Am J Transl Res 2021;13(9):10816-10822
www.ajtr.org /ISSN:1943-8141/AJTR0131550

Original Article

Clinical efficacy of tanshinone capsules combined with varying concentrations of 5-ALA-PDT in the treatment of cystic acne

Yan Yao[1*], Jing Zuo[2*], Li Chen[1]

[1]*Department of Dermatology, Affiliated Hospital of Nanjing University of Chinese Medicine, Nanjing 210029, Jiangsu Province, China;* [2]*Department of Ophthalmology, Affiliated Hospital of Nanjing University of Chinese Medicine, Nanjing 210029, Jiangsu Province, China.* [*]*Equal contributors and co-first authors.*

Received February 7, 2021; Accepted May 11, 2021; Epub September 15, 2021; Published September 30, 2021

Abstract: Objective: To investigate the clinical effectiveness and safety of tanshinone capsules combined with varying concentrations of 5-aminoketovaleric acid photodynamic therapy (5-ALA-PDT) in the treatment of cystic acne. Methods: A total of 97 patients with cystic acne treated in our hospital were enrolled in the study and divided into group A (n = 34, tanshinone capsules combined with 5% 5-ALA-PDT), group B (n = 31, tanshinone capsules combined with 7.5% 5-ALA-PDT), and group C (n = 32, tanshinone capsules combined with 10% 5-ALA-PDT). The number of skin lesions, the global acne grading system (GAGS) scores, the clinical effectiveness, the adverse reactions, and the recurrence rates were compared among the three groups. Results: The number of skin lesions and the GAGS scores were lower in all three groups at two weeks, one month, and three months of treatment ($P<0.05$), and the numbers of skin lesions in groups B and C were significantly lower than the number in group A ($P<0.05$). The clinical effectiveness in groups B and C was better than it was in group A ($P<0.05$), and the overall effective rates in groups B and C (87.10% and 87.50%) were significantly higher than the overall effective rate in group A (41.18%) ($P<0.05$). The adverse reaction rates in groups A and B (5.88% and 6.45%) were significantly lower than the adverse reaction rate in group C (25.00%) ($P<0.05$), and the recurrence rate in group A (17.65%) was significantly higher than the recurrence rates in groups B and C (3.23% and 0.00%) ($P<0.05$). Conclusions: Tanshinone capsules combined with 7.5% 5-ALA-PDT showed the optimal clinical effectiveness and safety in the treatment of cystic acne.

Keywords: Tanshinone capsules, 5-aminoketovaleric acid photodynamic therapy, clinical effectiveness, safety

Introduction

Acne is a chronic inflammatory skin disease caused by *Cutibacterium acnes* infection and abnormal cortical secretions, resulting in localized skin conditions such as acne, papules, pustules, nodules and cysts involving hair follicles and sebaceous glands. Acne occurs in about 90% of adolescents to varying degrees [1]. Cystic acne is the most severe type of acne with cysts as the main lesion type. The lesions are relatively large, with localized pain and more pronounced swelling, mostly aggregated cysts and nodules, which tend to result in hyperpigmentation, severe hyperplastic scarring or depressed scarring after the lesions break down and become full of pus. Cystic acne has a long course and is prone to recurrence, which affects facial aesthetics and is detrimental to patients' physical and mental health [2, 3].

Medications such as antibiotics, sex hormones, and retinoids, as well as aesthetic procedures such as lasers, alpha hydroxyl acid, and red light combined with blue light irradiation, are often used clinically to relieve the symptoms of cystic acne. However, patients are prone to develop a tolerance to a medication and experience adverse effects. In contrast, hormone treatment, keratolytic and lipid removal treatment usually work longer. Patients may have low compliance due to prolonged treatment, which is not conducive to good clinical outcomes, and the treatment can also impair normal liver and kidney function as well as hormone secretions. Therefore, it is important to seek effective, safe and reliable treatments.

According to Traditional Chinese Medicine, cystic acne is related to blood stasis and phlegm clotting and is especially closely associated with blood stasis. The main active ingredient of tanshinone capsules is cryptotanshinone, which kills the acne bacillus and eliminates the inflammatory response. It has been shown that tanshinone is effective at relieving inflammation caused by *Propionibacterium acnes* in vitro [4]. 5-Aminoketovaleric acid photodynamic therapy (5-ALA-PDT) is a new efficacious and safe treatment option in dermatology, that is being gradually used in the treatment of severe acne [5]. However, there is no standard for the concentration of 5-ALA-PDT in the treatment of cystic acne. In this study, we analyzed the clinical effectiveness and safety of cystic acne treated with danshinone capsules combined with varying concentrations of 5-ALA-PDT in cystic acne patients.

