ORIGINAL ARTICLE

Bali Dermatology and Venereology Journal (*BDV*) 2020, Volume 3, Number 2, 26-30
ISSN.2622-5417

Published by DiscoverSys

The effectiveness of galactomyces ferment filtrate, dexpanthenol, and *Centella asiatica* combination serum in the treatment of post-acne hyperpigmentation

We Sagara Dewi[1*], Ivan Kurniadi[1], Anis Irawan Anwar[1]

ABSTRACT

Background: Acne vulgaris is a chronic inflammation of the pilosebaceous gland that may result in non-inflammatory and inflammatory lesions. A hypermelanotic reaction to skin inflammation causes post-acne hyperpigmentation (PAH). It can occur secondary to the inflammation process and, depending on the severity, may persist for a prolonged period.

Objective: To determine the effectiveness of galactomyces ferment filtrate (GFF), dexpanthenol, and *Centella asiatica* combination serum in the treatment of PAH

Methods: This was a placebo-controlled randomized clinical trial. Sixty-eight subjects were divided into two groups: the experimental group received combination serum while the control group received a placebo for eight weeks. Three drops of serum were applied to the area with PAH twice daily in the morning and night. The melanin, erythema, roughness, and L*, a*, and b* scores were assessed objectively using mexameter, chromameter and skin analyzer every two weeks. Pearson's correlation test and independent T-test were used to assess the trend of the parameters and compare the results of both groups.

Results: The results of statistical calculations using the Pearson correlation test showed the treatment group showed a significant decreasing trend of the melanin and spots score. Both groups showed a significant decreasing trend in erythema, L* score and roughness. However, no significant difference was found between both groups in all parameters.

Conclusion: The combination serum may decrease the melanin and spot scores suggesting that it affects the melanocyte activity. It has shown good efficacy in treating PAH.

Keywords: Acne vulgaris, post-acne hyperpigmentation galactomyces ferment filtrate, dexpanthenol, *Centella asiatica*
Cite this Article: Dewi, W.S., Kurniadi, I., Anwar, A.I. 2020. The effectiveness of galactomyces ferment filtrate, dexpanthenol, and *Centella asiatica* combination serum in the treatment of post-acne hyperpigmentation. *Bali Dermatology and Venereology Journal* 3(2): 26-30. DOI: 10.15562/bdv.v3i2.25

[1]Department of Dermatology and Venereology, Faculty of Medicine, Universitas Hasanuddin, Indonesia

*Corresponding to:
We Sagara Dewi; Department of Dermatology and Venereology, Faculty of Medicine, Universitas Hasanuddin, Indonesia;
wesagaradewi@yahoo.com

Received: 2020-06-29
Accepted: 2020-11-02
Published: 2020-12-10

INTRODUCTION

Acne vulgaris (AV) is a disorder of the pilosebaceous unit, chronic, and characterized by open and closed comedones, inflammatory papules, pustules, nodules, or cysts affecting both adults and adolescents. Acne pathophysiology is complex, includes increased sebum production, follicular hyperkeratosis, *Propionibacterium acnes* proliferation, and reactive inflammation.[1,2] Acne is one of the most common conditions treated by a dermatologist, and it affects people without regard to race or ethnicity. Although it mostly occurs during adolescence, AV may persist until adulthood, with 50.9% prevalence in 20-29 year-old females and 26.3% in 40-49 years of age range.[3]

The occurrence of post-acne hyperpigmentation (PAH) is a special concern among darker skin patients with acne.[4,5] Lesions of inflammatory acne disrupt the basal layer of the epidermis, causing melanocytes to increase melanin production.[1] PAH is common in patients with darker skin and can persist for months or years. Dyschromias that cause emotional and psychological distress, such as PAH, can significantly impact individuals' health-related quality of life.[6]

Darker skin types of the patients (Fitzpatrick type 3-6) have an increased inflammatory acne lesions incidence which predisposes to pigmentation development, scars and keloids compared to the fair skin types who manifest with more erythema. However, an active acne phase shows signs of resolution, pigmentation and erythema in darker skin prototypes is a very common manifestation along with atrophic acne scars.[7] Hyperpigmentation of the dermis can take years to fade to normal, while the variant of epidermal can occur up to 6-9 months. PAH is generally clinically apparent a few weeks after erythema from acne subsides. The patient may withdraw from group settings owing to the social stigma attached to this cosmetically displeasing condition in severe cases.[8]

