

Ocular Adverse Effects in Patients with Systemic Isotretinoin in King Khaled Hospital, Hail, Saudi Arabia, 2018 - 2019

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Received: August 30, 2019; **Published:** September 03, 2019

Abstract

Aim: The aim of the study is to evaluate the ocular adverse effects in patients with isotretinoin use in Hail, Saudi Arabia.

Materials and Methods: During a cross sectional study the data were collected through the patient attended to derma clinics and using isotretinoin at dosages of 10 - 20 mg/kg/day for 4 months, a total of 30 Saudi patients were examined in three visits before start, within 1 month and After 1 month of the treatment course. History taking for any symptoms of dry eye and any other abnormalities associated with it. Vision acuity for each eye, tear break up time, corneal exam SPK (Superficial Punctate Keratitis), tear meniscus, and meibomian gland dysfunction. The data analyzed by using (SPSS) version 24.

Results: There were no changes related to visual acuity, vision quality, corneal examination, stringy mucus discharge or redness in any of the cases. Results of examining the patients after one month of stopping the treatment shows that 20% developing meibomian gland dysfunction and there were 50% patients having difficulty wearing contact lenses. A decrease of tear Meniscus was observed in 77 % of patients. Tear break up time was more than 10 seconds in 77%. Subjective symptoms such as burning sensation increased up 30%, regarding the foreign body sensation 37% of them began feeling that during therapy, then it declined to 23%. While transient blurring of vision observed in 13% of them.

Conclusion: The analysis showed that the use of isotretinoin is associated with short term ocular side effects. It is important to inform the patients about these side effects and the importance of the follow up with ophthalmologist during the treatment period.

Keywords: Isotretinoin; Acne Vulgaris; Ocular Adverse Effect; Dry Eye

Introduction

A Retinoids is a form of vitamin A which make a big transformation in the dermatological therapeutics, the focus on Isotretinoin which is the drug that used to treat patients with severe acne vulgaris [1-3]. However, its used for several skin disorders not only for the treatment of severe acne vulgaris. A lot of people now use Isotretinoin so, it's important to be perceptible of the adverse effects, toxicities and management issues related to its use [2,3]. Ocular adverse effect highly related with Isotretinoin use. Sometimes these effects are considerable reason to cessation the drug. Blepharoconjunctivitis and dry eye symptoms are the most common ocular adverse effects and occur in 20% - 50% of patients usually at the third to fifth weeks of therapy [4]. Who approve that many adverse effect are associated with it: abnormal meibomian gland secretion, blepharoconjunctivitis, corneal opacities, decreased dark adaptation, decreased tolerance to contact lenses, decreased vision, increased tear osmolarity, meibomian gland atrophy, myopia, ocular discomfort, ocular sicca, photophobia [5,6].

Citation: Jluwi Saud Almasaud., et al. "Ocular Adverse Effects in Patients with Systemic Isotretinoin in King Khaled Hospital, Hail, Saudi Arabia, 2018 - 2019". *EC Ophthalmology* 10.10 (2019): 801-806.

Methodology

Setting

The present study was conducted in King Khaled hospital, Hail city, Kingdom of Saudi Arabia, from June 2018 to May 2019, to determine ocular adverse effect of isotretinoin.

Sampling

A total of 40 Saudi male and female patients attended to outpatient dermatology clinics to treat acne vulgaris. Written informed consent was obtained from each patient and the study was conducted by Patients were excluded if they were had any history of ophthalmologic abnormality, uses any other drugs that can affect the eye or had any previous ocular surgery.

Data collections

Data were collected through the patient attended to dermatology clinics and use isotretinoin at dosages of 10 - 20 mg/kg/day for 4 months, there were three visits for each patients before, during 1 month, and at the end of the use, 10 patients were excluded from the study, eight of them did not complete the follow up while two patients stopped using of the drug.

Each visit consists of: Taking a history of drug dose, burning sensation, foreign body sensation, transient blurring vision, stringy mucus discharge, change in vision, redness, and difficult wearing contact lenses. By examination: vision acuity for each eye, tear break up time, corneal exam SPK (superficial punctate keratitis), tear meniscus and meibomian gland.

Data analysis

An excel sheet will be used for data management. The data will be analyzed using Statistical Package for Social Sciences (SPSS) version 24. A cronbach's Alpha was used to assess the reliability.

