

Effects of Oral Retinoids on Ocular Surface, Assessment through Ocular Surface Disease Index (OSDI) Questionnaire

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ABSTRACT

Objective: Oral retinoids commonly prescribed for acne vulgaris have many side effects. The objective of this study was to determine effect of oral retinoids on ocular surface.

Methodology: This quasi-experimental study, conducted at department of ophthalmology and dermatology HBS Medical & Dental College from August 2023 to July 2024, a total of 109 acne patients who were prescribed oral retinoids were included. Tear film break up time (TBUT) and ocular surface disease index (OSDI) scores were calculated at baseline and three months after therapy to determine effect of oral retinoids on ocular surface and presence of dry eyes. Data were analyzed using SPSS 22.

Results: Mean age of patients was 28.40 ± 9.81 years. There were 23 (21.10%) males and 86 (78.90%) females. Mean baseline and three months follow up TBUT were 24.13 ± 6.31 and 10.33 ± 6.04 seconds, respectively ($p < 0.001$). Mean baseline and three months follow up OSDI scores were 3.03 ± 2.13 and 22.80 ± 10.32 , respectively ($p < 0.001$). Frequency of dry eyes in acne patients treated with oral retinoids after three months of therapy was 82 (75.23%). The most common ocular complaint of the patients was gritty sensation in the eyes 33 (30.28%) followed by itching in the eyes 22 (20.18%) and burning sensation in the eyes 17 (15.61%).

Conclusion: Dry eyes occurred in 75.23% users of oral retinoids showing a major effect of these agents on ocular surface.

Key words: Acne vulgaris, Dry eye, Retinoids.

Authors' Contribution:

^{1,2}Conception; Literature research; manuscript design and drafting; ^{2,3}Critical analysis and manuscript review; ⁴Data analysis; Manuscript Editing.

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Article info:

Received: July 08, 2024
Accepted February 20, 2025

Cite this article. Rana AM, Ahmed M, Hameed MA. Effects of Oral Retinoids on Ocular Surface, Assessment through OSDI Questionnaire. J Islamabad Med Dental Coll. 2025; 14(1): 18-23.

DOI: <https://doi.org/10.35787/jimdc.v14i1.1243>

Funding Source: Nil

Conflict of interest: Nil

Introduction

Acne vulgaris is a prevalent issue among teenagers, pregnant women and anybody experiencing hormonal fluctuations for whatever cause affecting 9.4% of the global population making it the 8th most prevalent disease across the globe.¹ The apparent appearance of acne, together with its symptoms and subsequent effects, all add to the psychological impact of the illness. Additionally, the costs

associated with its management further add to the overall burden of the condition.²

There are several medications that are used for the treatment of acne vulgaris including topical & oral antibiotics, oral contraceptives, spironolactone, benzoyl peroxide, topical retinoids and oral retinoids.³ Amongst these, retinoids are most commonly used and they treat acne by exerting their anti-inflammatory and immune regulation

ability and inhibiting the activity of the sebaceous glands.⁴ Retinoids at one end is highly beneficial for managing acne but has various side effects often limiting its prescription by physicians and use by the patients.⁵ Eyes have sebaceous glands called the “Meibomian glands” that help in stabilizing and protecting the ocular surface by contributing to form the tear film.⁶ Since the retinoids have direct effects on the activity of the sebaceous glands, there is an increased risk of developing ocular complications with the use of these agents, in particular the instability of the ocular surface.⁷ These ocular side effects include blurred vision, nyctalopia, dry eye, light sensitivity, blephroconjunctivitis, contact lens intolerance, photophobia, foreign body sensation, keratoconjunctivitis sicca, corneal ulceration, corneal opacification and rarely papilloedema.⁷ Various methods and techniques have been reported in previous literature that help in determining the stability of tear film and the ocular surface including the “Schirmer’s test”, “tear film breakup time (TBUT)” and “ocular surface disease index (OSDI)”, to name a few.⁸ In Pakistan, although acne is widely treated by physicians and dermatologists, yet there is no practice of getting the regular ophthalmologist reviews during the course of treatment of acne by oral retinoids. This study thus focuses on determining the effect of oral retinoids on ocular surface based on OSDI questionnaire to document the burden of various adverse effects of oral retinoids on the ocular surface which may help educating the patients regarding possible ocular effects of retinoids and raise the awareness among acne treating physicians to emphasize on the importance of regular ocular check-ups by ophthalmologist during the course of treatment of acne by oral retinoids.

