doi.org/10.36721/PJPS.2023.36.2.SP.607-611.1

Efficacy of topical 30% salicylic acid in combination with minocycline in moderate to severe acne

Jiaoli Yang, Xue Xu*, Zudong Meng and Yufang Liu
Department of Dermatology, Renmin Hospital, Hubei University of Medicine, Hubei, China

Abstract: To evaluate the efficacy of topical 30% salicylic acid plus minocycline in moderate to severe acne. One hundred patients with moderate to severe acne from February 2020 to February 2021 were retrospectively analyzed. They were assigned (1:1) to receive either topical 30% salicylic acid plus minocycline (combination group) or minocycline (mono therapy group). The acne scores, physician subjective and objective scores, efficacy, quality of life, incidence of adverse reactions, recurrence, and satisfaction in both groups were compared. The combination group had lower Global Acne Grading System (GAGS) scores, erythema scores and papulopustular scores than the mono therapy group. Combined therapy was associated with lower erythema absolute value and erythema index, more skin water content and less transcutaneous water loss versus minocycline. Higher efficacy, acne symptoms scores, and quality of life were observed with combination therapy versus mono therapy ($P<0.05$). The two groups had a similar incidence of adverse reactions and recurrence. Combination therapy showed a higher appearance satisfaction versus mono therapy. The efficacy of topical 30% salicylic acid plus minocycline for moderate to severe acne was better versus minocycline.

Keywords: Moderate and severe acne, topical 30% salicylic acid, minocycline, acne score, quality of life, adverse reactions, recurrence, satisfaction.

INTRODUCTION

Acne is a chronic inflammatory disease that occurs in the sebaceous glands of hair follicles and is highly susceptible to disfiguring skin damage, which seriously affects patients psychologically and socially (Jing *et al*., 2019). Studies assessing the effect of acne, especially facial acne, on psychological health, found a range of abnormalities including depression, lack of self-confidence, suicidal ideation, anxiety, psychosomatic symptoms, low self-esteem, embarrassment and social inhibition, which improve with effective treatment (Jiang *et al*., 2021). Acne treatments include systemic therapies (oral antibiotics and retinoid), topical therapies (benzoyl peroxide) and physical modalities (laser therapy and chemical peeling). Currently, retinoic acid and antibiotics are the mainstays of treatment for acne in clinical practice, in which minocycline hydrochloride capsules are commonly used in the treatment of moderate to severe acne. Minocycline hydrochloride is tetracycline and semi-synthetic drug that inhibits sebum secretion and promotes the reduction of free fatty acids in the skin, with potent antibacterial effects (S and Y, 2021). Since acne is a chronic disease that requires prolonged therapy, treatment adherence in patients therefore is a major concern, along with side effects would lead to recurrence of acne, patient dissatisfaction, and increased medical costs. In recent years, it has been suggested (Jiang *et al*., 2021) that the new supra molecular salicylic acid possesses more significant effects in the treatment of acne with less recurrence. Herein, the efficacy of topical 30% salicylic acid plus minocycline in the treatment of moderate to severe acne was investigated (WJ *et al*., 2020).

MATERIALS AND METHODS

General data

One hundred patients with moderate to severe acne in our hospital from February 2020 to February 2021 were retrospectively analyzed. The patients were divided into two groups based on the medication method: topical 30% salicylic acid combined with minocycline medication (combination group) and mono therapy with minocycline alone (mono therapy group), with 50 cases each group. The patients in the combination group were aged 14 to 30 years, with a mean age of (22.32±3.56) years, including 24 females and 26 males. The combination group had 21 cases of 34-46 kg and 29 cases of 47-57 kg in terms of weight, 29 cases of 1-3 years and 21 cases of 4-6 years in terms of disease duration, 23 cases of moderate acne and 27 cases of severe acne in terms of disease degree, and 22 cases of grade II and 28 cases of grade III in terms of acne grading. The patients in the mono therapy group were aged 15 to 31 years, with a mean of (23.01±3.51) years, including 23 females and 26 males. The mono therapy group had 20 cases of 34-46 kg and 30 cases of 47-57 kg in terms of weight, 28 cases of 1-3 years and 22 cases of 4-6 years in terms of disease duration, 24 cases of moderate acne and 26 cases of severe acne in terms of disease degree, and 23 cases of grade II and 27 cases of grade III in terms of acne grading. The two groups showed no significant differences in general information ($P>0.05$).

**Corresponding author:* e-mail: xueyuyidu598@163.com

Inclusion and exclusion criteria

Inclusion criteria: Male and female patients aged 15to35 years with moderate to severe facial acne vulgaris defined by the Investigator Global Assessment (IGA) scale of 3 or 4; Patients had ≥10 inflammatory lesions (papules, pustules, or nodules) and ≥10 no inflammatory lesions (open and closed comedones) on the face.

