

EFFICACY OF ORAL METFORMIN VERSUS ORAL DOXYCYCLINE IN TREATING ACNE VULGARIS

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ABSTRACT

Background: Acne vulgaris is a common inflammatory disorder of the pilosebaceous unit that may cause scarring and psychological distress.

Objective: To compare the efficacy of oral metformin with oral doxycycline in patients with moderate-to-severe acne vulgaris.

Methods: This randomized controlled trial was conducted in the Outpatient Department of Dermatology, Lahore Medical and Dental College/Ghurki Trust Teaching Hospital, Lahore. A total of 96 patients aged 12–40 years were enrolled through non-probability consecutive sampling and randomly allocated into two equal groups. Group A received oral metformin 500 mg twice daily, while Group B received oral doxycycline 100 mg once daily for 12 weeks.

Results: The mean total lesion count in the metformin group decreased from 35.20 ± 11.73 at baseline to 21.96 ± 8.93 at 8 weeks and 14.24 ± 7.69 at 12 weeks. In the doxycycline group, it declined from 38.40 ± 11.35 to 25.92 ± 9.62 and 15.84 ± 8.62 , respectively. Significant reductions in total, inflammatory, and non-inflammatory lesion counts were observed within both groups ($p < 0.001$). At 12 weeks, no significant differences were found between the groups in total lesion count ($p = 0.502$), inflammatory lesion count ($p = 0.639$), or non-inflammatory lesion count ($p = 0.070$).

Conclusion: Both oral metformin and oral doxycycline significantly reduced acne lesion counts and severity over 12 weeks, with no significant difference in final clinical outcomes.

KEYWORDS: Acne vulgaris, metformin, doxycycline, total lesion count, inflammatory lesions, Patients

INTRODUCTION

Acne vulgaris is a chronic, inflammatory disorder of the pilosebaceous unit. It is characterized primarily by a plugging of the follicles and raised inflammatory lesions such as papules, pustules, nodules, and scars (1). Almost half of the teens who develop acne go on to have acne as adults. Some 70-80% of adolescents suffer from acne (2). Acne can be a chronic condition for some patients, with a long-term psychological, social and physical impact. The formation of acne is initiated by a series of events that take place in the pilosebaceous unit (3), which include increased production of sebum and changes in the composition of the fatty acids produced in the sebum. Fluctuations in hormones, increased follicular keratinization (4) and alterations in both innate and adaptive immune-system responses are observed. These are coupled processes which prevent the normal functioning of the pilosebaceous unit and damage the follicles. This causes an excess of sebum, fatty acids and lipids in the layers of the skin, resulting in inflammatory and non-inflammatory lesions. Reducing scarring and psychological effects, as well as providing the patient with the best possible appearance, are the main objectives of treatment. The main

aims of treatment are to stop the formation of follicular hyperkeratosis and to lower the amount of fatty acids and sebum released, which will result in fewer comedones. There are many methods of topical and systemic treatment for acne vulgaris. Common treatments for mild acne are topical benzoyl peroxide, retinoids, salicylic acid, azaleic acid, clindamycin and 5% dapsone (5). For moderate to severe acne, the systemic treatment options include isotretinoin, tetracycline, doxycycline, metformin, and hormone therapy in the form of oral contraceptive and/or antiandrogen medications (6). Inflammatory or mild inflammatory acne can also be treated with lasers and light therapy. New research has indicated that there is a strong link between insulin resistance and acne. Hyperinsulinemia, or elevated blood insulin levels, upregulate the levels of insulin-like growth factor-1 (IGF-1) in the blood and decreases insulin-like growth factor-binding protein 3 (IGFBP3) (7). This directly influences keratinocyte growth and death, and can stimulate the release of growth hormone, glucocorticoids and androgens related to the development of acne.

