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Efficacy of Oral Isotretinoin in Steroid-Induced Rosacea: Clinical outcomes and Safety

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ABSTRACT

Steroid-induced rosacea is a common dermatological disease. Various treatment methods are used with different efficacy. To assess the effectiveness and safety of oral isoretinion in treatment of steroid-induced rosacea. An interventional prospective project implemented in Dermatology outpatients' clinic in Tikrit Teaching hospital and private Dermatology clinic in Tikrit city-Iraq within period of ten months from 1st of February to 30th of November, 2025 on convenient sample of sixty patients with steroid-induced rosacea. Assessment was done by use of clinical scoring system investigator global assessment erythema score before and after treatment. The mean score of erythema before treatment was (3.4) which was significantly declined to (1.4) after oral isoretinoin therapy ($p<0.001$). The side effects were mild cheilitis and dryness that shown by most of the patients after treatment and mild relapses were shown only by 13.3% of patients. Low dose oral isoretinoin is effective and safe agent in treatment of steroids-induced rosacea.

INTRODUCTION

Rosacea is a prevalent dermatological disorder characterized by ongoing, recurrent lesions in the face's vasculature (Meyer-Hoffert & Schröder, 2021). The etiology of this persistent skin disorder is undetermined, and it presents with a range of clinical signs (Steinhoff et al., 2011). Capillary enlargement and flushing are the initial symptoms of rosacea. Telangiectasia then develops, and reddish patches continue, especially on the nose and cheeks. Erythema endures as a result of recurrent vasodilation and telangiectasia (Geng et al., 2024).

The following environmental factors can make rosacea worse: hot temperatures, ultraviolet rays, foods with spice, drinking alcohol, and potentially tobacco. Papules, pustules, and rhinophyma are common phases of rosacea, while each person's progression is unique. Women are more likely to

get rosacea as a result of applying various beauty products without considering their negative impact (Kwon et al., 2020). Several internal and external variables may be associated with the phenotypic presentation of rosacea, and population-level investigations generally point to an inherited susceptibility for the condition (Chang et al., 2015).

Surveys indicate that 1% to 10% of individuals are affected by rosacea, with the ailment being less prevalent among those with darker skin tones. It is unknown how common rosacea is in the Middle East (Albaqshi et al., 2020). Additionally, rosacea sufferers have a lower quality of life than the general population. Rosacea is a persistent inflamed central face skin condition that can be very difficult to control, despite recent improvements in management (Assiri et al., 2024).

Steroid-induced rosacea (SIR) can occur from prolonged topical steroid treatment for more than two months; pro-inflammatory cytokine production and rebound vasodilation have been suggested as aetiology (Bhat et al., 2011). In particular, the danger is increased when applied to the face due to a fragile corneal layer and significant skin permeation through several sebaceous glands (Souto et al., 2022). Using topical steroids on areas with thin layers of skin, such the face, or using high-potency steroids for a long time are known to raise the risk of adrenocortical insufficiency (Hameed, 2013).

Erythema, capillary dilatation, scaling, papules, pustules, and perioral and periocular dermatitis resembling rosacea are its hallmarks. Though these conventional treatments are slow-acting and typically inefficient, it can be treated by stopping the use of steroids and by using a range of therapeutic agents, including topical antibiotics, oral tetracycline antibiotics, and antihistamines (Xu et al., 2023). It was shown that tetracycline medication frequently proves beneficial for steroid-induced rosacea condition, indicating a potential involvement of skin bacteria in its causation (Mochizuki et al., 2025).

Retinoids, derivative of vitamin A, are extensively utilised for acne vulgaris and psoriasis, and have long been established as effective treatments for numerous dermatological disorders, including photoaging, actinic keratosis, and ichthyoses (Chu et al., 2021). Due to conflicting findings from multiple researches, the efficacy of these substances in treating rosacea is currently debatable. Although some writers have reported encouraging results, retinoids are not widely used for rosacea because of a number of issues, chief among them being local adverse effects and a dearth of solid data from extensive studies (Chang et al., 2012). Most people agree that using retinoids to treat rosacea is effective, although it is still not allowed (Anzengruber et al., 2017).

