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Research Article

EVALUATION OF EFFICACY AND SAFETY OF *AVCO ACNE GEL* FOR ACNE: AN OPEN, SINGLE CENTRIC, NON COMPARATIVE STUDY FOR 8 WEEKS

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ABSTRACT

Acne is a common disease of the pilosebaceous units of the skin and topical therapy is recommended for the management of acne with comedolytic, anti-inflammatory agents, along with antimicrobials. However, topical application of these drugs leads to frequent adverse effects and also, there is an emergence of antibiotic resistance by Propionibacterium acnes. Furthermore, systemic antimicrobial usage has been causally associated with various adverse events. *AVCO Acne Gel* is a herbal formulation containing, Activated Virgin Coconut Oil derived from catalytic activity of lipase on virgin coconut oil (Malaysian Patent MY-140578-A). The present study was planned to evaluate the efficacy and safety of *AVCO Acne Gel* in management of acne vulgaris.

This study was an open, single centric, non-comparative clinical trial conducted at the Ellead skin research centre, Ellead Co., Ltd. 272-1, Sehyneo-dong, Boondang-gu, Seongnam-si, Gyeonggi-do, Korea from July2, 2010 to October 6, 2010. Twenty one patients consisting of 9 males and 12 females, aged 15 to 38 were included in the study. Children below 18 years of age, patients already on medication or therapy, patients with preexisting severe skin diseases or cancer, patients prone to irritants and allergic, patients exposed to UV rays or laser and on treatment with AHA or salicylic acid, patient with stressful lifestyle and those who refused to give informed consent were excluded from the study. Pregnant and lactating women were also excluded from the study. A baseline history was obtained in order to determine the patient's eligibility for enrolment in the trial. Thereafter all patients underwent a clinical examination and thorough skin examination was done. All patients were advised to apply *AVCO Acne Gel* topically over the lesions, once in a day for a period of 8 weeks. All patients were followed up every two weeks and during each follow-up visit, local skin examination (dermatological assessment), instrumental assessment (sebumeter and digital photography) and subject self assessment (questionnaire) was done. The predefined primary outcome measures were acne grading, reduction of papule, pustule count and skin sebum with subject self assessment of satisfaction, Improvement and sensory evaluation. The predefined secondary outcome measures were incidence of adverse events and compliance to the treatment. Statistical analysis was done according to intention-to-treat principles.

This study observed significant reduction in the acne grading (1.50 to 0.77; $p<0.001$), papule count (12.52 to 5.24; $p<0.001$), pustule count (5.38 to 1.33; $p<0.001$), skin sebum (107.07 to 84.21; $p<0.001$) after 8 weeks of application. In addition, there was a better subject self satisfaction and improvement. The overall response to the treatment also recorded a significant improvement from the second week onwards. There were no clinically significant short and long-term adverse reactions (either reported or observed), during the entire period of study and excellent patient compliance to *AVCO Acne Gel* was also observed. Based on these observations, it may be concluded that the *AVCO Acne Gel* has anti-acne activity. It is also clinically effective and safe for external usage in acne vulgaris.

Keywords: P.acne, acne, clinical, pustule, papule, sebum

INTRODUCTION

Acne is a common disease of the pilosebaceous units of the skin and acne is an end result of the interplay of multiple factors. The pathogenesis of acne vulgaris is multifactorial, including increased sebum production, comedogenesis, P. acnes proliferation, and inflammation[1]. P. acnes play an important role not only in the process of inflammation but also in the formation of comedones. P. acnes contribute to the inflammatory nature of acne by inducing monocytes to secrete pro-inflammatory cytokines including interleukin (IL)-1b, IL-8, and tumour necrosis factor (TNF)-a[2]. Excessive sebum production secondary to sebaceous gland hyperplasia is the first abnormality to occur[3]. Subsequent hyperkeratinization of the hair follicle prevents normal shedding of the follicular keratinocytes, which then obstruct the follicle and form an inapparent microcomedo[4]. Lipids and cellular debris soon accumulate within the blocked follicle and this microenvironment encourages colonization of P. acnes, which provokes an immune response through the production of numerous inflammatory chemomediators. Inflammation is further enhanced by follicular rupture and subsequent leakage of lipids, bacteria, and fatty acids into the dermis. The clinical diagnosis of acne is based on the history and a physical examination. Acne most commonly develops in areas with the greatest concentration of sebaceous glands, which include the face, neck, chest, upper arms, and back[5].

