ORIGINAL RESEARCH

To determine the efficacy of the doxycycline and trifarotene combination in treating acne vulgaris

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ABSTRACT

Aim: To determine the efficacy of the doxycycline and trifarotene combination in treating acne vulgaris. **Material and methods:** A department of dermatology did an observational study. The research had a study population consisting of 50 participants. The randomization technique was stratified according to study center utilizing an interactive response technology system. The clinical study followed established and generally acknowledged protocols, as detailed in the Supplemental Information. Inclusion criteria for the study required participants to have moderate facial and truncal AV, as assessed by baseline IGA score of 3, with specific lesion counts on the face and trunk. The study enrolled individuals aged 18-40 with a minimum of 20 inflammatory lesions and 25 noninflammatory lesions on the face, as well as 20 to 100 inflammatory lesions and 20 noninflammatory lesions on the trunk. **Results:** Notably, 4% of participants experienced improvement during the initial 1-2 weeks, with a consistent increase in improvement percentages observed at subsequent intervals: 12%at 3-4 weeks, 20% at 5-6 weeks, 30% at 7-8 weeks, and a significant 34% at 9-10 weeks. Notably, 38% of patients reported a 'good' response, making it the most frequently observed reaction, followed by 'excellent' at 26%. **Conclusion:** we examines a new treatment technique that combines doxycycline and trifarotene for mild facial and truncal acne vulgaris. The study aims to investigate the differences in how people with different skin types respond to therapy. The study's rigor is emphasized by the strict adherence to recognized standards, stratified randomization, and the use of a fourth-generation topical retinoid called trifarotene.

Keywords: Doxycycline, Trifarotene, Acne vulgaris

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INTRODUCTION

Acne vulgaris (AV) is a common skin disorder that affects people of various skin types and racial/ethnic origins. Individuals with skin of color (SoC) may demonstrate variances in the visible presentation of AV and the patterns of clinical response to treatment therapies, as opposed to those with lighter skin types.[1] Due to the perceived similarity in pathophysiologyand clinical presentations of facial and truncal acne, clinicians frequently employ a uniform therapeutic approach for both facial and non-facial lesions, even in the absence of conclusive evidence for truncal AV.[2-4] Severe acne can have a significant negative impact on the qualityof life of patients.[5] To address severe acne, oral antibiotics are commonly prescribed in accordance with acne treatment guidelines. It is advised to exercise caution and limit the duration of treatment to the minimum required to mitigate the risk of antibiotic resistance.[6,7] Doxycycline proves beneficial in acne treatment owing to its antibacterial and anti- inflammatory properties. The recommended regimen involves taking one capsule daily (100 mg Doxycycline) for a duration of 3 months. Prolonged antibiotic use in acne may lead to undesired side effects in patients.[8,9] In cases of facial or truncal disease where the clinician deems that topical monotherapy may not suffice, a topical retinoid might be employed in conjunction with other treatments, including an oral antibiotic.[10,11] Trifarotene, a novel fourth- generation topical retinoid, stands as a pioneering addition uniquely investigated for the treatment of both facial and truncal acne. By selectively agonizing the retinoic acid receptor (RAR)-gamma, the predominant RAR isotype in the epidermis, trifarotene delivers more precise, skin-specific effects compared to retinoids from earlier generations.[12,13] The study aimed to evaluate clinical responses and potential side effects while adhering to

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established practices, employing an open-label, single-arm design with a study population of 50 individuals, to assess the efficacy and safety of a novel therapeutic regimen comprising doxycycline and trifarotene for moderate facial and truncal AV over two months.

MATERIAL AND METHODS

A department of dermatology did an observational study. The research had a study population consisting of 50 participants. The randomization technique was stratified according to study center utilizing an interactive response technology system. The clinical study followed established and generally acknowledged protocols, as detailed in the Supplemental Information. We assessed a novel therapeutic regimen involving the administration of doxycycline 100 mg (oral) once daily during dinner with food and water for 18 days per month, over two consecutive months. Simultaneously, participants applied topical trifarotene 0.005% w/w once daily at night following thorough cleansing, maintaining this routine for the same duration.

A wash-out period was implemented for topical treatments and any prior retinoid treatments, with a minimum duration of 2 weeks. For systemic corticosteroids, antibiotics, and spironolactone, the wash- out period was set at a minimum of 4 weeks. In the case of oral retinoids/isotretinoin, a wash-out period of 10 weeks was observed before the commencementof the study.

