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ORIGINAL RESEARCH

Effectiveness of Photodynamic Therapy, 2% Salicylic Acid, and Their Combination for Moderate Acne

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Objective: This study aimed to investigate the effectiveness of photodynamic therapy combined with 2% salicylic acid for treating moderate acne.

Methods: This retrospective study included outpatients with moderate acne who consulted the Department of Dermatology at Suining First People's Hospital in Sichuan Province between April 2019 and December 2019. The patients were grouped into the photodynamic group, the salicylic acid group, and the combination therapy group, according to whether they received aminolevulinic acid photodynamic therapy, a 2% supramolecular salicylic acid topical masque applied once daily for 10 minutes and then washed off for four consecutive weeks, 2% salicylic acid therapy, or both treatments combined. The overall effective rate was calculated as the percentage of patients with a 60% or greater reduction in skin lesions. Adverse reactions were also collected.

Results: A total of 66 patients were included, with 22 patients in each group. The combination therapy group had an overall effective rate of 72.73%, which was higher compared to the photodynamic group at 40.91% and the salicylic acid group at 22.73% (5 cases, $P < 0.003$). The skin lesions decreased in the photodynamic group, salicylic acid group, and combination therapy group by 11.72±4.80%, 8.62±3.16%, and 15.12±7.61% (P=0.01) at week one; 26.26±5.52%, 24.19±5.88%, and 33.11±8.90% (P=0.01) at week two; 42.63 ±7.25%, 39.21±9.91%, and 47.31±9.15% (P=0.01) at week three; and 58.84±9.45%, 52.35±8.75%, and 65.97±7.20% (P=0.01) at week four. Some patients experienced mild discomfort (redness, itching, pain), but no severe adverse reactions were reported.

Conclusion: Photodynamic therapy combined with 2% salicylic acid therapy reduced the number of skin lesions in patients with moderate acne more than either treatment alone. The combination therapy may be tolerable with no severe adverse reactions.

Keywords: photochemotherapy, salicylic acid, acne vulgaris, treatment outcome, skin care, adverse effects

Introduction

Acne vulgaris is the eighth most common skin disease globally, with a prevalence of 9.4%. Epidemiological studies indicate that 27–96% of adolescents experience acne at some point.[1] This chronic inflammatory condition affects the pilosebaceous follicles and typically presents during adolescence.[2] Clinically, acne manifests as papules, pustules, nodules, cysts, and other types of rashes, mainly on the face, neck, upper back, and chest.[3] These lesions can result in scarring and pigmentation, often requiring prolonged treatment. Acne not only impacts the skin but also leads to psychological and social distress due to concerns about appearance. The severity of acne has been reported to negatively correlate with patients' quality of life, with greater severity causing a more significant decline.[4] Therefore, it is imperative to take active and effective therapeutic measures to treat acne.

The primary goal of acne treatment is to reduce the number of lesions, prevent scarring, and enhance the skin's overall appearance, ultimately improving the patient's quality of life. Various treatment methods are available, and the specific approach may vary depending on the severity and type of acne, as well as individual factors such as age, skin type, and medical history.[5] The clinical treatment of acne often involves antibiotics, retinoids, and other topical or systemic therapies, all of which have demonstrated efficacy.[6] However, long-term use of antibiotics can easily lead to drug resistance and reduce their therapeutic effect, so treatment guidelines have limited their use to a maximum of three

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months.[7] The use of retinoids is limited by factors such as the younger age of pediatric patients and teratogenicity in women of childbearing potential, both of which restrict their application.[8] To avoid these effects, physical therapies such as those involving chemical peels with acids, including salicylic acid, glycolic acid, or lactic acid, have become an ideal choice.[9,10] In particular, salicylic acid, which has been demonstrated to be effective in several studies.[11–13] It works by penetrating the pilosebaceous unit due to its lipophilic nature, promoting exfoliation through disruption of intercellular desmosomal connections between corneocytes, thereby reducing follicular blockage. Additionally, it exerts anti-inflammatory effects by inhibiting cyclooxygenase enzymes, which decreases the production of pro-inflammatory prostaglandins.[14] However, the quality of evidence for their efficacy is generally low.[15] In addition to its physical peeling effects, salicylic acid appears to reduce the proportions of microbial species such as Staphylococcus, Ralstonia, and Streptococcus on the skin, thereby restoring a healthier microbial balance.[10]

