

Persistent Effects of Adapalene Gel After Chemical Peeling with Glycolic Acid in Patients with Acne Vulgaris

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Abstract: We investigated the usefulness of adapalene gel as maintenance therapy following chemical peeling with glycolic acid in patients with acne vulgaris. The study period was 14 weeks. The subjects were 23 patients with mild to moderate acne vulgaris (1 male, 22 females). After chemical peeling (CP) of the face was performed 3 times at 2-week intervals, adapalene was applied for 6 weeks using a randomized, double-blind half-side method. On the day of observation, dermatologists examined dermal findings, and measurement was conducted using instruments to analyze the physiological skin function. After the third session of CP was completed, both the inflammatory and non-inflammatory lesion counts significantly decreased. Subsequently, on the adapalene-treated side there were no change in the inflammatory and non-inflammatory lesion counts after the CP 3 times, but on placebo-treated side, there significant increase in the inflammatory and non-inflammatory lesion counts. Concerning the results of measurement with instruments, the sebum capacity significantly decreased after the third session of CP. Subsequently, there were no changes after the 6-week application of adapalene or a placebo. These results suggest that post-CP adapalene application is an effective acne treatment method to improve efficacy and treatment adherence.

Keywords: Acne vulgaris(AV), chemical peeling(CP), adapalene.

INTRODUCTION

Acne vulgaris is frequent in clinical practice. It is a chronic, inflammatory dermal disease involving sebaceous hair follicles [1]. Its clinical characteristics include seborrhea, comedones, red papules, and pustules [1]. This disease frequently develops on the faces and thoracic/dorsal regions of persons aged 10 to 29 years, and is experienced by more than 90% of Japanese persons [2,3].

Chemical peeling (CP) is a technique to treat dermal symptoms related to acne, pigment anomalies, and photoaging or cosmetically improve the skin (anti-aging, reduction of spots/dullness, and improvement in the skin quality) [4]. In patients with acne, the thickening cornified layer of the hair follicle infundibularis exfoliated, reducing sebum retention in hair follicles. In particular, this procedure is effective for pimples [4]. Glycolic acid belongs to α -hydroxy acids, with the smallest molecular weight. It is appropriate for peeling of the most superficial (level 1) and superficial (level 1,2) layers [5]. Neither systemic toxicity nor serious complications have been reported, and various products are commercially available. In 2008, the Japanese Dermatological Association prepared the "Guidelines for Acne Vulgaris Treatment" for Japanese [6]. Concerning inflammatory/non-inflammatory lesion, glycolic and salicylic

acids (macrogol base) were recommended as recommendation grade C1 (recommended as options, although there was little evidence) [5-7]. On the other hand, adapalene (6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthoic acid), a naphthoic acid derivative [8], was approved as an external retinoid preparation in Japan in 2008 [9]. In patients with acne, this drug corrects the alteration of the hyperkeratinization process of the hair follicle infundibular, reducing microcomedones, comedones and inflammatory lesions. Furthermore, it was also strongly recommended as maintenance therapy after the reduction of inflammation. In the guidelines, the recommendation grade was established as A (Strongly recommended to perform (there should be at least one level I or II study that supports effectiveness)) [5-7]. However, no study has compared CP with adapalene, although CP may exhibit immediate actions on comedones and cosmetic effects such as whitening [4]. In this study, we used an external adapalene preparation (recommendation grade A) after CP, which reduces lesion in the early phase, and examined its usefulness for acne vulgaris treatment.

SUBJECTS AND METHODS

Subjects

The subjects were 23 patients with mild to moderate acne, aged over 20 years, in whom there was no laterality in the acne count, and from whom written informed consent was obtained in the Department of Dermatology, Wakayama Medical University between 2009 and 2010. Patients were excluded if they had cyst, scar, and keloids, or other dematologic conditions requiring systemic treatment.