Materials and methods

Baseline data

Ninety-seven patients with cystic acne admitted to our hospital were recruited as the study cohort and divided into group A (n = 34, tanshinone capsules combined with 5% 5-ALA-PDT), group B (n = 31, tanshinone capsules combined with 7.5% 5-ALA-PDT), or group C (n = 32, tanshinone capsules combined with 10% 5-ALA-PDT) according to the 5-ALA-PDT concentration each patient was administered. Inclusion criteria: (1) Patients who had the disease > six months, (2) patients 16-35 years old, and (3) patients with severe acne. Exclusion criteria: (1) patients with autoimmune diseases, such as dermatomyositis and lupus erythematosus, (2) patients with systemic skin diseases, such as vitiligo and psoriasis, (3) patients who used an antibiotic treatment in the previous one month prior to their participation in this study, (4) patients who underwent a retinoid treatment within the last 6 months, (5) patients undergoing glucocorticoid treatment, (6) patients with an intolerance to 5-ALA-PDT treatment, (7) patients with severe liver and kidney dysfunction or malignancy, (8) patients with a porphyrin allergy or photosensitivity, (9) women who were pregnant or lactating, and (10) patients who withdrew from the study. This study was approved by the Medical Ethics Committee of the Affiliated Hospital of Nanjing University of Chinese Medicine. The study cohort and their families signed a written informed consent form before participating in the research.

Methods

Groups A, B, and C were treated with tanshinone capsules combined with 5%, 7.5%, and 10% 5-ALA-PDT, respectively. (1) Tanshinone capsules (Approval No. Z13020110, manufacturer: Hebei Xinglong Xili Pharmaceutical Co., Ltd.) two weeks of treatment: 4 capsules per time, b.i.d for 8 weeks, followed by 3 capsules per time, b.i.d for 4 weeks. (2) 5-ALA-PDT therapy: After facial cleaning, the patients with facial abscesses were placed in a supine position. The lesions and surrounding skin were re-cleaned using water for injection, and aminolevulinic acid hydrochloride for topical powder (specification: 118 mg, approval No. H2007-0027, manufacturer: Shanghai Fudan-Zhangjiang Bio-Pharmaceutical Co., Ltd.) and saline were prepared as 5-aminoketovaleric acid (5-ALA) with the concentrations of 5%, 7.5%, and 10%. Sterilized cotton balls were applied on the lesions and expanded outward by 0.5 cm. One milliliter of liquid was dripped and soaked using sterile desiccated cotton, and then medical gauze was applied externally, followed by sealing with plastic film, which was protected from light for 4 hours. The sealing was removed, and a LEDIA photodynamic device (Model: LED-IA, output wavelength: 633 nm, manufacturer: Wuhan YAG Photoelectric Technology Co., Ltd.) was used for the irradiation with an energy density of 100 J/cm^2 and an irradiation distance of 10 cm, and the light spot was adjusted to completely cover the lesion during the treatment according to the area of the lesion. The treatment was performed every 1 to two weeks for 4 times, and the skin lesions were protected from light for 72 hours after the irradiation.

Outcome measurement

(1) Before the treatment, the numbers of lesions on the patients were recorded at two weeks, one month, and three months of treatment, and the lesion severity was assessed using global acne grading system (GAGS) scores [6], with the chest and upper back (scored as 3), the forehead (scored as 2), the left cheek (scored as 2), the right cheek (scored as 2), the chin area (scored as 1), and the nose (scored

Table 1. Comparison of the baseline data among the three groups ($\bar{x}$±s; *n*, %)

