

EFFICACY OF TOPICAL METFORMIN VERSUS TOPICAL CLINDAMYCIN IN THE TREATMENT OF ACNE VULGARIS: A SPLIT-FACE STUDY

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ABSTRACT

Background: Acne vulgaris is a common inflammatory dermatosis that affects adolescents and adults, often requiring effective topical therapies. Objective: To evaluate and compare the efficacy of 30% topical metformin cream with 2% topical clindamycin in the management of mild to moderate acne vulgaris using a split-face study design. Methods: The quasi-experimental study was performed in the Department of Dermatology, Ghurki Trust Teaching Hospital, Lahore. Sixty subjects (120 facial sides) with a mean age of 22.14 ± 5.48 years (age range 14–36 years), having mild to moderate facial acne, were selected. The patients used 30% metformin cream on the right cheek and 2% topical clindamycin on the left cheek for 12 weeks and were followed for 16 weeks. The lesion count (total, inflammatory, and non-inflammatory) was recorded at baseline, week 4, week 8, week 12, and week 16. Both interventions showed significant efficacy against acne lesions; however, metformin exhibited higher efficacy, especially for inflammatory lesions. By week 12, metformin significantly outperformed clindamycin in reducing inflammatory lesions (5.13 ± 2.46 vs. 6.89 ± 3.23 ; $p < 0.001$) and total lesion counts (14.09 ± 6.21 vs. 15.87 ± 6.73 ; $p = 0.017$). At week 16, metformin maintained superior improvement, with lower total lesion counts (8.42 ± 5.38 vs. 10.82 ± 5.48 ; $p < 0.001$), inflammatory lesions (2.60 ± 1.66 vs. 4.58 ± 2.69 ; $p < 0.001$), and non-inflammatory lesions (5.93 ± 4.79 vs. 6.82 ± 5.09 ; $p = 0.011$). The Global Acne Assessment Score (GAAS) was also in favor of metformin, as 60.0% of metformin-treated sides obtained "Almost clear" status after 12 weeks, while 18.3% of sides treated with clindamycin did. After 16 weeks, 96.7% of metformin-treated sides versus 83.3% of sides treated with clindamycin had obtained "Almost clear" status, which shows superior and sustained effectiveness of metformin. Conclusion: It is concluded that topical 30% metformin cream was more effective than topical 2% clindamycin in lowering lesion numbers and GAAS scores.

KEYWORDS: Acne vulgaris, Metformin, Clindamycin, Split-face study, Inflammatory lesions, GAAS score.

INTRODUCTION

Acne vulgaris is one of the most common chronic inflammatory skin diseases worldwide, affecting about 80–90% of adolescents and a large proportion of adults. Acne is a common dermatological condition that can have serious adverse psychological, self-esteem, and social functioning implications. Hence, there is a need to integrate viable and affordable treatment interventions into the social structure as a societal health concern [1]. The disease arises due to the multifactorial interaction between increased sebum secretion, follicular hyperkeratinization, Cutibacterium acnes proliferation, and increased inflammation. Contemporary first-line therapy options are the use of a regimen of topical retinoids, benzoyl peroxide, and antibiotics such as clindamycin [2]. However, there has been an issue of overreliance on antibiotics in terms of antibiotic resistance, decreased effectiveness over time, and disturbance in skin microbial balance. This makes it necessary for newer and safer alternatives without antibiotics to be considered. Acne vulgaris is a chronic inflammatory skin disease that affects hair follicles and sebaceous glands [3]. The major features of this skin disease are comedones, papules, pustules, nodules, and scars

