PAPER DETAILS

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ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Efficacy and Safety of Topical Dapsone Versus Topical Tetracycline in Mild to Moderate Acne Vulgaris: A Retrospective Analysis

Hafif ve Orta Şiddette Akne Vulgariste Topikal Dapsona Karşı Topikal Tetrasiklinin Etkinliği ve Güvenliği: Retrospektif bir Analiz

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ABSTRACT

Aim: *In this study, we compared the efficacy and side effects of topical 7.5% dapsone and 3% tetracycline in patients with mild and moderate acne.*

Material and Methods: *The hospital's clinical Ethics Committee approved the study. A total of 100 subjects aged 12–40 were enrolled in the study, and each group contained 50 subjects who applied to the dermatology clinic with the complaint of acne from 01.09.22 to 30.11.22, were diagnosed with mild and moderate acne and were treated with topical 7.5% dapsone or 3% tetracycline for at least 12 weeks.*

Results: *A statistically significant difference was found between the 2 groups regarding acne scores and lesion numbers at the end of the treatment (p=0.006 for acne score, 0.002 for open comedones and <0.001 for other types of lesions). There was also a significant difference between the 2 groups regarding patients with an acne score of 0 or 1 after 12 weeks of treatment (p=0.007). At the end of the first month, there was a difference between the 2 groups regarding erythema, dryness and burning/stinging side effects (respectively p=0.009, 0.009 and <0.001).*

Conclusion: *Our results suggest that topical 7.5% dapsone is effective in treating mild to moderate acne and is safe in terms of side effects compared to topical 3% tetracycline.*

Key words: *topical dapsone; acne and dapsone; tetracycline and dapsone; topical tetracycline*

ÖZET

Amaç: *Biz bu çalışmada hafif ve orta şiddetli akne hastalarında7,5 dapson ve3 tetrasiklin'in etkinlik ve yan etkilerini karşılaştırdık.*

Gereç ve Yöntem: *Çalışma hastanenin Etik Kurulu tarafından onaylandı. Çalışmaya sivilce şikâyetiyle 01,09,22–30,11,22 tarihleri arasında dermatoloji polikliniğine başvuran, hafif ve orta şiddetli akne tanısı alan ve tedavisinde7,5 dapson veya3 tetrasiklin kullanılan, 1240 yaş arasında, her grupta 50 hasta olacak şekilde toplam 100 hasta alındı.*

Bulgular: *İki grup arasında tedavi sonundaki akne skorları ve lezyon sayıları açısından istatistiksel anlamlı fark bulundu (akne skoru için p=0,006, açık komedonlar için 0.002 ve diğer tüm lezyon tipleri için <0,001). Aynı zamanda 12 haftalık tedavi sonunda akne skoru sıfır ve bir olan hastalar açısından da gruplar arasında anlamlı fark vardı (p=0,007). Tedavinin 1. ayının sonunda iki grup arasında eritem, kuruluk ve yanma/batma hissi açısından fark bulundu (sırasıyla p=0,009, 0.009 and <0,001).*

Sonuç: *Bizim sonuçlarımız hafif ve orta şiddetli akne tedavisinde topikal3 tetrasiklinle karşılaştırmada topikal7,5 dapsonun daha etkili ve yan etkiler açısından daha güvenli olduğunu göstermektedir.*

Anahtar kelimeler: *akne ve dapson; tetrasiklin ve dapson; topikal dapson; topikal tetrasiklin*

Introduction

Acne vulgaris (AV) is a chronic inflammatory disease of the hair follicle and sebaceous glands[1]. The prevalence of acne is 12% in women and 4% in men[2]. Since sebaceous glands are more common in places such as the face, pectoral region and back, acne is also an effective factor in social life and has psychological interactions[3]. Acne treatment can be summarized under 3 main headings as topical treatments, systemic antibiotics and systemic isotretinoin. Topical tetracycline has both antimicrobial and anti-inflammatory properties. Dapsone (4-amino 4-diphenyl sulfone), which

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shows its effect by competitively inhibiting dihydropteroate synthetase against para-aminobenchoic acid, is a drug from the sulfone group discovered in 1908 and has both anti-inflammatory and antimicrobial activity[4–6]. It is known to inhibit neutrophil chemotaxis by different pathways[7, 8]. This study compared the efficacy and side effects of topical 7.5% dapsone and topical 3% tetracycline in patients with mild and moderate AV.

Material and Methods

Ethics Approval

Our study was approved by the clinical research ethics committee.