Methodology

This quasi-experimental study was conducted at “Departments of Ophthalmology and Dermatology”

HBS Medical & Dental College from August 2023 to July 2024 after taking approval from the ethical review board. For calculation of appropriate sample size for the study, WHO sample size calculator was used by using following formula:

For calculation, following parameters were used:

- Confidence interval = 95%
- Absolute precision = 7%
- Anticipated frequency of dry eye with oral retinoids = 83.4%⁹

Calculation gave the sample size of 109 patients who were selected for the study through “non-probability consecutive sampling” technique.

Inclusion criteria: Patients of age ≥ 18 years, both males and females, who were planned to put on oral retinoids therapy for acne vulgaris were included in the study.

Exclusion criteria: Patients who had recent ocular surgery, OSDI ≥ 13 , TBUT ≤ 10 seconds, pregnant females, lactating mothers, ongoing ocular surface infection, already being treated with ocular lubricants and already taking topical or oral retinoids were excluded from the study.

After inclusion in the study, baseline characteristics of the patients including history of smoking and nature of occupation were documented. To assess the effects on ocular surface and presence of dry eyes with oral retinoids use, following parameters were assessed in all the study participants at baseline and 3 months after the treatment.

1. **“Ocular Surface Disease Index (OSDI):** It is a twelve-question index (Figure 1) that has a score ranging from 0 to 100. OSDI score ≥ 13 was considered as having dry eyes.¹⁰
2. **“Tear film breakup time (TBUT):** A fluorescein strip was applied to the bulbar conjunctiva's lower region for this test. The patient was then told to sit for an eye examination under a slit lamp while blinking normally for a few seconds. The time between the appearance of the "first dark spot" and the last blink was recorded, and it was used for visualization and analysis. TBUT

of ≤ 10 seconds was considered as having dry eyes.¹¹

In addition, at three months follow up, patient complains related to their ocular health were also documented. In case of presence of dry eyes or any other complaint, appropriate treatment was provided to the effected patients.

“Data were analyzed using Statistical Package for Social Sciences (SPSS) 22.00. Quantitative data (age, TBUT and OSDI score) was represented using mean \pm standard deviation. Qualitative data (gender, history of smoking, nature of occupation, patient complains and presence of dry eyes) were represented by using percentage and frequency. To compare baseline and 3 months post-therapy TBUT and OSDI score, paired sample t-test was used. Frequency of dry eyes was stratified using age, gender, history of smoking and nature of occupation to deal with effect modifiers and post-stratification comparison was performed using chi-square test. A p-value of ≤ 0.05 was considered as statistically significant.

Ethical approval for the study was obtained from the Ethical & Research Committee of HBS Medical and Dental College, Islamabad (Appl#EC18.B/1, 8th Aug 23).

Results

A total of 109 patients were included in the study. Mean age of the study participants was 28.40 ± 9.81 years. There were 23 (21.10%) males and 86 (78.90%) females. Baseline characteristics of study participants are given below (Table. I)

Mean baseline TBUT of study participants was 24.13 ± 6.31 seconds while at three months follow up it was 10.33 ± 6.04 seconds. Mean OSDI score at baseline was 3.03 ± 2.13 while at three months follow up it was 22.80 ± 10.32 (Table. II)

Based on the three months post-therapy values of TBUT and OSDI score, frequency of dry eyes in acne patients treated with oral retinoids after three months of therapy was 82 (75.23%). Stratification

of frequency of dry eyes by age, gender, history of smoking and nature of occupation is given (Table.III)

The most common complaint of the patients who were using oral retinoids therapy for acne was gritty sensation in the eyes 33 (30.28%) followed by itching in the eyes 22 (20.18%) and burning sensation in the eyes 17 (15.61%) while 27 (24.77%) of the patients did not have any complain related to their eyes. (Figure. 1)