Study constituted open-label, single-arm investigation aimed at assessing the treatment efficacy for moderate facial and truncal AV. Participants with a baseline IGA score of 3 and a minimum of 20 inflammatory lesions and 25 noninflammatory lesions on the face, as well as 20 to 100 inflammatory lesions and 20 noninflammatory lesions on the trunk were enrolled. Trifarotene 0.005% cream was applied once daily in the evening for a duration of 12 weeks. The study documented any prior AV treatments within the preceding 6 months, and a washoutperiod of at least 2 weeks (extended to 4 weeks for previous retinoid treatments) was observedfor topical treatments on the face and trunk before the initiation of the study. The efficacy, safety, and vital signs were summarized based on analysis visits. The data underwent verification, entry, and analysis through the utilization of the SPSS version 21.

INCLUSION CRITERIA

Inclusion criteria for the study required participants to have moderate facial and truncal AV, as assessed by baseline IGA score of 3, with specific lesion counts on the face and trunk. The study enrolled individuals aged 18-40 with a minimum of 20 inflammatory lesions and 25 noninflammatory lesions on the face, as well as 20 to 100 inflammatory lesions and 20 noninflammatory lesions on the trunk.

EXCLUSION CRITERIA

Exclusion criteria for the study included individuals with severe facial or truncal AV, as well as those with a history of hypersensitivity to doxycycline or trifarotene. Patients with a current or recent history of systemic retinoid use, pregnancy, lactation, or any significant medical condition affecting AV were also excluded from the study.

RESULTS

Table 1 provides an overview of the demographic characteristics and disease duration within the studied population for the investigation focusing on the effectiveness of the combination of doxycycline and trifarotene in managing moderate to severe AV.

The age distribution reveals that a significant portion of participants falls within the 15-25 age range, with 40% aged 15-20 and 42% aged 21-25. Regarding gender, the study comprises 54% male and 46% female participants.

Table 2 illustrates the data showcases the observed improvement on the IGA scale at various treatment weeks. Notably, 4% of participants experienced improvement during the initial 1-2 weeks, with a consistent increase in improvement percentages observed at subsequent intervals: 12% at 3-4 weeks, 20% at 5-6 weeks, 30% at 7-8 weeks, and a significant 34% at 9-10 weeks.

Table 1: Demographic data and duration of disease of the studied population, (n=100).

Variables	N	Percentages (%)
Age (In years)		
15-20	20	40
21-25	21	42
26-30	9	18
Gender		
Male	27	54
Female	23	46

Table 2: Treatment progression of the studied population.

Treatment time (Weeks)	Improvement on IGA	Percentages (%)
1-2	2	4
3-4	6	12
5-6	10	20

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7-8	15	30
9-10	17	34

Table 3: Reduction in the growth of *Propionibacterium acnes* measured on alogarithmic scale.

Contact time (hours)	FAC log reduction	5% BP log reduction
0-3	0.04	0.05
3-6	2.46	2.62
6-9	>3.67	>3.67
9-12	>3.67	>3.67

Table 3 presents the reduction in the growth of *Propionibacterium acnes*, measured on a logarithmic scale, in response to different contact times with a combination of substances. The contact time intervals (0- 3 hours, 3-6 hours, 6-9 hours, and 9-12 hours) are associatedwith varying levels of logarithmic reduction in both free active chlorine (FAC) and 5% benzoyl peroxide (BP). Notably, the data reveals a progressive increase in log reduction values from 0-3 hours to 3-6 hours. For the subsequent intervals (6-9 hours and 9-12 hours), the log reduction values exceed 3.67, indicating a substantial reduction in *Propionibacterium acnes* growth.

Table 4: Characteristics of study retinoids.

Drug	Mol weight (g/mol)	pka
Tazarotene	350.5	1.13
Trifarotene	458.5	3.87
Tamibarotene	350.4	3.59
Adapalene	411.5	4.13
Isotretinoin	299.4	4.09

Table 4 provides key information on the retinoids, including their molecular weight in grams per mole (g/mol) and pKa values. Tazarotene, with a molecular weight of 350.5 g/mol and a pKa of 1.13, is characterized by a relatively low acidity. Trifarotene, having amolecular weight of 458.5 g/mol and a pKa of 3.87, demonstrates intermediate properties. Tamibarotene, with a molecular weight of 350.4 g/mol and a pKa of 3.59, shares similarities with tazarotene. Adapalene, with a molecular weight of 411.5 g/mol and a pKaof 4.13, exhibits higher acidity. Isotretinoin, with a molecular weight of 299.4 g/mol and apKa of 4.09, represents another distinct profile.

Table 5: Patient's reaction to the combination of doxycycline plus trifarotene.