Metformin is a biguanide that is widely used for treatment of diabetes mellitus (8). It works by decreasing IGF-1. For this reason, it can be applied topically or orally, and may prove to be useful for the treatment of acne vulgaris (9). Oral doxycycline is strongly recommended by key dermatology organizations and guideline bodies as a first-line, systemic option due to its ability to inhibit *Cutibacterium acnes* and reduce inflammation. Yet, oral metformin is not part of the current guidelines for treating acne. New studies are examining its beneficial effects in treating moderate to severe acne, especially when the underlying cause of the acne is insulin resistance and inflammation. Sadati et al. also made a comparison study with 40 participants. The severity of the disease was assessed using standardized tools like the Global Acne Grading System and Total Lesion Count at baseline and at the 2-month and 4-month follow-up visits. The mean score of GAGS was 24.10 ± 6.93 in the metformin group and 29.65 ± 11.72 in the doxycycline group ($p=0.076$). After one month of treatment, both groups showed improvement with mean GAGS scores of 19.30 ± 5.11 and 15.35 ± 7.61 for the metformin group and doxycycline group respectively, but this was not statistically significant ($p=0.061$). No meaningful difference was seen between the metformin and doxycycline groups ($p=0.634$) at the end of the study, as further reductions were observed in both groups with mean GAGS scores of 13.45 ± 4.22 for metformin and 14.70 ± 10.84 for doxycycline. There was no significant difference in the overall reduction in GAGS score from baseline between the metformin group (the mean score change was -10.65 ± 6.29) and the doxycycline group (the mean score change was -14.95 ± 12.89 , $p=0.188$). The baseline TLC value was similar in the groups: 40.15 ± 23.98 in patients under metformin and 47.50 ± 36.86 in patients under doxycycline ($p=0.459$). At the one-month evaluation, TLC decreased to 27.10 ± 19.39 and 21.05 ± 15.20 , respectively ($p=0.279$). Lesion counts also decreased at the end of the follow-up period in the metformin group (14.10 ± 10.57) and the doxycycline group (14.30 ± 13.90 ; $P=0.959$). The average reduction in TLC was -26.05 ± 16.57 for metformin and -33.20 ± 29.81 for doxycycline ($p=0.354$) (10). Amin et al performed a study and found the efficacy of oral doxycycline to be 64.2% (12). However, Robinson et al. found that the effectiveness of metformin therapy was 71.4% (11).

OBJECTIVE

To compare the efficacy of oral metformin versus oral doxycycline in treating moderate-to-severe acne vulgaris.

METHODOLOGY

This Randomized controlled trial was conducted in the outpatient Department of Dermatology, Lahore Medical and Dental College, Ghurki Trust Teaching Hospital, Lahore from March 2026 to June 2026. A sample size calculation was performed for comparing two population proportions at a 5% level of significance, 80% statistical power and 1:1 allocation ratio. The number of patients required was based on expected efficacy of 86% for oral metformin and 64.2% for oral doxycycline, and was calculated to be 96 per group with 48 participants in each arm of the study. Non-probability consecutive sampling was used for patients' enrollment. Eligible participants were then randomly assigned to treatment group by the lottery method. Both males and females, between 12-40 years of age, whose acne vulgaris was clinically diagnosed as moderate to severe with facial involvement were included. Patients with inflammatory or non-inflammatory acne lesions (open and closed comedones, papules, pustules, nodules, or cysts) were eligible for participation. Patients who had a known allergy or sensitivity to Metformin or Doxycycline were not included. Other exclusion criteria included those undergoing an acne therapy of either systemic or topical origin within the past month before the study. The study did not include pregnant and lactating females.

Data Collection

The study began upon approval from the Hospital Institutional Review Board. All adult participants gave informed written consent. Participants under the age of 18 were accompanied by a parent/legal guardian who provided written consent, and the participant provided assent. Patients were screened to see if they met the criteria for moderate-to-severe acne vulgaris at the Dermatology Outpatient Department. An extensive history was taken, which included age, sex, marital status, length of time with acne, history of therapy received, other medical conditions, and current medications. A complete dermatological examination was carried out, and BMI was calculated. The Global Acne Grading System and Total Lesion Count were used to evaluate acne severity at baseline. All pictures were taken under identical lighting, distance, camera position and facial orientation conditions to enable reliable comparison at follow-up. The patients who met the inclusion criteria were randomized into two groups of equal size. Patients who satisfied the inclusion criteria were randomly divided into two equal groups. For 12 weeks, Group A was treated with oral metformin 500mg twice a day, and Group B was

