EVALUATION THE EFFECT OF ACITRETIN ON OCULAR SURFACE PARAMETERS IN PSORIATIC VULGARIS PATIENTS

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DISSERTATION SUBMITTED IN PARTIAL FULLFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF MEDICINE

(OPHTHALMOLOGY)

UNIVERSITI SAINS MALAYSIA

2021

DISCLAIMER

I hereby certify that the work in this my own except for the quotations and summaries which have been duly acknowledged.

Date: …...……

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ACKNOWLEDGEMENTS

Thanks to Allah, the Most Merciful, and Most Gracious and with His blessings has allowed me to complete this dissertation. It gives me much privilege and pleasure to express my gratitude to my supervisor, Dr Khairy Shamel Sonny Teo for his great guidance, contribution and constructive criticism throughout the preparation and completion of this study. I would also like to forward my utmost gratitude and appreciation to my co-supervisor, Dr Akmal Haliza bt Zamli, for their consistent and proper guidance, support and relentless assistance. Special thanks also to Dr Rajalingam Ramalingam head of department from Dermatology in Hospital Tengku Ampuan Afzan (HTAA) and Dr Wan Noor Hasbee Wan Abdullah, as well as Dr Zulrusydi, Hospital Raja Perempuan Zainab 2 (HRPZ) for allow me to collect data from their site.

My sincere thanks to all the support staffs in Ophthalmology clinic at Hospital Tengku Ampuan Afzan, Hospital Raja Perempuan Zainab 2 (HRPZ) and HUSM, for their assistance during the completion of this dissertation and also not forgetting all the participants involved in this study.

Last but not least, my special thanks to my dear family members who has been the pillar of my strength since the very beginning especially my beloved husband, Mohd Shaiful Nizam bin Mamat Nasir and my precious son and daughter, Irsyad Anaqi and Khaulah Addeena for their patience and the time they had sacrificed, encouragement, understanding and constant love throughout this journey.

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ABSTRAK (BAHASA MELAYU)

Objektif: Mengkaji kesan ubat acitretin terhadap parameter permukaan mata merangkumi aspek masa yang diambil untuk lapisan filem air mata hilang integriti (Tear Break up Time (TBUT)), penghasilan air mata daripada kelenjar lakrimal (Schirmer Test), dan markah 'Ocular Surface Disease Index (OSDI) pada pesakit Psoriasis vulgaris.

Reka bentuk: Analisa prospektif terhadap 29 pesakit psoriasis vulgaris yang memerlukan tambahan rawatan ubat acitretin. Hasil yang diambil kira termasuk data demografi, kategori psoriasis dan jangka masa rawatan yang diterima oleh pesakit sebelumnya; masa yang diambil untuk lapisan filem air mata hilang integriti (Tear Break up Time (TBUT)), penghasilan air mata daripada kelenjar lakrimal (Schirmer Test), dan markah 'Ocular Surface Disease Index (OSDI) pada pesakit Psoriasis vulgaris pada perjumpaan pertama, 3 bulan dan 6 bulan seterusnya.

Keputusan: Tiada perbezaan purata yang ketara terhadap lapisan filem air mata hilang integriti (Tear Break up Time (TBUT)), penghasilan air mata daripada kelenjar lakrimal (Schirmer Test) dan markah Ocular Surface Disease Index (OSDI) pada pesakit Psoriasis vulgaris yang dirawat dengan acitretin selama 6 bulan.

Kesimpulan: Terapi Acitretin selama 6 bulan tidak memberi kesan terhadap integriti permukaan mata dan lapisan filem air mata pesakit psoriasis vulgaris.

Kata kunci: Acitretin, Psoriasis Vulgaris, permukaan mata, tear Break-up Time, Schirmers test, Ocular Surface Disease Index (OSDI)

ABSTRACT (ENGLISH)

Objective: To evaluate the effect of oral acitretin on ocular surface parameters which are, time of tear film to loss it integrity (by Tear Break up Time (TBUT)), production of tears by lacrimal gland (by Schirmer test), and score for Ocular Surface Disease Index (OSDI) in psoriatic vulgaris patients.