Study Design

The study was conducted retrospectively by scanning patient files. The files of the patients aged 12–40 years who applied to the dermatology outpatient clinic with the complaint of acne between 01.09.2022 and 30.11.2022 were diagnosed with mild and moderate AV, had Investigator's Static Global Assessment (ISGA) scores between 2–4 and was treated with topical 7.5% dapsone or topical 3% tetracycline (drugs were administered only once a day) were included in the study. Those younger than 12 and older than 40 years, those with nodulocystic acne and severe acne, those who received other acne treatments and those who had facial treatments (energy-based device, peeling, dermabrasion, epilation, etc.) in the 3 months before the first examination, and those who used systemic corticosteroid, retinol-containing or acidic cosmetic products were not included in the evaluation. A hundred patient files were evaluated, with 50 patients in each group. In our study, we used information such as demographic characteristics in the patient files, ISGA scores before treatment and at the end of each month during 12 weeks of treatment, the number of non-inflammatory lesions, including open and closed comedones, the number of inflammatory lesions including papules and pustules, and side effects and severity scores (0-none, 1-mild, 2-moderate, 3-severe) at the end of each month control. Patients with an ISGA score of 0 or 1 at the end of treatment were considered "recovered patients" or "clinical success."

Examination of the patients, determination of the severity of the disease, treatment and follow-up were performed by the same doctor (S. H.). Treatment was not discontinued in any of the patients in the study due to side effects.

Statistics

Data were entered in the software IBM Statistical Package for Social Sciences (SPSS) program version 25 (IBM© Corp., Armonk, NY, USA) and this program was used for statistical analysis. Discontinuous variables were expressed in numbers and percentages, while continuous variables were expressed in mean +/– standard deviation. P value <0.05 was considered statistically significant. Chi-squared test was used to investigate independent variables for discontinuous variables. Whether the groups conformed to normal distribution in terms of continuous variables was assessed using the Kolmogorov-Smirnov test, and The Wilcoxon test was used when investigating dependent groups in terms of variables that did not conform to the normal distribution, and the Mann Whitney U test was used when investigating independent groups.

Results

A hundred patients were included in the study, with 50 patients in each group. The age was 23.94 +/– 7.78 years in the group using dapsone, while it was 22.70 +/– 8.38 years in the group using tetracycline. There were 32 male patients in the study, 19 (38%) in the dapsone group and 13 (26%) in the tetracycline group. There was no statistically significant difference between the groups regarding age and gender (p=0.357 and 0.198, respectively). Detailed demographic data are shown in Table 1.

Table 1. *Demographics and general data*

	Dapsone (n=50)	Tetracysline (n=50)
Age (years, mean ± sd)	23.94±7.78	22.70±8.38
Gender (n / %)		
Male	19/38	13/26
Female	31/62	37/74
Initial ISGA values (mean ± sd)	2.74±0.72	2.84±0.65
2 (n /%)	21/42	15/30
3 (n /%)	21/42	28/56
4 (n /%)	18/16	7/14
Initial NNL[1] (mean ± sd)	40.84±9.83	43.90±9.45
Open comedone	10.52±2.89	11.66±3.47
Closed comedone	30.32±7.10	32.24±6.38
Initial NIL[2] (mean ± sd)	35.58±6.29	37.84±7.48
Papule	13.24±1.76	13.84±2.39
Pustule	22.34±4.63	23.40±4.60
Initial TNL[3] (mean ± sd)	76.44±15.94	81.16±15.12

[1]NNL-Number of noninflammatory lesions, [2]NIL-Number of inflammatory lesions, [3]TNL-Total number of lesions.

Table 2. *Investigator's Static Global Assessment scores, clinical cure rates, lesion counts, and percentile reductions at the end of treatment*

mean ± sd	Dapsone	Tetracycline
ISGA	1±0.90	1.54±1.01
Percentage reduction	65±30.45	46±36.51
Clinical success (n / %)	38/76	25/50
NNL	9.30±10.56	18.30±10.13
Percentage reduction	78.43±22.93	57.36±24.64
Open comedone	3.08±3.15	5.10±3.38
Percentage reduction	72.62±26.54	56.16±27.03
Closed comedone	6.22±7.54	13.20±7.60
Percentage reduction	80.38±22.23	57.84±26.14
NIL	6.86±8.38	12.90±8.27
Percentage reduction	81.80±21.39	63.74±27.03
Papule	2.98±3.42	5.44±3.35
Percentage reduction	78.32±23.92	59.86±26.51
Pustule	3.84±5.19	7.46±5.41
Percentage reduction	83.97±20.95	65.85±29.57
TNL	16.16±18.81	31.20±17.60
Percentage reduction	79.99±22.04	60.61±24.21

There was no statistically significant difference between the 2 groups in terms of ISGA values, open and closed comedones, non-inflammatory lesions, papules, pustules, inflammatory lesions and total lesions before the treatment (p=0.400, 0.095, 0.181, 0.100, 0.111, 0.151, 0.066 and 0.091, respectively, Table 1).