treated with oral doxycycline 100mg once a day for 12 weeks. Participants were instructed on the use and adherence with medications, potential side effects, and the need for regular follow-up appointments. Patients were re-evaluated after 4 and 12 weeks. GAGS score, TLC, treatment adherence and adverse effects were documented on a pre-designed data collection proforma at every visit. The primary outcome was treatment efficacy at 12 weeks. The efficacy was evaluated by the decrease in GAGS score and Total Lesion Count from baseline. A clinically significant response was considered as severe to moderate or moderate to mild acne. Secondary outcomes included mean decrease in GAGS score, mean decrease in TLC, adherence to treatment, and frequency of adverse effects in each treatment group.

Data Analysis

The data were entered and analysed in SPSS version 27.0. Numeric variables such as age, Bmi, duration of acne, GAGS score and Total Lesion Count were reported as mean $\pm$ s.d or median (iqr), as appropriate. Qualitative variables such as sex, marital status, acne and treatment effects, and side effects were represented in frequencies and percentages. For quantitative data, the independent-samples t-test was used for comparisons between the two groups and the paired-samples t-test was used for within-group comparisons from baseline to 12 weeks. Between-group comparisons for categorical outcomes (including treatment efficacy and side effects) were based on the chi-square test or Fisher's exact test. Possible effect modifiers were controlled for by stratifying the data based on age, sex, marital status, body mass index, baseline acne severity, and duration of the disease. An appropriate statistical test was used to perform post stratification comparisons. A p-value <0.05 was considered statistically significant.