Pigmen irregular dispersion after cutaneous inflammation or melanin overproduction results

in PAH. When PAH is confined to the epidermis, there is an increase in the production and transfer of melanin to surrounding keratinocytes. Although the exact mechanism is unknown, this rise in melanocyte activity is stimulated by prostanoids, cytokines, chemokines and other inflammatory mediators, as well as reactive oxygen species that are released during the inflammatory process.[9]

The treatment of PAH needs to be started at an early phase with the proper regimen for these patients to prevent darkening progressivity, achieve early resolution, and make a necessary decision before taking on laser resurfacing or other acne scars treatment method.[7] Sunscreens with broad-spectrum protection form a mandatory mainstay in the PAH treatment in darker skin. Adherence to sunscreen is strongly suggested in early treatment phases. Topical lightening agents, retinoids, and topical antioxidants commonly used to treat PAH.[10] Effective strategies for PAH treatment include using topical depigmenting agents for three months as first-line treatment. Therefore, there are still tremendous gaps in understanding the basic science of PAH and other alternative treatments in reducing the severity of PAH that still ensues. This study was aimed to assess the effectiveness of galactomyces ferment filtrate (GFF), dexpanthenol, and *Centella asiatica* combination serum in the treatment of PAH.

METHODS

Study Design

This double-blind, placebo-controlled, randomized clinical trial was carried out in the Dermatology and Venereology outpatient clinic of Universitas Hasanuddin Hospital, Makassar, South Sulawesi, Indonesia, from February-May 2019.

Subjects

Non-pregnant females with skin type Fitzpatrick type 3-6 with post-acne hyperpigmentation and a minimum of 8-hour indoor working hours were screened to be included in this study. The subjects were excluded from participation if they had a history of cosmetic topical acne medication in the past 14 days and a history of oral corticosteroids, antibiotics, and contraception in the past 30 days. The subjects were also instructed to avoid applying any topical preparations other than the products in this study, including cosmetics that could worsen the severity of PAH.

Study Protocol

Subjects were instructed to wash their face with water and cleanser, which the researcher provided, then apply three drops of combination serum that contain GFF, dexpanthenol and *C.asiatica*. Patients were not allowed to apply any material on the face, except broad-spectrum sunscreen with SPF 35, which was applied in the morning one minute after applying the serum. The sunscreen usage as photoprotection to protect from photosensitivity risk, sunburn and inhibit the pigmentation induced by UV light. Each day, subjects washed their face with the cleanser, rinse, and pat dries, then apply three drops of combination serum.

Each subject returned to the hospital every 14 days for eight weeks of the treatment (T0, T14, T28, T42, and T56) for safety and efficacy assessments. The severity of acne vulgaris and degree of post-inflammatory hyperpigmentation were subsequently examined clinically by using chromameter and mexameter. Also, skin health status measurement was assessed using the *Magic Mirror Skin Analyzer®*. This study was approved by the Ethical Commission of Universitas Hasanuddin.

Chromameter®

Chromameter exerts three wavelengths, 450 nm, 560 nm, and 600 nm and collects the reflected light to produce a tristimulus color analysis, resulting in three parameters: L* (Luminosity), which denotes color brightness (0 for black to 100 for white), a* which denotes red-green color (+60 for red to -60 for green), and b* which denotes changes along the yellow-blue axis (+60 for yellow to -60 for blue).[11]

Mexameter®

This instrument is equipped with 16 diodes that emit wavelengths with 568 nm, 660 nm, and 880 nm, each corresponding to green, red, and infrared spectrum. Melanin index and erythema index were computed from the absorbed and reflected values of the red and infrared wavelengths and the green and red spectrum.[11]

Magic Mirror Skin Analyzer®

Magic mirror skin analyzer is a professional and high-tech instrument that measures skin conditions objectively and scientifically based on the theory of skin morphology. This device can comprehensively analyze the user's skin by adopting image analysis technology, integrated graphics, and optical principles to provide a basis for skin treatment and beauty. It has a patent of three spectral analyses in RGB/UV/PL. Scanners and sensors can simultaneously analyze the patient's pores, RGB spot, sebum, wrinkles pigmentation, moisture, elasticity, color, and temperature through face recognition. In this study, we only evaluated the improvements of spot score and roughness of the skin in both groups.

