Cerrahpaşa Med J 2024; 48(1): 46-49 ORIGINAL ARTICLE

Topical 5% Dapsone Applied Twice Daily for Facial Acne Vulgaris: More Effective on Inflammatory Lesions and Quicker in Female Patients

Defne Özkoca[1], Nazlı Caf[2], Zuhal Metin[3], Ayşenur Özdil[4], Işıl Göğem İmren[5], Selami Aykut Temiz[6], Mahmut Sami Metin[3], Koray Durmaz[7], Hanife Merve Akça[8], Tuğba Kevser Uzunçakmak[9], Zekayi Kutlubay[10]

[1]Zonguldak Atatürk State Hospital, Dermatology and Venerology Clinic, Zonguldak, Türkiye
[2]Diyarbakır Dağkapı State Hospital, Dermatology and Venerology Clinic, Diyarbakır, Türkiye
[3]Department of Dermatology and Venerology, Kırşehir Ahi Evran University Medical Faculty, Kırşehir, Türkiye
[4]Department of Public Health, İstanbul University-Cerrahpaşa, Cerrahpaşa Medical Faculty, İstanbul, Türkiye
[5]Denizli State Hospital, Dermatology and Venerology Clinic, Denizli, Türkiye
[6]Ereğli State Hospital, Dermatology and Venerology Clinic, Konya, Türkiye
[7]Bozüyük State Hospital, Dermatology and Venerology Clinic, Bilecik, Türkiye
[8]Department of Dermatology and Venerology, Karamanoğlu Mehmet Bey University Medical Faculty, Karaman, Türkiye
[9]Şişli Memorial Hospital, Dermatology and Venerology Clinic, İstanbul, Türkiye
[10]Department of Dermatology and Venerology, İstanbul University-Cerrahpaşa, Cerrahpaşa Medical Faculty, İstanbul, Türkiye

Cite this article as: Özkoca D, Caf N, Metin Z, et al. Topical 5% dapsone applied twice daily for facial acne vulgaris: More effective on inflammatory lesions and quicker in female patients. *Cerrahpaşa Med J.* 2024;48(1):46-49.

Abstract

Objective: Topical 5% dapsone is an effective alternative in the treatment of facial acne vulgaris. The aim of this study is to determine the impact of gender and age of the patient on the treatment efficacy of dapsone gel, as well as its efficacy on types of lesions.

Methods: Patients with mild-to-moderate facial acne vulgaris lesions, aged between 12 and 40 years of age were included in this multicenter study. Patients received 5% dapsone gel twice daily treatment for 8 weeks. Follow-up consultations were in weeks 2 and 8. The number of inflammatory and non-inflammatory lesions and the Global Evaluation of Acne Scale (GEAS) score of the patients were noted in each visit.

Results: A negative correlation was found between age and the treatment response of inflammatory lesions in week 2 (rs = −0.201; P = .008). Inflammatory lesions responded to treatment more compared to non-inflammatory lesions both on week 2 and week 8 (P-values both <.001). Female patients had a greater decline in both the number of inflammatory lesions and the total number of lesions on week 2 (P < .001 and P = .039 respectively). An at least 1 grade decline in the GEAS score was observed significantly more in the female patients on week 2 compared to male patients (P = .033).

Conclusion: Topical dapsone is more effective in the treatment of inflammatory lesions than of the non-inflammatory lesions, and female patients have a quicker response.