Design: A prospective analysis of 29 patients with psoriasis vulgaris who need step up treatment to oral acitretin. Outcome measures included patients' demographic data, types and duration of previous treatment for psoriasis received before, tear break-up time (TBUT), Schirmers' test, and Ocular Surface Disease Index (OSDI) at baseline, 3 months and 6 months of treatment.

Result: : No statistically significant changes were found in mean for TBUT, Schirmers test and OSDI in psoriasis vulgaris patient treated with oral acitretin for 6 months durations.

Conclusion: Ocular surface integrity and tear film are not affected by 6 months therapy with oral acitretin in psoriasis vulgaris patients.

Keywords: Acitretin, Psoriasis Vulgaris, Ocular Surface, Tear Break-up Time, Schirmers test, Ocular Surface Disease Index (OSDI).

Chapter 1

INTRODUCTION

INTRODUCTION

1.1 Background of Psoriasis

Psoriasis vulgaris is a chronic, incurable, immune-mediated skin disease with multisystem disorder with dermatological involvement. Prevalence of psoriasis in the world is between 2% to 5% (1,2). As it is a lifelong disease, it has a negative impact on patients' quality of life. Approximately 2.0% to 3.0% of the world's population is affected by this disease (1). The prevalence variable among differ population and ethnic groups worldwide whereby higher prevalence rates are found in western countries; the distribution ranges from 2.2% in the U.K to as high as 4.5% in Norway (1). The prevalence of psoriasis among patients in the United States is 2.2% to 3.15%, while lower rates were observed in Latin Americans, Indians, and Africans (Egypt and Tanzania) (1). In Asia, the prevalence is less than 0.5% (1). The wide variation in estimates of prevalence between regions may be attributed to the differences in ethnic or racial composition, genetics, and environmental and climate conditions (1,2). Based on latest Malaysian Psoriasis Registry (MPR) 2007 to 2016, mean age were 35 years old with a male: female ratio of 3:2 while the ethnic distribution were 51.1% in Malay populations, 26.3% in Chinese, and 17.3% in Indian (3). However worldwide, there was no sexual or ethnic predilection reported (3).

The aggravating factors for psoriasis are caused by either one or multiples factors. The most common aggravating factor reported was stress (70.3%), followed by sunlight (36.2%), infection (25.5%), trauma (9%), drugs (8.6%), alcohol (4.1%), topical medication (3.8%) and pregnancy (2.7%) (3). Stress has been found to be an important aggravating factor in up to 60% of psoriasis and it was found to be related with dysregulation of immune and abnormal neuroendocrine response (3,4). Pathogenesis of psoriasis is due to proinflammatory activation,

and characterised by uncontrolled proliferation of keratinocytes (4). Apart from the above aggravating factors, the severity of disease will also depend on the concomitant involvement of metabolic diseases (4).

Clinical type of psoriasis can be classified either based on the type of lesion and the location of disease involvement. In Malaysia, most common clinical presentation is chronic plaque psoriasis (85.1%), followed by guttate psoriasis (2.9%), erythrodermic psoriasis (1.7%), and pustular psoriasis (1.0%) (3). The severity of psoriasis is based on the body surface area involvement whereby it is defined as mild, moderate, severe or erythrodermic. In Malaysia Psoriasis Registry, evaluation of percentage body surface area (BSA) involvement of psoriasis showed 31.2% had less than 2% BSA involved, 28.9% between 2 to 10%, 15.3% more than 10%, and 3.1% were erythrodermic (>90% BSA involved), while the remaining 21.4% was unknown (3). The most common body region involved was the lower limbs (81.1%), followed by the scalp (78.8%), upper limbs (74.1), the trunk (72.7%), and the face and neck (49.7%) (3).

Apart from skin, it is known that psoriasis affects other system as well including the eye. An estimated 10% of psoriasis patient has ocular involvement in which arthropathic and pustular psoriasis type being the 2 highest association (5). The etiopathogenetic mechanism that contributes to development of ocular manifestations include, direct eye involvement with psoriatic plaques, psoriasis-related immune-mediated inflammatory processes, and complications of psoriasis treatments such as oral retinoid and phototherapy (5,6)

S. Abbagani et al from southern India in their study on ocular comorbidities revealed that ocular manifestations were seen in 87.07% cases with psoriasis vulgaris, 86.79% with scalp psoriasis, and 43.75% with palmoplantar psoriasis (7). They also found out that statistically significant

ocular features incidence rate increase according to the duration of psoriasis as well as the severity of the disease base on Psoriasis Area Severity Index (PASI) score (7).

