

Effect of isotretinoin on tear film stability in acne vulgaris patients

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Abstract

The purpose of the study was to assess and compare tear film stability and lid margin diseases before and after using topical and oral isotretinoin in acne vulgaris patients.

A quasi-experimental study was conducted from August 2022 to June 2023 at the Department of Ophthalmology and Dermatology, Madina Teaching Hospital, Faisalabad. A total of 60 females with acne vulgaris with stable tear films ranging from 15 to 25 years that received topical or oral isotretinoin (IT) were included through non-probability convenient sampling. Preassessment of Tear break time (TBUT) and lid margin diseases was carried out. After 4 weeks of using topical or oral isotretinoin, a post treatment evaluation was performed. Data was analyzed by paired sample t-test and independent t-test using SPSS version 27.

Results of this study showed that TBUT decreased after topical and oral isotretinoin treatment ($P < 0.001$, $P < 0.001$) respectively. Mean TBUT after topical and oral isotretinoin was 8.1500 ± 1.16190

and $6.5167 \pm .98276$ respectively. Results also showed a significant difference between topical and oral isotretinoin ($P < 0.001$) as oral isotretinoin had more effect on TBUT and lid margin diseases than topical isotretinoin.

The study concluded that there was a significant decrease in TBUT after the usage of topical as well as oral isotretinoin. The study also concluded that oral isotretinoin had more effect in TBUT and lid margin disease in comparison with topical isotretinoin

Keywords

Dry eye, Lubrication, Acne vulgaris, Isotretinoin.

1. INTRODUCTION

Acne vulgaris is a common skin disease that frequently recurs as an inflammatory condition of the sebaceous glands, which predominantly induce follicular obstruction and excessive oil excretion (Saitta P, Keehan P *et al.*, 2011; Dreno B. *et al.*, 2017). Particularly affected areas include the

face, chest, and back. Acne vulgaris appearance includes comedones, nodules, pustules, and papules (Strauss JS *et al.*, 2006; El-Tonsy *et al.*, 2018). The various medical approaches for treating acne include topical, systemic medication, and therapies using light (Fox L *et al.*, 2016). Topical retinoids involve the application of medication that is applied directly to the skin such as retinoic acid, adapalene, tretinoin, and isotretinoin are administered either separately or in addition with the use of antibiotics (See JA *et al.*, 2018; Aslam I *et al.*, 2015). They are useful in treating mild to moderate acne vulgaris and can also be used to manage numerous skin diseases over time (Zaenglein AL *et al.*, 2016). For more severe cases, systemic treatments such as antimicrobial, retinoid, and hormone replacement therapy can be used separately or in addition to topical medications (Thiboutot *et al.*, 2018). In addition, the attempts of carotenoid therapy in which all those naturally occurring fat soluble vitamins containing Flora and Fauna respectively such as *Daucus Carota*, *Lycopersicum*, *Esculentum Magnifera Indica*, *Habitat Hippoglossus*, etc.

The tear film is a thin fluid layer approximately 3µm thick and 3µl in volume that covers the outer mucosal surfaces of the eye. The tear film, which protects the eye from the surrounding environment, covers the ocular surface and also serves to moisten the eye to ensure a well-ordered surface for vision and the well-being of the conjunctiva and cornea (Dartt DA *et al.*, 2013). It consists of three main components. Meibomian glands create the outer lipid layer, which serves to decrease tear evaporation. The lacrimal glands create the middle aqueous layer which lubricates, nourishes and washes away debris.

Conjunctival goblet cells form the inner mucin layer. Mucin improves tear film spreading over the corneal epithelium by regulating surface tension (Yokoi *et al.*, 2014).

Dry eye syndrome, also referred to as Dry eye disease (DED), is a complex state that affects the ocular surface. It causes discomfort, impaired vision, and disruption in the tear film, which can lead to harm to the surface of the eye. The condition is related to higher osmolality and mild inflammation of the eye surface (Perry HD *et al.*, 2008; Clayton JA *et al.*, 2018). The incidence of DED is greater in females, ranging from 1.33 to 1.74 times more frequent compared to men. Additionally, it is more prevalent in Asian populations compared to Caucasian populations, and the rates of occurrence increase as individuals age (Stapleton F. *et al.*, 2017; Hashemi *et al.*, 2014).

The eye is shielded and safeguarded by a fold of skin called the eyelid. Eyelids perform multiple functions such as moisturizing and cleansing the eye of tears and protecting of eyes (Mathers WD *et al.*, 1991). They also serve to distribute tear drainage, shield the surface of the eye, and contribute to its aesthetic appearance (Ducker L *et al.*, 2022). The eyelids possess glands that produce lubricating fluid for the eye's surface. There are three distinct types of glands within the eyelids. The sweat glands, also known as Moll glands, can be found opening into the follicles that produce hair or the outer edge of the eyelid. Similarly, the sebaceous glands, referred to as Zeiss glands, are placed within the root of follicles. These external glands, Molls and Zeiss, are

prone to infection and blockage of their ducts due to cell waste and mucous (Bowling B. *et al.*, 2016).