Results

A total of 40 patients, 30 of them completed the study 9 of patients didn't complete the follow up for unrelated reasons and 1 patient stop used the drug. The mean of age are of 25 (range 18-38 years) with standard deviation ± 5 , and 25 (83.30%) of precipitant was females (See table 1). Majority of the patients were with high school educational level 16 (53.30%), while the other were with bachelor degree. There were no changes related to visual acuity, vision quality, corneal examination, stringy mucus discharge or redness in any of the cases. Only 6 (20%) of the patients develop Meibomian gland during treatment and after one month of stop using the treatment. On the other hand, there were 4 (13.30%) patients has difficult wearing contact lenses before the treatment and this percentage has increased with treatment up to 15 (50%) and the same in the last visit (See table 2).

Gender	N (%)	Mean \pm Standard Deviation	Range (Min-Max)
Female	25 (83.30%)	25 \pm 5	18 - 38
Male	5 (16.70%)		

Table 1: Showing the Socio-demographic data.

Adverse effect	Visits, N (%)		
	1 st	2 nd	3 rd
Meibomian Gland	0 (0.00%)	6 (20.00%)	6 (20.00%)
Difficult Wearing Contact Lenses	4 (13.30%)	15 (50.00%)	15 (50.00%)

Table 2: Showing the examination result of meibomian gland, and difficult wearing contact lenses.

A decrease of tear Meniscus was observed in 20 (66.70%) and 23 (76.70%) of patients before and after one month of stop the treatment respectively. Tear break up time was more than 10 seconds. in 30 (100%) of cases during treatment and this percentage decreased to 23 (76.70%) participant in the last visit (See table 3).

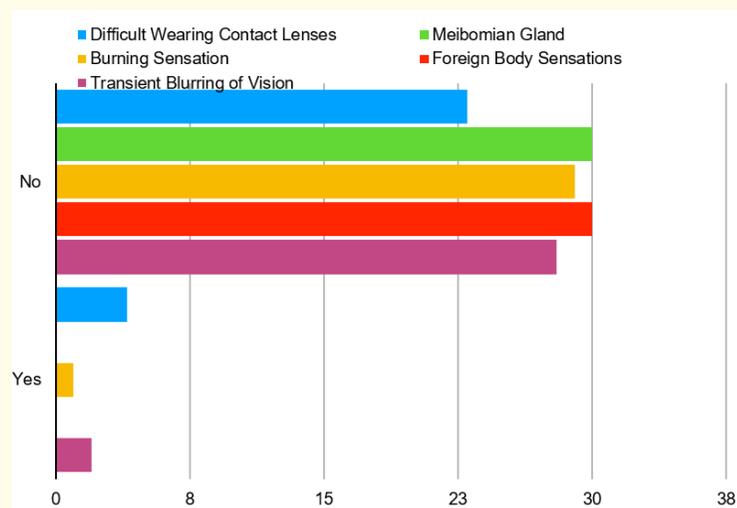
Adverse effect		Visits, N (%)		
		1 st	2 nd	3 rd
Tear Meniscus	= 1mm	30 (100%)	10 (33.30%)	7 (23.30%)
	< 1 mm	0 (0.00%)	20 (66.70%)	23 (76.70%)
Tear Break Up Time	< 10 sec.	30 (100%)	0 (0.00%)	7 (23.30%)
	> 10 sec.	0 (0.00%)	30 (100%)	23 (76.70%)

Table 3: Showing the Examination result of Tear meniscus, and Tear break up time.

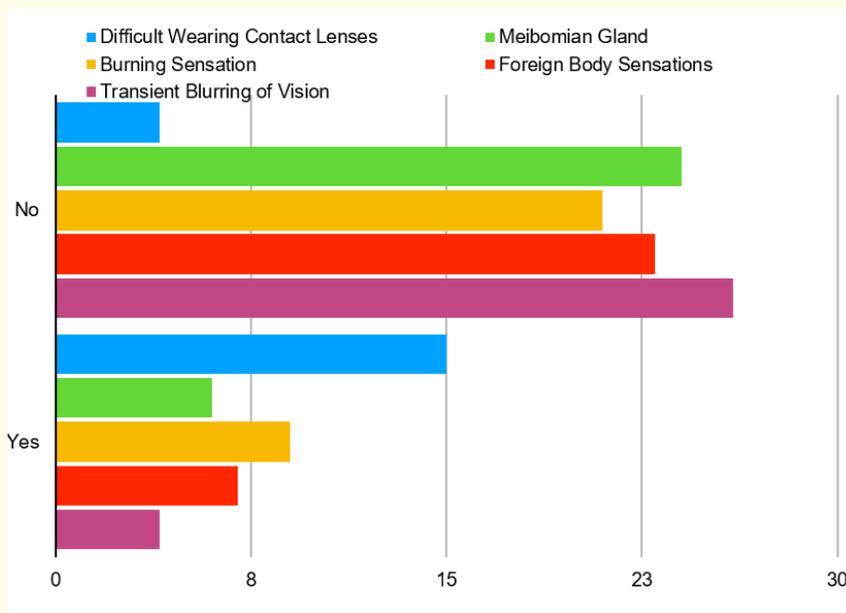
Subjective symptoms such as burning sensation occurred in 1 (3.30%) of the patients before the treatment. While during the treatment it's increased to 8 (26.70%) and keeps increasing until it is reached 9 (30%) cases in last visit. Regarding the foreign body sensation, none of them had it in the first visit, while 11 (36.70%) of them began feeling that after starting the therapy, then it declined to 7 (23.30%) cases at the last visit. Transient blurring of vision observed in 2 (6.70%) of cases before the treatment and increased to 3 (10%) during the therapy, until reached 4 (13.30%) patients after one month of stop using it (see table 4). The changes in (Meibomian Gland, Difficult Wearing Contact Lenses, Burning Sensation, Foreign Body Sensations, Transient Blurring of Vision) before and after, are shown in graph 1 and 2.