Psoriasis may affect any other parts of the eye including the eyelid, conjunctivae, cornea, uvea, and lens. The most common eye presentation in psoriasis patient in a few studies showed that blepharitis as most common presentation for eyelid involvement, whereas corneal involvement may develop secondary to dryness, trichiasis, or conjunctiva involvement [6-9]. Ghalamkapour et al in their recent study on ocular findings in psoriasis revealed that dry eye syndrome was significantly higher in psoriasis patient group as compared to control group (6). They found that higher incidence of dry eyes associated with PASI score, facial, nail involvement, with the duration of the disease which received treatment either methotrexate, acitretin and other treatment modalities in psoriasis (6). Apart from dry eye, other common eye association with psoriasis include uveitis, and cataractous lens [6-9].

Treatment of psoriasis include either topical treatment, phototherapy or systemic treatment such as methotrexate, acitretin, and cyclosporine, including biological therapies such as etanercept, infliximab, adalimumab, and ustekinumab.(3) Almost all patients are treated with topical medications which are the first line therapy in psoriasis. The most widely used topical treatments are emollients (82.5%), followed by tar preparations (79.6%), topical corticosteroids for areas other than face and flexures (72.3%), keratolytics (67.8%), vitamin D analogues such as calcipotriol (22.4%), and dithranol (0.8%) (3). Phototherapy was used in 6.1% of patients for example narrowband UVB, broadband UVB, oral psoralen-UV-A (PUVA) and topical or bath PUVA (3). These treatment modalities allow the dermatologist to have a wide therapeutic option that increases the possibilities of control of patients with serious and extensive psoriasis (10). Acitretin (23.9%) become second line treatment preferred beside methotrexate (69.4%), as it is very useful option either used as monotherapy or in combination with other systemic

drugs or in sequential therapy (10). Acitretin differ from other biologic agent as not being a direct immunosuppressant and maintaining very long-term responses (3,10).

1.2 Retinoid and Acitretin in psoriasis

Retinoids are a group of nonsteroid hormone compounds related to retinol (vitamin A and its metabolites) are potent natural regulators of cellular activities. Retinoids was first synthesized in 1970s for it use in the treatment of skin cancer. It used then extended to the treatment of proliferative disease such as psoriasis as it exert effect on keratinization, cell proliferation and inflammation, and immune regulation. It has antiproliferative activity and effect on cell differentiation, especially in epithelial tissues (10). Synthetic oral retinoids development had successful clinical application in the management of severe and recalcitrant dermatoses for dermatotherapy (11). Oral isotretinoin (13-cis retinoic acid), representative of the first retinoid generation, is presently regarded as the drug of choice for the treatment of severe forms of acne and rosacea, whereas oral acitretin, representative of the second retinoid generation, is the drug of choice for the treatment of severe forms of psoriasis, Darier's disease and other keratinization disorders (Table 1) [11-14].

Acitretin (etretin), (C_{21} H_{26} O_3, [g/mol]) trade names Soriatane and Neotigason is a second generation monoaromatic retinoid. It is a free acid form and an active metabolite of its precursor etretinate, which is used in the treatment of severe psoriasis and other dermatoses (refer Figure 1; chemical structure retinoid) [10-12].

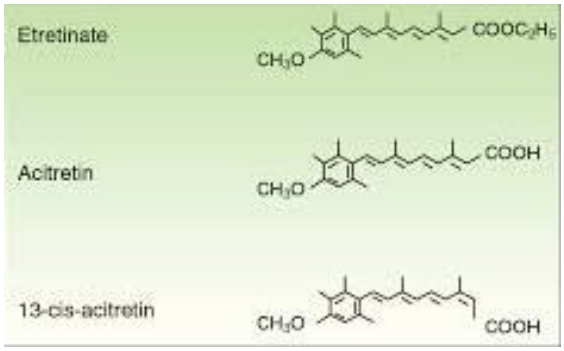


Figure 1; Chemical structure of retinoid; Etretinate, Acitretin, and Isotretinoin (13-cis acitretin)

In 1980s, etretinate was the only available second generation retinoid, and was rarely used due to its associated side effects and the adverse pharmacokinetics (long half-life, high lipophilicity and long teratogenic potential even after the end of therapy). Acitretin is the most important metabolite of etretinate and has even better pharmacokinetic characteristics at a comparable efficacy profile. Due to this reason, only acitretin is available as a systemic retinoid in most European countries and has been so since 1988.