When each group was investigated in terms of pre– and post-treatment ISGA values, open and closed comedones, non-inflammatory lesions, papules, pustules, inflammatory lesions and total lesion counts, statistically significant differences were found for each group separately in terms of ISGA values and all lesion types (p<0.001 for all).

When the 2 groups were compared in terms of ISGA values and percent decrease in ISGA values at the end of treatment, a statistically significant difference was found between the groups (p=0.006 and 0.005, respectively), and the decrease was greater in the dapsone group. Likewise, it was also examined whether there was a difference between the groups in terms of the number of lesions and the percentage decreases in the number of lesions, and a statistically significant difference was found between the groups (p=0.002 for open comedones, p<0.001 for others). The reduction in lesions was more common in the group using dapsone. Data on this subject are detailed in Table 2.

Patients with an ISGA score of 0 or 1 (recovered patient) after 12 weeks of treatment in each group were evaluated, and it was examined whether there was a difference between the groups in this respect. A statistically significant difference was found between the 2 groups regarding patients who recovered (p=0.007). The number of recovered patients who used dapsone was higher in the group. Details are given in Figure 1.

Table 3. *Side effect data at monthly checkups*

	Dapsone			Tetracycline		
n / %	End of 1st m	End of 2nd m	End of 3rd m	End of 1st m	End of 2nd m	End of 3rd m
Erythema	9/18	5/10	0/0	21/42	6/12	3/6
mild	4/8	5/10	0/0	6/12	4/8	3/6
moderate	3/6	0/0	0/0	5/10	1/2	0/0
severe	2/4	0/0	0/0	10/20	1/2	0/0
Dryness	9/18	3/6	0/0	21/42	5/10	3/6
mild	6/12	2/4	0/0	8/16	2/4	2/4
moderate	3/6	1/2	0/0	5/10	1/2	1/2
severe	0/0	0/0	0/0	8/16	2/4	0/0
Burning/stinging	8/16	5/10	1/2	26/52	9/18	3/6
mild	7/14	5/10	1/2	16/32	6/12	3/6
moderate	1/2	0/0	0/0	2/4	2/4	0/0
severe	0/0	0/0	0/0	8/16	1/2	0/0

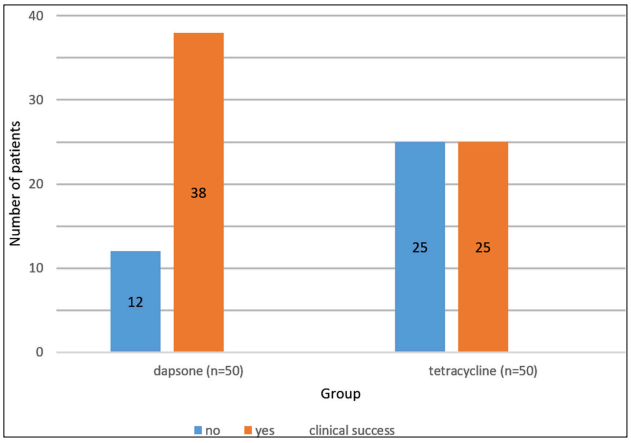

Figure 1. *Clinical success data by groups.*

When the 2 groups were evaluated in terms of erythema, there was a difference at the end of the 1st month (p=0.009, erythema was more common in the tetracycline group), there was no difference at the end of the 2nd month (p=0.749), and there was a difference at the end of the 3rd month (p=0.022, in the dapsone group no erythema was found). When the 2 groups were evaluated in terms of dryness side effects, it was found that there was a statistically significant difference between the groups at the end of the 1st month control (p=0.009, dryness was more common in the tetracycline group), but there was no difference in the 2nd and 3rd month controls (p=0.461 and 0.110, respectively). Considering whether there is a statistically significant

difference between the groups in terms of burning and stinging side effects, there is a statistically significant difference at the end of the 1st month ($p<0.001$); this side effect is more common in the tetracycline group), but there is no difference in the controls at the end of the 2nd and 3rd months ($p=0.249$ and 0.161, respectively). Data on side effects seen at monthly controls are detailed in Table 3.