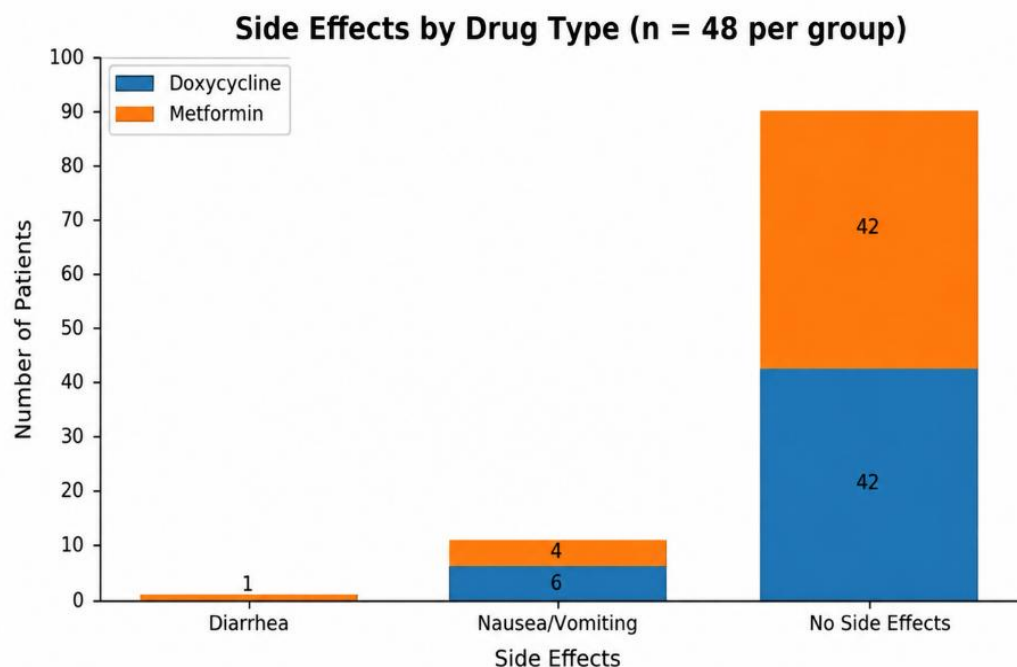
RESULTS

The Gender distribution was similar in both the groups with majority of the subjects being female in the Metformin group (77.1%) and Doxycycline group (70.8%) ($p = 0.485$). There was a significant difference between the marital status ($p < 0.001$) with higher proportion of married participants in Metformin group (33.3%) than in the Doxycycline group (2.1%). There was no significant difference in smoking status between groups ($p = 0.273$): 12.5% of patients in the Metformin group and 20.8% of patients in the Doxycycline group reported having smoked. Regarding duration of acne, in both groups, the majority of patients had acne of more than 12 months duration (56.3% in the Metformin group, 52.1% in the Doxycycline group) with no statistically significant difference between the groups ($p = 0.083$). As far as topical treatment history, Benzoyl Peroxide use was only reported in the Metformin group (12.5%), and Clindamycin use was more common in the Metformin group (33.3%) than the Doxycycline group (20.8%) with statistically significant difference ($p = 0.008$). Likewise, there was only one group of patients who used tetracycline systemically before randomization: Metformin (12.5%), while the Doxycycline group reported no prior systemic use of tetracycline, which was statistically significant ($p = 0.011$). Retinol use was also reported in the Metformin group only (12.5%), but no one in the Doxycycline group reported using retinol, and this difference was statistically significant ($p = 0.011$).

Table 1: Patient Characteristics and Drug Type (48 per group; N=96)

Variable	Categories	Metformin (n, %)	Doxycycline (n, %)	p-value
Gender	Male	11 (22.9%)	14 (29.2%)	0.485
	Female	37 (77.1%)	34 (70.8%)	
Marital Status	Yes	16 (33.3%)	1 (2.1%)	<.001
	No	32 (66.7%)	47 (97.9%)	
Smoking Status	Yes	6 (12.5%)	10 (20.8%)	0.273
	No	42 (87.5%)	38 (79.2%)	
Duration	3–6 months	4 (8.3%)	0 (0.0%)	0.083
	6–12 months	17 (35.4%)	23 (47.9%)	
	>12 months	27 (56.3%)	25 (52.1%)	
Topical Agent	Benzoyl Peroxide	6 (12.5%)	0 (0.0%)	0.008
	Clindamycin	16 (33.3%)	10 (20.8%)	
	N/A	26 (54.2%)	38 (79.2%)	
Systemic	Tetracycline	6 (12.5%)	0 (0.0%)	0.011
	N/A	42 (87.5%)	48 (100.0%)	

Variable	Categories	Metformin (n, %)	Doxycycline (n, %)	p-value
Retinol	Yes	6 (12.5%)	0 (0.0%)	0.011
	No	42 (87.5%)	48 (100.0%)	



The figure demonstrates that both treatment groups were generally well tolerated, with the majority of patients in each group reporting no adverse effects. In the Metformin group (n=48), 42 patients (87.5%) experienced no side effects, while 4 patients (8.3%) reported nausea or vomiting and 1 patient (2.1%) reported diarrhea. In the Doxycycline group (n=48), 42 patients (87.5%) had no side effects, 6 patients (12.5%) reported nausea or vomiting, and no cases of diarrhea were observed.

Table 2: Lesion Count Results by Drug

Variable	Mean ± SD	Min	Max	Mean Rank (Metformin)	Mean Rank (Doxycyclin)	p-value
TLC_BASELINE	36.80 ± 11.54	18	64	23.54	27.46	0.341
TLC_8	23.94 ± 9.40	8	57	22.54	28.46	0.150
TLC_12	15.04 ± 8.12	2	46	24.12	26.88	0.502
INF_BASELINE	16.64 ± 8.82	4	37	27.56	23.44	0.315
INF_8	9.24 ± 6.13	0	30	26.18	24.82	0.740
INF_12	4.86 ± 4.65	0	22	26.46	24.54	0.639
N-INF_BASE	20.24 ± 9.36	2	43	20.18	30.82	0.010
N-INF_8	14.58 ± 7.03	2	30	20.54	30.46	0.015
N-INF_12	10.22 ± 5.72	1	26	21.78	29.22	0.070