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Exclusion criteria included males/females aged 19 years or younger and pregnant or lactating women. The purpose and contents of this study were examined and approved by the Ethic Review Board of Wakayama Medical University in accordance with the Helsinki Declaration.

Methods

The study period was 12 weeks. Chemical peeling with 40% glycolic acid (pH3.2) was performed 3 times at 2-week intervals [9]. From 2 weeks after the completion of CP, adapalene or a placebo (supplied by Galderma, Inc.) was applied to the half-face before bedtime every day for 6 weeks. Each drug was randomly assigned using the double-blind method.

EVALUATION

The severity of acne was evaluated according to the guidelines [6]. The exanthema count and skin condition were examined by dermatologists every two weeks (total: 7 times). For physiological skin function analysis, the water content (%) was measured using a CORNEOMETER®, the sebum capacity ($\mu\text{g}/\text{cm}^2$) using a SEBMETER®, and the transepidermal water loss (TEWL) (g/cm^2) using a TEWAMETER® (Multi-probe adaptor, Courage + Khazaka Co., Ltd., Cologne, Germany) at the start of this study, 2 weeks after the completion of the third session of CP, and 6 weeks after the start of adapalene application (total: 3 times) in a room with constant temperature (22 ~ 23°C) and humidity (relative humidity 40 ~ 45%).

STATISTICAL ANALYSIS

Statistical analysis was conducted using Wilcoxon’s t-test. A p-value <0.05 was regarded as significant.

RESULTS

The subjects were 23 patients with acne vulgaris (1 male, 22 females), with a mean age of 25.3 ± 5.8 (standard deviation) years.

Changes in the Lesion

Time dependent changes in the inflammatory lesion are shown in Fig. (1). After the completion of the third session of CP (6th week), the lesion significantly decreased in comparison with the pre-study value ($p < 0.001$). Subsequently, there was a significant decrease after the 6-week (12th week) application of adapalene in comparison with the pre-study value ($p < 0.01$). However, 6 weeks (12th week) after the start of application in adapalene group, there was no significant difference in comparison with the value after the third session of CP (6th week), although there was a slight decrease from 2 weeks after the start of application (8th week). In the placebo group, the lesion significantly increased in comparison with that after the third session of CP (12th week) ($p < 0.01$).

The changes in the non-inflammatory lesion are shown in Fig. (2). After the third session of CP (6th week), the non-inflammatory lesion significantly decreased in comparison with the pre-study value ($p < 0.001$). Subsequently, there were significant decreases after the 6-week (12th week) application of adapalene or the placebo in comparison with the pre-study value ($p < 0.01$). In the adapalene group, there was no significant difference in comparison with the value after the third session of CP (6th week), although there was a slight decrease. In the placebo group, the exanthema was significantly greater than after the third session of CP (6th week) ($p < 0.05$).

