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Efficacy and Safety of Salicylic Acid (20%) Chemical Peel Solution in Treatment of Moderate

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Abstract

Background and objectives: Rosacea is a chronic skin disorder characterized by persistent facial erythema, telengectesia, inflammatory papules and pustules, facial flushing. This study aimed to evaluate the clinical effectiveness of 20% salicylic acid chemical peel in comparison to combined effect of oral doxycline 100mg capsule and topical metronidazole 0.75% gel in the treatment of moderate rosacea. **Methods:**An open label comparative therapeutic trial which has been done at Erbil Dermatology Teaching Center outpatient clinic during the period from March of 2017 to January 2018 on forty patients with moderate rosacea. Full history and clinical examinations were done for every patient. Patients were randomly allocated to two groups: group A underwent salicylic acid chemical peeling every 3 weeks for a series of four sessions using 20% salicylic acid and group B received oral doxycline 100mg capsule and topical metronidazole 0.75% gel once daily for a series of 12 weeks. Treatment efficacy was assessed at last session according to IGA score of rosacea. **Results:** Forty patients; their age ranged from 23 to 68 years. Before treatment, all patients in both treatment groups were classified as having a moderate grading of rosacea. At the last visit, according to investigator's global assessment, treatment success in terms of a clear, or mild final result was obtained in a significantly larger proportion of those patients treated with 20% salicylic acid group compared with doxycline capsule and topical metronidazole gel. **Conclusions:**The findings in our study indicated that 20% salicylic acid peel is more efficacious in treatment of moderate rosacea than combined doxycline 100mg capsule and metronidazole 0.75% gel. Also chemical peel is easier to use and has less cost.

Keywords: Salicylic acid 20%, Metronidazole gel 0.75%, Doxycline 100 mg capsule, Moderate rosacea, Erbil.

Introduction

Rosacea is a term used to encompass a group of signs and symptoms that include persistent erythema of the convexities of the face, telangiectasias, inflammatory papules and pustules, a tendency toward frequently flushing of the face, non-pitting facial edema, various types of ocular inflammation, and phymatous changes of the nose, ears, forehead, chin or eyelids[1]. Rosacea is a very common disease it is more common in light-skinned than darker-skinned persons , although it may occur in all skin types including black people more commonly affects women than men however rhinophyma is much more common in men[2]. There is a wide range in the estimated prevalence of rosacea (0.1–22%) likely due to differences in case definitions[3].

Rosacea is mainly a disease of young to middle-aged adults but it occurs in patients of all ages, including children[2]. Triggering factors of rosacea may include hot or cold temperature, sunlight, wind, hot drinks, exercise, spicy food, alcohol, emotions, cosmetics, topical irritants, menopausal flushing, and medications that promote flushing. There are four rosacea subtypes: erythematotelangiectatic, papulopustular, phymatous, and ocular[4].

The etiology of rosacea is not known because of obvious clinical difference among the rosacea varieties, the etiologic and pathophysiologic variation has been hypothesized Such variations may include reactivity of facial vasculature, matrix composition or connective tissue structure of the dermis, pilosebaceous unit, prominent colonization by demodex mite , or a combination of factors that change the cutaneous reaction to rosacea provoking factors[1,4]. Although environmental factors contribute to the development of rosacea, there is also a strong genetic component (46%)[5]. There may be subtle histologic changes

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in the erythemato telangiectatic type of rosacea and are commonly restricted to vascular ectasia and mild edema a more obvious perivascular and perifollicular lymphohistiocytic infiltrate appears in the inflammatory papulopustular type in some cases there may be prominent sebaceous hyperplasia[1]. The disease is chronic; lasting for years with episodes of activity followed by inactive intervals of different duration. No accepted treatment is accessible to treat the flushing episodes of rosacea; surgical modalities, such as dermabration, laser and scalpel operation are used for treatment of telengectasia and phymas the treatment of inflammatory rosacea usually involves systemic treatment with oral antibiotics such as erythromycin, tetracycline and/or topical antibiotics including metronidazole and clindamycine, oral isotretinoin may be indicated in severe cases[6]. Salicylic acid SA is a beta-hydroxy acid an organic aromatic carboxylic acid with hydroxyl group in the beta position it solubilizes intercellular cement, decease corneocytes adhesion, leads to sloughing of the superficial layers of epidermis followed by activation of epidermal basal cells and underlying fibroblast stimulate fibrosis[1]. SA has anti-inflammatory ,antimicrobial and antifungal properties Various preparations of SA have been used for peeling purposes in ethyl alcohol solutions containing 10%, 20%, 30%, 40%, and 50% (w/v) SA[7-9]. Metronidazol, a topical nitroimidazole FDA approved topical treatment of rosacea and can be applied once or twice daily available as a 0.75% gel, cream, or lotion and as a 1% cream or gel for the[1,4].