Table 1. Fitzpatrick skin type in both groups

Fitzpatrick skin type	Treatment group	Placebo	Total	P-value
III	7 (20.6)	10 (29.4)	17 (25.0)	
IV	19 (55.9)	22 (64.7)	41 (60.3)	0.114
V	8 (23.5)	2 (5.9)	10 (14.7)	
Total	34 (100)	34 (100)	68 (100)	

Table 2. The trend in various parameters over time

Parameter	Group	Pearson correlation	p-value
Melanin	Treatment	-0.245	0.001*
	Placebo	-0.138	0.072
Erythema	Treatment	-0.192	0.012
	Placebo	-0.219	0.004*
L* (Luminosity)	Treatment	0.377	0.000*
	Placebo	0.189	0.014*
Spots score	Treatment	-0.182	0.017*
	Placebo	-0.053	0.491
Roughness	Treatment	-0.363	0.000*
	Placebo	0.196	0.010*

*Significant if p<0.05

Table 3. Results of different parameters after eight weeks of treatment

Parameter	Group	Mean ± SD	p-value
Melanin	Treatment	264.8 ± 58.3	0.895
	Placebo	266.6 ± 52.7	
Erythema	Treatment	338.8 ± 84.4	0.456
	Placebo	353.2 ± 73.8	
L*	Treatment	58.9 ± 3.1	0.182
	Placebo	57.5 ± 5.2	
a*	Treatment	13.1 ± 2.2	0.341
	Placebo	13.6 ± 2.1	
b*	Treatment	18.2 ± 1.5	0.313
	Placebo	17.8 ± 1,6	
Spots	Treatment	39.1 ± 10.9	0.391
	Placebo	41,2 ± 9.2	
UV spot	Treatment	91.5 ± 11.9	0.483
	Placebo	93.3 ± 9.0	
Roughness	Treatment	56.3 ± 7.3	0.163
	Placebo	58.9 ± 7.6	

Statistical Evaluation

Data analysis was performed using Statistical Package for Social Sciences (SPSS) 25.0 for Windows (SPSS Inc. Chicago, IL, USA), where Independent t-test for comparison of treatment results between groups A and B; Pearson's Correlation test to assess the trend of change in score variables and chi-square test to compare the distribution of skin types were done. A p-value <0.05 was considered significant.

RESULTS

A total of 68 subjects participated in the study. Subjects were divided into two groups, group A (experimental) and group B (placebo). Subjects with mild to moderate acne vulgaris and post-acne hyperpigmentation ranging from 16-26 years. The average age for group A and group B was 21.5±2.03 years and 21±2.19 years, respectively, with no significant difference between both groups (p=0.441). Table 1 shows the Fitzpatrick skin type distribution in both groups. No significant difference in Fitzpatrick skin type was observed between both groups (p=0.114).

Table 2 shows the trend over time of the examined variables as assessed by Pearson's correlation test. The melanin and spots score of the treatment group showed a significant decrease after eight weeks of treatment (p<0.05). Both groups showed a significant decrease in erythema, L* score, and roughness (p<0.05).

Table 3 shows the comparison of all parameter values between both groups at the end of the study. No significant difference was seen in all parameters between both groups (p>0.05).

DISCUSSION

Inflammation sequelae on the post-acne phase signify the emergence of clinical manifestation as post-acne hyperpigmentation and pigmented scars. This condition is exaggerated in dark skin type. Early evaluation to address the pigmentary after acne effect needs topical lightening and sun protection. Treatment of PAH with interventional therapies for darker skin to achieve an optimum outcome and use aggressive modalities are replaced by safer option, less aggressive, and repeated treatments are conducted by physicians all through an inflammation controlled stage to optimize result and minimize complication.[12] This study examined the effect of GFF, dexpanthenol, and *C. asiatica* combination serum in treating post-acne hyperpigmentation compared to placebo.

Pearson's analysis of our data showed that the treatment group showed a significant decreasing trend of melanin index and spot score after eight

Published by DiscoverSys | *BDV* 2020; 3(2): 26-30 | doi: 10.15562/bdv.v3i2.25

weeks of the combination serum application, which was not evident in the placebo group. Interestingly, the L* score was found to decrease significantly in both groups. Unlike the L* score, which merely describes the color between black and white, the melanin index shows the skin's melanin content and may serve as one of the parameters of skin repigmentation.[13] A study comparing the melanin index of vitiligo patients showed that patients with higher melanin index had a higher chance of repigmentation.[5] Thus, this study suggests that while in terms of the white-black color spectrum, the results of both groups did not show a significant difference, the melanin index in the treatment group showed a more significant decreasing trend compared to the placebo group.