Vitamin A derivative	Receptor target	Indication
Isotretinoin (13-*cis* retinoic acid)	RAR agonist	Severe acne Rosacea (e.g. phymatous, granuloma, fulminant, steroid-induced; Morbihan disease) Pityriasis rubra pilaris
Alitretinoin (9-*cis* retinoic acid)	RAR agonist and RXR agonist	Severe chronic hand-eczema (therapy-refractory under potent topical steroids) Pityriasis rubra pilaris Darier's disease
Acitretin 9-(4-Methoxy-2,3,6-trimethylphenyl)-3,7-dimethylnona-2,4,6,8-tetraenol acid	RAR agonist	Severe therapy-resistant keratization disorders Psoriasis (e.g. pustular, palmoplantar, erythrodermic) Hyperkeratosis palmoplantaris Pityriasis rubra pilaris Darier's disease Ichthyosis Lichen ruber
Bexarotene (4-[1-(3,5,5,8,8-Pentamethyltetralin-2-yl) ethenyl]-benzooic acid)	RXR agonist	Cutaneous T-Cell Lymphoma CD30+-lymphoproliferative diseases with multifocal lesions

Table 1: Systemic retinoid therapy. Abbreviations: RAR agonist, retinoic acid receptors agonist; RXR agonist, retinoid X receptors agonist.

Acitretin shows strong effects in pustular psoriasis and erythrodermic psoriasis. In studies by Beckenbach and Sbidian et al, low-dose acitretin was applied (0.2–0.3 mg/kg body weight daily) to patients with isolated nail-psoriasis for six months, and it showed good results, with a response rate of over 50% (15,16). Acitretin is available in oral capsule formulation (10–25

mg). Compared to other conventional systemic treatments, acitretin is not suggested as a first choice for monotherapy in psoriasis vulgaris.

For the pharmacokinetic of acitretin, its bioavailability is 20–90% after oral intake and enhanced by fat rich food. [14-16]. It reaches peak plasma levels in 1 to 4 hours. The absorbed drug is bound more than 99% to plasma proteins. The half-life of acitretin is 2to 4 days, which is much shorter than that of etretinate (120 days). As compared to etretinate, acitretin 50 times less lipophilic thus enabling it to be eliminated more rapidly. It is metabolised to 13-cis-acitretin, which is interconvertible with acitretin, and both are widely distributed in the body and then excreted in feces and urine. One month after cessation of therapy, the residual plasma concentration falls below detection limit, thereby lowering the risk of teratogenicity [14-19].

The mechanism of action of acitretin also remains unknown. It enters the cells by non-receptor-mediated endocytosis where it binds to cytosolic proteins, which carry it to nucleus, and there it activates nucleic acid receptors. Two classes of retinoid nuclear receptors have been identified: retinoic acid receptors (RAR) and retinoid X receptors (RXR) (refer Table 1) (10). Acitretin binds to RAR and RXR nuclear receptors, activating all 3 subtypes (α, β, and γ) and modulating the transcription of the genes that code for various proteins involved in the pathogenesis of psoriasis (14). Retinoid receptors regulate transcription of genes bearing short DNA sequences in their promoter region known as asretinoic acid response elements [14-16],[18],[19]. Among all retinoid, acitretin have same mechanism of action with isotretinoin, in term of targeted receptor which is retinoic acid receptor (RAR) (refer Table 1) (10).