Another physical therapy approach is photodynamic therapy, which involves the use of a topical photosensitizer in combination with a light source and oxygen.[16] Various photosensitive chemicals can be used for this therapy.[17] Aminolevulinic acid-based photodynamic therapy has gained particular popularity in China,[18] showing clinical improvement of lesions and good tolerability.[19] For mild-to-moderate acne, both topical and physical treatments have been shown to be effective.[20] However, combination treatments are considered particularly beneficial.[8]

The wide range of available acne treatment options has led to a lack of consensus regarding the most effective type and concentration of acid for treating acne-prone skin.[21] Despite suggestions that combination treatments are preferable, most previous studies on moderate acne have compared single treatments,[22–24] with few studies examining the benefits of combination treatments.[21] Therefore, further studies are needed to provide evidence on the effectiveness of specific treatments and the benefits of combination therapy. This study aimed to investigate the effectiveness of photodynamic therapy combined with 2% salicylic acid in treating moderate acne.

Materials and Methods

Study Design and Participants

This retrospective study enrolled outpatients with moderate acne who consulted the Department of Dermatology at Suining First People's Hospital in Sichuan Province for acne treatment between April 2019 and December 2019. The patients were divided into three groups according to the treatment they received: the photodynamic group, the salicylic acid group, and the combination therapy group. This study was approved by the Ethics Committee of Suining First People's Hospital in Sichuan Province. As this study involved only the review of existing medical records without direct patient contact, the Ethics Committee determined that it posed minimal risk to patients and did not adversely affect their rights or welfare; therefore, the requirement for obtaining written informed consent was waived. All patient data were anonymized, and confidentiality was strictly maintained following institutional and ethical guidelines.

The inclusion criteria were: 1) patients diagnosed with moderate acne based on the Pillsbury grading system (Table 1) which classifies acne severity based on lesion type and distribution;[25] 2) patients who received either one of the two treatments or a combination of both; 3) patients aged 16 years or older. The Pillsbury system was selected for its clinical simplicity and wide acceptance in dermatological practice, allowing consistent assessment across our patient population. Although other grading systems, such as the Global Acne Grading System, exist, the Pillsbury system's focus on lesion

Table 1 Pillsbury Clinical Grading System

Grade I	Mild	The skin lesions mainly consist of acne, accompanied by a small number of papules and pustules, with a total of <30 skin lesions.
Grade II	Moderate	Based on grade I, there are moderate amounts of papules and pustules, with a total number of skin lesions ranging from 31 to 50.
Grade III	Moderate	The number of papules and pustules increases based on grade II, and a small number of nodules appear, with several <3. The total number of skin lesions ranges from 50 to 100.
Grade IV	Severe	Based on the above types of skin lesions, the number of nodules increases, cystic lesions appear, the total number of nodules and cysts is >3, and the total number of skin lesions is greater than 100.

Note: Grade II–III acne was considered moderate acne for inclusion in this study.

morphology and severity was particularly suited to the objectives of this study.[25] Patients were excluded if they could not adhere to treatment due to severe adverse reactions, poor compliance, or health reasons, including women who were pregnant or breastfeeding. Those with keloid scars, severe psychiatric disorders, or serious systemic diseases affecting the hematopoietic, cardiovascular, cerebrovascular, or endocrine systems were also excluded. Additionally, patients who had used oral or topical antibiotics, isotretinoin, or other retinoid therapies within the previous four weeks were not included, ensuring an adequate washout period before enrollment. Patients who received any aesthetic medicine or cosmetology treatments during the study period or before completion of skin measurements were likewise excluded.

Procedure

All patients washed and, if necessary, disinfected their faces with 75% ethanol, then punctured and drained the acne to remove the secretions.

During the treatment period, all patients were instructed to follow the same standardized skincare routine. They were advised to cleanse their face twice daily using a mild, fragrance-free, non-medicated facial cleanser and to avoid harsh soaps, exfoliating products, or cosmetic treatments. No specific face cream was provided. The use of any other topical creams, ointments, or cosmetic products was not permitted unless prescribed as part of the treatment protocol.