When the patients with side effects in each group were compared in terms of severity of side effects, there was no statistically significant difference in terms of severity in patients with both erythema, dryness and burning/stinging at the end of the 1st and 2nd-month controls ($p=0.426$ and 0.361, respectively, in patients with erythema, $p=0.093$ and 0.449 in patients with dryness, $p=0.199$ and 0.346 in patients with burning/stinging). This comparison could not be made, as no erythema and dryness were observed in patients using dapsone at the end of the 3rd-month controls. Similarly, statistical comparison could not be made between the groups of patients using dapsone and patients who were burning/stinging since this side effect was very rare.

Discussion

There was no statistically significant difference between the two groups compared in our study in terms of demographic characteristics, pre-treatment ISGA scores and the number of lesions. When each group was evaluated in isolation, a statistically significant difference was found in ISGA values and the number of lesions before and after 12 weeks of treatment, and this shows that both treatment modalities are effective in treating mild and moderate acne separately. However, when the 2 groups are evaluated in terms of ISGA values and percentage reductions at the end of treatment, as well as the number of lesions and percentage reductions, it is seen that topical 5% dapsone is more effective than topical 3% tetracycline. When the 2 groups are compared in terms of side effects, it is observed that the side effects are less common in the group using dapsone, especially in the control at the end of the first month of treatment.

In the literature review, no previous studies of efficacy and side effects of topical 5% dapsone and topical 3% tetracycline were found. Most studies with topical dapsone have compared the drug to placebo.

Stein Gold LF[9], Eichenfield LF[10] evaluated 4340 AV patients in two randomized, double-blind controlled studies for once-daily use of 7.5% dapsone and placebo and they find a significant improvement in both ISGA values and the number of non-inflammatory and inflammatory lesions in the dapsone group at the end of 12 weeks of treatment.

Draelos et al.[11] showed that 5% dapsone used twice a day had a significant effect on acne scores compared to the control group (decrease of 40.5% and 32.8%, respectively) in a multicenter, 12-week, double-blind, randomized, phase 3 study in which 3010 individuals were evaluated. The study observed a significant decrease in non-inflammatory (32% and 24%) and inflammatory (47.5% and 41.8%) acne lesions in the dapsone group compared to the control group. In the follow-ups, they did not see any abnormality (even in those with G-6PD deficiency) in laboratory tests. Side effects such as 21.8% dryness, 20% erythema, 1.4% burning sensation, 1% itching and 0.1% irritation were observed in the dapsone group.

In a placebo-controlled, randomized study conducted by Gita Faghihi et al.[12], they investigated the efficacy and side effects between systemic 20 mg/day isotretinoin + 5% dapsone and systemic 20 mg/day isotretinoin + placebo in a 12-week treatment period in 58 patients with moderate and severe acne aged 18–25 years. While the decrease in the number of non-inflammatory and inflammatory lesions at the end of the treatment was significantly higher in the dapsone group than in the other group, no difference was found between the placebo group regarding a decrease in acne score. They found that the efficacy was greater in female patients. In the dapsone group, they observed a burning sensation in 7 patients (24.13%), mild erythema in 4 patients (13.79%), and mild dryness in 3 patients (10.34%). No abnormality was observed in hemoglobin levels in the follow-ups of the patients.

Lucky et al.[13] investigated the efficacy of 5% dapsone applied topically twice daily in a multicenter, 12-month phase 3 study, and at the end of the 12 th month, they observed a 58.2% decrease in inflammatory lesions, a 19.5% decrease in non-inflammatory lesions and a 49% reduction in the total number of lesions. Mostly mild application area side effects were observed in 13.8% of the patients ((2.9% dryness, 2.5% redness-rash, 2.3% sunburn, 1.6% stinging, 1.6% erythema and 1.4% itching).

Conclusion

When the results of our study and the other studies mentioned above are evaluated, it is suggested that topical dapsone is effective in treating mild and moderate AV and is safe regarding side effects compared to topical 3% tetracycline.

The authors do not recommend topical antibiotics for treating acne due to the risk of resistance development. However, topical antibiotics in combination with topical retinoids or topical benzoyl peroxide are recommended.

Limitations of the study

One limitation is the study's retrospective nature. Because the study was conducted in a specific country, that is, at a specific geographic latitude, the results cannot be generalized to the whole world. There were no severe acne patients in the study, so the results do not apply to severe acne. The results cannot be generalized to other age groups since the study was conducted on patients within the age group 12–40 only.

No supports were received for the study from any person and/or institution.

The study has no conflicts of interest (due to a single author).

All authors have approved this final version of the article and have given permission for it to be submitted to you for publication.

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