Doxycycline, a second-generation tetracycline, exhibits its antimicrobial, antiangiogenic and anti-inflammatory properties and is FDA approved treatment of rosacea[10] and could be considered for all severities of inflammatory papules/pustules, inflamed phyma and ocular features of rosacea. Dosage is not specified, the standard formulations of $\geq$ 50 mg, have antibiotic activity, doxycycline is also available in 40-mg modified-release dose, which is considered to have anti-inflammatory but not antibiotic activity, and reduced gastrointestinal side-effects vs. doses $\geq$ 50 mg[11]. The aim of this study was to assess the effectiveness and safety of chemical peels (using salicylic acid 20%) in comparison to combined effect of doxycline 100mg capsule and topical metronidazole 0.75% gel in the treatment of moderate rosacea.

Patients and Methods

A randomized comparative trial of efficacy of 20% salicylic acid in comparison to combined doxycycline capsule and metronidazole gel as a treatment of moderate rosacea was conducted in Erbil dermatology teaching center in Erbil city. The time of the study was from March 2017 to January 2018. Both gender patients aged, 18 years and older, with moderate grading facial rosacea were included in the study according to investigators global assessment of rosacea IGA score, Table [16].

Table (1): Investigators global assessment of rosacea.

Score	Definition	Description
0	Clear	No papules and/or pustules; no or residual erythema; no or mild to moderate Telengectasia
1	Minimal	Rare papules and/or pustules; residual to mild erythema; mild to moderate Telengectasia
2	Mild	Few papules and/or pustules; mild erythema; mild to moderate telangiectasia moderate telangiectasia
4	Moderate	Pronounced number of papules and/or pustules; moderate erythema; mild to moderate telangiectasia
5	Moderate to severe	Many papules and/or pustules, occasionally with large inflamed lesions; moderate erythema; moderate telangiectasia
6	Severe	Numerous papules and/or pustules occasionally with confluent areas of inflamed lesions; moderate or severe erythema; moderate or severe telangiectasia

This is a descriptive score provides an integrated assessment of moderate rosacea based on the severity of the principal symptoms: inflammatory lesions, erythema, and telangiectasia. The severity of erythema in this score is rated on a

4-point scale (0=none; either no visible erythema or minimal residual erythema. 1= mild; Slight erythema either centrofacial or generalized to whole face. 2= moderate; Pronounced erythema either centrofacial or generalized to whole face. 3=Severe; Severe erythema/red to purple hue, either centrofacial or generalizeto whole face). Telangiectasia assessment was done with the same method6. Patients excluded from the study if they had: mild rosacea, severe rosacea, steroid rosacea, pregnant and lactating females, active infection with herpes simplex virus, history of keloid and hypertrophic scar, hypersensitivity to treatment component. The procedure was described in detail, all patients provided written informed consent a detailed history was taken from each patient regarding age, gender, duration, Triggers of rosacea, previous treatments, modalities of previous treatment (topical, systemic treatment or combined).

Patients were allocated randomly to one of the two groups: Group A: included 20 patients, they underwent 20% salicylic acid peels every 3 weeks, four peeling sessions were conducted during procedure. Patients were asked to close their eyes while lying down in a 45° semi-reclining position. Degreasing was done by scrubbing with cotton gauze soaked with 96% ethyl alcohol Vaseline was used to protect lip and nasolabial folds, peel was then applied over the face starting over the forehead, right cheek, left cheek, chin, nose, upper lip, and lastly the infraorbital areas, using nearly 1 mL for each session gauze were used for application. The total length of the peeling sessions was from 3 to 5 minutes the patients then asked to wash their faces with water. They were then asked to dry the face and they were asked to apply a sunscreen on their faces before leaving the hospital they were asked not to apply any other topical or use systemic treatments for rosacea.