Keywords: Acne vulgaris, dapsone, gender, topical

Introduction

Acne vulgaris is a chronic disease caused by the inflammation of the pilosebaceous unit. Its estimated prevalence worldwide is 9.4%, which increases up to 85% among adolescents. Several treatment modalities, including topical and systemic modalities, are used in the treatment of acne vulgaris; yet the chronicity of the disease complicates treatment.[1,2]

Received: January 30, 2023 **Revision Requested:** April 10, 2023
Last Revision Received: April 11, 2023 **Accepted:** December 24, 2023
Publication Date: April 26, 2024
Corresponding author: Defne Özkoca, Zonguldak Atatürk State Hospital, Dermatology and Venerology Clinic, Zonguldak, Türkiye
e-mail: defneozkoca@yahoo.com
DOI: 10.5152/cjm.2024.23010

Dapsone is an anti-inflammatory synthetic sulpha-drug that has been long used orally in the treatment of many dermatological diseases. It has been used in the treatment of nodulocystic acne vulgaris before the use of systemic retinoids as well. However, its side effects, mainly methemoglobinemia and hemolysis, prevent its widespread systemic use. The topical formulations of dapsone, 5% and 7.5%, have a better safety profile and can be used in acne vulgaris along with other chronic cutaneous diseases. The 5% dapsone gel has been found to be safe and effective in the treatment of inflammatory acne vulgaris.[3-9]

The aim of this study is to evaluate the efficacy of twice daily use of topical 5% dapsone gel in the treatment of mild-to-moderate acne vulgaris and to determine the impact of gender and age on the treatment efficacy of dapsone gel on the inflammatory and non-inflammatory acne vulgaris lesions in the short term (2 weeks of treatment) and long term (8 weeks of treatment).

Methods

Patient Selection

Patients aged 12 to 30 years, with mild to moderate acne vulgaris (having 20 to 50 inflammatory and 20 to 100 non-inflammatory lesions) who were not actively undergoing any treatment modality, who were willing to participate in this study and who were able to come to the follow-up visits were included in this study. The study period was limited with 4 months; patients were included and followed up in this study between August 1, 2022, and December 1, 2022. Patients with severe nodulocystic acne or those who have recently developed new nodules and cysts; patients under treatment with other modalities; patients with symptoms of an underlying hormonal disturbance (hirsutism, alopecia or menstrual irregularities); patients under the age of 12 or over the age of 40; patients with forms of acne other than acne vulgaris (such as acne rosacea); patients with a diagnosed malignancy or who are immunosuppressed; pregnant and nursing patients; illiterate patients who cannot sign the informed consent; and patients who may not use the drug twice daily or who cannot come to the follow-up consultations were excluded from this study.

Treatment Centers Involved

This is a multicenter study performed at multiple government hospitals in Türkiye. The centers involved in this study were the dermatology outpatient clinics of Zonguldak Atatürk State Hospital, Diyarbakır Dağ Kapı State Hospital, Denizli State Hospital, Ereğli State Hospital, Bozhöyük State Hospital, Karamanoğlu Mehmet Bey University Hospital. and Kırşehir Ahi Evran University Hospital

Treatment Regimen

The patients were instructed to apply dapsone 5% gel twice daily after having cleansed their faces with soap or an over-the-counter cosmetic cleanser. The drug is to stay on the face for at least 10 to 12 hours; the patients were instructed not to wash the drug off until the second dose. The use of any other topical or systemic acne treatment was prohibited. The patients were only allowed to apply a sunscreen that is suitable for acne-prone skin. The patients were treated for at least 8 weeks.

Patient Evaluation

The names, ages, and gender of each patient were noted on the initial visit. The initial visit was on day 0, and the follow-up visits were on week 2 in order to evaluate the immediate effects of the drug and on week 8 in order to evaluate the long-term effects of the drug. The number of inflammatory lesions, the number of non-inflammatory lesions, and the total number of lesions (inflammatory and non-inflammatory lesions) along with the Global Evaluation of Acne Scale (GEAS) score were noted at each visit. Any side effects experienced were also noted at the given visit. Global Evaluation of Acne Scale is a scoring system that was developed by Dreno et al[10]; acne vulgaris patients are graded from 0 to 5 with this scale. Only the patients with GEAS scores of 1 (minimal disease), 2 (mild disease), and 3 (moderate disease) were included in this study. Patients with a score of 1 have a few comedones or papules; a score of 2 have comedones, papules, or pustules on less than one half of the face; and a score of 3 have comedones, papules, or pustules on more than half of the face.