[4]. It is estimated that about 90% of adolescents develop acne, and over half of them persist in adulthood [5]. The disease may cause irrevocable scarring, which is very ruinous to emotional well-being and psychosocial development [6]. Lesions are most usually present in the face and trunk [7]. The pathogenesis of acne vulgaris integrates four core processes, including amplified sebum production, excess secretion of keratin in hair follicles, inflammation, and *Propionibacterium acnes* colonization [5]. Moreover, personal traits, environmental conditions, and genetic susceptibility might have an important impact on disease development and progression. The processes cause the impairment of the normal operation of the pilosebaceous unit, leading to the formation of microcomedones, which then form comedones and inflammatory lesions [6]. Topical therapy is usually used to treat mild acne. Isotretinoin, tetracycline, doxycycline, and hormonal treatment like combined oral contraceptives and antiandrogens are only used in moderate and severe or nodulocystic disease. Non-inflammatory or mildly inflammatory acne can be treated with the help of light-based or laser therapies [8]. Recent research has pointed to insulin resistance as another cause of acne pathogenesis. Insulin and IGF-1 boost the androgen production and lower the sex hormone-binding globulin hepatic synthesis. Hyperinsulinemia raises the IGF-1 and lowers the IGF binding protein-3, which directly interferes with the growth and death of keratinocytes. Such hormonal changes can activate the factors associated with the development of acne, such as androgens, growth hormone, and glucocorticoids [9]. Metformin is a biguanide that is usually prescribed to manage diabetes mellitus and induces a decrease in IGF-1 levels and enhances insulin resistance. By so doing, metformin can be of therapeutic use in the treatment of acne [10]. EL-Komy et al. examined the success of topical metformin gel in a split-face trial that included 27 female patients. The study participants rubbed metformin gel on one side of the face and a placebo on the other side every night for 12 weeks. The number of lesions was recorded at the baseline, after every four weeks, and at one-month follow-up. The metformin-treated group became considerably better in the inflammatory and non-inflammatory lesions [11,12]. This is a split-face trial to compare topical metformin and topical clindamycin in patients having *acnes vulgaris*. The design permits direct within-patient comparison, reducing inter-individual variability and improving the reliability of outcome assessment. The efficacy of clindamycin on the treatment of *Propionibacterium acnes* has steadily decreased over the last 40 years [13].

Objective

The objective pertains to evaluating the efficacy of 30% metformin cream and 2% topical clindamycin for the management of acne in a split face pattern.

Methodology

This quasi-experimental study design was conducted at the Department of Dermatology, Ghurki Trust Teaching Hospital, Lahore, from March 2026 to July 2026. A sample size of 60 facial sides (30 in each group) was calculated using a 95% confidence interval and taking the expected mean decrease in inflammatory lesion count as 7.03 ± 3.91 in the metformin side (10) versus 2.63 ± 2.05 in the clindamycin side (13). A nonprobability consecutive sampling method was used.

Inclusion Criteria

1. Individuals who presented with mild to moderate facial acne, including inflammatory and non-inflammatory lesions.
2. Participants aged 12 to 45 years.

Exclusion Criteria

1. Patients with nodulocystic (severe) acne.
2. Patients who had used topical or systemic acne therapy during the previous month.
3. Patients with a history of micro needling, chemical peeling, or laser procedures within the last six months.
4. Patients with known hypersensitivity to metformin or clindamycin.

Data Collection

Patient recruitment was started after approval from the Institutional Ethics Committee. A total of 60 facial sides (30 patients in each group) with mild to moderate acne were approached with a written informed consent, and all signed the consent. All participants were given a structured proforma that contained details of demography and clinical characteristics. Before the treatment, the severity of acne was measured with the Global Acnes Assessment Score, and standardized clinical photographs were taken. The subjects used the treatments given at 12 weeks and were followed up to 16 weeks. The same clinical scoring system and photographic documentation were used to evaluate treatment effectiveness at baseline and 4, 8, 12, and 16 weeks in order to compare them with each other in standard ways.

Data Analysis

The entry and analysis of data were done with SPSS version 27.0. The presentation of the data was done using descriptive statistics. Qualitative variables (gender, treatment response, patient satisfaction, and side effects) were calculated in terms of frequencies and percentages. Mean and standard deviation were determined in the case of quantitative variables (age, duration of illness, GAAS scores of inflammatory, non-inflammatory, and total lesions). Data were stratified in terms of age, gender, and length of illness. A post-stratification paired t-test was used to compare the IGA score at baseline and the end of the final endpoint. The chi-square test was used to measure the efficacy of treatment, and a p-value was calculated to measure statistical significance.