Mean age	28.40 \pm 9.81 years
< 45 years	88 (80.73%)
≥ 45 years	21 (19.27%)
Gender	
Male	23 (21.10%)
Female	86 (78.90%)
History of smoking	
Yes	17 (15.60%)
No	92 (84.40%)
Nature of occupation	
Indoor	65 (59.63%)
Outdoor	44 (40.37%)

Parameter	Baseline	3-months post-therapy	p-value
TBUT	24.13 \pm 6.31 seconds	10.33 \pm 6.04 seconds	< 0.001
OSDI	3.03 \pm 2.13	22.80 \pm 10.32	< 0.001

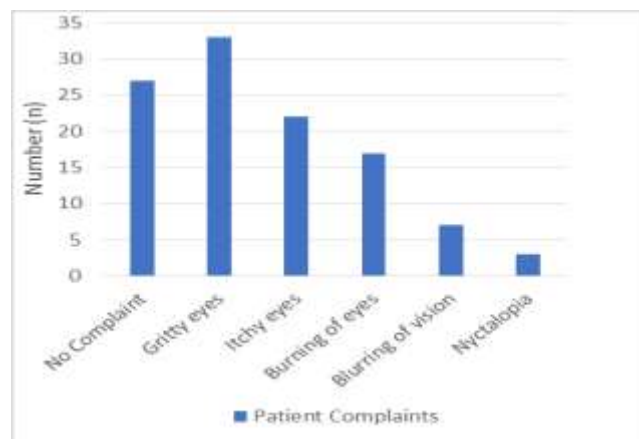


Figure 1: Ocular complaints of oral retinoid users

Table III: Dry eyes with oral retinoids use and it's stratification			
Dry eyes at 3-months post-therapy follow up			
Yes		82 (75.23%)	
No		27 (24.77%)	
Stratification by age			
Dry eyes	< 45 years (n = 88)	≥ 45 years (n = 21)	p-value
Yes	68 (77.27%)	14 (66.67%)	0.312
No	20 (22.73%)	7 (33.33%)	
Stratification by gender			
Dry eyes	Male (n = 23)	Female (n = 86)	p-value
Yes	21 (91.30%)	61 (70.93%)	0.044
No	2 (8.70%)	25 (29.07%)	
Stratification by history of smoking			
Dry eyes	Yes (n = 17)	No (n = 92)	p-value
Yes	15 (88.24%)	67 (72.83%)	0.176
No	2 (11.76%)	25 (27.17%)	
Stratification by nature of occupation			
Dry eyes	Indoor (n = 65)	Outdoor (n = 44)	p-value
Yes	40 (61.54%)	42 (95.45%)	< 0.001
No	25 (38.46%)	2 (4.55%)	

Discussion

Oral retinoid therapy is a well-recognized and most commonly prescribed medication for the treatment of "acne vulgaris" which is a highly common dermatological condition.^{12,13} Present study focused on determining the effect of oral retinoids on ocular surface in the local population. In present study, average age of the patients suffering from acne who were prescribed oral retinoids was 28 years. This corresponds to the fact "acne vulgaris" primarily affects younger population.^{14,15} Majority of the patients who had acne were females. This finding is in line with the finding of multiple studies showing clear female predominance in acne patients.^{16,17} In terms of changes in TBUT and OSDI scores, it was observed that patients who were treated with oral retinoids had significant reduction in TBUT from the baseline ($p < 0.001$) and significant increase in OSDI scores from the baseline ($p < 0.001$). This change in ocular surface

assessment indices is consistent with the findings observed by Amatya et al. and Caglar et al.^{18, 19} In a study conducted by Zakrzewska et al, it was found that although OSDI scores increased significantly from baseline similar to present study but the difference between baseline and post-retinoid therapy TBUT was not statistically significant which is not in line with the findings of present study.²⁰ Frequency of dry eyes after retinoid therapy was observed to be at 75.23% in this study. AlMasoudi et al. reported it at 83.4% which is higher but comparable.⁹ Contrarily, Zakrzewska et al. reported this at 41.66% which was much lower as compared to present study.²⁰ There was no statistically significant difference in terms of frequency of dry eyes after oral retinoid therapy between age groups or by history of smoking. However, among male patients, frequency of post-retinoid therapy dry eyes was significantly higher which is contrary to the fact that women are more likely to suffer from dry eye disease as compared to men.^{21, 22} Similarly, frequency of post-retinoid therapy dry eyes was significantly higher in patients who worked outdoors which is consistent with the fact that working outdoors is a major risk factor for developing dry eye disease.^{23,24}

