Original Article

Evaluation of Tear Function among Acne Vulgaris Patients Undergoing Treatment with Isotretinoin

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Abstract

Purpose: To evaluate the effect of Isotretinoin on tear secretion among patients with Acne Vulgaris.

Patients and Methods: In this prospective study patients who were candidate for Isotretinoin (Accutane) therapy for two months underwent complete eye examination. The best corrected visual acuity was measureed and slit lamp examination of anterior segment, evaluation of tear break-up-time and Schirmer's test were performed. The post surgical examination carried out two months post therapy consisted of complete eye examination and evaluation of dry eye level.

Results : Thirty nine patients entered the study. There were 5 patients complaining of eye strain before treatment, which rose to 19 patients after Isotretinoin therapy ($P < 0.001$). The tear break up time was 13 ± 1 seconds which decreased to 9 ± 1 seconds ($P < 0.001$) after therapy and the Schirmer's test mean reading was 22 ± 2 mm, which was reduced to 18 ± 5 mm ($P < 0.001$) after treatment. There were 4 patients with blepharitis before the treatment which rose to 19 patients after the end of Isotretinoin treatment ($P < 0.001$).

Conclusion: Isotretinoin usage (0.5 - 1 mg/kg for two months) impairs the tear secretion and causes dry eye and blepharitis among patients. Considering the young age of patients using this drug, some of them candidates for keratorefractive surgery, a history of Isotretinoin usage should be considered before commencing the surgery. We recommend postponing the refractive surgery among these patients until the signs of dry eye are subsided.

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Introduction

Isotretinoin is a synthetic derivative of vitamin A (B-cis- Retinoic Acid) which is mostly used to treat Acne Vulgaris in young patients [1]. This drug causes a reduction in oil secretion by skin sebaceous glands therefore reducing the severity of Acne Vulgaris. Pilosebaceous glands are the main affected part of the skin in patients with Acne Vulgaris. The mechanism of Acne formation is not well known but several theories have been suggested. One theory is the increase in oil secretion which is more than the capacity of exit ducts and causes the accumulation of oil in extracellular space around secretary cells [2]. Another theory points to skin bacterial flora as the cause of Acne Vulgaris. In this theory the lipase formation by propionibacterium causes the breakdown of the secreted oil by pilosebaceous glands, which causes the subsequent Acne formation [2]. Another theory is the irregularity among squamous cells in the entrance of oil canals which causes the closure of canals [2]. This causes the oil to become trapped inside the gland and form the Acne [2]. Some reasurchers think the pathogeneses of Acne is multi factorial and it is caused by all causes discussed above [3].

Nowadays Isotretinoin is the forefront of drugs used to treat Acne Vulgaris [1-3]. Isotretinoin can modify the Acne formation as a drug which changes the proliferation of squamous cells. This drug has antibacterial activity and increases the secretion of peroxides and inhibits the propionibacterium growth [3]. It also modifies the oil secretion from pilosebaceous glands [1]. Isotretinoin has some side effects on liver [4], heart and blood vessels [4] and also causes dry skin. Eyes are one of the most common affected organs. It causes dry eye and blepharoconjunctivitis [1]. Other eye problems caused by this drug are reduced vision, contact lens intolerance, unusual secretion of meibomian glands, corneal and lens opacity, choroidal neovascularization and pupil edema [2, 5-7]. One rare side effect is the change of corneal curvature which is reversible after drug termination [3]. The use of drug in children and pregnant women is prohibited. In this prospective study the effect of Isotretinoin on tear break up time as well as Schirmer's test among patients who used the drug to treat Acne Vulgaris was studied.

Patients and Methods

This study was performed as a before-after cross sectional study on patients with Acne Vulgaris coming to Novin Didegan Eye Clinic from 2009 to 2010, who were candidates for Isotretinoin treatment for at least a two months period. The study was approved by the Novin Didegan Eye Clinic ethics committee and all patients gave informed consent before entering the study.

All patients with a history of antihistamine, beta-blocker, systemic carbonic anhydrase and antihypertensive agents usage were excluded from the study. All patients underwent complete eye examination and history taking before the treatment started. The complete eye exam included Uncorrected Visual Acuity (UCVA) and Best Corrected Visual Acuity (BCVA) measurements using Snelen chart (Auto chart projector Nidek CP 670), as well as complete slit lamp examination, applanation tonometry and fundus examination with dilated pupil. Any sign of blepharitis was categorized based on table 1. The tear secretion was tested using Schirmer's 1 test which studies the liquid portion of tear.