Statistical Analysis

Analyses were performed using The Statistical Package for Social Sciences version 21.0 software (IBM Corp.; Armonk, NY, USA). The numerical variables were demonstrated with mean, standard deviation, minimum value, maximum value, median, and the categoric variables were demonstrated with frequency and percentage. The histogram, Q-Q graphic, Shapiro–Wilk, and Kolmogorov–Smirnoc tests were used for analyzing the distribution of the numerical variables. Mann–Whitney *U*-test was used to compare the numerical independent groups, and Spearman Correlation test was used to determine the correlation between the numerical variables. Pearson's chi-square test and Fisher's exact test were used to analyze the difference between categorical variables. Friedman test was used for dependent groups, Wilcoxon test was also used if necessary, and Bonferroni correction was applied. A *P*-value of less than .05 was accepted as statistically significant.

Ethics

The approval of Kent University Ethics Committee was taken before the initiation of the study (Approval No: E-60116787020-237049, Date: July 26, 2022). Informed consent was obtained from all patients or their legal guardians.

Results

Demographics

A total of 175 patients were included in this study. The mean age of the patients was 20.9 ± 4.6 years; the youngest patient was 12 years old and the eldest was 37 years old. Thirty-five (20%) of the patients were male and 140 (80%) were female.

The Relationship of Treatment Efficacy to Age

The decrease in the number of non-inflammatory and inflammatory lesions was analyzed separately in week 2 and week 8. A statistically significant negative correlation was found between age and the decrease in the number of inflammatory lesions in week 2 (rs = −0.201; $P = .008$); thus the treatment efficacy of topical dapsone in the treatment of inflammatory lesions decreases with increasing age. The relationships were insignificant for inflammatory lesions on week 8, and the non-inflammatory lesions on weeks 2 and 8 ($P = .28$, .065, and .091 respectively).

The Relationship of Treatment Efficacy to Gender

Before the initiation of the study, there was no statistically significant difference between the genders in terms of the number of inflammatory lesions. At week 2, the mean decline in the number of inflammatory lesions in males was 27.3% and in females it was it 37.4%; the difference was statistically significant ($P < .001$) (Table 1). At week 8, the mean decline in the number of inflammatory lesions in males was 67.5% and in females it was 67.4%; this difference was statistically insignificant.

Again, there was no statistically significant difference between genders in the number of non-inflammatory lesions at the initiation of the study. The differences between genders in the mean decline

Table 1. Treatment Efficacy for Inflammatory Lesions in Terms of Gender

		Male	Female	*P*
Week 0-week 2	Mean ± SD Min-Max (median)	27.3 ± 22.5 0-80 (22.2)	37.4 ± 43.6 −233-100 (50)	<.001
Week 0-week 8	Mean ± SD Min-Max (median)	67.5 ± 17.9 19.1-100 (73.3)	67.4 ± 44.9 −233-100 (75)	.078

Table 2 Treatment Efficacy for the Total Number of Lesions in Terms of Gender

		Male	Female	*P*
Week 0-week 2	Mean ± SD Min-Max (Median)	18 ± 17.6 −11.1-57.1 (16.7)	23.5 ± 25 −135.3-68.6 (24)	.039
Week 0-week 8	Mean ± SD Min-Max (Median)	53 ± 17 −9.1-78.6 (55)	50.1 ± 31.1 −135.3-100 (54.6)	.895

in the number of non-inflammatory lesions in weeks 2 and 8 were statistically insignificant (*P*-values .656 and .728, respectively).

