androgenetic alopecia and dry eye. Based on our study, we can recommend that patients with female androgenetic alopecia should be examined and monitored for dry eye to maintain ocular surface homeostasis and whenever a problem is detected treatment should be started to prevent serious consequences. In our study, we evaluated the correlation between the severity of androgenetic alopecia patients and the results of dry eye tests; however, we found no statistically significant differences related with the severity of the disease.Herein, also the postmenopause's effect was evaluated. Among healthy women significant differences in dry eye test results were evident between post menopausal women. However, there were no significant differences in dry eye between female androgenetic alopecia patients whether or not they were postmenopausal. All female androgenetic alopecia patients had worse dry eye test results. These results suggest that clinicians should test female androgenetic patients for dry eye regardless of whether or not they are postmenopausal.The major limitation of our study was the small sample size. Nevertheless, post hoc analysis was conducted to determine the power of the statistics. Most of the statistics were in acceptable power. Despite the limitations, to our knowledge, only few studies to date has evaluated the relationship between dry eye and female androgenetic alopecia; therefore, we believe that our study will give a lead to further research in the topic.

Conclusion

Female androgenetic alopecia patients had significantly different dry eye test results compared with healthy women. All androgenetic alopecia patients regardless of their age ,results were similar to those of women in the postmenopause. Thus the results support the assumption of relationship between dry eye and female androgenetic alopecia. However, prospective studies with larger sample sizes are needed for evaluation of relationship between dry eye & female androgenetic alopecia.

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