The growing number of side effects significantly limits the therapeutic application of isotretinoin, even if it is a very effective treatment for different dermatological disorders. Its teratogenicity is its most distinguished consequence. Additional recorded adverse reactions include ophthalmic, mucocutaneous and musculoskeletal effects in addition to liver and hematology changes (Rajput & Anjankar, 2024). Although there are fewer studies and a lack of standardization in the vehicle, preparation, and treatment plan, the proof supporting topical retinoid therapy for rosacea is fascinating but insufficient. This study aimed to assess the effectiveness and safety of oral isoretinion in treatment of steroid-induced rosacea.

METHODS

This study was an interventional prospective project implemented in Dermatology outpatients' clinic in Tikrit Teaching hospital and private Dermatology clinic in Tikrit city-Iraq within period of ten months from 1st of February to 30th of November, 2025. All patients with steroid-induced rosacea presented to clinics were the study population. Adult patients with history of prolonged topical corticosteroid use, clinical diagnosis of steroid induces rosacea with typical clinical

findings (erythema skin atrophy telangiectasia inflammatory papules and pustules with burning sensation) and stopping steroids since one month duration were inclusion criteria. Exclusion criteria were pregnancy and lactation, history of liver diseases, history of hyperlipidemia, prior use of oral isotretinoin use during previous 6 months before study, lost to follow up and patients refused to participate. The study protocol received approval from the Ethics Committee of Medical College/Tikrit University (No.151, date 1/2/2025), hospital administration, patient's written informed consent and management of treatment side effects. This study included convenient sample of sixty patients with steroid-induced rosacea after eligibility to inclusion and exclusion criteria. Information of selected patients were collected directly by researchers and fulfilled in questionnaire designed by the researcher and included the following data: general characteristics of patients (age, gender, duration of steroids use and erythema score before treatment) and treatment outcomes of oral isortetinoin (erythema score after treatment, time to improve, side effects, relapses rate 3 months after stopping treatment and duration of treatment). The researcher diagnosed the steroid-induced rosacea depending on clinical findings (erythema skin atrophy telangiectasia inflammatory papules and pustules with burning sensation). Oral isotretinoin (0.2-0.3 mg/kg/day) for 8 to 16 weeks was prescribed by researcher with use of sunscreen, emollients, gentle cleanser regularly. Assessment was done by use of clinical scoring system IGA erythema score (investigator global assessment) before and after treatment. The researcher followed the outcomes every four weeks and treatment duration was ranging between two to four months. Side effects and relapses were followed up and diagnosed by researcher (clinical history and examination). The data collected were analyzed statistically by Statistical Package of Social Sciences software version 26. Categorical variables were analyzed using Chi square or Fishers exact tests, while paired t-test was applied for analyzing continuous variables. Level of significance was 0.05 or less.

RESULTS AND DISCUSSION

This study included sixty patients with steroid-induced rosacea presented with mean age of (35.1 years); 23.3% of patients were in age of less than 30 years, 41.7% of them were in age group of 30-39 years, 30% of patients were in age group 40-49 years and 5% of them were in age of 50 years and more. Female patients were more than males (81.7% vs. 18.3%). Mean steroids use duration was (2.2 years); 48.3% of them had steroids duration of 1-3 years. Mean erythema score before treatment was (3.4); 8.4% of patients had mild erythema, 43.3% of patients had moderate erythema and 48.3% of them had severe erythema. (***Table 1***)

Table 1. General Characteristics of Patients With SIR

Variable	No.	%
Age mean±SD (35.1±7.1 years)		
<30 years	14	23.3
30-39 years	25	41.7
40-49 years	18	30.0
≥50 years	3	5.0
Gender		
Male	11	18.3
Female	49	81.7
Duration of steroid use mean±SD (2.2±1.6 years)		
<1 year	19	31.7

1-3 years	29	48.3
>3 years	12	20.0
Erythema score before treatment mean±SD (3.4±0.6)		
Mild erythema	5	8.4
Moderate erythema	26	43.3
Severe erythema	29	48.3
Total	**60**	**100.0**