There was no statistically significant difference between genders in terms of the total number of lesions at week 0. The mean decline in the total number of lesions on week 2 was 18% in males and 23.5% in females. This difference was statistically significant, *P* = .039. However, the difference was insignificant for week 8, *P* = .895. (Table 2)

There was no statistically significant difference between genders in terms of the GEAS scores at weeks 0, 2, and 8. An at least 1 grade decline (for example, from a score of 3 to 2) was observed in 28.6% of the male and 48.6% of the female patients in week 2; this difference was statistically significant (*P* = .033). However, there was no statistically significant difference between genders in terms of GEAS score decline in week 8. (Table 3)

Table 3. At Least 1-Grade Decline in Global Evaluation of Acne Scale Score in Terms of Gender

GAES Score		Male (n = 35)	Female (n = 140)	*P*
Week 0-week 2				.033
	No Decline	25 (71.4)	72 (51.4)	
	At least 1 point decline	10 (28.6)	68 (48.6)	
Week 0-week 8				.589
	No Decline	4 (11.4)	21 (15)	
	At least 1 point decline	31 (88.6)	119 (85)	

GAES, Global Evaluation of Acne Scale.

The Relationship of Treatment Efficacy to Lesion Type

The decrease in the number of lesions on week 2 was 41.2% for inflammatory lesions, 1.6% for non-inflammatory lesions, and 22.4% for the total number of lesions. The treatment efficacy of topical dapsone is statistically superior in inflammatory lesions compared to non-inflammatory lesions on week 2 (*P* < .001). The decrease in the number of lesions on week 8 was 67.4% for inflammatory lesions, 30.3% for non-inflammatory lesions, and 50.7% for the total number of lesions. The treatment efficacy of topical dapsone was statistically superior in inflammatory lesions compared to non-inflammatory lesions on week 8 (*P* < .001). Table 4 summarizes the difference in treatment efficacy between lesion types in weeks 2 and 8.

Side Effects

The side effects that were questioned during the follow-up period were erythema, burning, desquamation, tingling, and erosions. None of the patients complained of any side effects in the follow-up visits. Topical dapsone gel has a tolerable safety profile without any major and minor adverse effects.

Discussion

The 5% topical formulation of dapsone has already been proven to be effective in the treatment of acne vulgaris.[3-9] One of the aims of this study was to determine if there was a difference, if any, in the treatment efficacy between inflammatory and non-inflammatory lesions of acne vulgaris, which would guide the physicians in patient selection. In this study, we have revealed that the decrease in the number of inflammatory lesions was statistically significantly greater than the decrease in the number of non-inflammatory lesions both short-term (week 2) and long-term (week 8). Previously, Draelos et al[5] reported that the number of inflammatory and non-inflammatory acne vulgaris lesions declined starting as early as the second week of treatment. They have reported observing the greatest decline in the number of inflammatory lesions, starting from the second week until the twelfth week of treatment, although this has not been statistically proven.[5] Another study to examine the superior efficacy of topical dapsone gel on inflammatory lesions was performed by Taylor et al,[11] however, the study involved the use of once daily 7.5% formulation of dapsone gel. The authors reported an earlier effect of the drug on the inflammatory lesions. However, this difference became unremarkable with the continuation of the treatment. On the contrary, we report that dapsone gel is more effective on inflammatory lesions both in early and long-term treatment. Only 1 study has found topical dapsone treatment to be more effective on non-inflammatory lesions. Moore et al[12] investigated the treatment efficacy of 7.5% dapsone gel on truncal acne vulgaris lesions in pre-adolescents (aged between 9 to 11 years). We still conclude that 5% topical dapsone gel has superior efficacy both with short-term and long-term treatment in the treatment of the inflammatory lesions of facial acne vulgaris lesions on patients older than 12 years.