Topical therapy is recommended for the management of acne (especially for non-inflammatory comedones and mild to moderate inflammatory acne) and comedolytic, anti-inflammatory agents, alongwith antimicrobials are preferred drugs. Tretinoin is the most effective available topical comedolytic agent, but topical application leads to frequent erythema, peeling, and burning of the skin. During the past few decades, many reports have documented an emergence of antibiotic resistance by P. acnes during treatment of acne[6-8]. Furthermore, systemic antimicrobial usage has been causally associated with various short-term and long-term adverse events[9]. Recently, new retinoids with additional anti-inflammatory action are being co-administered with antibiotics to reduce the risk of bacterial resistance[8]. Therefore, an agent which can inhibit P. acnes growth and suppress the inflammatory response will provide promising benefits to patients with acne vulgaris. Herbs have been used for many purposes, including medication, nutrition, flavouring, beverages, and fragrance. Much of the early interest in functional foods and nutraceuticals was based on the medicinal uses of herbs. *AVCO Acne Gel* is a herbal formulation containing, Activated Virgin Coconut Oil derived from catalytic activity of lipase on virgin coconut oil (Malaysian Patent MY-140578-A). The present study was planned to evaluate the efficacy and safety of *AVCO Acne Gel* in management of acne vulgaris.

MATERIALS AND METHODS

Aim of the study

This study was aimed to evaluate the clinical efficacy, short and long-term safety of *AVCO Acne Gel* in newly diagnosed and previously treated cases of acne vulgaris.

Study design

This study was an open, single centric, non-comparative clinical trial conducted at the Ellead Co., Ltd. Ellead skin research centre, 272-1, Sehyneo-dong, Boondang-gu, Seongnam-si, Gyeonggi-do, Korea from July2, 2010 to October 6, 2010, as per the ethical guidelines of the Declaration of Helsinki. The study protocol, case report forms (CRFs), regulatory clearance documents, product-related information and informed consent forms were submitted to the Institutional Ethics Committee and approved by the same.

Inclusion criteria

Twenty one patients consisting of 9 males and 12 females, aged 15 to 38 were included in the study, conducted at the Ellead skin research centre, Ellead Co., Ltd. 272-1, Sehyneo-dong, Boondang-gu, Seongnam-si, Gyeonggi-do, Korea from July2, 2010 to October 6, 2010. A written informed consent was obtained from all patients.

Exclusion criteria

Children below 18 years of age, patients already on medication or therapy, patients with preexisting severe skin diseases or cancer, patients prone to irritants and allergic, patients exposed to UV rays or laser and on treatment with AHA or salicylic acid, patient with stressful lifestyle and those who refused to give informed consent were excluded from the study. Pregnant and lactating women were also excluded from the study.

Study procedures

A baseline history was obtained in order to determine the patient's eligibility for enrolment in the trial. The baseline assessment included personal data, a description of symptoms and details of past medical history (family history of acne, history of possible exacerbating factor/s, etc.). Thereafter all patients underwent a clinical examination and thorough skin examination was done by two dermatologists for standard acne grading[10] and clinical grading (presence of inflamed papules and pustules). Further the patients underwent instrumental assessment to verify sebum removal effect by using Sebumeter® (SM810, Courage & Khazaka, Germany). The device measures the amount of sebum per unit area (microgram/cm^2) by photometric reflection method. Also a digital photography was conducted to asses overall improvement in acne by using DSLR camera and photographic system. A subject self assessment for satisfaction, improvement and sensory effect was also conducted by using researcher-provided questionnaire at 2, 4, 6 and 8 weeks, rating -1 for bad, 0 for no change and 1 for good. Patients were advised to apply *AVCO Acne Gel* topically over the lesions, once in a day for a period of 8 weeks. Patients were followed up every two weeks and during each follow-up visit, local skin examination was done and observations recorded in the structured case record sheet. All patients were reviewed clinically at the end of 8 weeks.