Exclusion criteria: acne fulminans, acne conglobata, secondary acne, or dysplastic naevi; systemic acne treatment with oral is otretino in within 6 months or oral antibiotics in the past 1 month; history of facial procedures like dermabrasion, chemical, or laser peels; phototherapy within 1 month; topical treatments other than medicated cleansers within 14 days; female patients who were pregnant or nursing; history of photosensitive diseases, porphyria, or porphyrin sensitivity.

Mono therapy group

Patients were given 50mg of minocycline hydrochloride capsules orally twice daily. One course of treatment consisted of 4 weeks and all patients were given a total of 2 courses of treatment.

Combination group

Patients were also given 50 mg of minocycline hydrochloride capsules orally twice daily. The treatment duration was identical to that of the mono therapy group. Additionally, the patients were treated with topical 30% supramolecular salicylic acid. After facial cleaning, the patient lay flat, with the hair wrapped with a towel and the eyes protected with wet gauze. An appropriate amount of water was added to 30% supra molecular salicylic acid (BRODA, Shanghai Ruizhi Medical Technology Co., Ltd.) and the face was massaged during the application process for 5~10min. The reaction of the lesions in the treatment area was closely observed, and the endpoint reaction was a white cream reaction and the appearance of uniform erythema in the treatment area. Thereafter, the massage was stopped, and after waiting for 10~20min, the face was cleaned and then cold sprayed for 10min. The treatment was performed every 2 weeks, with 4 treatment sessions for one course of treatment. The patients were given one course of treatment in total.

Observational indicators

The patients were followed up for 2 months. 1) Acne score. Global Acne Grading System (GAGS) was used to evaluate the severity of acne, with a total score of 1-36 points. The higher the scores, the more severe the symptoms (LI *et al*., 2020); 2) Physician subjective score the evaluation was performed based on the severity of erythema and papulopustularity, each with 0~4 points. The higher the score, the more severe the symptoms (SHI and ZHANG, 2020); 3) Physician objective score. The absolute value of erythema on both sides of the face was measured using the VISIA skin tester, and the erythema index, skin water content, and transcutaneous water loss on both sides of the face were measured using the Derma lab Cortex noninvasive skin tester; 4) Quality of life. Acne-specific quality of life questionnaire (Acne-QOL) was used to assess the patients' quality of life, which included acne symptoms, self-perception, emotional function, and social function, each with a full score of 30 points, 30 points, 24 points and 30 points, respectively, and a total score of 114 points. The higher the scores, the better the quality of life (Yu, 2020); 5) Occurrence of adverse reactions and recurrence; 6) Appearance satisfaction. Self-made questionnaires with a total score of 0~10 points were used, with 0~3 points indicating unsatisfied, 4~6 points indicating satisfied and 7~10 points indicating highly satisfied.

Efficacy assessment criteria

Cured: the patient's skin was smooth, clean, and non-oily, and the number of skin lesions was reduced by 90.5~100%; markedly effective: the patient's skin glossiness and cleanliness were increased significantly, the oiliness decreased significantly, and the number of skin lesions decreased by 70%~89%; effective: the patient's skin glossiness and cleanliness increased, the oiliness decreased, and the number of skin lesions decreased by 30%~69%; ineffective: no changes in skin glossiness, cleanliness and oiliness, and 0-29% reduction or increase in the number of lesions in patients were observed (WU *et al*., 2020).

Ethical approval

This study has been approved by Renmin Hospital, Hubei University of Medicine ethics committee. Patients and their families were informed of the research content and voluntarily signed the informed consent. All the methods were carried out in accordance with the Declaration of Helsinki.

STATISTICAL ANALYSES

SPSS 21.0 was used for data analyses. Count data were expressed as rates and analyzed using the chi-square test or rank sum test. Measurement data were expressed as ($x \pm s$) and analyzed using the t-test or F-test. α=0.05 was used as the baseline for significant differences.

RESULTS

Comparison of acne scores and physician subjective scores

The GAGS scores, erythema scores, and papulopustular scores of patients in both groups were decreased after medication ($P<0.05$), with lower results observed in the combination group than the mono therapy group ($P<0.05$) (table 1).