Present study shows that oral retinoids have major effect on the ocular surface health. Based on this it is strongly recommended that all the patients with acne who are planned to be treated with oral retinoids should have ophthalmological assessment before, during and after the therapy to ensure maintenance of ocular surface health and avoid development of dry eyes.

The few limitations of this study are it was a single center study with limited sample size, follow up period was short and there was no control arm.

Conclusion

Frequency of dry eyes is high among users of oral retinoids showing a major effect of these agents on ocular surface

References

1. Alshammrie FF, Alshammari R, Alharbi RM, Khan FH, Alshammari SK. Epidemiology of acne vulgaris and its association with lifestyle among adolescents and young adults in Hail, Kingdom of Saudi Arabia: A community-based study. *Cureus*. 2020;12(7):e9277. <https://doi.org/10.7759/cureus.9277>
2. Layton AM, Thiboutot D, Tan J. Reviewing the global burden of acne: how could we improve care to reduce the burden? *Br J Dermatol*. 2021;184(2):219-225. <https://doi.org/10.1111/bjd.19477>.
3. Leung AK, Barankin B, Lam JM, Leong KF, Hon KL. Dermatology: how to manage acne vulgaris. *Drugs Context*. 2021;10:2021-8-6. <https://doi.org/10.7573/dic.2021-8-6>.
4. Bagatin E, Costa CS. The use of isotretinoin for acne - an update on optimal dosing, surveillance, and adverse effects. *Expert Rev Clin Pharmacol*. 2020;13(8):885-897. <https://doi.org/10.1080/17512433.2020.1796637> .
5. Bremner JD. Isotretinoin and neuropsychiatric side effects: Continued vigilance is needed. *J Affect Disord Rep*. 2021;6:100230. <https://doi.org/10.1016/j.jadr.2021.100230>.
6. Gupta PK, Periman LM, Lain E, Donnenfeld E, Hovanesian J, Kim T, et al. Meibomian gland dysfunction: a dermatological perspective on pathogenesis and treatment outlook. *Clin Ophthalmol*. 2021;15:4399-4404. <https://doi.org/10.2147/OPTH.S327407>. <https://doi.org/10.2147/OPTH.S327407>.
7. Lamberg O, Strome A, Jones F, Mleczek J, Jarocki A, Troost JP, et al. Ocular side effects of systemic isotretinoin - a systematic review and summary of case reports. *J Dermatolog Treat*. 2023;34(1):2213364. <https://doi.org/10.1080/09546634.2023.2213364>. <https://doi.org/10.1080/09546634.2023.2213364>.
8. Verjee MA, Brissette AR, Starr CE. Dry eye disease: early recognition with guidance on management and treatment for primary care family physicians. *Ophthalmol Ther*. 2020;9(4):877-888. <https://doi.org/10.1007/s40123-020-00308-z>. <https://doi.org/10.1007/s40123-020-00308-z>.
9. AlMasoudi RM, Bahaj RK, Kokandi AA. Patients' awareness of the ocular side effects of isotretinoin therapy: a study from Saudi Arabia. *Cureus*. 2022;14(4):e24628. <https://doi.org/10.7759/cureus.24628>.
10. Aberame AR, Bhandary SV, Rao LG, Gupta C. Assessment of prevalence of dry eye among medical students using ocular surface disease index questionnaire - Is COVID-19 to be really blamed? *Indian J Ophthalmol*. 2023;71(4):1450-1453. https://doi.org/10.4103/ijo.ijo_2824_22
11. Handayani AT, Valentina C, Suryaningrum IGAR, Megasafitri PD, Juliari IGAM, Pramita IAA, et al. Interobserver reliability of tear break-up time examination using "smart eye camera" in Indonesian remote area. *Clin Ophthalmol*. 2023;17:2097-2107. <https://doi.org/10.2147/OPTH.S412233>.
12. Scott-Emuakpor R, Vuthaluru K, Nagre A, Jawed I, Patel PA, Sidhu HK. Role of oral retinoids in treatment of acne vulgaris with a bioinformatics-based perspective of personalized medicine. *Cureus*. 2023;15(4):e38019. <https://doi.org/10.7759/cureus.38019>
13. Adelman MJ, Sivesind TE, Weber I, Bosma G, Hochheimer C, Karimkhani C, et al. Prescribing patterns of oral antibiotics and isotretinoin for acne in a Colorado hospital system: retrospective cohort study. *JMIR Dermatol*. 2023;6:e42883. <https://doi.org/10.2196/42883>.
14. Ip A, Muller I, Geraghty AWA, McNiven A, Little P, Santer M et al. Young people's perceptions of acne and acne treatments: secondary analysis of qualitative interview data. *Br J Dermatol*. 2020;183(2):349-356. <https://doi.org/10.1111/bjd.18684>.
15. Zhu Z, Zhong X, Luo Z, Liu M, Zhang H, Zheng H, et al. Regional, and national burdens of acne vulgaris in adolescents and young adults aged 10-24 years from 1990 to 2021: a trend analysis. *Br J Dermatol*. 2024 Sep 13:ljae352. <https://doi.org/10.2196/42883>.
16. Chang J, Nock MR, Cohen JM, Bunick CG. Acne accounts for an almost 2.5-fold higher proportion of dermatology visits among adult females compared to adult males in the United States: A study of the national ambulatory medical care survey from 2002-2016. *PLoS One*. 2023;18(9):e0290763. <https://doi.org/10.1371/journal.pone.0290763> .
17. Dabash D, Salahat H, Awawdeh S, Hamadani F, Khraim H, Koni AA, et al. Prevalence of acne and its impact on quality of life and practices regarding self-treatment among medical students. *Sci Rep*. 2024;14(1):4351. <https://doi.org/10.1038/s41598-024-55094-6>.
18. Abuallut II, Dibaji MQ, Assiri A, Mawkili W, Najmi AY, Ageeli SA, et al. Oral isotretinoin-associated ocular effects and risk factors: a cross-sectional study. *Clin Ophthalmol*. 2024;18:4041-4052. <https://doi.org/10.2147/OPTH.S491757>.
19. Caglar C, Senel E, Sabancilar E, Durmus M. Reduced ocular surface disease index (OSDI) scores in patients with isotretinoin treatment. *Int*