The acute toxicity of retinoid is comparable to vitamin A intoxication (15). The adverse effects of therapeutically used systemic retinoids are similar. Systemic retinoids are highly teratogenic

especially when consumption early in pregnancy. It usage is known to reduce the efficacy of oral contraceptives, especially progesterone-only, thus additional effective contraception must be advocated to patients who are within childbearing age or planning to conceived (15). Blood donation prohibition is recommended as well within the two years after termination of retinoid treatment due to etretinate is highly lipophilic state and has a very long half-life. This is also relevant for acitretin as there is evidence that acitretin is metabolised to etretinate by the consumption of alcohol during acitretin treatment (15,16). Other major side-effects from the systemic use of retinoids are mucocutaneous xerosis, conjunctivitis, loss of hair and alteration of laboratory values, such as an elevation of transaminases and triglyceride levels (15,16). Additionally, an association between long-term retinoid treatment and the appearance of disorders in bone metabolism and development of extra skeletal ossifications has been reported (16).

1.3 Acitretin and dry eyes in psoriasis

Retinoic acid reported to improve cornea surface keratinization, improve epithelial defect of cornea and help in stability of precornea tear film layer as well as promotes cornea surface hydration.(20) These effects achieved provided appropriate concentration dissolved via local of systemic absorption to eye.(20) On the other hands, retinoid also do caused reduced meibomian gland secretion which subsequently may lead to distruption of tear production and lead to dry eye symptoms. As we know, instability of pre cornea tear film as a cause for persistent epithelial defect and if left untreated may cause cornea scarring or even worst secondary bacterial infection end up with debilitating poor vision. As acitretin part of these retinoid acid and chemically related to vitamin A thus we can postulate that usage of this systemic treatment may caused ocular surface distruption.

In 2002, Gartaganis et al, conducted a study on ocular surface effect of short term oral acitretin in patients with severe dermatoses (11). They evaluated the ocular surface parameters including Schirmer's test, Tear Break up Time, Rose Bengal and Contrast Sensitivity (11). The study showed no significant different between pre values and post treatment after 2 months. However, this study considered as short-term study and they didn't specified specific type of dermatoses. They concluded that, for short term administration of oral acitretin, tear film function, ocular surface integrity and visual acuity were not affected (11).

Ghalamkarpour et al (2019) in their study, evaluated ocular abnormalities in patients with psoriasis compared to healthy controls, as well as determining its association with medications, age, sex, duration and severity of the disease and joint involvement (6). They assessed ocular abnormalities in term of ocular surface problem using an ocular surface disease index (OSDI) questionnaire, and also a thorough ophthalmological evaluation including ocular fundus and anterior segment, Schirmer test and Tear Break-Up Time (TBUT) comparing between psoriasis group and normal healthy population. They found that mean values of Schirmer and TBUT tests for both eyes were significantly lower in patients with psoriasis compared to the healthy controls. Also, significantly higher OSDI scores were observed in the patients compared to the control group. Thus this study concluded that dry eye disease was more frequent for both eyes of the psoriatic patients in comparison with the healthy controls (6). Further analyses of the psoriasis group, revealed that ocular findings were significantly associated with the type of treatment in both eyes whereby it was more frequent in patients treated with methotrexate, followed by acitretin, biologic drugs, cyclosporine, phototherapy and topical corticosteroid, respectively (6).