Adverse effect	Visits, N (%)		
	1 st	2 nd	3 rd
Burning Sensation	1 (3.30%)	8 (26.70%)	9 (30.00%)
Foreign Body Sensations	0 (0.00%)	11 (36.70%)	7 (23.30%)
Transient Blurring of Vision	2 (6.70%)	3 (10.00%)	4 (13.30%)

Table 4: Showing the Examination result of Burning sensation, foreign body sensations, and transient blurring of vision.



Graph 1: Subjective symptoms before the treatment.



Graph 2: Subjective symptoms after the treatment.

Discussion

Isotretinoin is treatment used to treat people who have acne vulgaris its causes an atrophy of sebaceous gland acini and a decrease in sebum production. Otherwise it’s alters meibomian gland function and structure [7]. A study on rabbits after systemic treatment with isotretinoin, histopathological evaluation found degenerative changes in the meibomian gland acini [8]. Fraunfelder, La Braico, and Meyer [4] evaluated 1741 case reports received from spontaneous reporting systems. The most common ocular complaints involved visual changes, including blurred vision and refractive changes. The next largest grouping involved the cornea, including keratitis and corneal opacities. The third group involved eyelids and conjunctiva, including blepharoconjunctivitis. More serious ocular adverse reactions included papilledema, pseudotumor cerebri, and white or gray subepithelial corneal opacities; all of these are reversible if the drug is discontinued [4]. Acute unilateral cataract [9], uveitis and scleritis [4] are rare side effects that can be seen during isotretinoin treatment.

In our study we find There were no changes related to visual acuity and vision quality. There was no difference in the corneal examination in any of the cases during the treatment, also the stringy mucus discharge and redness. Maybe this due to the small number of patients. Reports on the effects of isotretinoin on tear breakup time have been inconsistent. Whereas Milson., *et al.* [10] found a normal tear breakup time, Ensink., *et al.* [11] and Egger., *et al.* [12] reported a decreased tear breakup time. In the Aylin., *et al.* [13] found a significant reduction in tear breakup time values during treatment when compared with values at baseline, at the end of treatment, and at 30 days after the end of the treatment. In the current study we found a decrease of Tear break-up time in the end of treatment in 23 (76.70%) of the cases. Recently, Fraunfelder., *et al.* [14] have extensively classified the adverse ocular effects related to systemic isotretinoin use. In Tongabay., *et al.* [15] they compared the most commonly encountered adverse ocular effects of systemic isotretinoin, when administered at different doses. One patient experienced blurred vision, one patient had severe blepharoconjunctivitis, and one patient had contact lens intolerance, all of whom were in the high-dose group. The most common adverse ocular effects related to systemic isotretinoin use

are blurred vision, refraction problems (myopia), contact lens intolerance, and reduced accommodation [4]. In a study by Fraunfelder, *et al.* 39 of 237 patients were reported to have blurred vision and four patients developed transient myopia [4,14,15]. In our study the most common adverse effects is difficult wearing of contact lenses 15 (50.00%), then burning sensation 9 (30.00%), after that foreign body sensation 7 (23.30%), and the least was for meibomian Gland 6 (20.00%). Many of dermatological diseases are treated with retinoids, various studies have shown their association with ocular side effects. Patients who undergo this treatment should be carefully selected, in addition to the importance of describing the least possible dose and less time which is sufficient for treatment. The physician should inform their patients about the possible side effects associated. Also, it's important to aware the patients about the importance of following up with the ophthalmologist to detect any changes and early intervention for treatment [5].

Conclusion

The analysis of data showed that, the use of isotretinoin is associated with short term ocular side effects. It is important to inform the patients about these side effects. Also, the importance of the follow up with ophthalmologist during the treatment period and therefore early detection and treatment.

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Volume 10 Issue 10 October 2019

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