Group B: 20 patients included they were instructed to apply metronidazole 0.75% gel once daily in conjunction with oral doxycycline 100 mg capsule for 12 weeks.

All patients had been followed for 12 weeks and assessed according to IGA score. Specially designed questionnaire was used for collection of information, and data analyzed by using Statistical Package for Social Sciences (SPSS) version 22 and the results were compared between patients with different variables, Chi square and independent samples t-tests were performed to compare between the two groups, a p-value ≤ 0.05 was regarded as statistically significant. Ethical considerations informed verbal consent was obtained from each patient who enrolled in the study after a detailed explanation about the aim of the study was given. The study was approved by ethical committee of the Kurdistan board of medical specialties.

Results

The study population involved 40 patients; twenty patients were included in group A and 20 patients in group B, all patients completed the study. Their age ranged from 23 to 68 years. The mean age of the two groups were (45.9± 11.21) of these 40 patients 7 (17.5%) patients were male and 33 (82.5%) were female, Table 2.

Table (2): Association between study groups and gender.

Gender	Study group		Total	p-value
	Group A	Group B	No. (%)	
	No. (%)	No. (%)		
Male	3(15%)	4(20%)	7(17.5%)	0.67
Female	17(85%)	16(80%)	33(82.5%)	
Total	20(100%)	20(100%)	40(100%)	

The duration of rosacea in years for the two groups was: Group A the duration was < 1year in 6(30.0%) cases, 2-5 year in 8(40.0%) cases, > 5 years in 6(30.0%) cases. Group B the duration was < 1year in 7(35.0%) cases, 2-5 years in 8(40.0%) cases, > 5 years in 5(25.0%) cases (Table 3).

Table (3): Association between study groups and duration.

Duration	Study group		Total	p-value
	Group A	Group B		
	No. (%)	No. (%)		
≤1year	7(35%)	6(30%)	13(32.5%)	0.92
2-5 years	8(40%)	8(40%)	16(40%)	
> 5 years	5(25%)	6(30%)	11(27.5%)	
Total	**20(100%)**	**20(100%)**	**40(100%)**	

Group A: Seven (35%) patients did not receive any previous treatment while 7(35%) and 6(30%) patients had received previous topical treatment or topical and systemic treatment respectively

Group B: Three (15%) patients did not receive any previous treatment while 9(45%) and 8(40.0%) patients had received previous topical treatment or topical and systemic

treatment respectively,Table 4.

Table (4): Association between study groups and previous treatment.

Previous treatment	Study group		Total	p- value
	Group A No. (%)	Group B No. (%)		
None	7(35%)	3(15%)	10(25%)	0.34
Topical	7(35%)	9(45%)	16(40%)	
Topical & oral	6(30%)	8(40%)	14(35%)	
Total	20(100%)	20(100%)	40(100%)	

At the last visit, success was recorded according to the IGA rating of clear , and mild and it was achieved in a significantly greater proportion of patients treated with 20% salicylic acid chemical peel{ clear 15(75%), mild 4(15%) patients compared with combined doxycline 100mg capsule and topical metronidazole 0.75% gel {clear 8(40%), mild 5(25%)}. There was statistically significant association between the results of the two groups (p-value 0.03). Nearly twice as many 20% salicylic acid group (75%) received an IGA score of clear at last available visit, Figure1, 2 compared with combined doxycline 100 mg capsule and topical metronidazole (0.75%) gel group (40%). By contrast 7(35%) of patients with combined oral doxycline capsule and topical metronidazole gel had a score of moderate (not responding) compared with 1 (5%) patient20% salicylic acid group at last visit, Table 5.

Table (5): Association between study groups and treatment outcome.

Treatment outcome	Study group		Total	p-value
	Group A No. (%)	Group B No. (%)		
Cleared	15(75%)	8(40%)	23(57.5%)	0.03
Mild	4(20%)	5(25%)	9(22.5%)	
Moderate	1(5%)	7(35%)	8(20%)	
Total	20(100%)	20(100%)	40(100%)	

Figure (1): Sixty five years old male patient who rated as having moderate grading of rosacea according to IGA score underwent four sessions of 20% salicylic acid chemical peel every three weeks.