1.4 Dry eyes in psoriasis and ocular surface parameters

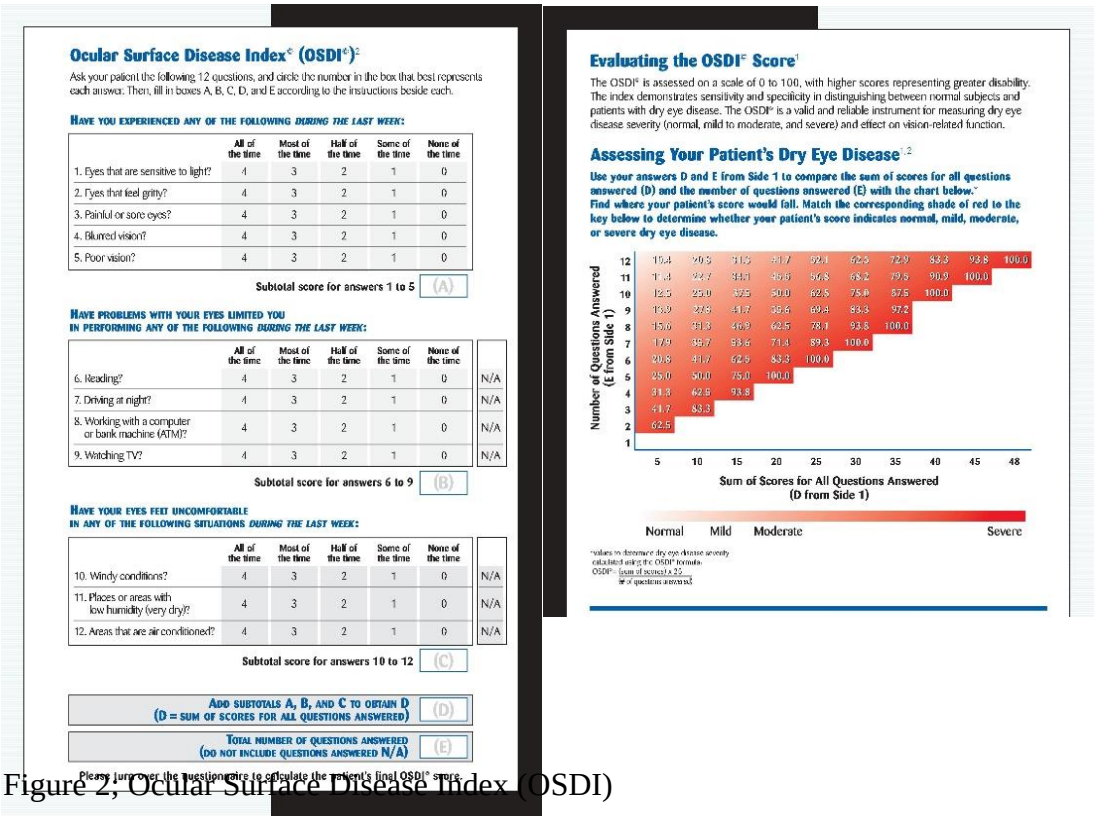
Ocular surface parameters are parameters that are used to quantify the hydration state of the ocular surface by measuring tears function. Tears is important for ocular surface regularity and maintainance of good vision. The hydration state of the eyes can be disturbed either by the disease itself or side effect of medications that is needed to treat the disease. In psoriasis patients, there are numerous aggravating factors that can lead to ocular symptoms specifically dry eyes. S. Abbagani et al in their study on ocular morbidities in psoriasis patient found out that 44.7% of patient have dry eyes (7). They proved that it is statistically significant that dry eyes related with increasing number of years of the disease and increasing PASI score (7). The use of biologic agents as well as retinoid in the treatment of psoriasis also contribute to development of dry eyes (6,20). The use of retinoid in psoriasis patients causing detrimental effect on meibomian gland as it result in cell death, atrophy of acini, hyposecretion of oil and altered gene expression leading to dry eye syndrome (20).

Based on Asian Dry Eyes Society, dry eye is defined as a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface (12). Dry eye disease is diagnosed by the combination of symptoms and an unstable tear film. Dry eye symptoms assessed by Ocular Surface Disease Index (OSDI), or McMonnies questionnaire, Women's Health Study Questionnaire, or the recently reported dry eye-related QOL score (DEQS), while unstable tear film characterised by decreased TBUT (12).

Tear break-up time (TBUT) is measured using a fluorescein dye as a standard method. To minimise the effect on the tear volume and TBUT, a small quantity of the dye (less than 2 mL) should be administered with a pipette or wetted fluorescein strip. After the dye is instilled, the subject is instructed to blink three times to ensure adequate mixing of the dye with the tears. The time interval between the last blink and appearance of the first dark spot on the cornea is measured using a stopwatch. The mean value of the three measurements should be used. Cutoff value of less than 5 seconds is used for the diagnosis of dry eye (12).

Schirmer test primarily measures aqueous tear secretions and useful for determination of aqueous deficient dry eye (12). The Schirmer test done using dry filter strip that need to be placed temporally in each lower fornix. The average distance at which the paper was wet in both eyes after 5 min recorded as the Schirmer value of the subject (6,21,22).