*TLC=Total Lesion Count

*INF= Inflammatory Lesion

*N-INF= Non Inflammatory Lesion

At baseline, the mean Total Lesion Count (TLC) was slightly higher in the Doxycycline group (mean rank = 27.46) compared to the Metformin group (mean rank = 23.54). Still, the difference was not statistically significant

($p = 0.341$). Similar nonsignificant differences persisted at 8 weeks ($p = 0.150$) and 12 weeks ($p = 0.502$), although both groups showed a marked reduction in mean TLC over time (from 36.80 ± 11.54 at baseline to 15.04 ± 8.12 at 12 weeks). For Inflammatory Lesion Counts (INF), the Metformin group had a slightly higher baseline mean rank (27.56) than the Doxycycline group (23.44), but the difference was nonsignificant ($p = 0.315$). This pattern continued at 8 weeks ($p = 0.740$) and 12 weeks ($p = 0.639$), with both groups showing consistent declines in lesion numbers over time. In contrast, Non-Inflammatory Lesion Counts (N-INF) revealed significant differences between groups. At baseline, the Doxycycline group had a notably higher mean rank (30.82) than the Metformin group (20.18), with the difference being statistically significant ($p = 0.010$). This significant difference persisted at 8 weeks ($p = 0.015$) but was no longer statistically significant at 12 weeks ($p = 0.070$). Both treatment groups demonstrated reductions in non-inflammatory lesions over the study period.

Table 3: Descriptive Statistics, Mean Ranks, and Friedman Test Results for Lesion Counts by Drug

Drug	Variable	Time Point	Mean $\pm$ SD	Min	Max	Mean Rank	p-value
Metformin	Total Lesion Count (TLC)	Baseline	35.20 $\pm$ 11.73	18	64	3	<0.001
		8 Weeks	21.96 $\pm$ 8.93	8	38	2	
		12 Weeks	14.24 $\pm$ 7.69	2	28	1	
	Inflammatory Lesion (INF)	Baseline	18.60 $\pm$ 10.02	5	37	3	<0.001
		8 Weeks	9.56 $\pm$ 6.68	0	25	1.92	
		12 Weeks	5.28 $\pm$ 4.87	0	17	1.08	
	Non-Inflammatory Lesion (NINF)	Baseline	16.80 $\pm$ 8.09	2	38	2.74	<0.001
		8 Weeks	12.24 $\pm$ 6.70	2	30	2.06	
		12 Weeks	8.92 $\pm$ 5.48	2	26	1.2	
Doxycyclin	Total Lesion Count (TLC)	Baseline	38.40 $\pm$ 11.35	26	63	3	<0.001
		8 Weeks	25.92 $\pm$ 9.62	14	57	2	
		12 Weeks	15.84 $\pm$ 8.62	7	46	1	
	Inflammatory Lesion (INF)	Baseline	14.68 $\pm$ 7.09	4	33	3	<0.001

	8 Weeks	8.92 ± 5.63	2	30	2	
	12 Weeks	4.44 ± 4.48	0	22	1	
Non-Inflammatory Lesion (NINF)	Baseline	23.68 ± 9.42	7	43	2.98	<0.001
	8 Weeks	16.92 ± 6.67	7	30	2.02	
	12 Weeks	11.52 ± 5.76	1	24	1	