Isotretinoin, also known as 13-cis-retinoic acid, is a medication primarily used to treat severe skin conditions such as acne (Bron AJ *et al.*, 2017; GurleviKU *et al.*, 2022). However, it is important to note that isotretinoin can have side effects related to the eyes, specifically dry eye disease and instability in the tear film. These side effects occur due to various mechanisms, including decreased tear production, alterations in sensory and involuntary tear secretion, swelling of the glands, and direct toxicity through tears (Ruiz *et al.*, 2020). The primary action of isotretinoin is to reduce oil secretion, resulting in decreased oil production on the skin. This can lead to a condition called meibomian gland dystrophy, where the glands responsible for producing the oily component of tears become dysfunctional. The changes in the oily and mucin layers due to Meibomian gland dysfunction (MGD) can disrupt the normal functioning of the tear film, leading to an evaporative dry eye. This condition occurs when tears evaporate too quickly from the surface of the eye due to a compromised tear film (Bayhan SA *et al.*, 2016).

The study aimed to find out the effect of topical and oral isotretinoin on tear film stability as patients undergoing treatment with isotretinoin have potential complaints including dryness, red eyes, foreign body sensation, irritation, excessive tearing, and light sensitivity.

2. MATERIALS AND METHODS

A Quasi-Experimental study was conduc-

ted at the Ophthalmology and in Dermatology Madina Teaching Hospital, Faisalabad. The study duration was from August 2022 to June 2023. A sample size of 60 was calculated through the Rao soft formula. A total of 60 Females with acne vulgaris having stable tear films with ages ranging from 15 to 25 years received topical or oral isotretinoin. They were included through non-probability convenient sampling. Individuals with skin diseases like acne rosacea and dermatitis, acne vulgaris patients who are using Macrolide and Fusidic medication, unstable tear film, previous eyelid disease including stye, chalazion, keratoconjunctivitis sicca, Stevens-Johnson syndrome, screen user, pregnant ladies, contact lens user, history of refractive surgery including LASIK, PRK and patient using stress medication like Citalopram, dapoxetine were excluded. Data was collected through a self-designed proforma for dry eye and lid margin diseases. A written informed consent was taken from each patient before collecting the data. After confirming the status of acne vulgaris, subjects were distributed into two categories, each group included 30 subjects, one group received topical isotretinoin while the other group received oral isotretinoin once a day for one month. Pre-assessment included tear break-up time and evaluation of lid margin diseases. Eyelid diseases such as stye, chalazion, and blepharitis were evaluated with the direct illumination technique of a slit lamp. All patients were given follow-up for 4 weeks and advised to use topical isotretinoin at bedtime and oral isotretinoin once a day for 4 weeks. A post-treatment evaluation was taken after 4 weeks of using topical isotretinoin and oral isotretinoin.

Statistical analysis:

The Data was analyzed by paired sample t-test and independent t-test using SPSS version 27.

3. RESULTS AND DISCUSSION

The mean age of acne vulgaris subjects who received treatment was 20.3833±2.49128 as shown in Table 1.

Table 1. Age of Subjects

	N	Minimum	Maximum	Mean	Std. Deviation
Age	60	15.00	25.00	20.3833	2.49128

On application of the normality test, the Shapiro-Wilk test was >0.05. So paired sample T-test and independent sample T-test were utilized. 60 eyes of 30 subjects received topical isotretinoin at bedtime once in a day. The mean value before

TBUT was 11.5833±1.12433 sec and after was 8.1500±1.16190 sec. There is a significant decrease of 3.4333 sec in TBUT after the use of topical isotretinoin as a P value <0.05 (p<0.001). The results are described in Table 2 and Figure 1.