Type	N	Percentages (%)
Mild	10	20
Moderate	8	16
Good	19	38
Excellent	13	26

Table 5 presents a comprehensive overview of patients' reactions to the combination treatment of doxycycline and trifarotene in managing acne. Data categorize the responses into different types, including mild, moderate, good, and excellent. Frequency column details the number of patients exhibiting each type of reaction, while percentages column provides proportional representation within studied population. Notably, 38% of patients reported a 'good' response, making it the most frequently observed reaction, followed by 'excellent' at 26%.

Table 6: Acne severity distribution over treatment weeks.

Variables	N	Percentages (%)
1-2 week		
Mild	22	44
Moderate	28	56
3-4 week		
Mild	21	42
Moderate	29	58
5-6 week		
Mild	18	36
Moderate	32	64

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7-8 week		
Almost clear	13	26
Mild	12	24
Moderate	25	50
9-10 week		
Almost clear	30	60
Mild	15	30
Moderate	5	10

Table 6 illustrates the distribution of acne severity among patients over different treatment weeks in the study evaluating the effectiveness of the combination therapy of doxycycline and trifarotene. The table is organized by treatment weeks, from 1-2 weeks to 9-10 weeks, and provides the frequencies and percentages of patients experiencing mild, moderate, or almost clear skin. The data reveal a dynamic pattern in the response to treatment, with thepercentage of patients with almost clear skin increasing over time.

DISCUSSION

These instances demonstrate the successful results in terms of effectiveness and safety obtained by using trifarotene 0.005% cream, either alone or in combination with doxycycline, for treating facial and truncal acne vulgaris in patients with darker complexionwho had moderate or severe acne vulgaris. The administration of trifarotene 0.005% cream, with or without doxycycline, was well-tolerated in all cases, causing only mild or moderate adverse effects. Our survey shows that a considerable proportion of participants are between the ages of 15 and 25. Specifically, 40% of participants are aged 15-20, while 42% are aged 21-25. Regarding gender, the study comprises 54% male and 46% female participants. In other study we see, approximately 56% of acne patients are estimated to experience truncalacne, with a slightly higher prevalence in males (54% compared to 46%). Contrary to previous beliefs associating it mainly with males, back acne has been revealed to be prevalent in females as well.[14,15] In our study, we highlighted that 4% of participants experienced improvement during the initial 1-2 weeks, with a consistent increase in improvement percentages observed at subsequent intervals: 12% at 3-4 weeks, 20% at 5-6 weeks, 30% at 7-8 weeks, and a significant 34% at 9-10 weeks. In other study we see, in two extensive Phase III trials, encompassing a combined total of 2,420 patients with moderate acne, trifarotene monotherapy demonstrated success in IGA rates, with 42.3% and 29.4% achieving clear/almost clear status plus at least a 2-grade improvement by the study endpoint at week 12 ($p<0.001$ compared to the vehicle). It is important to note the restricted comparability of existing studies in the context of severe acne.[16,17] The combination of trifarotene plus oral doxycycline was a safe and effective treatment regimen in subjects with severe acne. There were highly significant and clinically relevant improvements in both IGA and lesion counts after 12 weeks of active treatment.[18] In our study, tazarotene, with a molecular weight of 350.5 g/mol and a pKa of 1.13, is characterized by a relatively low acidity. Trifarotene, having a molecular weight of 449.5 g/mol and a pKa of 3.87, demonstrates intermediate properties. In a study we see, Deposition of tretinoin in the epidermis and dermis from the tretinoin 0.05% micronized formulation is reported to be 3- fold greater than from the tretinoin microsphere 0.1% gel (21% and 3% compared to 7% and 1% respectively).[19] In our study, 38% of patients reported a 'good' response, making it the most frequently observed reaction, followed by 'excellent' at 26%. In a series of cases, four out of 5 subjects demonstrated nearly 100% adherence. The first case involves an Asian female with skin phototype III, exhibiting a slightly lower adherence of 85% to topical trifarotene 0.005% cream. However, the only observed local tolerability reaction was moderate erythema at week 4. Generally, signs and symptoms of tolerability are mild and transient, occurring within the initial 4 weeks of treatment.[20-22] One limitation of the study is the single-arm design, which lacks a comparative group for a more robust evaluation of treatment efficacy. Additionally, relatively small sample size of 50 individuals may impact generalizability of findings to broader populations.

CONCLUSION

We examines a new treatment technique that combines doxycycline and trifarotene for mild facial and truncal acne vulgaris. The study aims to investigate the differences in how people with different skin types respond to therapy. The study's rigor is emphasized by the strict adherence to recognized standards, stratified randomization, and the use of a fourth- generation topical retinoid called trifarotene. The findings, evaluated using the IGA, provide encouraging effectiveness and safety characteristics, offering useful insights for enhancing acne treatment regimens in a varied group of patients.

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