To perform the test, Whatman paper (Whatman W&K Ballston Filter Paper No. 42) was placed for 5 minutes in the lateral inferior portion of both eyes while the patient was looking at a distant object and blinked normally. The reading was then performed and if less than 10 mm of the paper was wet it was determined as positive (sign of dry eye).

The Tear Break-Up Time (T) test was performed before Tetracaine eye drop. After soaking the eye with fluorescein the patient was asked to blink several times for fluorescein to spread and the corneal surface was illuminated with cobalt blue light and observed using a slit lamp. The time for the appearance of spots in green colored cornea was measured. The time between the last blink and the appearance of the black spots was recorded. If this time was less than 10 seconds the test was considered positive (dry eye). The intraocular pressure was then measured using indirect fundoscopy. Patients were then given 0.5 -1 mg/kg Isotretinoin based on the severity of their Acne Vulgaris for a 2 months period and the same eye examinations were repeated at the end of two months. The data were analyzed using SPSS program version 17.0 (SPSS Co, Chicago, Illinois.).

Results

This study was performed on 78 eyes form 39 patients treated with Isotretinoin. The average age of participants was 24 ± 0.5 years with 97.3 % of patients being female and 2/7 % being male. The average tear break up time was 13 ± 1 seconds before treatment which was reduced to 9 ± 1 seconds after the treatment.The difference was statistically significant ($P < 0.001$) based on Mann-Whitney Test (Table 2).

The average Schirmer's test results was 22 ± 2 mm before and 18 ± 5 mm after the treatment with the difference being statistically significant ($P < 0.001$) (Table 2), (Figure1).

Thirty five patients did not have blepharitis signs before the start of the study and 4 patients had mild signs of blepharitis. After the treatment 20 patients did not have any sign of blepharitis, 14 patients had weak signs, 3 had moderate and 2 had severe blepharitis (Table 2), (Figure 2). The difference was statistically significant ($P < 0.001$) based on Mann-Whitney test.

Before the start of the study 13 % of patients had dry eye symptoms like foreign body sensation, burning eyes and other symptoms which increased to 49 % after treatment ($P < 0.001$) (Figure 3).

Table 1: The method for classification of blepharitis among patients.

Patients' findings	Score	Classification
No sign	Zero	-
Inflammation + redness or telangiectasia of eye lid margin	+ 1	Mild
Above signs + secretion on the margin of eyelid	+ 2	Moderate
Above signs + follicular conjunctiva and cellular corneal margin	+ 3	Severe

Table 2: Test results and eye complications among patients before and after treatment.

Variables	Pre	Post	P
Mean TBUT ± SD, Sec	13 ± 1	9 ± 1	< 0.001*
Mean Schimer's Test ± SD, mm	22 ± 2	18 ± 5	< 0.001*
Blepharitis, N (%)			
0	35 (90)	20 (51)	< 0.001*
1	4 (10)	14 (36)	
2	0 (0)	3 (8)	
3	0 (0)	2 (5)	
Dryness, N (%)	5 (13)	19 (49)	0.001**

* Based on Mann-Whitney test.
** Based on Mac-Nemar test.

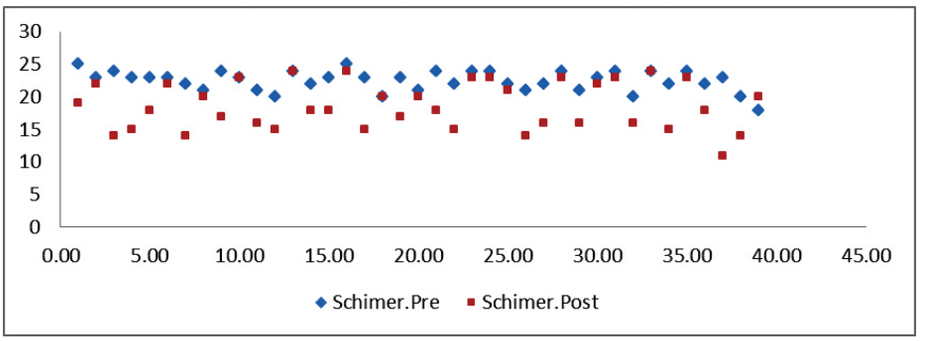

Figure 1: The treatment's effect on Schirmer's test.