RESULTS

Table 1: Descriptive Statistics of Study Participants (N = 60)

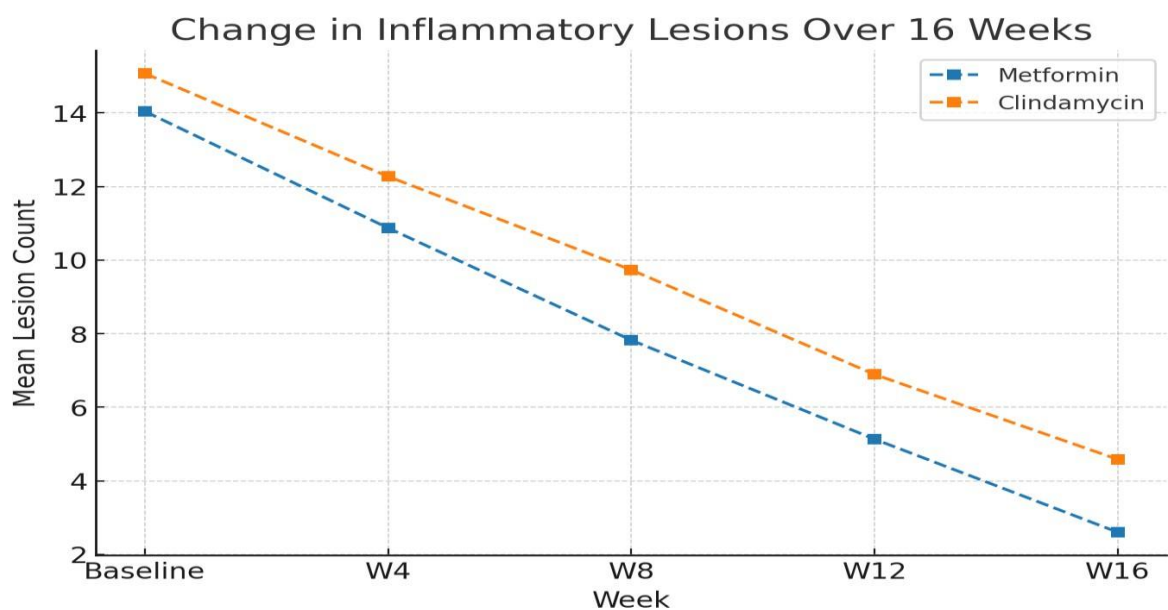
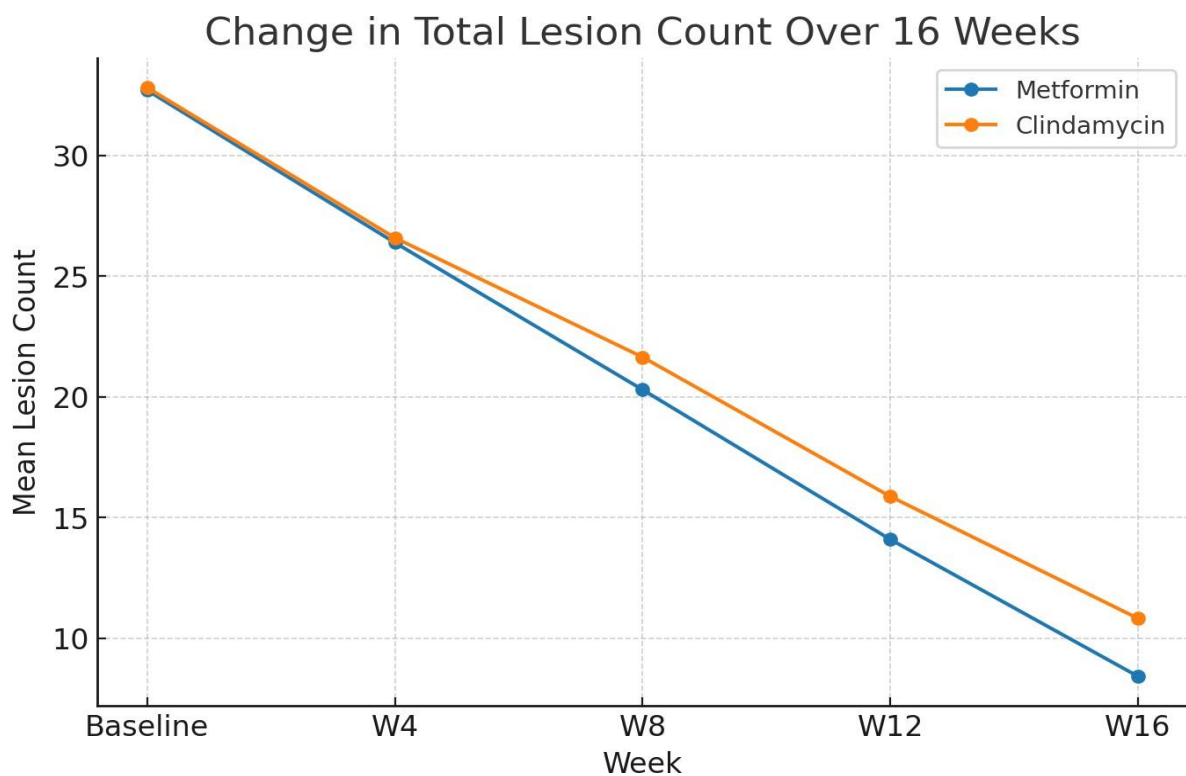
Variable	Category / Value	n	%	Mean $\pm$ SD	Min–Max
Age (years)		60	–	22.14 $\pm$ 5.48	14 – 36
Gender	Male	9	15.0		
	Female	51	85.0		
Marital Status	Married	14	23.3		
	Unmarried	46	76.7		
Duration of Acne	6–12 months	34	56.7		
	>12 months	26	43.3		
Previous Topical Agent Use	Azelaic acid	2	3.3		
	Azithromycin	1	1.7		
	Benzoyl Peroxide	4	6.7		
	Clindamycin	23	38.3		
	None	30	50.0		
Previous Systemic Treatment	Macrolides	5	8.3		
	None	55	91.7		
Previous Retinol Use	Yes	4	6.7		
	No	56	93.3		