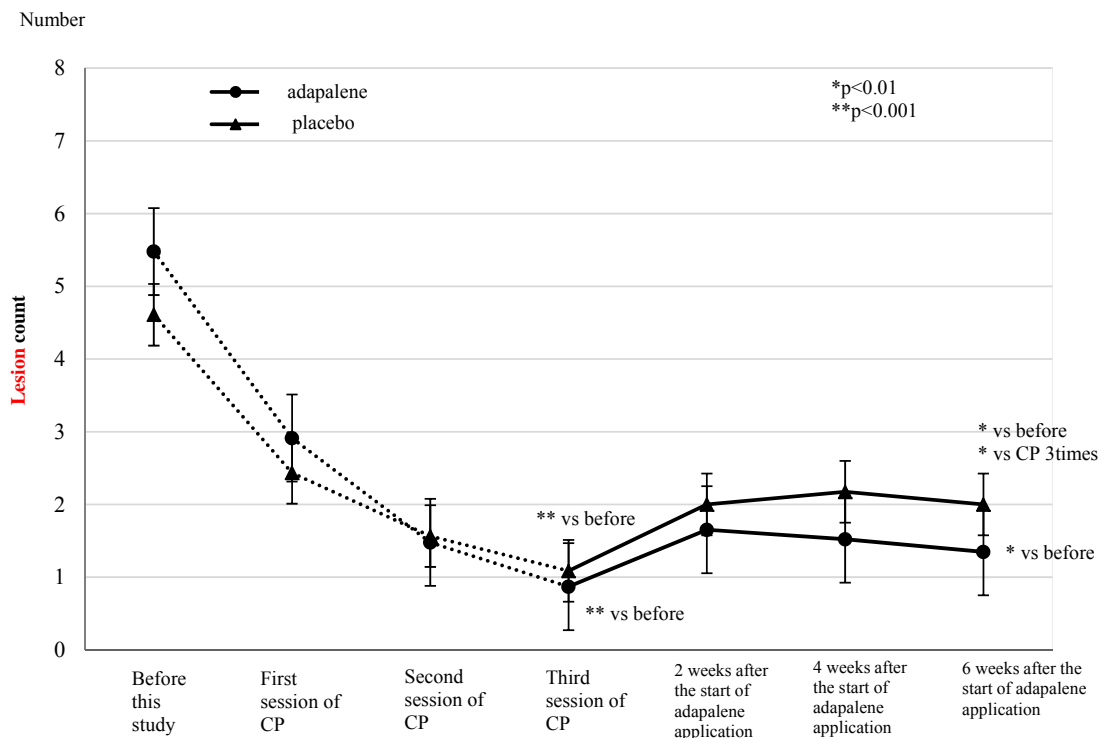


Fig. (1). Changes in the inflammatory lesion count (N=23).

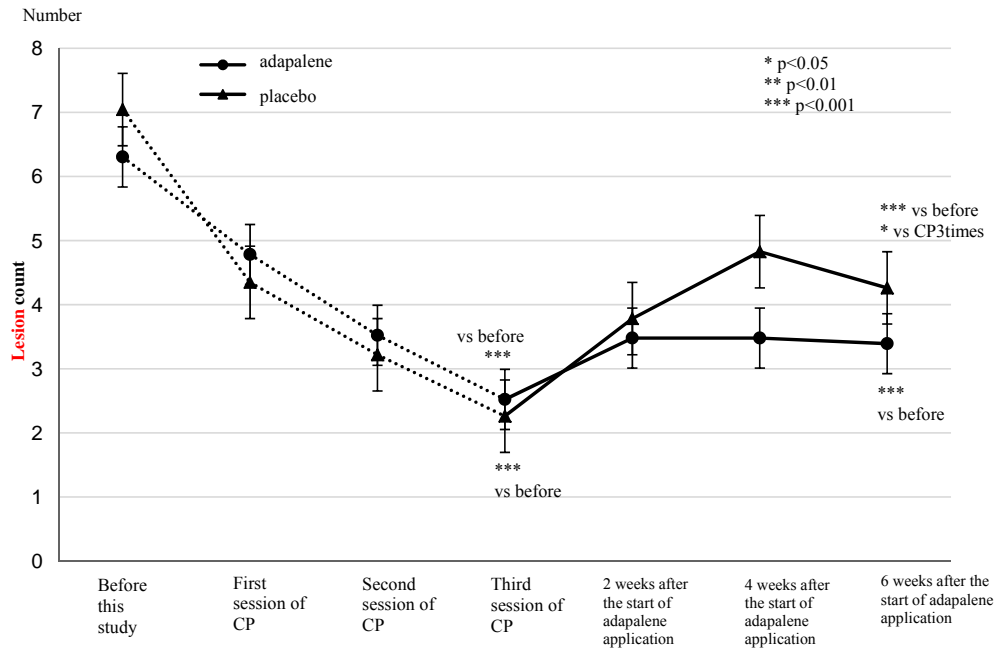


Fig. (2). Changes in the non-inflammatory lesion count (N=23).