Patients in the photodynamic group received photodynamic therapy once a week for four consecutive weeks using aminolevulinic acid hydrochloride topical powder (trade name: ALA, specification: 118 mg/bottle, lot number: 190702, Shanghai Fudan-Zhangjiang Bio-Pharmaceutical Co., Ltd.) at a concentration of 5%. The photosensitizer was evenly applied to the skin lesions, protected from light, and covered with plastic wrap for 2 hours before red light irradiation with a photodynamic therapy device (Wuhan Yage Optic & Electronic Co., Ltd., wavelength (633±10) nm, power density 60–100 mW/cm^2) at 60–70 mW/cm^2 for 20 min, 10 cm from the tip of the nose. Protective goggles were worn during treatment. After the treatment, an ice compress was applied for 20 minutes, and patients were instructed to avoid light for 48 hours, to pay attention to sun protection, and to moisturize the skin.

Patients in the salicylic acid group were treated once a day for four consecutive weeks with a 2% salicylic acid acne-removal and oil-control masque (100 g, 2% supramolecular salicylic acid, water-washable, ZHUHAI YASHA Bio-Technology Co., Ltd.) applied to the skin lesions on the face. After 10 minutes, the solution was washed off. During treatment, the area where the 2% salicylic acid was applied was closely observed, and any adverse reactions were recorded. If any burning, redness, swelling, pain, itching, or other symptoms occurred, they were treated promptly.

Patients in the combination therapy group received photodynamic therapy once a week, in combination with a 2% salicylic acid treatment applied once daily for four consecutive weeks. Photodynamic therapy was initially applied as described above. The skin was then cooled with an ice compress for 20 minutes, followed by the external application of 2% salicylic acid, as described above.

During the treatment period, all patients were instructed to avoid consumption of spicy, sweet, and fried foods, to eat more vegetables and fruits, ensure a light diet, to maintain a reasonable work and rest schedule, strictly avoid staying up late, and to pay attention to protection from the sun after treatment.

Data Collection and Outcomes

The number of facial skin lesions (acne, papules, pustules, and nodules) was counted by the same dermatologist at each follow-up visit. The treatment effectiveness was determined by the percentage reduction in skin lesions before and after treatment according to the following formula:

Reduction rate of skin lesions = (total number of skin lesions before treatment - total number of skin lesions after treatment)/total number of skin lesions before treatment × 100%.[12]

The treatment effects were defined as follows: Cure: reduction of skin lesions ≥ 90%; Significant therapeutic effect: 60% ≤ reduction of skin lesions < 90%; Improved: 20% ≤ reduction of skin lesions < 60%; Ineffective: reduction of skin lesions < 20%. The overall effective rate was calculated as the Cure rate plus the significant therapeutic effect rate.

Records were kept of the number of skin lesions and adverse reactions experienced by the patients before treatment and at the end of the first, second, third, and fourth weeks. The type of adverse reaction, such as erythema, edema, pain,

itching, and the number of cases were also recorded. The incidence of adverse reactions was calculated as the percentage of patients who experienced adverse events, using the following formula:

Incidence of adverse reactions (%) = (Number of patients with adverse reactions / Total number of patients in the study) × 100.

Statistical Methods

Statistical analyses were performed using SPSS 20.0 software (IBM Corporation). The measurement data were recorded as mean and standard deviation (SD), and the count indicators were expressed as *N* (%). A one-way analysis of variance (ANOVA) was used to compare overall differences between groups for each test indicator. If the overall difference was statistically significant, a multiple comparison between groups was further performed using the least significant difference (LSD) method. The Chi-squared test was used to compare rates between groups, and when necessary, it was supplemented by Fisher's exact test for direct P-value calculation. The rank-sum test was applied for comparisons of ordinal data. A two-sided P-value of < 0.05 was considered statistically significant at a significance level of 0.05.

Results

Initially, 68 patients were included in the study, of whom 2 were excluded because they did not complete the subsequent follow-up; ultimately, 66 patients were included in the analysis.

There were three groups of patients: the photodynamic group (n = 22), the salicylic acid group (n = 22), and the combination therapy group (n = 22). There were no significant differences in age, gender, or the number of skin lesions among the three groups ($P > 0.05$).

The total effective rates for the three groups at the fourth week are shown in Table 2. The rates were 40.91% in the photodynamic group, 22.73% in the salicylic acid group, and 72.73% in the combination therapy group. The differences between the groups were statistically significant ($P = 0.003$).