Group	Number of cases	Sex		Age (years)	Duration of disease (years)	BMI (kg/m^2)
		Male	Female			
Group A	34	20 (58.82)	14 (41.18)	21.68±5.89	3.28±0.91	21.52±2.11
Group B	31	17 (54.84)	14 (45.16)	22.52±6.96	2.94±0.76	21.55±1.99
Group C	32	19 (59.38)	13 (40.63)	21.85±6.87	2.93±0.78	21.74±2.56
t		0.023		0.146	1.947	0.092
P		0.880		0.865	0.148	0.912

as 1) as the factor scores. The scores for skin lesions in the same area were: no lesions, 0 points, ≥1 acne, 1 point; ≥1 papule, 2 points; ≥1 pustule, 3 points; ≥1 cyst or nodule, 4 points. Individual area score = factor score × lesion score, and the total score is the sum of the individual area score. (2) The patients' treatment efficacy was assessed at three months of treatment [7]: a reduction of more than 90% in the number of lesions and the GAGS score was considered cured. A reduction of 71% to 90% was considered significant improvement. A reduction of 25% to 70% was considered effective. A reduction of less than 25% was considered ineffective. Total effective rate = Cured + significant improvement. (3) Any adverse reactions as well as the recurrence of cystic acne were recorded at a 6-month follow-up, including erythema, temporary hyperpigmentation, and local edema.

Statistical methods

All the data were processed using SPSS 22.0 statistical software. The count data were expressed as (*n*, %), and the comparisons were performed using χ^2 tests. The measurement data were expressed as ($\bar{x}$±s), and the comparisons within and between groups were performed using paired t-tests and t-tests with independent samples, respectively. The comparisons at the different time points were performed using repeated measures analyses of variance (ANOVA) with *post hoc* LSD-t tests. The statistical graphs were made using GraphPad Prism 8.0. Statistically significant differences were expressed using $P<0.05$.

Results

Baseline data

There were 34 patients in group A, with the age of 21.68±5.89 years, duration of disease of 3.28±0.91 years, and body mass index (BMI) of 21.52±2.11 kg/m^2. There were 31 patients in group B, with the age of 22.52±6.96 years, duration of disease of 2.94±0.76 years, and BMI of 21.55±1.99 kg/m^2. There were 32 patients in group C, with the age of 21.85±6.87 years, duration of disease of 2.93±0.78 years, and BMI of 21.74±2.56 kg/m^2. Gender, age, disease duration, and BMI did not differ significantly among the three groups ($P>0.05$) (**Table 1**).

Number of skin lesions

Significant differences were observed in the number of skin lesions when compared at the time points, between the groups, and between the time-group interactions ($P<0.05$). *Post hoc* LSD-t tests showed that the number of lesions was lower in all three groups at two weeks, one month, and three months of treatment compared with the pre-treatment values ($P<0.05$), and groups B and C showed lower numbers of lesions compared with group A ($P<0.05$, **Table 2**; **Figure 1A**).

GAGS scores

Significant differences were observed in the GAGS scores when compared at the time points, between the groups, and between the time-group interactions ($P<0.05$). The *post hoc* LSD-t tests showed that the GAGS scores were significantly lower in the three groups at two weeks, one month, and three months of treatment compared with their pre-treatment values ($P<0.05$), and the GAGS scores in groups B and C were significantly lower compared with the GAGS scores in group A ($P<0.05$) (**Table 3** and **Figure 1B**).

Clinical effectiveness

The clinical effectiveness in groups B and C was better than the clinical effectiveness in group A ($Z = 3.381, 3.485$, $P<0.05$), and the

Table 2. Comparison of the number of skin lesions at the different time points (pcs; $\bar{x}\pm s$)

Group	Number of cases	Before treatment	two weeks of treatment	one month of treatment	three months of treatment
Group A	34	71.35±12.40	55.85±14.81$^{\Delta}$	28.50±9.18$^{\Delta}$	23.15±7.30$^{\Delta}$
Group B	31	69.87±14.11	40.39±11.38$^{\Delta,*}$	17.97±5.67$^{\Delta,*}$	12.19±3.16$^{\Delta,*}$
Group C	32	71.09±13.73	40.13±11.94$^{\Delta,*}$	17.03±5.13$^{\Delta,*}$	11.38±2.83$^{\Delta,*}$
F	$F_{time\ point}$ = 680.381, $F_{interaction}$ = 4.272, $F_{intergroup}$ = 19.298				
P	$P_{time\ point}$<0.001, $P_{interaction}$<0.001, $P_{intergroup}$<0.001				

Note: $^{\Delta}$compared with pre-treatment, $P<0.05$; *compared with group A, $P<0.05$.