Table 1: Comparison of acne scores and physician subjective scores (points, x ± s)

Groups	N	Time point	GAGS score	Erythema score	Papulopustular score
Combination group	50	Before treatment	50.05±8.60	3.32±0.57	2.56±0.41
		After treatment	10.41±1.50#*	1.70±0.21#*	0.85±0.14#*
Monotherapy group	50	Before treatment	50.26±8.86	3.38±0.74	2.52±0.33
		After treatment	19.60±3.14	2.75±0.26	1.18±0.86

Note: #means compared with the corresponding values before treatment within the group, $p<0.05$; *means compared with the Monotherapy group after treatment, $p<0.05$

Table 2: Comparison of physician objective scores (x ± s)

Groups	N	Time point	Erythema absolute value	Erythema index	Skin water content	Transcutaneous water loss
Combination group	50	Before treatment	57.23±6.26	14.52±2.03	55.30±4.35	21.31±3.04
		After treatment	28.02±7.23#*	12.14±2.32#*	71.35±4.23#*	12.37±2.55#*
Monotherapy group	50	Before treatment	55.14±5.32	14.23±2.41	54.72±4.66	20.62±2.70
		After treatment	40.42±8.03	13.75±2.78	65.80±3.16	14.12±2.36

Note: #means compared with the corresponding values before treatment within the group, $p<0.05$; *means compared with the Monotherapy group after treatment, $p<0.05$

Table 3: Comparison of clinical efficacy [n (%)]

Groups	N	Cured	Markedly effective	Effective	Ineffective	Total effective rate
Combination group	50	8(16.00)	19(38.00)	18(36.00)	5(10.00)	45(90.00)
Monotherapy group	50	5(10.00)	16(32.00)	13(26.00)	16(32.00)	34(68.00)
Z						2.003
P						0.045

Comparison of physician objective scores

The two groups of patients had lower erythema absolute value and erythema index, more skin water content (P<0.05), and less transcutaneous water loss (P<0.05) after treatment, with better results observed in the combination group in contrast to the control group (P<0.05) (table 2).

Comparison of clinical efficacy

The overall effective rate of treatment for patients in the combination group was 90.00% (45/50), which was higher than that of 68.00% (34/50) in the mono therapy group (Z=2.003, P<0.05) (table 3).

Comparison of quality of life

The acne symptoms, self-perception, emotional function, and social function scores of patients in both groups were elevated after treatment (P<0.05), with higher outcomes obtained in the combination group than in the mono therapy group (P<0.05) (table 4).

Comparison of the incidence of adverse reactions and recurrence

The two groups showed no significant differences in the incidence of adverse reactions (8.00% (4/50) vs. 4.00% (2/50)) ($\chi2$=0.177, P>0.05) and in the recurrence rate (2.00% (1/50) vs. 8.00% (4/50)) ($\chi2$=0.842, P>0.05) (table 5).

Comparison of appearance satisfaction

Patients in the combination drug group had 98.00% (49/50) higher satisfaction with appearance than that of 72.00% (36/50) in the monotherapy group (Z=3.013, P<0.05) (table 6).

DISCUSSION

In recent years, the incidence of acne has been increasing due to the changes in people's lifestyles. The main pathogenesis is that estrogen affects fatty skin, obstructs hair follicles, and increases the adhesion of follicular funnel glial cells, which consequently promotes the activity of follicular sebaceous glands. The face of adolescents is a high prevalence site for acne, and as the development of one's self-esteem and self-confidence lies in puberty, adolescents are more psychologically vulnerable to the adverse effects of the disease. Previous research has shown (XU *et al*., 2019) that acne is highly predisposed to adverse psychological effects and the degree of impact increases with its severity. To the best of our knowledge, antibiotics are commonly used in the treatment of acne. Minocycline belongs to a kind of

Table 4: Comparison of quality of life (score, x ± s)

Groups	N	Time point	Acne symptoms	Self-perception	Emotional function	Social function
Combination group	50	Before treatment	13.42±2.35	11.60±1.62	12.63±2.30	10.05±1.74
		After treatment	23.58±3.40#*	22.66±3.78#*	20.2±3.53#*	26.57±3.24#*
Monotherapy group	50	Before treatment	13.47±2.30	11.63±1.67	12.60±2.22	10.18±1.80
		After treatment	17.04±2.51	14.38±2.70	15.73±2.75	16.62±2.13

Note: #means compared with the corresponding values before treatment within the group, p<0.05; *means compared with the Monotherapy group after treatment, p<0.05

Table 5: Comparison of the incidence of adverse reactions and recurrence [n (%)]

Groups	N	Adverse reactions				Recurrence
Combination group		Erythema	Itching	Dizziness	Total incidence	
	50	1(2.00)	1(2.00)	2(4.00)	4(8.00)	1(2.00)
Monotherapy group	50	1(2.00)	0(0)	1(2.00)	2(4.00)	4(8.00)
χ^2					0.177	0.842
P					0.674	0.359

Table 6: Comparison of appearance satisfaction [n (%)]

Groups	N	Very satisfied	Satisfied	Unsatisfied	Total satisfaction
Combination group	50	41(82.00)	8(16.00)	1(2.00)	49(98.00)
Monotherapy	50	29(58.00)	7(14.00)	14(28.00)	36(72.00)
Z					3.013
P					0.003

tetracycline antibiotic, which is a broad-spectrum antibiotic that effectively inhibits sebum secretion and maintains the balance of facial fat. Supra molecular salicylic acid is a natural anti-inflammatory agent with a light skin irritation under supra molecular chemical technology, which facilitates clinical control of salicylic acid concentration and provides favorable conditions for its absorption and utilization. It has been suggested (Zhuang, 2019). that compared with minocycline hydrochloride treatment, supra molecular salicylic acid treatment combined with minocycline hydrochloride treatment yields more significant results, better promotes quality of life and satisfaction in patients with moderate to severe acne, with a high safety profile.