Primary and secondary outcome measures

The predefined primary outcome measures were acne grading, reduction of papule, pustule count and skin sebum with subject self assessment of satisfaction, Improvement and sensory evaluation. The predefined secondary outcome measures were incidence of adverse events and compliance to the treatment.

Adverse events

All local and systemic adverse events, reported or observed by patients were recorded with information about severity, time of onset, duration and action taken regarding the study drug. Relation of adverse events to study medication was predefined as "Unrelated" (a reaction that does not follow a reasonable temporal sequence from the administration of the drug), "Possible" (follows a known response pattern to the suspected drug, but could have been produced by the patient's clinical state or other modes of therapy administered to the patient), and "Probable" (follows a known response pattern to the suspected drug that could not be reasonably explained by the known characteristics of the patient's clinical state).Patients were allowed to voluntarily withdraw from the study, if they had experienced serious discomfort during the study or sustained serious clinical events requiring specific treatment. For patients withdrawing from the study, efforts were made to ascertain the reason for dropout. Non-compliance (defined as failure to take less than 80% of the medication) was not regarded as treatment failure, and reasons for non-compliance were noted.

Statistical analysis

Statistical analysis was done according to intention-to-treat principles. Changes in various parameters from baseline values and values after the 2, 4, 6 and 8 weeks were analyzed by "Paired t test". The minimum level of significance was fixed at 99% confidence limit and a 2-sided p value of <0.05 was considered significant. The values are expressed in the sequence as: mean score (M) at 2, 4,6 and 8 weeks, standard deviation (SD) at baseline, 2, 4 and 8 weeks. In all graphs, the baseline value is 0.00.

RESULTS

Twenty one patients were included in this study and no patients were lost to follow up. The age range was 15-38 years (Table 1). There was a female preponderance in the study and total 9 (42%) males and 12 (58%) females were included in the study.

Table 1: Subjects demographics

Age	15-20	21-30	31-38
Number of patients	10	9	2
Percentage	33.3	30.0	6.7

It was observed that from fourth week onwards there was significant reduction in the acne grading from 1.50 to 0.77 (p<0.001, Fig 1).

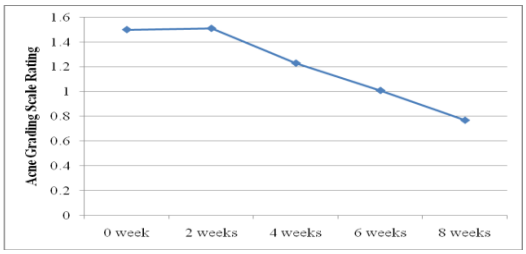

Figure 1: Effect of *AVCO Acne Gel* on Acne score

Also significant reduction in papule count from 12.52 to 5.24 (p<0.001; Fig 2), pustule count from 5.38 to 1.33 (p<0.001; Fig 3), skin sebum from 107.07 to 84.21 (p<0.001; Fig 4) was observed from second week, sixth week and eighth week respectively (Table 2).