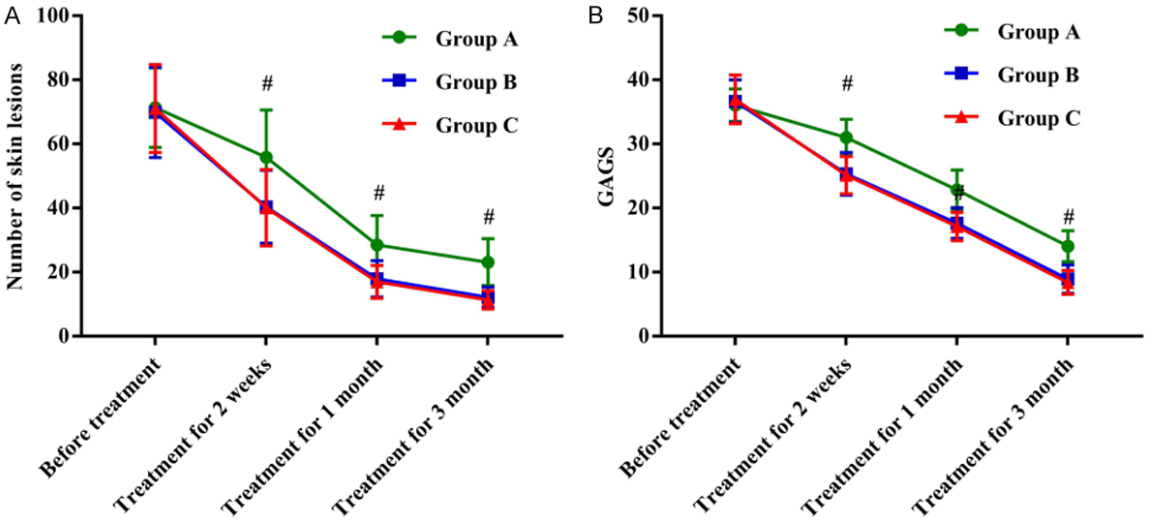

Figure 1. Comparison of the number of skin lesions and GAGS at the different time points. **Figure 1** shows that the number of lesions (A) and GAGS (B) before the treatment in the three groups were not significantly different ($P>0.05$). The numbers of lesions and GAGS at two weeks, one month, and three months of treatment in the three groups were significantly different ($P<0.05$). #Compared with group A, $P<0.05$.

Table 3. Comparison of the GAGS scores at different time points in the three groups ($\bar{x}\pm s$)

Group	Number of cases	Before treatment	two weeks of treatment	one month of treatment	three months of treatment
Group A	34	36.06±2.56	31.03±2.83$^{\Delta}$	22.85±3.10$^{\Delta}$	14.06±2.40$^{\Delta}$
Group B	31	36.65±3.35	25.35±3.34$^{\Delta,*}$	17.65±2.40$^{\Delta,*}$	8.94±2.22$^{\Delta,*}$
Group C	32	36.97±3.78	25.13±2.92$^{\Delta,*}$	17.13±2.21$^{\Delta,*}$	8.41±1.86$^{\Delta,*}$
F	$F_{time\ point}$ = 3075.180, $F_{interaction}$ = 13.472, $F_{intergroup}$ = 33.382				
P	$P_{time\ point}$<0.001, $P_{interaction}$<0.001, $P_{intergroup}$<0.001				

Note: $^{\Delta}$compared with pre-treatment, $P<0.05$; *compared with group A, $P<0.05$.

overall effective rates of groups B and C (87.10% and 87.50%) were significantly higher compared with the overall effective rate of group A (41.18%) ($P<0.05$) (**Table 4**).

Adverse reactions and recurrence

Group C (25.00%) showed an increased incidence of adverse reactions compared with groups A and B (5.88% and 6.45%) ($P<0.05$), and group A (17.65%) showed an increased recurrence rate compared with groups B and C (3.23% and 0.00%) ($P<0.05$, **Table 5**).

Discussion

5-ALA-PDT treats acne by exogenously giving ALA to patients. Since sebaceous glands and

Table 4. Comparison of the treatment efficacy levels among the three groups (*n*, %)

Group	Number of cases	Cured	Markedly effective	Effective	Ineffective	Total effective rate
Group A	34	7 (20.59)	7 (20.59)	9 (26.47)	11 (32.35)	14 (41.18)
Group B	31	14 (45.16)	13 (41.94)	2 (6.45)	2 (6.45)	27 (87.10)*
Group C	32	15 (48.39)	13 (40.63)	2 (6.45)	2 (6.45)	28 (87.50)*
Z/χ^2			17.386			19.961
P			<0.001			<0.001

Note: *compared with group A, $P<0.05$.

