

## BENEFFICIAL EFFECTS OF TOPICAL AGENTS ON MILD TO MODERATE ACNE

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**Summary.** *Introduction: Alpha hydroxy acids (AHA) are a special group of organic acids found in many natural nutriment. They have been described in literature for the treatment of a number of conditions in which abnormal keratinization consistently contributes to pathogenesis. These include ichthyoses, warts, psoriasis, eczema and acne. Adapalene modulates cellular keratinization and inflammatory processes, and thus is highly comedolytic and anti-inflammatory. This latter effect is due to inhibition of the lipoxigenase activity and also to the oxidative metabolism of arachidonic acid. Aims: The aim of present study was to compare the efficiency and skin tolerance of a topical alpha hydroxy acid preparation and topical retinoid adapalene on mild to moderate acne, all in order to reduce acne. Experimental part: Group consisted of 35 subjects who were divided in two sub-samples. Within the first experimental sub-group 2ml of 40% solution of AHA (Dr Murad fruit acids 40%) was applied to all subjects (Nsg1=15), once a week. Within second experimental sub-group), 0,05% Adapalene (Ainol cream) was applied to all subjects (Nsg2=20), once a day. Testing areas were 5x5 cm, left and right cheek, parallel. Therapy lasted for 7 weeks. For data statistical analysis and interpretation of results, software program "SPSS version 13" was used. Results were expressed through the descriptive statistics, as simple frequencies, while for establishing of statistically significant differences, t test of significance was used. Results: The results of this study showed that alpha hydroxy acid and adapalene had a significant effect in the treatment of mild to moderate acne by reducing the number of lesions (non-inflamed and inflamed). Furthermore, fewer side-effects were experienced by patients treated with AHA when compared to adapalene. Conclusion: Topical AHA and topical adapalene had overall efficiency and superior therapeutic dimension.*

**Key words:** *Acne vulgaris, alpha hydroxy acids, adapalene*

### Introduction

Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous unit that affects at least 85 percent of adolescents and young adults (1). Distribution of acne lesions is limited to areas with well-developed sebaceous glands including face, back, chest and upper arms. It characteristically occurs in these sites with both non-inflammatory and inflammatory skin lesions (2). Hyperkeratinisation plays an important role in the pathogenesis of acne, and is usually a result of decreased desquamation due to increased corneocyte cohesion (3). Excessive sebum production is one of the major factors contributing to the formation of primary lesions (4,5). Topical treatments are usually effective for most patients with mild to moderate facial acne. Alpha hydroxy acids (in further text AHA) ability to decrease corneocyte cohesion provides the rationale for their use in the treatment of acne (6,7). Unlike true keratolytics, alpha hydroxy acids decrease corneocyte cohesion at the lower levels of the stratum corneum (potentially dislodging comedones and preventing their formation) as well as

improving the skin surface cosmetically (8,9,10). Topical retinoids have been used to successfully treat acne for almost three decades. In the beginning, a retinoid was a compound of similar structure and action to retinol (vitamin A) (11). Changes in the carboxylic group, the poly-ethylene chain, and the aromatic ring can result in the modification of the original molecule. The new synthetic retinoid molecules have little resemblance to retinol but nonetheless are included in this family because they have the ability to bind with or activate retinoid receptors (12). The main aims of the present study were to compare the efficiency of applied preparations (topical alpha hydroxy acid preparation and topical retinoid adapalene), skin tolerance and to monitor the undesirable effects which could affect the quality of life in subjects in treatment of mild to moderate acne.

### Experimental Part

Examination was performed in the Cabinet for venereal and skin diseases and department of esthetic medi-

cine of Health centre in Niš. Selection of subjects was based on clinical analysis and anamnestic data (subjects with mild to moderate facial acne). Differences in sex haven't been taken into account, because influence of hormones hasn't been monitored. Group consisted of 35 subjects divided in two sub-groups. Within the first experimental sub-group (in further text SG1), 2ml of 40% solution of AHA was applied to all subjects (Nsg1=15), once a week. Within the second experimental sub-group (in further text SG2), 0,05% Adapalen was applied to all subjects (Nsg2=20), once a day. Testing areas were 5x5 cm, left and right cheek, paralel. Seven weekly peeling sessions were carried out in each patient, while analysis, clinical examination and marks inserting in the protocol of research, were performed once a week. All subjects got through the complete treatment, as required by protocol. Symptoms which included number of comedones, papules, greasy face look, erythemes, desquamation and sensation of pulling were monitored. Comedones, papules and greasy face look were monitored as criteria of treatment's efficiency, while erythemes, desquamation and sensation of pulling were monitored as undesirable effects which could negatively affect the quality of life. The aim of present study was to compare the efficiency and skin tolerance of a topical alpha hydroxy acid preparation and topical retinoid adapalen in mild to

moderate acne. For data statistical analysis and interpretation of results, software program "SPSS version 13" was used. Results were expressed through the descriptive statistics, as simple frequencies, whereas t test of significance was used for establishing the statistically significant differences.