In this study, female patients experienced greater treatment efficacy compared to male patients on the second week of treatment. Both the decline in the inflammatory and total number of lesions, along with at least 1 grade decline in the GEAS score, were statistically significantly more than males in the females on week 2. In alignment with what we have found, Tanghetti et al[13] also reported superior treatment efficacy in females with the topical use of 5% dapsone gel twice daily. Both the inflammatory and non-inflammatory lesions of acne vulgaris have been reported to significantly

Table 4 Treatment Efficacy According to Lesion Type

		Inflammatory Lesions	Non-Inflammatory Lesions	Total Number of Lesions	*P*
Week 0-week 2	Mean ± SD Min-Max (median)	41.2 ± 40.8 −233.3-100 (50)	1.6 ± 39.6 −200-66.7 (0)	22.4 ± 23.7 −135.3-68.6 (23.1)	<.001
Week 0-week 8	Mean ± SD Min-Max (median)	67.4 ± 40.9 −233.3-100 (75)	30.3 ± 42.7 −140-100 (40)	50.7 ± 28.8 −135.3-100 (55)	<.001

decrease more in female patients compared to male patients after 12 weeks of dapsone 5% gel treatment. Other studies revealing superior efficacy of dapsone gel in female patients investigated the once daily use of the 7.5% topical formulation.[13,14] Tanghetti et al[14] reported superior efficacy of topical 7.5% dapsone gel in females compared to males, on both inflammatory and non-inflammatory acne vulgaris lesions after 12 weeks of treatment.[14] Likewise, Draelos et al. reported that treatment response to 7.5% dapsone gel was greater in female patients.[15] In alignment with the previous literature, we also report superior treatment efficacy of dapsone gel in females at week 2. However, this difference was insignificant by week 8. Thus, 5% dapsone gel may be a good treatment alternative for female patients seeking a quick improvement in acne vulgaris lesions.

This study revealed a superior early treatment efficacy of 5% dapsone gel on the inflammatory lesions in younger patients compared to older patients. Previously, 2 studies have investigated the treatment efficacy of dapsone gel depending on the patient's age.[15,16] Del Rosso et al's16 study included adolescent and adult female patients who had been treated with 5% dapsone gel twice daily for 12 weeks. They report a statistically greater decline in the number of non-inflammatory and total lesions of acne vulgaris in the adult group compared to adolescents.[16] Draelos et al. have also subdivided their patients into adolescents and adults. Patients received once-daily 7.5% dapsone gel treatment, and at the end of the treatment, adult patients demonstrated a greater decline in the GEAS score.[15] Dapsone gel has been proven to be safe and effective in the treatment of adolescent patients as well.[17] However, according to the previous literature, adult patients have greater treatment success with topical dapsone treatment compared to adolescent patients.[15,16] Our study contradicts the previously established greater treatment efficacy in adult patients; but still, we did not categorize them as adolescents and adults, we just investigated the effect of age on treatment efficacy. Furthermore, we could only show decreased treatment efficacy in older patients only on the inflammatory lesions and on week 2. Therefore, we believe further studies are needed to comment on the effect of the patient's age on the treatment efficacy of dapsone gel.

In conclusion, the 5% topical formulation of dapsone is more effective in the treatment of inflammatory lesions of facial acne vulgaris than of the non-inflammatory lesions, both with short- and long-term treatment. Female acne vulgaris patients have an earlier increased earlier response to 5% dapsone gel compared to male patients.

Limitations

The limited sample size is a major limitation of this research.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Kent University (Approval No: E-60116787020-237049, Date: July 26, 2022).

Informed Consent: Informed consent was obtained from all patients or their legal guardians.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept and Design – D.Ö., N.C., Z.M.; Data Acquisition – D.Ö., N.C., I.G.İ., S.A.T., K.D., M.S.M., H.M.A.; Data Acquisition and Statistical Analysis – D.Ö., A.Ö.; Literature Search and Authorship – D.Ö., N.C., T.K.U., Z.K.

Declaration of Interests: The authors have no conflict of interest to declare

Funding: The authors declared that this study has received no financial support.