- Ophthalmol. 2017;37(1):197-202. <https://doi.org/10.1007/s10792-016-0263-y>.
20. Zakrzewska A, Wiącek MP, Słucznanowska-Głąbowska S, Safranow K, Machalińska A. The effect of oral isotretinoin therapy on meibomian gland characteristics in patients with acne vulgaris. *Ophthalmol Ther.* 2023;12(4):2187-2197. <https://doi.org/10.1007/s40123-023-00737-6>.
 21. Kim H, An Y, Hwang WJ. Gender differences in dry eye disease symptoms associated with psychological health indicators among adults using mobile mental health apps. *PLoS One.* 2023;18(1):e0278921. <https://doi.org/10.1371/journal.pone.0278921>.
 22. Borrelli M, Frings A, Geerling G, Finis D. Gender-specific differences in signs and symptoms of dry eye disease. *Curr Eye Res.* 2021;46(3):294-301. . <https://doi.org/10.1080/02713683.2020.1801758>.
 23. Echieh CI, Etim BA, Echieh CP, Oyeniya T, Ajewole J. A comparative assessment of dry eye disease among outdoor street sweepers and indoor office cleaners. *BMC Ophthalmol.* 2021;21(1):265. <https://doi.org/10.1186/s12886-021-02025-y>.
 24. Shah S, Jani H. Prevalence and associated factors of dry eye: Our experience in patients above 40 years of age at a Tertiary Care Center. *Oman J Ophthalmol.* 2015;8(3):151-156. <https://doi.org/10.4103/0974-620X.169910>.