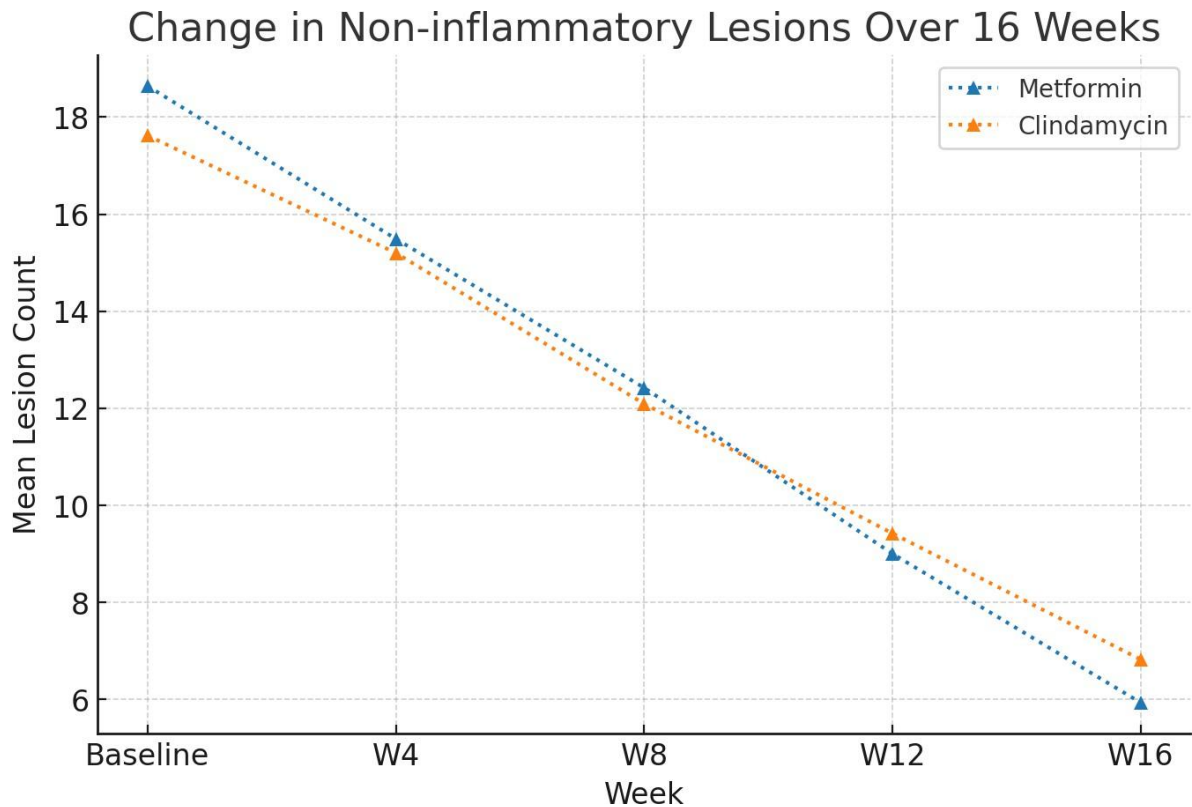
The study included 60 participants with a mean age of 22.14 ± 5.48 years (range 14–36 years). Most participants were female (85.0%) and unmarried (76.7%). More than half of the participants (56.7%) had acne duration between 6 and 12 months, while 43.3% had acne for more than one year. Half of the participants had no previous topical treatment history, while clindamycin was the most commonly used previous topical agent (38.3%). Only a small proportion had previous systemic treatment (8.3%) or retinol use (6.7%). Overall, the study population was predominantly young females with mild to moderate acne and limited prior exposure to systemic therapies.