The insignificant difference in L* score between both groups might be attributed to the physiological improvement of post-acne hyperpigmentation, which may occur early when the underlying condition is rapidly treated.[14] One possible explanation is that all subjects experienced mild to moderate acne vulgaris that led to mild hyperpigmentation that was treated early and adequately, leading to rapid improvement of the lesions. Thus, both groups, including the placebo group, showed a comparable improvement. Including patients with severe acne vulgaris, hence more severe hyperpigmentation, would be interesting to conduct in the future. We also found an insignificant difference in erythema scores between both groups. The early and adequate treatment of hyperpigmentation of acne vulgaris will help to reduce the erythema in acne vulgaris. Post-inflammatory hyperpigmentation can be alleviated or prevented. The underlying inflammatory conditions should be evaluated and treated as the first step to reduce the inflammation progression and post-inflammatory hyperpigmentation (which is an inflammatory consequence). If there is no evidence of inflammation or the inflammatory conditions subsides at diagnosis, the post-inflammatory hyperpigmentation treatment should be considered the next step.[15]

Moreover, Dexpanthenol is a water-soluble derivative of vitamin B5, activated and converted into pantothenic acid in the skin. Due to its restructuring, anti-inflammatory and moisturizing properties, Dexpanthenol may be effective in several diseases such as mild skin irritation, radiodermatitis and atopic dermatitis. It has been suggested that the reported beneficial effect of dexpanthenol on wound healing is the result of increased fibroblast proliferation and accelerated epithelialization; both processes are important for the cure of both deep and superficial wounds. Epidermal wounds treated with the dexpanthenol emulsion showed a reduction in erythema and a more and solid tissue regeneration.[16]

This study demonstrates the anti-melanogenic properties of the constituting components of the serum. Dexpanthenol has been shown to inhibit melanin synthesis by binding free radicals and peroxides that contribute to pigmentation.[17] *Centella asiatica* contains the major components of asiatic acid, asiaticoside and madecassic acid. In dermatology, these components are used to achieve preventive and therapeutic effects. Asiaticoside, one of the main components of *C. asiatica*, was shown to inhibit melanogenesis *in vitro*.[18] Furthermore, *C. asiatica* extract has an anti-inflammatory effect, bacteriostatic effect on *Cutibacterium acnes* (*C. acnes*), decrease follicular keratinocyte hyperproliferation, and increase wound healing effect. Therefore, *C. asiatica* may be useful to treat patients with acne vulgaris earlier to prevent PAH.[19] Galactomyces ferment filtrate further augments this effect by inhibiting tyrosine hydroxylase and dampening oxidative stress. It has been shown to improve skin brightness levels and reduce the amount of sebum and keratin in acne vulgaris.[20] As to date, these effects were only shown *in vitro*. This study laid novel clinical data on the synergistic depigmenting effect of these agents.

A large-scale study with varying degrees of post-acne hyperpigmentation, including those with severe acne vulgaris, is needed to establish the effectiveness of this regimen. More consistent or greater change in PAH tools reading may have become more apparent if a larger group of subjects were treated or if the changes were observed longer.

CONCLUSION

This double-blind, placebo-controlled, randomized clinical trial revealed that galactomyces ferment filtrate, dexpanthenol, and *C. asiatica* combination serum was an effective treatment option in lowering the melanin index of patients with post-acne hyperpigmentation. Although many treatment options are available for PAH, it takes months for PAH to resolve, even with adequate therapy. More randomized controlled clinical studies in large numbers of PAH patients would help provide standardized measurable outcomes for this indication.

FUNDING

None.

CONFLICT OF INTEREST

None declared.

AUTHORS CONTRIBUTION

All authors contributed to the publication of this research.