After using oral isoretinoin therapy, the mean erythema score of patients with SIR was (1.4); 63.3% of patients had faint erythema and 36.73% of patients had mild erythema. Mean time to improvement was (1.9 months); 48.3% of SIR patients improved after two months. The side effects were mild cheilitis and dryness that shown by most of the patients after treatment and mild relapses were shown only by 13.3% of patients. Mean duration of oral isoretinoin treatment was (3.2 months); 50% of patients had treatment duration of three months. (***Table 2***)

Table 2: Treatment Outcomes of Oral Isortetinoin.

Variable	**No.**	**%**
Erythema score after treatment mean±SD (1.4±0.5)		
Faint erythema	38	63.3
Mild erythema	22	36.7
Time to improve mean±SD (1.9±0.7 months)		
One month	18	30.0
Two months	29	48.3
Three months	13	21.7
Side effects		
Mild cheilitis and dryness	55	91.6
No	5	8.4
Relapse rate 3 months after stopping isotretinoin		
Mild relapse	8	13.3
No	52	86.7
Duration of treatment mean±SD (3.2±0.7 months)		
Two months	10	16.7
Three months	30	50.0
Four months	20	33.3
Total	**60**	**100.0**

As shown in table 2 and figures 1-3; there was a highly significant decline in erythema score of patients with SIR after using oral isoretinoin therapy ($p<0.001$); 48.3% of patients had severe erythema before treatment, while no patient had severe erythem after treatment, on other hand, no patient had faint erythema before treatment, while 63.3% of them had fain erythem after treatment by oral isoretinoin therapy. The mean score of erythema before treatment was (3.4) which was significantly declined to (1.4) after oral isoretinoin therapy ($p<0.001$).

Table 3. Erythema Score of SIR Patients Before and after Oral Isortetinoin Therapy.

Variable	Before		After		P value
	No.	%	No.	%	
Erythema score					
Faint erythema	0	-	38	63.3	**<0.001**[HS]
Mild erythema	5	8.4	22	36.7	
Moderate	26	43.3	0	-	
Severe erythema	29	48.3	0	-	

HS=Highly significant.

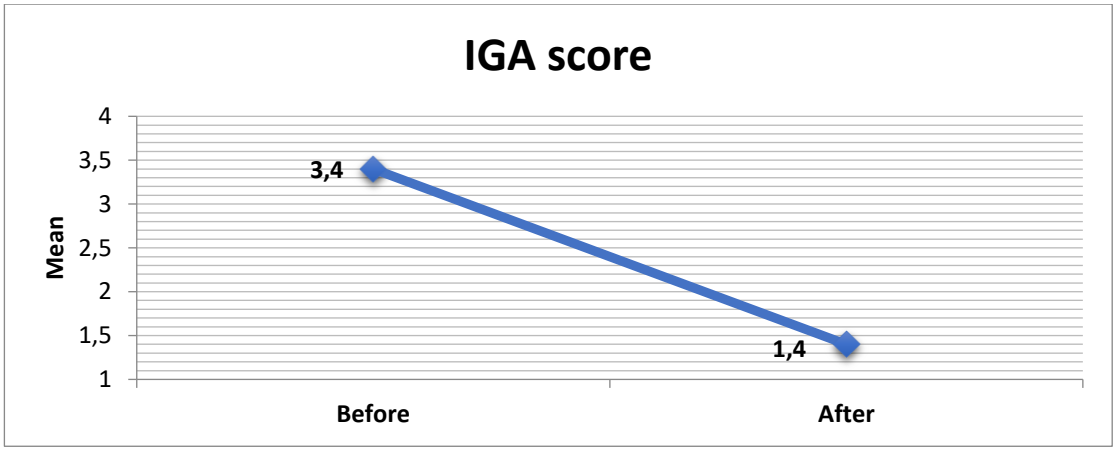

Figure 1: Erythema Score Before and After Treatment.