The reduction in skin lesions over the four weeks of treatment is shown in Table 3. There were significant differences between the groups at each time point. At week one, the reduction was 11.72±4.80% in the photodynamic group, 8.62 ±3.16% in the salicylic acid group, and 15.12±7.61% in the combination therapy group (P=0.01). At week two, the reduction was 26.26±5.52% in the photodynamic group, 24.19±5.88% in the salicylic acid group, and 33.11±8.90% in the combination therapy group (P=0.01). At week three, the reduction was 42.63±7.25% in the photodynamic group,

Table 2 Total Effective Rate of Skin Lesions in the Three Groups of Patients in the Fourth week

	Photodynamic Group (n=22)	Salicylic Acid Group (n=22)	Combination Therapy Group (n=22)	*P*
Cure, n	0	0	0	0.003
Significant therapeutic effect, n	8	5	16	
Improved, n	13	17	6	
Ineffective, n	0	0	0	
Total effective rate, %	40.91	22.73	72.73	

Table 3 The Reduction Rates of Skin Lesions at Different Treatment Time Points Among the Three Groups of Patients

Reduction Rates of Skin Lesions	Photodynamic Group (n=22)	Salicylic Acid Group (n=22)	Combination Therapy Group (n=22)	*P*
First week	11.72±4.80	8.62±3.16	15.12±7.61	0.01
Second week	26.26±5.52	24.19±5.88	33.11±8.90	0.01
Third week	42.63±7.25	39.21±9.91	47.31±9.15	0.01
Fourth week	58.84±9.45	52.35±8.75	65.97±7.20	0.01

39.21±9.91% in the salicylic acid group, and 47.31±9.15% in the combination therapy group (P=0.01). At week four, the reduction was 58.84±9.45% in the photodynamic group, 52.35±8.75% in the salicylic acid group, and 65.97±7.20% in the combination therapy group (P=0.01). This indicated that the reduction in skin lesions improved with treatment duration and improved most in the combination therapy group compared to the other two groups.

None of the patients in any of the groups experienced severe adverse reactions during treatment. Three patients in the photodynamic group experienced mild symptoms, including burning, redness, swelling, pain, and itching, which subsided after applying ice compresses or on their own after the treatment was completed. As the number of treatments increased, the symptoms of burning, redness, swelling, pain, and itching decreased. The 2% salicylic acid treatment caused mild dryness and itching, which subsided on their own after the treatment was over and did not require special care. During the combination treatment, some patients experienced mild symptoms, including redness, swelling, itching, and pain, which subsided after applying cold compresses. Given the low incidence and mild nature of these adverse events, as well as the relatively small sample size in each group, a formal statistical comparison of side effect frequency and severity was not performed. All reported symptoms were transient and resolved without intervention, supporting the good tolerability of all treatment regimens.

Discussion

This study found that each of the three treatments (photodynamic therapy, 2% salicylic acid therapy, and combination therapy) can reduce the number of skin lesions in patients with moderate acne. However, the combination therapy achieved the highest effective rate. These findings reveal that combination therapy may be effective and tolerable with no severe adverse reactions.

Both photodynamic therapy and chemical peeling were effective in treating acne.[26] This study aimed to evaluate whether the treatments were more effective when used in combination. Photodynamic therapy has become a popular treatment approach for moderate acne. A meta-analysis of three randomized controlled trials suggests that photodynamic therapy is an effective treatment for acne vulgaris, demonstrating a significant mean percentage reduction in inflammatory lesion count and a higher overall treatment response rate.[26] Yu Yan et al, reported that combining 5-aminolevulinic acid photodynamic therapy (ALA-PDT) with sequential 30% supramolecular salicylic acid (SSA) significantly reduced acne lesions, especially comedones and papules, compared to ALA-PDT alone, while also reducing adverse effects, such as erythema.[27] Similarly, our study found that combining photodynamic therapy with 2% salicylic acid achieved a higher effective rate and better lesion reduction than either treatment alone. However, the lower salicylic acid concentration may explain the more modest effectiveness compared to their results. These findings collectively support the enhanced efficacy of combination therapy in treating moderate acne. Zhang et al, reported that combining modified ALA-PDT with isotretinoin led to significantly improved lesion clearance compared to isotretinoin alone, particularly during the early treatment stages.[28] In that study, the 1-month effective rate of photodynamic therapy was 67.74%.[28] Although our study did not use isotretinoin, the higher effective rate observed in our combination therapy group compared to monotherapies similarly supports the enhanced efficacy of combination approaches. However, differences in drug selection and acne severity limit direct comparability. Another study suggests that photodynamic therapy provides long-term improvement across different types of acne, with 95.5% of cases achieving ≥60% lesion clearance—comparable to the effective rate observed in our study.[29] In our study, the effective rate of photodynamic therapy was 40.9%. Although this is lower than the rates reported in previous studies, several factors may account for this discrepancy. These include differences in treatment protocols (eg, light source intensity or application duration), patient adherence, or variations in acne severity across study populations. Additionally, our study was conducted retrospectively and in a real-world clinical setting, which may inherently differ from the more controlled environments of prospective clinical trials. Moreover, the inclusion criteria in our study may have selected patients with more persistent or treatment-resistant acne, potentially contributing to a lower observed response rate.[17] Despite this, the findings are still lower than the rates of previous studies, which supports the view that photodynamic therapy should be considered for moderate acne treatment. The differences in effective rates may be due to variations in study populations in terms of acne severity or patient characteristics. Chemical peeling is another practical approach for treating acne. A previous study using 2% salicylic acid reported an improvement rate of 51.01% after 12 weeks of treatment,[12] which is unfortunately not directly