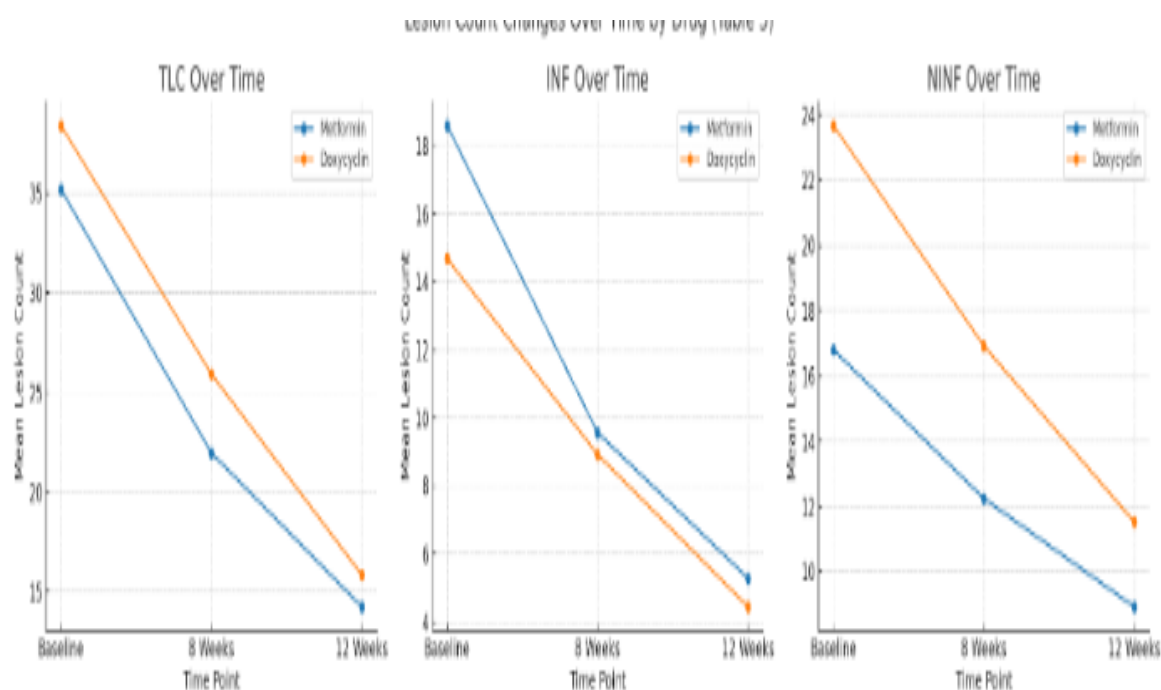


Table 4: GAAS and Cardiff Scores by Drug with p-values

Category	Metformin n (%)	Doxycyclin n (%)	Total n (%)	p-value
Baseline				0.018
Mild	0 (0.0%)	4 (8.3%)	4 (4.2%)	
Moderate	44 (91.7%)	44 (91.7%)	88 (91.7%)	
Severe	4 (8.3%)	0 (0.0%)	4 (4.2%)	
8 Weeks				0.086
Almost clear	20 (41.7%)	10 (20.8%)	30 (31.3%)	
Mild	23 (47.9%)	32 (66.7%)	55 (57.3%)	

Category	Metformin n (%)	Doxycyclin n (%)	Total n (%)	p-value
Moderate	5 (10.4%)	6 (12.5%)	11 (11.5%)	0.485
12 Weeks				
Almost clear	37 (77.1%)	35 (72.9%)	72 (75.0%)	
Mild	10 (20.8%)	13 (27.1%)	23 (24.0%)	
Moderate	1 (2.1%)	0 (0.0%)	1 (1.0%)	

Category	Metformin n (%)	Doxycyclin n (%)	Total n (%)	p-value
Baseline				0.020
Mild	4 (8.3%)	1 (2.1%)	5 (5.2%)	0.117
Moderate	23 (47.9%)	36 (75.0%)	59 (61.5%)	
Severe	21 (43.8%)	11 (22.9%)	32 (33.3%)	
8 Weeks				
Mild	33 (68.8%)	27 (56.3%)	60 (62.5%)	0.080
Moderate	14 (29.2%)	17 (35.4%)	31 (32.3%)	
Severe	0 (0.0%)	4 (8.3%)	4 (4.2%)	
No improvement	1 (2.1%)	0 (0.0%)	1 (1.0%)	
12 Weeks				
Mild	21 (43.8%)	31 (64.6%)	52 (54.2%)	
Moderate	6 (12.5%)	6 (12.5%)	12 (12.5%)	
No improvement	21 (43.8%)	11 (22.9%)	32 (33.3%)	