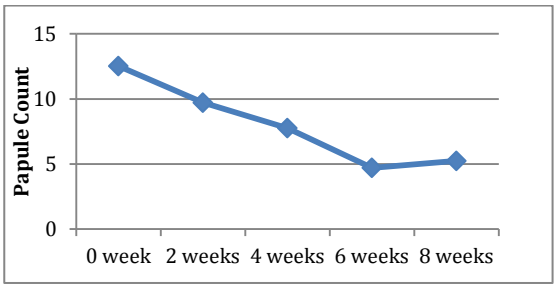

Figure 2: Effect of *AVCO Acne Gel* on Papule count

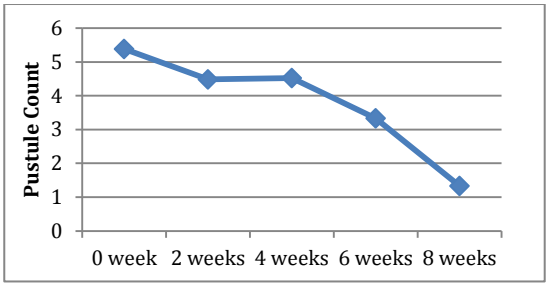

Figure 3: Effect of *AVCO Acne Gel* on Pustule count

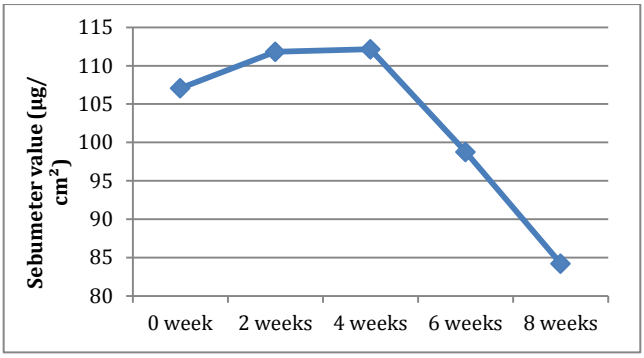

Figure 4: Effect of *AVCO Acne Gel* on Skin sebum

Table 2: Effect of *AVCO Acne Gel* on acne score, papule count, pustule count and skin sebum

Weeks	Acne Score (Mean ± SD)	Papule Count (Mean ± SD)	Pustule Count (Mean ± SD)	Skin Sebum (Mean ± SD)
0	1.50±0.70	12.52±5.20	5.38±3.93	107.07±45.13
2	1.51±0.63	9.71±4.36*	4.48±4.31	111.81±45.04
4	1.23±0.57***	7.76±3.40***	4.52±4.13	112.14±38.73
6	1.01±0.50***	4.71±2.53***	3.33±3.35*	98.76±39.28
8	0.77±0.51***	5.24±3.52***	1.33±1.62***	84.21±30.04*

Values expressed in Mean±SD for *n* = 21, significance ***p<0.001, **p<0.01, *p<0.05

The subject self assessment for satisfaction was observed increased from second week to eighth week (38% to 52.4%, Fig 5).

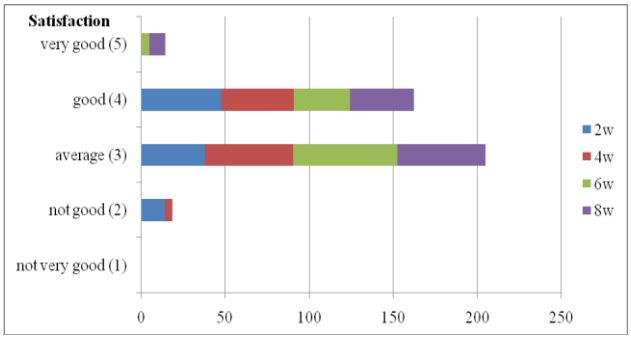

Figure 5: Effect of *AVCO Acne Gel* on Subject self assessment of satisfaction

Similarly overall improvement of acne prone skin after application was found to be satisfying upto eighth week (28.6% to 42.8%, Fig 6).