Results of this study showed that the GAGS scores, erythema scores, and papulopustular scores of patients in both groups were decreased after medication (P<0.05), with lower results observed in the combination group than the mono therapy group (P<0.05), which indicates that 30% supra molecular salicylic acid can rapidly control inflammation to effectively manage the condition, with fewer adverse reactions, no damage to the skin barrier function and liver function. Moreover, the overall effective rate of the combination group was 90.00% (45/50), which was higher than that of 68.00% (34/50) in the mono therapy group (Z=2.003, P<0.05). After treatment, higher scores of acne symptoms, self-perception, emotional function, and social function were observed in patients in the combination group than in the mono therapy group (P<0.05), indicating that salicylic acid combined with minocycline lowers the chronic inflammatory response, reduces the number of facial papules and pustules, mitigates facial erythema, peels off the immature and fragile keratin sheath to build a mature and healthy keratin sheath, repairs the skin barrier function to block various harmful irritants and promotes the efficacy of treatment in the early stage of treatment. The two groups showed no significant differences in the incidence of adverse reactions (8.00% (4/50) vs. 4.00% (2/50)) (χ2=0.177, P>0.05) and in the recurrence rate (2.00% (1/50) vs. 8.00% (4/50)) (χ2=0.842, P>0.05), suggesting that supra molecular salicylic acid has better topical tolerance and fewer side effects, with excellent effectiveness in preventing acne recurrence. Consistently, all these are in line with the previous results (Zhuang, 2019; XU *et al*., 2019).

CONCLUSION

In conclusion, the efficacy of topical 30% salicylic acid plus minocycline in the treatment of moderate to severe acne was superior to that of mono therapy with minocycline, which is worthy of clinical promotion.

REFERENCES

Jiang M, Duan JJ, Li L and Zeng XY (2021). Efficacy of

supra molecular salicylic acid combined with fire acupuncture. *in:* The treatment of mild to moderate acne. *Chin J. Integr. Dermatol. Venereol.*, **20**(5): 63-65.

Jing WW and Zhou AY (2019). Exploring the efficacy of salicylic acid conditioning and nourishing mask combined with minocycline in the treatment of moderate to severe acne. *Chin. Aesthet Med.*, **28**: 8-11.

Li J, Yu L, Han FX and Zhang Y (2020). Clinical efficacy of Quasi-long pulse width 1064 Nm Nd: Yag laser combined with supra molecular salicylic acid in the treatment of mild to moderate acne on the face. *Chin. J. Integr. Dermatol. Venereol.*, **19**(6): 68-71.

SLY (2021). Topical application of 20% supra molecular salicylic acid and oral minocycline hydrochloride combined with red and blue light for the treatment of 51 cases of moderate to severe acne. *Anhui. Med.*, **25**(7): 366-369.

Shi Y, Zhang W (2020). Efficacy of dual-wavelength intense pulsed light combined with 30% supra molecular salicylic acid in the treatment of acne and acne rosacea. *Chin J. Med. Aesthet. Beauty*, **26**(5): 4.

Wj W, Jj L and M Z (2020). Efficacy analysis of supra molecular salicylic acid combined with intense pulsed light in the treatment of moderate to severe acne. *J. Pract. Dermatol.*, **13**: 20-22.

Wu P-H, Wang L, Yu H-H, Wang Y, Li Q-J, Zhao W, Fang Y-F (2020). Evaluation of clinical effects of Millifire acupuncture in the treatment of post-acne scarring after grade iv severe acne. *Chin J. Plast. Surg.*, **10**(8): 5.

Xu LH, Xu TX, Guo YN and Huang H (2019). Efficacy of supra molecular salicylic acid peeling in the treatment of Rosacea. *J. Fujian Med. Univer.*, **53**(7): 76-79.

Yu Dy (2020). Efficacy and safety analysis of supra molecular salicylic acid combined with minocycline hydrochloride in the treatment of moderate-to-severe acne. *J. Pharmaceut. Forum*, **41**(5): 82-85.

Zhuang BY (2019). Intense pulsed light combined with 30% supra molecular salicylic acid for the treatment of mild to moderate acne on the face. *Chin J. Integr. Dermatol. Venereol.*, **18**(5): 350-353.