Analysis of the Physiological Skin Function

Changes in the Sebum Secretion

After the third session of CP, the sebum secretion significantly decreased in comparison with the pre-study value ($p < 0.05$). Subsequently, there were slight increases in both the adapalene and placebo groups, although there were no significant differences (Fig. 3).

Changes in TEWL

After the third session of CP, the TEWL value significantly decreased in comparison with the pre-study

value ($p < 0.05$). Subsequently, the values in the adapalene and placebo groups were significantly higher than after the third session of CP (Fig. 4).

Changes in the Cornified Layer Water Content

There was no significant difference in the cornified layer water content before and after this study.

Safety

During the study period, there were no side effects of CP. In the adapalene group, more than 90% (21/23) of the patients complained of dryness, desquamation, erythema, or

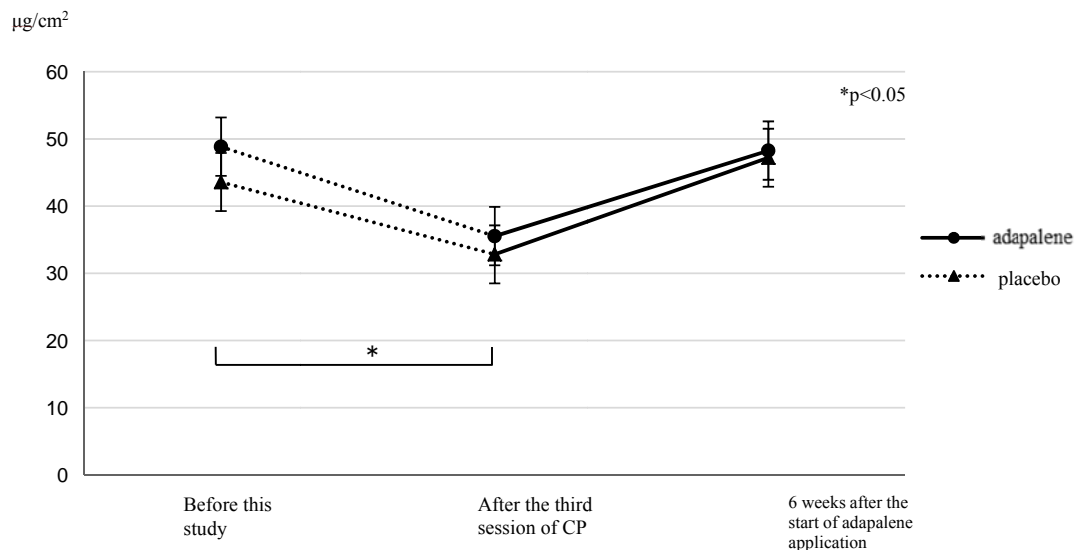


Fig. (3). Changes in the sebum secretion (N=23).