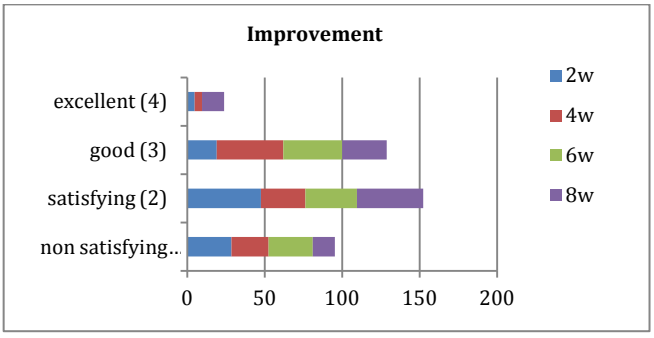

Figure 6: Effect of *AVCO Acne Gel* on Subject self assessment of Overall Improvement

The acne prone skin improvement throughout 8 weeks of treatment was found to be effective after 2 week (digital photograph, Fig 7).

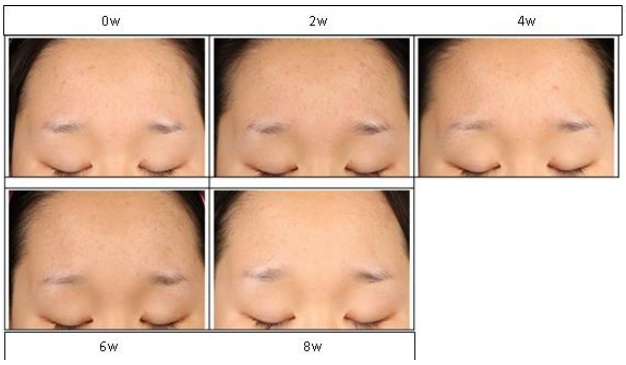

Figure 7: Effect of *AVCO Acne Gel* on acne prone skin over 8 weeks (Subject 11 – KHE)

There were no clinically significant short and long-term adverse reactions (either reported or observed), during the entire period of the study and excellent patient compliance to *AVCO Acne Gel* was observed.

DISCUSSION AND CONCLUSION

Acne vulgaris is a skin disorder with initial formation of microscopic microcomedo, which evolves into visible open comedones ("blackheads") or closed comedones ("whiteheads"). Subsequently, inflammatory papules, pustules and nodules also develop (nodulocystic acne consists of pustular lesions larger than 0.5 cm) and there may be presence of excoriations, post-inflammatory hyperpigmentation and scars[11]. The most commonly involved drugs are: anabolic steroids, corticosteroids, corticotropin, isoniazid, lithium, phenytoin, azathioprine, cyclosporine, phenobarbital, quinidine, tetracycline and vitamins (B1, B6, B12 and D2). Cosmetics and emollients may occlude follicles and cause an acneiform eruption. Topical corticosteroids may produce perioral dermatitis, a localized erythematous papular or pustular eruption[12]. As per the guidelines of The American Academy of Dermatology, primary acne vulgaris is classified into mild, moderate and severe grades. Mild acne is characterized by the presence of few to several papules and pustules (without nodules). Patients with moderate acne have too many papules and pustules (along with a few to several nodules) and with severe acne, patients have numerous or extensive papules and pustules (as well as many nodules).

The management of acne varies as per the severity and type of acne. Mild acne is generally responsive to aggressive topical treatment by an antibacterial and a comedolytic agent. Topical erythromycin and clindamycin are commonly used antibacterial agents. Benzoyl peroxide is the most commonly used comedolytic agent, but the major disadvantage is the resultant dermal irritation. This study observed significant reduction in the standard acne grading, papule count, pustule count and the amount of skin sebum after 8 weeks of application. In addition, there was a better subject self satisfaction and improvement. The overall response to the treatment also recorded a significant improvement from the second week onwards. There were no clinically significant short and long-term adverse reactions (either reported or observed), during the entire period of study and excellent patient compliance to *AVCO Acne Gel* was also observed. This favourable improvement in acne by *AVCO Acne Gel* might be due to synergistic actions of its ingredients. Based on these observations, it may be concluded that the *AVCO Acne Gel* has anti-acne activity. It is also clinically effective and safe for external usage in acne vulgaris.

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