At baseline, GAAS scores demonstrated that the majority of participants in both the Metformin and Doxycyclin groups were categorized as having moderate acne (91.7% in each group). Severe acne was observed in a small proportion of patients in the Metformin group (8.3%), while mild cases were present only in the Doxycyclin group (8.3%). This baseline difference between the groups was statistically significant ($p = 0.018$), indicating an imbalance in initial disease severity distribution. By 8 weeks, both groups showed clinical improvement with a clear shift toward lower severity categories. A higher proportion of patients in the Metformin group achieved an “almost clear” status compared to the Doxycyclin group (41.7% vs. 20.8%), whereas mild acne was more frequent in the Doxycyclin group (66.7% vs. 47.9%). However, this difference did not reach statistical significance ($p = 0.086$), although a trend favoring Metformin was observed. At 12 weeks, most patients in both groups achieved an “almost clear” status (77.1% in the Metformin group and 72.9% in the Doxycyclin group), with only a very small proportion remaining in the moderate category (2.1% vs. 0%). The difference between groups was not statistically significant ($p = 0.485$), indicating comparable efficacy of both treatments in improving GAAS outcomes over time. For Cardiff acne scores, baseline assessment showed a statistically significant difference between groups ($p = 0.020$), with moderate acne more common in the Doxycyclin group (75.0%) compared with the Metformin group (47.9%), while severe acne was more frequent in the Metformin group (43.8%) than in the Doxycyclin group (22.9%).

DISCUSSION

In this randomized controlled trial, 96 acne vulgaris patients received either oral metformin or oral doxycycline. Both treatments were effective in significantly reducing 12-weeks total, inflammatory and non-inflammatory lesion counts. A few demographic factors and acne severity measurements were different between the groups but overall the final clinical results were similar. Based on the present results, oral metformin is a possible alternative to doxycycline in certain patients with acne vulgaris, a non-antibiotic therapy. Security in sex distribution was also seen with 77.1% of the participants in the metformin group being female and 70.8% of the participants in the doxycycline group being male. However, much more patients were married in the metformin group than the doxycycline group. The use of benzoyl peroxide, clindamycin, systemic tetracycline and retinol was also more commonly reported among those taking metformin. These differences suggest that despite random allocation, there were not full equality of the groups at baseline. There may have been some patients that had developed partial response or treatment resistance in previous treatment, which could have affected their response to subsequent therapy. Both drugs resulted in significant decreases in total lesions. In the metformin group, the mean TLC decreased from 35.20 ± 11.73 at baseline to 21.96 ± 8.93 at 8 weeks and 14.24 ± 7.69 at 12 weeks, representing an approximate reduction of 59.5%. Similarly, the mean TLC in the doxycycline group decreased from 38.40 ± 11.35 to 25.92 ± 9.62 and 15.84 ± 8.62 , corresponding to a reduction of approximately 58.8%. Within group improvements at 12 weeks were statistically significant in both groups ($p < 0.001$), however the difference between the groups at 12 weeks was not significant ($p = 0.502$). The results in this study show that the number of acne lesions was virtually the same with the use of metformin and doxycycline (12).

The results were comparable with that of the randomized trial done by Sadati et al. which found that doxycycline and metformin both significantly decreased the severity of acne and the number of lesions without any significant differences between the overall efficacy of both drugs. A higher effect of doxycycline on inflammatory lesions, however, was seen in that study. The present study, however, resulted in similar reduction of inflammatory lesions in both groups. The inflammatory lesion count was reduced by around 71.6 % and 69.8 % respectively in the metformin and doxycycline groups. Mean inflammatory lesion counts at 12 weeks were 5.28 ± 4.87 and 4.44 ± 4.48 , respectively, and were not significantly different ($p = 0.639$). The variation between studies may be attributed to differences in the characteristics of the participants, treatment combinations, inflammatory burden at baseline, and methods of assessing the lesions. There was also a significant reduction in non-inflammatory lesions in both groups. The mean non-inflammatory lesion count declined from 16.80 ± 8.09 to 8.92 ± 5.48 in the metformin group and from 23.68 ± 9.42 to 11.52 ± 5.76 in the doxycycline group. The difference in non-inflammatory lesions between the two groups was significant at baseline and 8 weeks but not 12 weeks ($p = 0.070$). This indicates that both treatments had an effect of decreasing the number of comedonal lesions over time. This comparison should be interpreted in light of the baseline imbalance, however, and if done according to mean change or by controlling for baseline lesion counts would yield a more accurate measure of comparative efficacy (13,14).