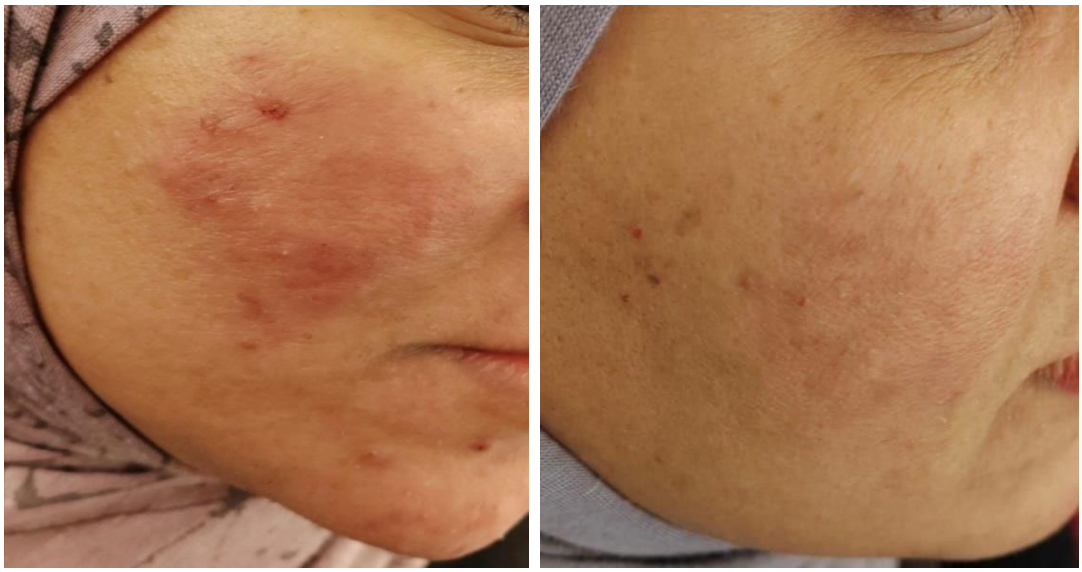

Figure 2. Effects of Oral Isoretinoin on SIR after Two Months Treatment.

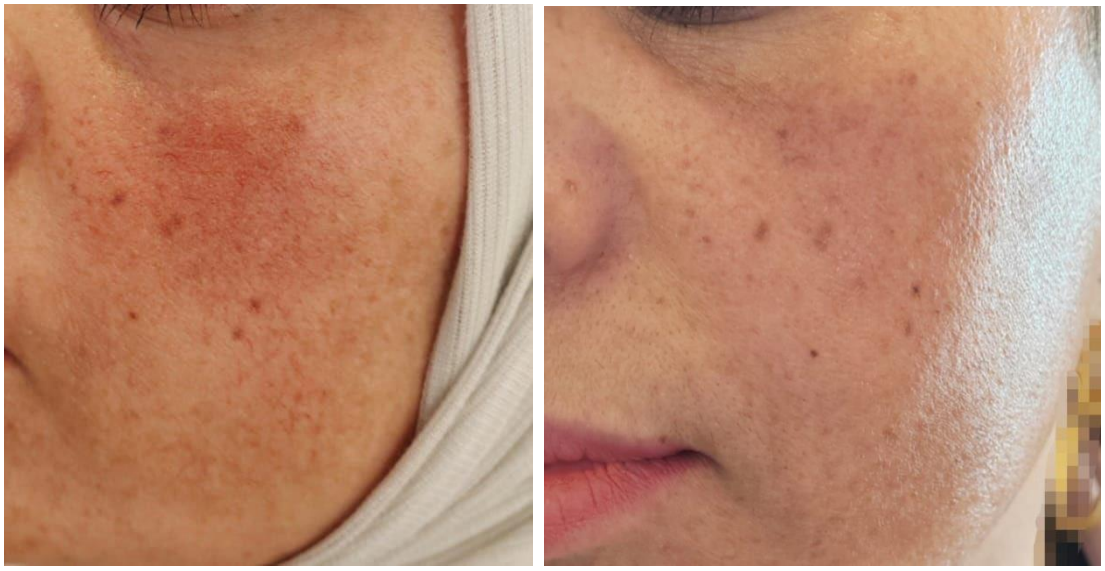

Figure 3. Effects of Oral Isoretinoin on SIR after One Month Treatment.