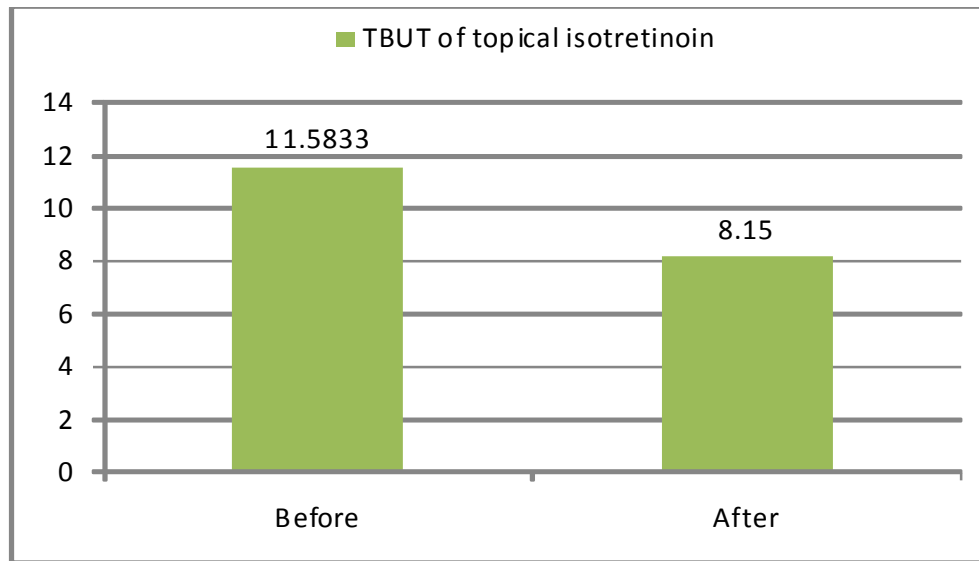


Fig- 1: Mean of TBUT before and after topical isotretinoin

Table 2. Mean of TBUT before and after topical isotretinoin

Paired Samples Test								
	Paired Differences					t	Df	Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
Before TBUT topical isotretinoin After TBUT topical isotretinoin	3.43	0.5634	0.07275	3.28777	3.57890	47.197	59	0.000

The remaining 30 subjects received oral isotretinoin once a day. The mean value of before TBUT was 11.6500±1.14721 sec which decreased by 5.1333 sec to 6.5167±.98276 sec. There is a difference of 5.1333 in a TBUT before and after

the use of oral isotretinoin as a P value <0.05 (p<0.001). The results show that a significant decrease in TBUT is seen after the use of oral isotretinoin. The Results are described in Table 3 and Figure 2.

Table 3. Mean of TBUT before and after oral isotretinoin

Paired Samples Test								
	Paired Differences					t	df	Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
Before and After TBUT oral isotretinoin	5.1333	0.85304	0.11013	4.91297	5.35370	46.613	59	0.000

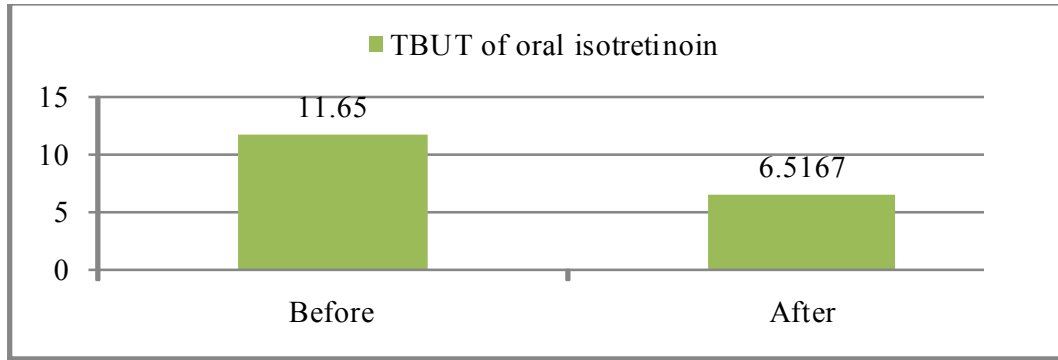


Fig-2: Mean of TBUT before and after oral isotretinoin

Mean TBUT after topical and oral isotretinoin was 8.1500 ± 1.16190 and $6.5167 \pm .98276$ respectively. There is a statistically significant difference in TBUT after topical and oral isotretinoin as $P < 0.05$ ($p < 0.001$) and oral isotretinoin had more effect on TBUT in comparison to topical and are explained in Table 4 and Figure 3.

Table 4. TBUT after topical and oral isotretinoin

Independent Samples Test									
	Levene's Test for Equality of Variances		t-test for Equality of Means						
	F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
								Lower	Upper
Equal variances assumed	1.35	0.24	8.31	118	<.001	1.63	0.196	1.24	2.02
Equal variances not assumed			8.31	114.84	<.001	1.63	0.196	1.24	2.02