Figure (2): Forty-three years old female patient who rated as having moderate grading of rosacea according to IGA score underwent four sessions of 20%salicylic acid chemical peel every three weeks.

The cutaneous side effects of both groups i.e. the number of participants who experienced itching, stinging and burning sensation did not differ in those who have been treated with 20 % salicylic acid chemical peel from those that have been treated with combined doxycline 100mg capsule and topical metronidazole 0.75% gel. (p-value > 0.81), Table 6.

Table (6): Association between study groups and cutaneous side effects.

Cutaneous side effects	Study group		Total	p-value
	Group A No. (%)	Group B No. (%)		
No	19(95%)	18(90%)	37(92.5%)	0.81
Yes	1(5%)	2(10%)	3(7.5%)	
Total	20(100%)	20(100%)	40(100%)	

Discussion

Rosacea is a very common chronic condition with periodic remissions and relapses, women are more commonly affected than men especially in the age range 36-50 years age[2,12,13]. In our study the mean age of patients was (45.9± 11.21) years, this was comparable with previous studies in Thiboutot[6] and Breneman[14]. Rosacea is a chronic dermatosis proposed pathomechanisms include abnormal skin innate immune responses, increased colonization by demodex mite, and unusual neurovascular dysregulation is often difficult to be treated topical and oral antibiotics, vascular laser treatment and topical alpha adrenoreceptor agonists are used to treat rosacea[1,4,14]. We compared the clinical effectiveness of 20% salicylic acid chemical peel with combined oral conventional doxycycline 100 mg capsule and metronidazole 0.75% gel for the treatment of moderate roscacea. The use of doxycycline in rosacea either alone or in combination with other therapies has been proven in several clinical trials doxycycline has antimicrobial and also anti-inflammatory effect through deceasing matrix metalloproteinase, inhibition of leukocyte chemataxis and decreasing production of proinflamatory cytokines[2,10]. Metronidazole gel is a widely used FDA approved therapy for the treatment of rosacea the mechanism of action of metronidazole is unclear in the treatment of rosacea it's a broad spectrum antibiotic has antimicrobial and anti-inflammatory effects in vitro studies have shown that metronidazole inhibits release of reactive oxygen species from neutrophil that cause injury of tissue at sites of inflammation its anti-inflammatory effect in rosacea may be contributed to this antioxidant effect[1,15-18]. In our study combined conventional dose oral doxycycline and topical metronidazole showed that they are effective in the treatment of rosacea success in terms of a clear, or mild final result according to IGA score was obtained in 40% and 25% of patients respectively.

salicylic acid has lipophilic and anti-inflammatory properties, it concentrates in pilosebaceous follicle induce improving in inflammatory lesions of rosacea through its keratolytic effect serve to resurface the upper layers of the epidermis stimulate dermal fibroblasts indirectly to deposit more collagen, elastin, and glycosaminoglycans in the papillary dermis thus causes improvement in vascular structure of rosacea[7,19,20]. Regarding 20% salicylic acid chemical peel in our study success in term of clear or mild final result according to IGA score is obtained in 75% and 20% of patients respectively. The cure rate among the patients allocated to 20 % salicylic acid chemical peel group was 75% compared with 40% among those treated with combined oral doxycycline and topical metronidazole gel and this difference of 35% was statistically significant (p-value= 0.03). Because there is no previous study comparing 20% salicylic acid chemical peel with combined orally administered doxycycline 100mg capsule and topical metronidazole 0.75% gel in treating rosacea, comparison of our study was not applicable. There were no differences in cutaneous side effects such as burning, stinging and itching between the two treatment groups systemic adverse effects reported included epigastric burning in three patients in the doxycycline group. No significant association was found between duration of rosacea before treatment and response to treatment groups. Limitations of our study include small sample size and lack of follow up. Though our study is regarded as first comparative study using 20% salicylic acid chemical peel in comparison with combination orally administered doxycycline capsule and topical metronidazole 0.75% gel in the treatment of rosacea.

Conclusions

The findings in our study indicate 20% salicylic acid chemical peels are more efficacious in treating moderate rosacea than combined oral doxycycline 100 mg capsule and topical metronidazole 0.75% gel. Also, chemical peel is easier to use and has lesser cost.

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