Table 5. Comparison of the occurrence of adverse reactions in the three groups (*n*, %)

Group	Number of cases	Erythema	Temporary hyperpigmentation	Local edema	Total incidence rate	Recurrence rate
Group A	34	1 (2.94)	1 (2.94)	0 (0.00)	2 (5.88)	6 (17.65)
Group B	31	1 (3.23)	1 (3.23)	0 (0.00)	2 (6.45)	1 (3.23)*
Group C	32	3 (9.38)	4 (12.5)	1 (3.13)	8 (25.00)*,#	0 (0.00)*
χ^2		0.507	1.526	0.256	4.935	7.675
P		0.476	0.217	0.613	0.026	0.006

Note: *compared with group A, $P<0.05$; #compared with group B, $P<0.05$.

epithelial cells reabsorb ALA, which is then converted into the photosensitizer protoporphyrin IX (Pp IX) via the heme synthesis pathway, and during red light (at a specific wavelength) irradiation, Pp IX produces free radicals as well as singlet oxygen, which selectively kills *Propionibacterium acnes*, thereby inhibiting sebaceous secretions and destroying the structure of the sebaceous glands [8, 9]. During photodynamic therapy (PDT), a red or blue light will be shined on the treatment area. Blue light is an effective exogenous stimulus, leading to the formation of endogenous porphyrins, and is 40 to 50 times more effective than red light, but less penetrating than red light. Therefore, blue light combined with red light contributes to the local anti-inflammatory effect [10, 11]. Although 5-ALA-PDT is clinically effective in the treatment of acne, PDT can still cause severe lesions, resulting in open lesions in the acne area that cannot be repaired by PDT. It was clinically found that 5-ALA-PDT is ineffective in the treatment of cystic acne, probably because the cystic patients had very thick cyst walls that would not break down, so the ALA could not be completely absorbed, leading to prolonged healing times and a low therapeutic efficacy.

Danshinone is mainly composed of fat-soluble salvia, which has the effect of removing blood stasis and relieving pain, regulating the endocrine system, activating the blood circulation, regulating menstruation, calming the mind, cooling the blood, reducing swelling, and maintaining a hormone balance. Tanshinone capsules are mainly composed of the ethanolic extract of *Salvia miltiorrhiza*, and have anti-inflammatory and antibacterial effects, can promote skin metabolism, improve microcirculation, have anti-androgenic effects as well as estrogenic activity, can inactivate acne-inflammatory substances such as *Staphylococcus* and *P. acne*, and have an inhibitory effect on the sebaceous glands [12-14]. After the oral administration of tanshinone capsules, they are absorbed through the gastrointestinal tract and transferred to the whole body more rapidly to reduce the serum testosterone, thus improving the symptoms of acne [15, 16]. It was clinically found that tanshinone combined with 5-ALA-PDT in the treatment of cystic acne can effectively improve the therapeutic effect and shorten the course of treatment, thus reducing the patients' economic burdens.

Studies have shown that the concentration of ALA should be kept between 2% and 20%, and the skin irritation caused by ALA increases with an increase in its concentration [17, 18]. In this study, the effects of 5-ALA-PDT at concentrations of 5%, 7.5%, and 10% in combination with tanshinone capsules were explored for the

treatment of cystic acne, respectively, and the results showed that the number of lesions and the GAGS scores were lower in all three groups at two weeks, one month and three months of treatment, and the numbers of lesions in groups B and C were significantly lower than the number of lesions in group A. The treatment efficacy of groups B and C was better than it was in group A, and the total effective rates in groups B and C (87.10% and 87.50%) were significantly higher than the total effective rate in group A (41.18%). The results of the study showed that tanshinone capsules combined with 7.5% and 10% 5-ALA-PDT for the treatment of cystic acne are more effective at reducing the number of lesions and improving the severity of acne lesions, and they have a more significant clinical effectiveness. Studies have shown that adverse reactions such as hyperpigmentation and erythema may occur when 5-ALA-PDT treatment is performed [5, 19, 20]. The occurrence of erythema is caused by the increased vascular permeability and capillary dilation in the superficial dermis caused by red light irradiation, and the hyperpigmentation is mainly induced by the accumulation of Pp IX in the epidermis caused by PDT [21-23]. In this study, the incidence rate of adverse reactions in groups A and B (5.88% and 6.45%) was significantly lower than it was in group C (25.00%). The recurrence rate in group A (17.65%) was significantly higher than the recurrence rates in groups B and C (3.23% and 0.00%). The results of the study suggested that tanshinone capsules with 7.5% 5-ALA-PDT resulted in fewer adverse effects and a lower cystic recurrence rate.