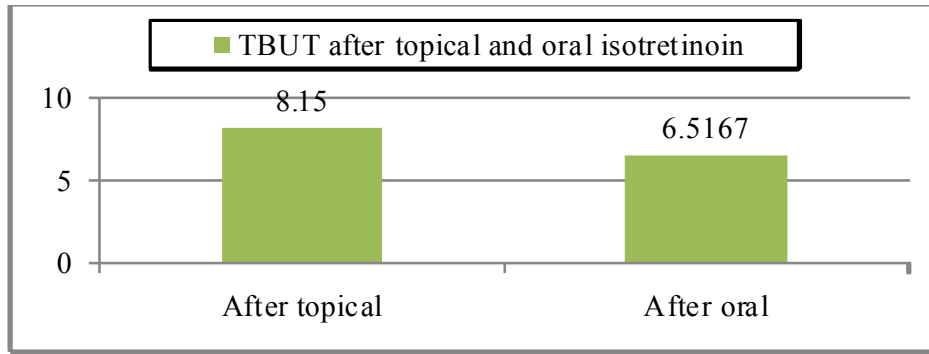


Fig- 3: TBUT after topical and oral isotretinoin

Among subjects given topical isotretinoin 78.3% (N=47) had no lid margin diseases and only 21.7% (N=13) had blepharitis. Among subjects given oral isotretinoin 40% (N=24) had no lid hav-

ing margin diseases, 25% (N=15) had blepharitis, 25% (N=15) had conjunctivitis and 10% (N=6) had blepharo conjunctivitis shown in Table 5 and Figure 4.

Table 5. Lid margin diseases after topical and oral isotretinoin

Lid margin diseases	Topical isotretinoin	Oral isotretinoin
	Percentage	Percentage
None	78.3	40.0
Blepharitis	21.7	25.0
Conjunctivitis	0	25.0
Blepharo conjunctivitis	0	10.0

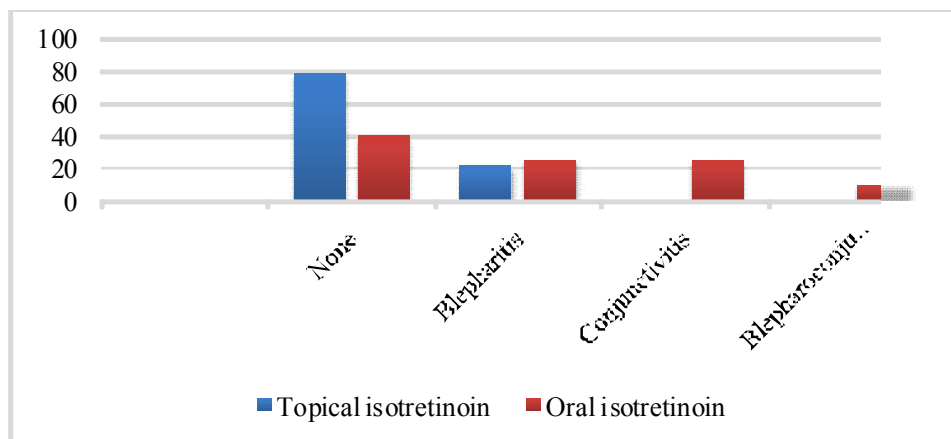


Fig-4: Lid margin diseases after topical and oral isotretinoin

Tear film provides lubrication, protection, and prevention against infectious beings. Treatment of acne vulgaris with topical and oral isotretinoin can impact tear film stability as well as lid margin diseases. Bayhan *et al* conducted 'Effects of topical acne treatment on the ocular surface in patients with acne vulgaris' in 2016. The study assessed the ocular adverse effects associated with the administration of a combination of topical retinoids and antibiotics in patients undergoing treatment of acne vulgaris. Results showed a significant decrease in TBUT from 11.93 sec to 6.65 sec with topical isotretinoin ($P < 0.001$). In comparison, the results of the current study also showed a significant decrease by 3.4333 sec in TBUT from 11.5833 sec to 8.1500 sec with topical isotretinoin given for 1 month ($P < 0.001$). In addition, the current study also showed that usage of oral isotretinoin considerably decreased TBUT from 11.6500 sec to 6.5167 sec ($P < 0.001$). Also, 25% of subjects using oral isotretinoin had blepharitis or conjunctivitis and 10% had blepharoconjunctivitis.

A study conducted by Duzgun *et al*, 'The effect of oral isotretinoin therapy on meibomian gland morphology and dry eye tests' in 2020. The study evaluated the impact of systemic isotretinoin on the structure of the meibomian gland and investigated its association with dry eye-related tests. Results of this study showed that meibography scores showed an optimistic association with the abnormalities of lid margin ($P < .001$) after using oral isotretinoin. The results of the current study also showed that 21.7% of subjects using topical isotretinoin given for 1 month had blepharitis.

4. CONCLUSION

The study concluded that there was a signifi-

ficant decrease in TBUT after the usage of topical as well as oral isotretinoin. The study also concluded oral isotretinoin had more effect in TBUT and lid margin disease in comparison to topical isotretinoin.

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