comparable to the effective rate used in this study. In this study the salicylic acid group achieved a total effective rate of 22.73%, which was lower than the rate found in the photodynamic group. However, higher concentrations of salicylic acid, such as 30%, have also been used effectively not only to treat acne but also acne scars and post-acne hyperpigmentation, demonstrating favorable outcomes in 76.4% of cases.[22] Some comparison studies suggest 30% salicylic acid is more effective than peeling with Jessner's solution (another chemical peel composed of salicylic acid, lactic acid, and resorcinol).[23,24] Jessner's solution works by removing the top layers of damaged skin and promoting epidermal renewal. It also improves acne by unclogging pores and reducing inflammation.[30] It is possible that the lower concentration used in our study (2%) contributed to the relatively modest effectiveness observed.[31] Future studies could explore optimal dosing to enhance therapeutic outcomes. Further studies are needed to establish whether higher concentrations of salicylic acid would achieve better effective rates in single and combination treatments.

Some studies have assessed combination therapies for treatment of moderate acne, such as photodynamic therapy in combination with isotretinoin, which showed improved effectiveness than the treatments in isolation.[32] Similarly, in our study, the combination therapy group was more effective than the single photodynamic therapy or the single 2% salicylic acid therapy group. Additionally, the combination therapy group showed a significantly better tendency to reduce skin lesions compared to the photodynamic group and the 2% salicylic acid therapy group. It was more effective in improving the skin lesions and facial skin condition. The adverse reactions were mainly manifested as burning, redness, swelling, pain, and itching. The symptoms were mild and tolerable and quickly disappeared after the treatment was completed. No severe adverse reactions were observed.

This study has some limitations. As a retrospective study, there may have been some bias in the inclusion of patients in the study. As a single-center study, the number of patients included was limited. Larger studies from multiple centers are needed to fully support the results of this study. Moreover, this study did not include objective skin measurements such as sebumeter or corneometer assessments, which could provide a more comprehensive evaluation of skin condition and treatment effects. Incorporating these tools in future research would strengthen the understanding of the treatments' impact.

Conclusion

In conclusion, treatment of patients with moderate acne vulgaris was effective using photodynamic therapy and 2% salicylic acid; however, the effectiveness was significantly improved by combining photodynamic therapy with 2% salicylic acid. The adverse reactions of all patients were mild and manageable. Therefore, this combination treatment may be effective and tolerable for treating moderate acne.

Data Sharing Statement

All data generated or analyzed during this study are included in this article.

Ethics Approval and Consent to Participate

This work has been carried out following the Declaration of Helsinki (2000) of the World Medical Association. This study was approved by the Ethics Committee of Suining First People's Hospital in Sichuan Province. As this study involved only the review of existing medical records without direct patient contact, the Ethics Committee determined that it posed minimal risk to patients and did not adversely affect their rights or welfare; therefore, the requirement to obtain distinct written informed consent was waived. All patient data were anonymized, and confidentiality was strictly maintained following institutional and ethical guidelines.

The Patient and Public Involvement Statement

This study does not involve any patient or publicly confidential information.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically

reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare that they have no competing interests.

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