Table 2: Total number of lesions before treatment and at every follow-up visit

Week	Lesion	Right side (Metformin) mean $\pm$ SD	Left side (Clindamycin) mean $\pm$ SD	(Topical) p value	Significance
W0 Baseline	Total Lesion Count	32.69 $\pm$ 8.87	32.80 $\pm$ 9.82	0.705	NS
	Inflammatory lesions	14.04 $\pm$ 6.50	15.07 $\pm$ 5.10	0.053	NS
	Non-Inflammatory lesions	18.64 $\pm$ 7.10	17.62 $\pm$ 6.85	0.421	NS
W4	Total Lesion Count	26.38 $\pm$ 7.90	26.58 $\pm$ 7.76	0.735	NS
	Inflammatory lesions	10.87 $\pm$ 4.84	12.27 $\pm$ 4.10	0.015	S
	Non-Inflammatory lesions	15.49 $\pm$ 5.81	15.20 $\pm$ 6.11	0.789	NS
W8	Total Lesion Count	20.29 $\pm$ 7.17	21.64 $\pm$ 7.89	0.117	NS
	Inflammatory lesions	7.82 $\pm$ 3.53	9.73 $\pm$ 3.58	<0.001	S
	Non-Inflammatory lesions	12.42 $\pm$ 5.52	12.09 $\pm$ 6.08	0.543	NS

W12 End	Total Count	Lesion	14.09 ± 6.21	15.87 ± 6.73	0.017	S
	Inflammatory lesions		5.13 ± 2.46	6.89 ± 3.23	<0.001	S
	Non-Inflammatory lesions		9.00 ± 5.36	9.42 ± 5.47	0.494	NS
W16 Follow-up	Total Count	Lesion	8.42 ± 5.38	10.82 ± 5.48	<0.001	S
	Inflammatory lesions		2.60 ± 1.66	4.58 ± 2.69	<0.001	S
	Non-Inflammatory lesions		5.93 ± 4.79	6.82 ± 5.09	0.011	S





At baseline (week 0), there was no statistically significant difference between the metformin-treated and clindamycin-treated sides for total, inflammatory, or non-inflammatory lesions ($p > 0.05$), confirming equal comparability at study initiation.