Data Availability Statement: The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

References

1. Alanazi MS, Hammad SM, Mohamed AE. Prevalence and psychological impact of acne vulgaris among female secondary school students in Arar city, Saudi Arabia, in 2018. *Electron Phys*. 2018;10(8):7224-7229. [CrossRef]
2. Williams HC, Dellavalle RP, Garner S. Acne vulgaris. *Lancet*. 2012;379(9813):361-372. [CrossRef]
3. Pickert A, Raimer S. An evaluation of dapsone gel 5% in the treatment of acne vulgaris. *Expert Opin Pharmacother*. 2009;10(9):1515-1521. [CrossRef]
4. Stotland M, Shalita AR, Kissling RF. Dapsone 5% gel: a review of its efficacy and safety in the treatment of acne vulgaris. *Am J Clin Dermatol*. 2009;10(4):221-227. [CrossRef]
5. Draelos ZD, Carter E, Maloney JM, et al. Two randomized studies demonstrate the efficacy and safety of dapsone gel, 5% for the treatment of acne vulgaris. *J Am Acad Dermatol*. 2007;56(3):439.e1-10. [CrossRef]
6. Thiboutot DM, Willmer J, Sharata H, Halder R, Garrett S. Pharmacokinetics of dapsone gel, 5% for the treatment of acne vulgaris. *Clin Pharmacokinet*. 2007;46(8):697-712. [CrossRef]
7. Kircik LH. Harnessing the anti-inflammatory effects of topical dapsone for management of acne. *J Drugs Dermatol*. 2010;9(6):667-671.
8. Lucky AW, Maloney JM, Roberts J, et al. Dapsone gel 5% for the treatment of acne vulgaris: safety and efficacy of long-term (1 year) treatment. *J Drugs Dermatol*. 2007;6(10):981-987.
9. Alexis AF, Burgess C, Callender VD, et al. The efficacy and safety of topical dapsone gel, 5% for the treatment of acne vulgaris in adult females with skin of color. *J Drugs Dermatol*. 2016;15(2):197-204.
10. Dréno B, Poli F, Pawin H, et al. Development and evaluation of a Global Acne Severity Scale (GEA Scale) suitable for France and Europe. *J Eur Acad Dermatol Venereol*. 2011;25(1):43-48. [CrossRef]
11. Taylor SC, Cook-Bolden FE, McMichael A, et al. Efficacy, safety, and tolerability of topical dapsone gel, 7.5% for treatment of acne vulgaris by Fitzpatrick skin phototype. *J Drugs Dermatol*. 2018;17(2):160-167.
12. Moore AY, Lain EL, McMichael A, et al. Once-daily dapsone 7.5% Gel for the Treatment of acne vulgaris in Preadolescent Patients: a Phase IV, Open-label, 12-week Study. *J Clin Aesthet Dermatol*. 2021;14(4):43-48.
13. Tanghetti E, Harper JC, Oefelein MG. The efficacy and tolerability of dapsone 5% gel in female vs male patients with facial acne vulgaris: gender as a clinically relevant outcome variable. *J Drugs Dermatol*. 2012;11(12):1417-1421.
14. Tanghetti E, Harper J, Baldwin H, Kircik L, Bai Z, Alvandi N. Once-daily topical dapsone gel, 7.5%: effective for acne vulgaris regardless of baseline lesion count, with superior efficacy in females. *J Drugs Dermatol*. 2018;17:1192-1198.
15. Draelos ZD, Rodriguez DA, Kempers SE, et al. Treatment response with once-daily topical dapsone gel, 7.5% for acne vulgaris: subgroup analysis of pooled data from two randomized, double-blind stu. *J Drugs Dermatol*. 2017;16(6):591-598.
16. Del Rosso JQ, Kircik L, Gallagher CJ. Comparative efficacy and tolerability of dapsone 5% gel in adult versus adolescent females with acne vulgaris. *J Clin Aesthet Dermatol*. 2015;8(1):31-37.
17. Raimer S, Maloney JM, Bourcier M, et al. Efficacy and safety of dapsone gel 5% for the treatment of acne vulgaris in adolescents. *Cutis*. 2008;81(2):171-178.