REFERENCE

1. Callender VD, Young CM, Kindred C, Taylor SC. Efficacy and safety of clindamycin phosphate 1,2% and tretinoin 0,025% gel for the treatment of acne and acne-induced post-inflammatory hyperpigmentation in patients with skin of color. *The Journal of Clinical Aesthetic Dermatology.* 2012 July;**5**(7):25-32.
2. Zaenglein AL, Thiboutot DM. Expert committee recommendations for acne management. *Pediatrics*. 2016;**188**:1188-119
3. Collier CN, Harper JC, Cantrell WC, Wang W, Foster KW, Elewski BE. The prevalence of acne in adults 20 years and older. *J Am Acad Dermatol*. 2008;**58**(1):56-9.
4. Halder RM, Nordlund JJ. Topical Treatment of Pigmentary Disorders. In: Nordlund JJ, Boissy RE, Hearing VJ, King RA, Oetting WS, Ortonne JP, editors. The Pigmentary System. p. 1163-74.
5. Bhargava P, Prakash C, Tiwari S, Lakhani R. Correlating melanin index to repigmentation potential: A novel prognostic tool in vitiligo. *Pigment International*. 2016;**3**(2):72-6.
6. Callender VD, St Surin-Lord S, Davis EC, Maclin M. Postinflammatory hyperpigmentation: etiologic and therapeutic consideration. *Am J Clin Dermatol*. 2011;**12**:87-99.
7. Shehnaz AZ. Chemical peels for post-acne hyperpigmentation in skin of color. *Journal of Pigmentary Disorder.*2015;**2**(2)1-5
8. Zawar VP, Agarwal M, Vasudevan B. Treatment of postinflammatory pigmentation due to acne with Q-switched Neodymium-doped Yttrium Aluminium Garnet in 78 Indian cases. *Journal of Cutaneous and Aesthetic Surgery.*2015;**8**:222-6
9. Davis EC, Callender VD. Postinflammatory hyperpigmentation, a review of the epidemiology, clinical features, and treatment options in skin of color. *J Clin Aesthet Dermatol*. 2010;**3**(7):20-7
10. Haldr RM, Richards GM. Topical agents used in the management of hyperpigmentation. *Skin Theraoy Lett*. 2004; **9**:1-3
11. Clarys P, Alewaeters K, Lambrecht R, Barel A. Skin color measurements: comparison between three instruments: the Chromameter®, the DermaSpectrometer® and the Mexameter®. *Skin research and technology*. 2000;**6**(4):230-8.
12. Arsiwala S. Acne scars: complications of treatment and their management of hyperpigmentation. *Jaypee Brothers Medical Publishers (P)Ltd*.New Delhi,India,2014.
13. Treesirichod A, Chansakulporn S, Wattanapan P. Correlation between skin color evaluation by skin color scale chart and narrowband reflectance spectrophotometer. *Indian J Dermatol*. 2014;**59**(4):339.
14. Davis EC, Callender VD. Postinflammatory hyperpigmentation: a review of the epidemiology, clinical features, and treatment options in skin of color. *The Journal of clinical and aesthetic dermatology*. 2010;**3**(7):20-31.
15. Chaowattanapanit S, Silpa-archa N, Kohli I, Lim HW, Hamzavi I. Postinflammatory hyperpigmentation: A comprehensive overview treatment options and prevention. *J AM Acad Dermatol*. 2017;**77**(4):607-21.
16. Oguz A, Uslukaya O, Alabal, et al. Topical N-acetylcysteine improves wound healing comparable to dexpanthenol: an experimental study. Int Surg. 2015;**100**:656-61.
17. Slyshenkov VS, Dymkowska D, Wojtczak L. Pantothenic acid and pantothenol increase biosynthesis of glutathione by boosting cell energetics. *FEBS Lett*. 2004;**569**(1-3):169-72.
18. Kwon KJ, Bae S, Kim K, An IS, Ahn KJ, An S, et al. Asiaticoside, a component of Centella asiatica, inhibits melanogenesis in B16F10 mouse melanoma. *Mol Med Report*. 2014;**10**(1):503-7.
19. Intachan P., Chokdeesumrit W., Comparison of the effectiveness of topical 5% *Centella Asiatica* gel versus topical 1% clindamycin gel in the treatment of acne vulgaris. J Med Health Si 2020: vol.27 No.1
20. Minji. L., et al., The Effects of essence-formed cosmetic ingredients containing the galactomyces ferment filtrate on skin improvements in keratinization, pores, sebum excretion, brightness and acne. Asian journal of beauty and cosmetology vol 12. 2014 (1): pg.77-84.