The Ocular Surface Disease Index (OSDI) Questionnaire, is designed to assess dry eye disease severity in a scale of normal, mild to moderate and severe (21). It is developed by the Outcomes Research Group at Allergen Inc. It is a 12-item questionnaire designed to provide rapid assessment of the symptoms of ocular irritation consistent with dry eye disease and their impact on vision- related functioning. The questionnaires are subdivided into three groups. The first group contains questions about the ocular symptoms of dry eyes syndrome, the second about the ocular symptoms while watching television or reading a book, and the third group contains the questions about ocular symptoms induced by environmental factors (Figure 2). The OSDI questionnaire is graded on a scale from 0 to 4, where 0 indicates none of the time; 1, some of the time; 2, half of the time; 3, most of the time; 4, all of the time. The total score of OSDI is calculated on the basis of the following formula: OSDI = [(sum of scores for all questions answered) × 100] / [(total number of questions answered) × 4] (23,24).



Ocular Surface Disease Index® (OSDI®)

Ask your patient the following 12 questions, and circle the number in the box that best represents each answer. Then, fill in boxes A, B, C, D, and E according to the instructions beside each.

HAVE YOU EXPERIENCED ANY OF THE FOLLOWING *DURING THE LAST WEEK*:

	All of the time	Most of the time	Half of the time	Some of the time	None of the time
1. Eyes that are sensitive to light?	4	3	2	1	0
2. Eyes that feel gritty?	4	3	2	1	0
3. Painful or sore eyes?	4	3	2	1	0
4. Blurred vision?	4	3	2	1	0
5. Poor vision?	4	3	2	1	0

Subtotal score for answers 1 to 5 (A)

HAVE PROBLEMS WITH YOUR EYES LIMITED YOU IN PERFORMING ANY OF THE FOLLOWING *DURING THE LAST WEEK*:

	All of the time	Most of the time	Half of the time	Some of the time	None of the time	
6. Reading?	4	3	2	1	0	N/A
7. Driving at night?	4	3	2	1	0	N/A
8. Working with a computer or bank machine (ATM)?	4	3	2	1	0	N/A
9. Watching TV?	4	3	2	1	0	N/A

Subtotal score for answers 6 to 9 (B)

HAVE YOUR EYES FELT UNCOMFORTABLE IN ANY OF THE FOLLOWING SITUATIONS *DURING THE LAST WEEK*:

	All of the time	Most of the time	Half of the time	Some of the time	None of the time	
10. Windy conditions?	4	3	2	1	0	N/A
11. Places or areas with low humidity (very dry)?	4	3	2	1	0	N/A
12. Areas that are air conditioned?	4	3	2	1	0	N/A

Subtotal score for answers 10 to 12 (C)

ADD SUBTOTALS A, B, AND C TO OBTAIN D (D = SUM OF SCORES FOR ALL QUESTIONS ANSWERED) (D)

TOTAL NUMBER OF QUESTIONS ANSWERED (DO NOT INCLUDE QUESTIONS ANSWERED N/A) (E)

Please turn over the questionnaire to calculate the patient's final OSDI® score.

Evaluating the OSDI® Score[1]

The OSDI® is assessed on a scale of 0 to 100, with higher scores representing greater disability. The index demonstrates sensitivity and specificity in distinguishing between normal subjects and patients with dry eye disease. The OSDI® is a valid and reliable instrument for measuring dry eye disease severity (normal, mild to moderate, and severe) and effect on vision-related function.

Assessing Your Patient's Dry Eye Disease[1,2]

Use your answers D and E from Side 1 to compare the sum of scores for all questions answered (D) and the number of questions answered (E) with the chart below.* Find where your patient's score would fall. Match the corresponding shade of red to the key below to determine whether your patient's score indicates normal, mild, moderate, or severe dry eye disease.