By week 4, a significant reduction in inflammatory lesions was observed on the metformin side compared to clindamycin ($p = 0.015$), though differences in total and non-inflammatory lesions were not significant. At week 8, metformin continued to show a significantly greater reduction in inflammatory lesions ($p < 0.001$), though total and non-inflammatory lesion counts remained statistically comparable. By week 12, metformin demonstrated superiority in both total lesion reduction ($p = 0.017$) and inflammatory lesions ($p < 0.001$), with no significant difference in non-inflammatory lesions. At week 16 follow-up, metformin maintained a significant advantage across all lesion categories: total ($p < 0.001$), inflammatory ($p < 0.001$), and non-inflammatory lesions ($p = 0.011$). This shows that metformin not only provided faster and stronger improvement in inflammatory lesions but also achieved sustained efficacy and broader benefits over time compared to clindamycin.

Table 3: Comparing the improvement of inflammatory lesions (papules, pustules, nodules) to non-inflammatory lesions (comedones) on Metformin and Topical Clindamycin sides

Improve ment	Inflammato ry lesions (Metformin) mean $\pm$ SD	Non- inflammato ry lesions (Metformin) mean $\pm$ SD	p-value (Metformi n)	Inflammato ry lesions (Clindamyci n) mean $\pm$ SD	Non- inflammato ry lesions (Clindamyci n) mean $\pm$ SD	p-value (Clindamyci n)
W12	-8.91 $\pm$ 6.50	-9.64 $\pm$ 7.10	0.494	-8.18 $\pm$ 5.10	-8.20 $\pm$ 6.85	0.494
W16	-11.44 $\pm$ 1.66	-12.71 $\pm$ 4.79	0.011	-10.49 $\pm$ 2.69	-10.80 $\pm$ 5.09	0.011

At week 12, there was a similar improvement in inflammatory and non-inflammatory lesions on both treatment sides ($p = 0.494$), suggesting early parallel benefits. However, by week 16, a statistically significant difference was noted ($p = 0.011$), with the metformin-treated side showing more improvement in both types of lesions. This indicates that both treatments had similar initial improvement in lesions, but metformin had more durable and sustained long-term improvement.

Table 4: Global Acne Assessment Score (GAAS) Severity Distribution

Time Point	Treatment	Almost Clear n (%)	Mild n (%)	Moderate n (%)
Baseline	Metformin	0 (0%)	8 (13.3%)	52 (86.7%)
	Clindamycin	0 (0%)	7 (11.7%)	53 (88.3%)
Week 4	Metformin	0 (0%)	24 (40.0%)	36 (60.0%)
	Clindamycin	0 (0%)	12 (20.0%)	48 (80.0%)
Week 8	Metformin	10 (16.7%)	38 (63.3%)	12 (20.0%)
	Clindamycin	7 (11.7%)	33 (55.0%)	20 (33.3%)
Week 12	Metformin	36 (60.0%)	24 (40.0%)	0 (0%)
	Clindamycin	11 (18.3%)	49 (81.7%)	0 (0%)
Week 16	Metformin	58 (96.7%)	2 (3.3%)	0 (0%)
	Clindamycin	50 (83.3%)	10 (16.7%)	0 (0%)

The patients in both groups had moderate severity levels of GAAS at baseline, which indicates that both groups had similar conditions before the treatment began. In terms of follow-up assessment of severity, metformin group showed early and greater improvement in GAAS severity compared to clindamycin. At 8 weeks of the study, more of the metformin group patients were categorized as “Almost Clear.” At 12 weeks, 60% of the patients from the metformin group were “Almost Clear,” while only 18.3% in the clindamycin group fell into the same category. At 16 weeks, all but 3.3% of metformin group patients were “Almost Clear,” while the clindamycin group saw 83.3% in the “Almost Clear” category.