In conclusion, tanshinone capsules combined with 7.5% and 10% 5-ALA-PDT in the treatment of cystic acne are superior to treatment with tanshinone capsules combined with 5% 5-ALA-PDT in terms of reducing the number of lesions and improving the severity of the symptoms, the treatment had a better clinical effectiveness. However, the treatment of cystic acne with tanshinone capsules combined with 7.5% 5-ALA-PDT had fewer adverse reactions and lower recurrence rates and was safer compared with tanshinone capsules +10% 5-ALA-PDT. Therefore, tanshinone capsules in combination with 7.5% 5-ALA-PDT were recommended in terms of clinical effectiveness and safety. However, the study cohort was small and the duration of the observation was not long, so these factors should be improved in future studies.

Disclosure of conflict of interest

None.

Address correspondence to: Li Chen, Department of Dermatology, Affiliated Hospital of Nanjing University of Chinese Medicine, No. 155, Hanzhong Road, Nanjing 210029, Jiangsu Province, China. Tel: +86-13611506199; E-mail: Dr13915963795@yeah.net

References

[1] Singer HM, Almazan T, Craft N, David CV, Eells S, Erfe C, Lazzaro C, Nguyen K, Preciado K, Tan B and Patel VA. Using network oriented research assistant (NORA) technology to compare digital photographic with in-person assessment of acne vulgaris. JAMA Dermatol 2018; 154: 188-190.

[2] Fournier JF, Clary L, Chambon S, Dumais L, Harris CS, Millois C, Pierre R, Talano S, Thoreau É, Aubert J, Aurelly M, Bouix-Peter C, Brethon A, Chantalat L, Christin O, Comino C, El-Bazbouz G, Ghilini AL, Isabet T, Lardy C, Luzy AP, Mathieu C, Mebrouk K, Orfila D, Pascau J, Reverse K, Roche D, Rodeschini V and Hennequin LF. Rational drug design of topically administered caspase 1 inhibitors for the treatment of inflammatory acne. J Med Chem 2018; 61: 4030-4051.

[3] Zheng Y, Yu E, Weng Q, Zhou L and Li Q. Optimization of hydrogel containing toluidine blue O for photodynamic therapy in treating acne. Lasers Med Sci 2019; 34: 1535-1545.

[4] Li Y and Zhou Y. The therapeutic effect of tanshinone IIA on Propionibacterium acnes-induced inflammation in vitro. Dermatol Ther 2018; 31: e12716.

[5] Serini SM, Cannizzaro MV, Dattola A, Garofalo V, Del Duca E, Ventura A, Milani M, Campione E and Bianchi L. The efficacy and tolerability of 5-aminolevulinic acid 5% thermosetting gel photodynamic therapy (PDT) in the treatment of mild-to-moderate acne vulgaris. A two-center, prospective assessor-blinded, proof-of-concept study. J Cosmet Dermatol 2019; 18: 156-162.

[6] Sule Afsar F, Seremet S, Demirlendi Duran H, Elif Yildirim F and Mumcu Sönmez N. Social appearance anxiety in adult patients with acne: a cross-sectional study. Acta Dermatovenerol Croat 2018; 26: 220-225.

[7] Ahmadvand A, Yazdanfar A, Yasrebifar F, Mohammadi Y, Mahjub R and Mehrpooya M. Eval-

uating the effects of oral and topical simvastatin in the treatment of acne vulgaris: a double-blind, randomized, placebo-controlled clinical trial. Curr Clin Pharmacol 2018; 13: 279-283.

[8] Zhang Y, Lin H, Guo X and Zou X. A case series pilot study on the combination of 5-aminolevulinic acid and photodynamic therapy (ALA-PDT) for treatment of vitiligo. An Bras Dermatol 2018; 93: 539-545.

[9] Osaki T, Takahashi K, Ishizuka M, Tanaka T and Okamoto Y. Antimalarial drugs enhance the cytotoxicity of 5-aminolevulinic acid-based photodynamic therapy against the mammary tumor cells of mice in vitro. Molecules 2019; 24: 3891.