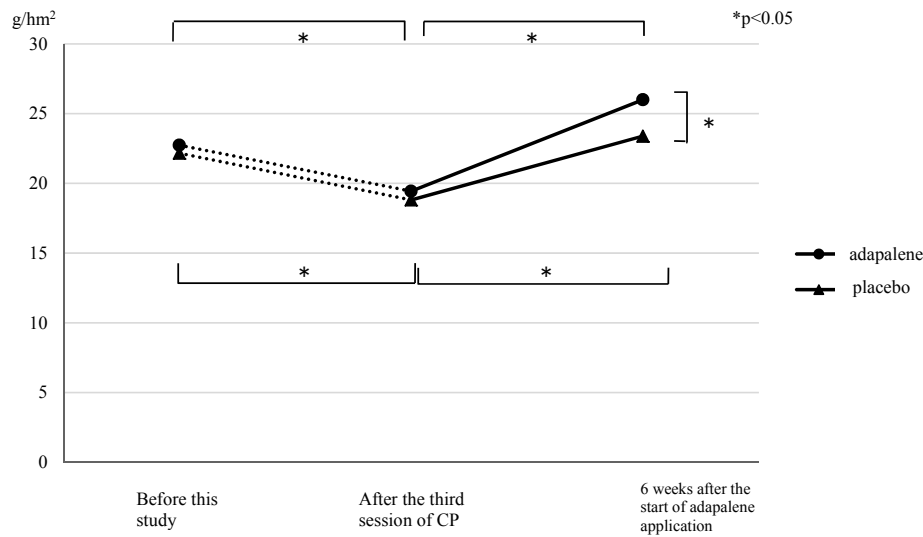


Fig. (4). Changes in the TEWL (N=23).

irritation within 2 weeks. However, in all patients, it was possible to continue treatment until the completion of this study.

DISCUSSION

Recently, patients have been strongly interested in acne treatment, and acne has been reviewed as an important dermal disease. Chemical peeling shows immediate actions on acne vulgaris, and its results are satisfactory for females and young patients, who have a strong esthetic sense. According to several studies, CP with glycolic acid significantly decreases the lesion count 2 weeks after the start of treatment; glycolic acid may exhibit more immediate actions compared to adapalene [10,11]. However, as a limitation of CP, continuous visits are required, which is stressful. In this study, we examined the usefulness of adapalene application as maintenance therapy following CP with glycolic acid. After the third session of CP, both inflammatory and non-inflammatory lesion significantly reduced. Subsequently, adapalene was applied for 6 weeks. The lesion count slightly increased with no statistical significance 2 to 4 weeks after the start of application, but there was a significant decrease in comparison with the pre-study value. These results suggest that adapalene application is useful for maintaining the therapeutic effects of CP.

Acne is often thought to affect the teenaged group. However, a significant number of patients either continue to experience acne or develop new-onset acne after the teenaged years. As acne frequently develops on the face, it influences the patient’s quality of life (QOL) [12]. In particular, QOL of most patients with post adolescent acne markedly reduces because of their strong esthetic sense [12,13].

In this study, the mean age of subjects are 25.3±5.8 (standard deviation) years, most of who have post-adolescent acne [14]. Irregular menstruation, mental stress, and

hormones, especially androgen, are closely involved in post-adolescent acne [15]. Androgen acts on the sebaceous gland, promoting sebum production and leading to comedones formation through the excessive cornification of hair follicles. Furthermore, marked mental stress enhances the production of corticotropin-releasing and adrenocorticotrophic hormones, increasing the secretion of androgen. As a result, acne exacerbates, reducing the treatment responsiveness [15].

For physiological skin function analysis, the sebum secretion, TEWL, and cornified layer water content were measured before this study, after the third session of CP, and after the completion of this study. The sebum secretion significantly decreased after the third session of CP. Subsequently, it increased after the application of adapalene/a placebo. As the facial secretion of sebum in patients with acne is higher than in healthy adults, sebum secretion is associated with the onset of acne [16]. Several studies have reported that retinoid/hormonal/laser therapies decrease sebum secretion through the destruction/reduction of the sebaceous gland, leading to the remission of acne. However, there are few studies on a CP-related decrease in sebum secretion [17]. A study indicated that glycolic acid penetrated pores of the skin, acting on the sebaceous gland cells and contributing to a decrease in sebum secretion [17]. There was a significant decrease in the TEWL after CP, whereas there was a significant increase following adapalene application. This was possibly because the side effects of adapalene, such as erythema, desquamation, and dryness, reduced the barrier function of the skin [9,18]. There were no changes in the water content before and after this study.

The results of this study suggest that the application of adapalene after CP remission of acne treatment is an effective acne treatment method to maintain and further improve treatment effect and adherence in patients wishing to completely cure acne earlier.

CONFLICT OF INTEREST

Adapalene and placebo were given by Galderma R&D, France.

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