*Values to determine dry eye disease severity calculated using the OSDI® formula: OSDI® = (sum of scores) x 25 / (# of questions answered)

Figure 2; Ocular Surface Disease Index (OSDI)

1.5 Rationale of Study

Current study was conducted as a mechanism to optimize care for psoriasis patient. In view of the widespread use in clinical practice, the adverse effects of retinoid, including ocular effects, should be studied thoroughly. This is particularly important because of the fact that many of the adverse effects of these drugs can be predicted, which suggests the need for systematic control of patients treated with vitamin A derivatives. The frequency of ocular side effects compels practitioners to consider periodic ophthalmological controls, particularly in patients with initial ocular symptoms. Such controls would provide the possibility of treating or reducing these adverse effects. Thus, existence of these study will help to elucidate the ocular surface problem in this group of population, factors contribute to it and important of regular eye assessment in these population. In the future, more awareness among patient with psoriasis to seek treatment for their eye problem and help to improve their quality of life for vision.

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Chapter 2

OBJECTIVES OF THE STUDY

2.1 General objectives

To evaluate the effect of acitretin on ocular surface parameters.

2.2 Specific objectives

2.21 To compare the mean Tear, Break Up Time (TBUT) at baseline, 3 months, and 6 months of treatment with acitretin in psoriasis vulgaris patient.

2.22 To compare the mean Schirmer test measurement at baseline, 3 months, and 6 months of treatment with acitretin in psoriasis vulgaris patient.

2.23 To compare the mean ocular surface disease index (OSDI) score at baseline, 3 months, and 6 months of treatment with acitretin in psoriasis vulgaris patient.

Chapter 3

MANUSCRIPT

3.1 TITLE PAGE

Effects of Oral Acitretin on Ocular Surface in Psoriasis Vulgaris Patients.

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Financial support and sponsorship: None.

Conflict of interests: There are no conflict of interests.

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3.2 ABSTRACT

Objectives: To evaluate the effect of oral acitretin on ocular surface parameters which are, time of tear film to loss it integrity (by Tear Break up Time (TBUT)), production of tears by lacrimal gland (by Schirmer test), and score for Ocular Surface Disease Index (OSDI) in psoriatic vulgaris patients.

Methods: A prospective analysis of 29 patients with psoriasis vulgaris who are on oral acitretin treatment. Outcome measures included patients' demographic data, types and duration of previous treatment for psoriasis received before, tear break-up time (TBUT), Schirmer's' test, and Ocular Surface Disease Index (OSDI) at baseline, 3 months and 6 months of treatment.

Results: No statistically significant changes were found in mean for TBUT, Schirmer's test and OSDI in patient treated with oral acitretin for 6 months durations.

Conclusion: Ocular surface integrity and tear film were not affected by 6 months therapy with oral acitretin in psoriasis vulgaris patients.

Key Words: Acitretin, Psoriasis Vulgaris, Ocular Surface, Tear Break-up Time, Schirmer's test, Ocular Surface Disease Index (OSDI).

3.3 INTRODUCTION

Psoriasis vulgaris is a chronic, incurable, immune-mediated skin disease with multisystem disorder mainly dermatological involvement. Ocular manifestations were seen in 87.07% cases with psoriasis vulgaris. [3] Abbagani in their study, they found out that the ocular manifestation in psoriasis patient strongly related with the duration of disease and severity of disease by Psoriasis Area Severity Index (PASI) score. [7] PASI score of more than 10 had higher prevalence of getting ocular symptoms which indirectly related to body surface area involvement (BSA).[7]

Acitretin (etretin), trade names Soriatane and Neotigason a second Generation monoaromatic retinoid is the only oral retinoid (synthetic vitamin A derivative) currently approved by the US Food and Drug Administration for the treatment of severe psoriasis.[25] Dosage of 25 mg/day combined with a phototherapy regimen is a standard treatment for severe plaque-type psoriasis and also pustular psoriasis.[25] As in Malaysia Clinical Practice Guideline for Psoriasis, recommended dosage is 0.5mg to 1mg per kg body weight per day with maximum dose of 75mg per day. There is role for a lower dose of acitretin in patients who are experiencing retinoid-related side effects and who are stabilized on a phototherapy regimen to 17.5mg/day. [26] In other study stated that, relatively high dose of acitretin was needed to show efficacy only after 8 weeks of treatment and it is used in longer duration to get full therapeutic effect. [25] According to Clinical Practice Guideline for Psoriasis Vulgaris June 2013, oral retinoid (Acitretin) is a treatment of choice after Methotrexate and phototherapy. It became better choice for the treatment of this disease in term of mean PASI score improvement.