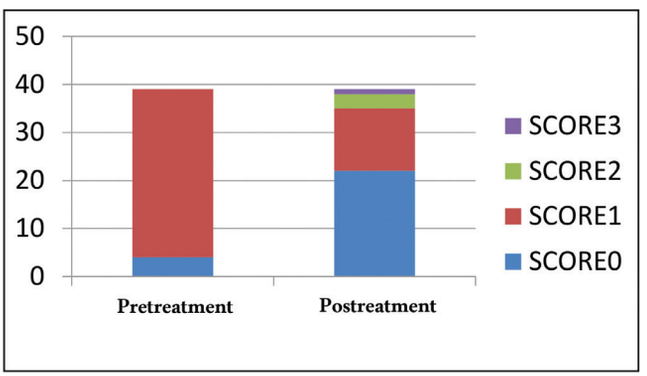

Figure 2: The treatment's effect on blepharitis among patients.

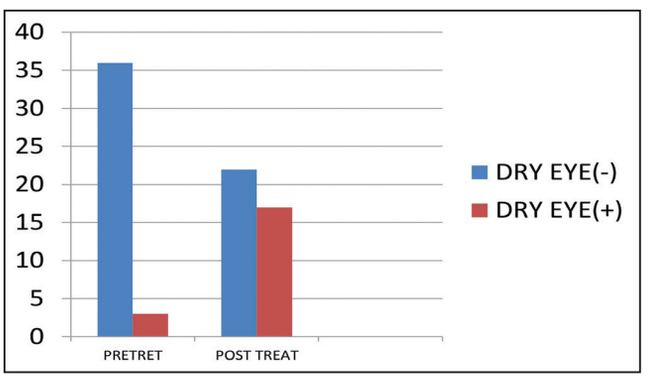

Figure 3: Dry eye before and after treatment.

Discussion

One of the most common side effects of Isotretinoin treatment is dry eye. The patients suffer from the symptoms of dry eye including foreign body sensation, feeling heavy eyelids, burning, itching, watering, dryness and a constant need for scrubbing their eyes and signs like redness of the eyes and blinking [6].

In our study the Schirmer's test and tear break up time tests changed significantly after a two months treatment with Isotretinoin, which is in line with other studies [1, 2]. The changes in tear break time test results may be due to changes in tear secretion by meibomian glands as reported by Kermer et al., including meibomian glands atrophy, reduced gland density and increased tear osmolarity [7]. In another study by Queiroga et al., [8] structural changes in cytology of conjunctiva was observed in patients treated with Isotretinoin.

The structural changes included a reduction of goblet cells and also reduction of cell nucleus size compared to cytoplasm which shows dysplastic changes of conjunctival cells.

Considering the changes in the liquid portion of tear demonstrated by Schirmer's test our findings were in contrast with other studies. Rismond et al. [9] have reported no change of lacrimal glands activity based on Schirmer's test among patients and they even reported increased liquid portion of the tear in some of their patients. They concluded that a reduction in meibomian glands activity after using Isotretinoin might cause a reactive over-secretion by lacrimal glands.

In a study by Chua et al. [1] increased eye secretion has been reported in patients treated using Isotretinoin. The exact mechanism of drug affecting the tear secretion by porcine and endocrine glands should be studied more before a solid conclusion could be reached on the mechanism of tear secretion changes among these patients. One aspect which might compromise the test results in studies is the use of dry eye medications.

One of Isotretinoin usage consequences is anterior or posterior blepharitis [3]. In a case report by Hazen et al.[10] the patient developed Keratitis- Ichthyosis- Deafness (KID) syndrome and the signs of blepharitis and keratitis developed to the point of neovascularization of cornea. In another study by Ellies et al. [5] on patients using Isotretinoin some patients developed blepharoker-atoconjunctivitis (BKC). In our study the eyelid's inflammation was caused by treatment which is in line with Ellies et al., findings [5].

Conclusion

Isotretinoin usage (0.5 - 1 mg /kg for two months) impairs the tear secretion and causes dry eye and blepharitis among patients. Considering the young age of patients using this drug, some of them candidates for keratorefractive surgery, a history of Isotretinoin usage should be considered before commencing the surgery. We recommend postponing the refractive surgery among these patients until the signs of dry eye are subsided.

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Footnotes and Financial Disclosures

Conflict of Interest:

The authors declare no conflict of interest with the subject matter of the present manuscript.