Discussion

In this split face study, both 30% topical metformin and 2% topical clindamycin showed better improvement in acne vulgaris after 12 weeks of treatment, and at 16 weeks after treatment, metformin had more reductions in inflammatory and total lesions. The split-face design had internal validity because both sides had a similar distribution of lesions at the baseline. Week 4 demonstrated a clear difference, with metformin demonstrating a much greater reduction in inflammatory lesions. This early sensitivity suggested that the anti-inflammatory and anti-lipogenic effects of metformin would be of clinical relevance after the first month of therapy. At week 8 and week 12, the greater metformin was superior because the reduction of inflammatory lesions was significantly greater than that of clindamycin, and the count of total lesions also showed improved results [14]. Such findings are consistent with the prior studies that suggest that metformin lowers sebum secretion, alters the activity of keratinocytes, and enhances the mechanisms of insulin-related pathways that directly address various aspects of the acne pathogenesis. By contrast, clindamycin is mainly an antibacterial and anti-inflammatory agent, and this effect is usually restricted by the emergence of bacterial resistance. This analysis was an indication of the global tendency of the decreasing efficacy of clindamycin due to the fact that it showed a lower upward trend compared to metformin during the treatment process [15]. At week 16, metformin was still showing sustained post-treatment improvement, and inflammatory lesions were almost non-existent. The number of lesions after the follow-ups revealed that there was more stable control in the long run on the metformin side, whereas clindamycin had indicated further improvement, but at a lower rate. The fact that metformin can alter the underlying metabolic and inflammatory processes instead of acting solely through antimicrobial action, also adds to the idea that the drug can be beneficial in the long-term. These were supported by scores of GAAS severity [16]. By week 12, most of the patients under Metformin therapy had changed their baseline moderate acne to almost clear, and by week 16, most of them had been declared as almost clear. Clindamycin improved, although at both time points an even smaller number of patients were in the almost clear category [17]. These tendencies indicate that metformin does not just help to decrease the number of lesions more efficiently, but also helps to achieve a faster transition to lower severity grades. In general, the research offers substantial evidence to suggest that topical metformin may be at the same level or even more effective than topical clindamycin in the treatment process of mild to moderate acne vulgaris [18]. The inflammatory lesions decrease, the improved long-term control, and the higher percentage of metformin turned to lower GAAS grades indicate the potential value of metformin as a valuable nonantibiotic therapeutic option that is particularly significant in light of the increasing antibiotic

resistance [19,20]. The results prove the necessity to introduce topical metformin into clinical practice and to continue the investigation with the help of larger randomized controlled trials. There were a number of limitations associated with this study that ought to be taken into consideration when interpreting the results. The sample size was also considered to be relatively small, which might not be generalizable to the larger populations. Since the study was a single-center study carried out in an outpatient dermatological department, the findings might not adequately reflect patients in other clinical and geographic areas. Although the quasi-experimental split-face study is effective in minimizing inter-individual variability, it still can be affected by local skin differences, variation in patient adherence, or other environmental factors inducing variations on one side of the face over the other.

CONCLUSION

It is concluded that topical 30% metformin cream demonstrated superior efficacy compared to 2% topical clindamycin in the treatment of mild to moderate acne vulgaris using a split-face design. Metformin produced greater reductions in inflammatory and total lesion counts, showed earlier clinical improvement, and achieved a higher proportion of “almost clear” GAAS severity scores by both week 12 and week 16. In contrast, clindamycin showed improvement but with comparatively slower and less pronounced reductions. The sustained post-treatment improvement on the metformin side further supports its therapeutic advantage.

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