[10] Fang CY, Chen PY, Ho DC, Tsai LL, Hsieh PL, Lu MY, Yu CC and Yu CH. miR-145 mediates the anti-cancer stemness effect of photodynamic therapy with 5-aminolevulinic acid (ALA) in oral cancer cells. J Formos Med Assoc 2018; 117: 738-742.

[11] Rosin FCP, Teixeira MG, Pelissari C and Corrêa L. Photodynamic therapy mediated by 5-aminolevulinic acid promotes the upregulation and modifies the intracellular expression of surveillance proteins in oral squamous cell carcinoma. Photochem Photobiol 2019; 95: 635-643.

[12] Quan M, Lv Y, Dai Y, Qi B, Fu L, Chen X and Qian Y. Tanshinone IIA protects against lipopolysaccharide-induced lung injury through targeting Sirt1. J Pharm Pharmacol 2019; 71: 1142-1151.

[13] Wu DM, Wang YJ, Han XR, Wen X, Li L, Xu L, Lu J and Zheng YL. Tanshinone IIA prevents left ventricular remodelling via the TLR4/MyD88/NF-κB signalling pathway in rats with myocardial infarction. J Cell Mol Med 2018; 22: 3058-3072.

[14] Ma J, Hou D, Wei Z, Zhu J, Lu H, Li Z, Wang X, Li Y, Qiao G and Liu N. Tanshinone IIA attenuates cerebral aneurysm formation by inhibiting the NF-κB-mediated inflammatory response. Mol Med Rep 2019; 20: 1621-1628.

[15] Lv C, Zeng HW, Wang JX, Yuan X, Zhang C, Fang T, Yang PM, Wu T, Zhou YD, Nagle DG and Zhang WD. The antitumor natural product tanshinone IIA inhibits protein kinase C and acts synergistically with 17-AAG. Cell Death Dis 2018; 9: 165.

[16] Liang R, Zhao Q, Jian G, Cheng D, Wang N, Zhang G and Wang F. Tanshinone IIA attenuates contrast-induced nephropathy via Nrf2 activation in rats. Cell Physiol Biochem 2018; 46: 2616-2623.

[17] Zhou W, Zhang S, Li J, Li Z, Wang Y and Li X. lncRNA TINCR participates in ALA-PDT-induced apoptosis and autophagy in cutaneous squamous cell carcinoma. J Cell Biochem 2019; 120: 13893-13902.

[18] Kawai N, Hirohashi Y, Ebihara Y, Saito T, Murai A, Saito T, Shirosaki T, Kubo T, Nakatsugawa M, Kanaseki T, Tsukahara T, Shichinohe T, Li L, Hirano S and Torigoe T. ABCG2 expression is related to low 5-ALA photodynamic diagnosis (PDD) efficacy and cancer stem cell phenotype, and suppression of ABCG2 improves the efficacy of PDD. PLoS One 2019; 14: e0216503.

[19] Nestor MS, Berman B, Patel J and Lawson A. Safety and efficacy of aminolevulinic acid 10% topical gel versus aminolevulinic acid 20% topical solution followed by blue-light photodynamic therapy for the treatment of actinic keratosis on the face and scalp: a randomized, double-blind study. J Clin Aesthet Dermatol 2019; 12: 32-38.

[20] Wanitphakdeedecha R, Tavechodperathum N, Tantrapornpong P, Suphatsathienkul P, Techapichetvanich T, Eimpunth S and Manuskiatti W. Acne treatment efficacy of intense pulsed light photodynamic therapy with topical licochalcone A, l-carnitine, and decanediol: a spilt-face, double-blind, randomized controlled trial. J Cosmet Dermatol 2020; 19: 78-87.

[21] Mathew ML, Karthik R, Mallikarjun M, Bhute S and Varghese A. Intense pulsed light therapy for acne-induced post-inflammatory erythema. Indian Dermatol Online J 2018; 9: 159-164.

[22] Moy LS, Frost D and Moy S. Photodynamic therapy for photodamage, actinic keratosis, and acne in the cosmetic practice. Facial Plast Surg Clin North Am 2020; 28: 135-148.

[23] Fabbrocini G and Cacciapuoti S. Evaluation, prevention, and management of acne scars: issues, strategies, and enhanced outcomes. J Drugs Dermatol 2018; 17: s44-48.