Discussion

Searching for new treatment agents of steroids-induced rosacea is essential in planning for preventive strategies of long term steroids topical treatment. Steroid Induced Rosacea (SIR) is marked by intense inflammation following the cessation of topical steroids, accompanied by inflammatory manifestations such as erythema, papules, pustules, and burning sensations, and may also involve heightened sebaceous activity and proliferation of Demodex mites (Paiva-Santos et al., 2023).

In present study, mean age of patients with steroid-induced rosacea was (35.1 years). This mean age is higher than mean age of (28.3 years) for patients with SIR reported by previous Iraqi study (Hameed, 2014). This difference might be attributed to higher use of topical steroids agents nowadays by women for cosmetic reasons. Our study showed that female patients with SIR were more than males (81.7% vs. 18.3%). Similarly, previous study implemented in South Korea which revealed higher predominance of women with SIR as compared to men (Shim et al., 2012). Current study found that mean steroids use duration by patients with SIR was (2.2 years). It was shown that steroids-induced rosacea disease duration lasts from months to years (Rathi & Kumrah, 2011).

The present study found that mean erythema score of patients with SIR before treatment was (3.4) and mean erythema score was (1.4) after using oral isoretinoin therapy (decline by 59%), with highly significant decline ($p<0.001$). This finding is consistent with results of recent systematic review and met-analysis study conducted in United States of America and Canada which reported that low dose of oral isoretinoin (≤0.5 mg/kg/day) was effective in reducing mean erythema score (47% decline) with 16 weeks treatment duration (King et al., 2025). In our study, 8.4% of patients with steroids induced rosacea had mild erythema, 43.3% of patients had moderate erythema and 48.3% of them had severe erythema, while after oral isoretinoin treatment, 63.3% of patients had faint erythema and 36.73% of patients had mild erythema with highly significant difference ($p<0.001$).

Consistently, two recent systematic review and meta-analysis literatures carried out in Italy and Indonesia revealed a profound effect of low dose isoretinoin in treatment of rosacea (Bangun & Bangun, 2024; Sticchi et al., 2025). Present study found that mean time to steroids-induced rosacea improvement after oral isoretinoin treatment was (1.9 months), while mean duration of oral isoretinoin treatment was (3.2 months). These findings are close to reports of previous American

review study which documented that low dose oral isoretinoin is effective in treatment of steroids-induced rosacea within improvement duration of two to three months. In our study, oral isoretinoin therapy of SIR was mostly accompanied be mild adverse effects (mild cheilitis and dryness). These findings are in agreement with results of various literatures which all reported the safety of oral isoretinion therapy in treatment of rosacea (Kapała et al., 2022). Our study showed mild relapses in 13.3% of patients with steroids-induced rosacea after oral isoretinoin therapy. This relapse rate is better than findings of recent systematic review and met-analysis study implemented in United States of America and Canada of (35%). With consistent use over time, isoretinoin reduces demodex activity, erythema, and sebaceous gland size and inflammation by downregulating TLR-2. It also gradually improves skin barrier function by reducing proinflammatory oxidised squalene, reducing irritating free fatty acids, and normalising follicular differentiation, which enhances epiderma barriers (Chakmakchi et al., 2025) To avoid recurrence, low dose of oral isoretinoin (0.07 mg/kg/day) was shown an efficacy with low rate of side effects and it was associated with better quality of life and less use of multiple antibiotics therapies (Bagatin et al., 2020).

CONCLUSION

In conclusion, low dose oral isoretinoin is effective and safe agent in treatment of steroids-induced rosacea. Oral isoretinoin is obviously reducing the erythema score of steroids-induced rosacea. This study recommended further projects on effectiveness of and safety of oral isoretinoin in treatment of rosacea.

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Conflict of interest

Declared none.

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