Previous studies also confirmed the beneficial effect of metformin that was suggested in the present study. Among the patients who were treated with metformin as an adjunctive therapy, Robinson et al. found a decrease in total lesion count of 71.4% compared with 65.3% in the control group with a non-statistically significant difference. They found that the use of metformin might enhance the metabolic and anti-inflammatory pathways associated with moderate to severe acne. Sharma et al. also showed that women who suffered from polycystic ovarian syndrome and were undergoing treatment with metformin had a significant decrease in acne severity (15). The population of their study, however, included only women with PCOS while the present study recruited both males and females and excluded patients with a clearly defined metabolic or endocrine disease. Clinical improvement was also shown by assessment using the Global Acne Assessment Scale. At baseline, moderate acne was present in 91.7% of both groups while severe acne was present in only the metformin group and mild acne was present in only the doxycycline group, which was significantly different at baseline ($p = 0.018$). Nearly all patients with an almost-clear status at 12 weeks were on metformin (77.1%) or doxycycline (72.9%) therapy (16). In the metformin group, only one patient remained in the moderate category of acne and none of the patients in the doxycycline group had moderate acne. There was no significant difference between groups ($p = 0.485$), which means the two groups had similar clinical efficacy at the end of treatment.

The results in Cardiff were not the same. The baseline rates were higher for severe acne-related impairment in the metformin group and for moderate impairment in the doxycycline group. The number of patients with "mild impairment" was higher at 12 weeks in the metformin group (43.8%) than in the doxycycline group (64.6%), and the "no improvement" category was more common in the metformin group. The Cardiff Acne Disability Index focuses more on the impact acne has on quality of life and psychosocial functioning than the actual severity of the acne (17). It is possible, therefore, that an immediate improvement in the number of lesions is not associated with an immediate improvement in perceived disability. However, the coding and interpretation of the "no improvement" category should be cross-checked as it did not seem to fit the marked objective improvement of the lesion counts and GAAS categories. Both treatments were generally safe to use. 87.5% of patients in both groups experienced no adverse effects (18). Diarrhea was reported in one patient treated with metformin, and nausea or vomiting occurred in 8.3% of those who took metformin and 12.5% of those who took doxycycline. The incidence of gastrointestinal intolerance was fairly low for the present study, as reported in previous studies that nearly one-third of patients have gastrointestinal symptoms when treating with metformin (19). Since both drugs were well tolerated with no major complications, there were no major issues with their adverse-effect profile. The negative effect of one participant in the metformin group was not included, however, and should be

verified prior to final analysis. The similar improvement seen with metformin in the current study is therefore clinically significant, as metformin does not directly contribute to the development of antibiotic resistance, but rather through metabolic, hormonal and anti-inflammatory mechanisms (20).

LIMITATIONS

This study had several limitations. It was conducted at a single tertiary-care centre with a relatively small sample size, which may limit the generalizability of the findings. Despite random allocation, the treatment groups differed at baseline in marital status, previous acne treatments, non-inflammatory lesion counts, and acne severity, which may have influenced the comparison of treatment outcomes. The study was not blinded, creating the possibility of observer and participant bias. The 12-week follow-up period was insufficient to assess long-term effectiveness, recurrence, scarring, or delayed adverse effects. Metabolic and hormonal factors, including insulin resistance, blood glucose, androgen levels, and polycystic ovarian syndrome, were not systematically evaluated, although these factors may affect the response to metformin.

CONCLUSION

Over the course of 12 weeks, the total, inflammatory, and non-inflammatory lesion counts of patients with acne vulgaris were found to be significantly reduced by oral metformin and oral doxycycline, respectively. Significant improvement was observed within both groups, while no statistically significant difference was found between the treatments in final lesion counts or GAAS outcomes. Both drugs were generally well tolerated, with only mild gastrointestinal adverse effects. These results suggest that oral metformin might be a good non-antibiotic alternative to doxycycline, especially for people who can't take antibiotics or have metabolic problems that go along with them.

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