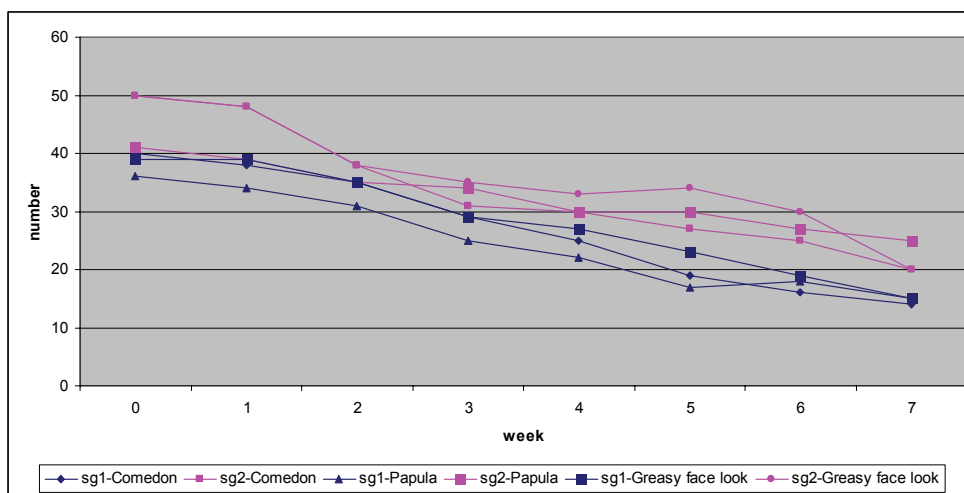
**Results**

The results of this study showed positive changes in both sub-groups.

In Table 1, graphs 1 and 2 show a decrease in the number of symptoms in both sub-groups, except in variables erythema, desquamation and sensation of pulling in second sub-group, where certain increase in number of symptoms between the initial state and second week, initial state and third week and initial state and second week of treatment, respectively, was noticed. T-tests which evaluated the significance of differences in variables at the beginning and at the end of treatments (tables 2 and 3) show significant decrease of symptoms in both sub-groups, except in variables erythema and sensation of pulling, in second sub-group, where significance (p=0.06) is near to the critical value of significance (p=0.05).

Table 1. Comparative review of treatment effects of SG1-AHA 40% & SG2-adapalen

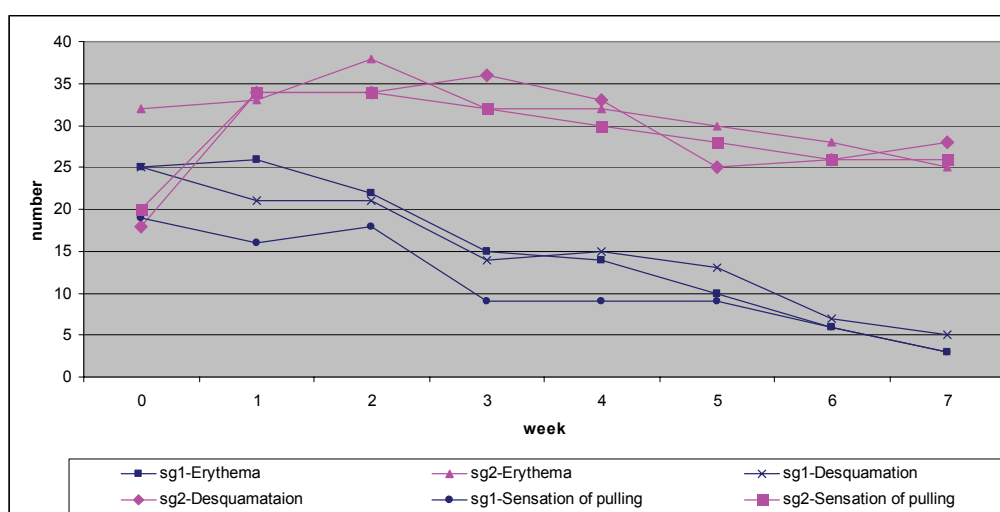
Variables/Number	0. week	1. week	2. week	3. week	4. week	5. week	6. week	7. week
	SG <sub>1</sub> /SG <sub>2</sub>	SG <sub>1</sub> /SG <sub>2</sub>	SG <sub>1</sub> /SG <sub>2</sub>	SG <sub>1</sub> /SG <sub>2</sub>	SG <sub>1</sub> /SG <sub>2</sub>	SG <sub>1</sub> /SG <sub>2</sub>	SG <sub>1</sub> /SG <sub>2</sub>	SG <sub>1</sub> /SG <sub>2</sub>
Comedon	40/50	38/48	35/38	29/31	25/30	19/27	16/25	14/20
Papula	36/40	34/39	31/35	25/34	22/30	17/30	18/27	15/25
Greasy face look	39/50	39/48	35/38	29/35	27/33	23/34	19/30	15/20
Erythema	25/32	26/33	22/38	15/32	14/32	10/30	6/28	3/25
Desquamation	25/18	21/34	21/34	14/36	15/33	13/25	7/26	5/28
Sens. of pulling	19/20	16/34	18/34	9/32	9/30	9/28	6/26	3/26



Graph 1. Number of comedones, papules and greasy face look as criteria of treatment efficiency.

Table 2. t test of SG1 (AHA 40%), between initial state and seventh week of treatment

Variables	First sub-group (SG <sub>1</sub> ) – AHA 40%										
	Mean G 1:0	Mean G 2:7	t-value	df	p	Valid N G 1:0	Valid N G 2:7	Std.Dev. G 1:0	Std.Dev. G 2:7	F-ratio variances	p variances
Comedone	2.60	0.87	9.28	28.00	0.00	15.00	15.00	0.63	0.35	3.23	0.04
Papula	2.33	0.93	7.06	28.00	0.00	15.00	15.00	0.72	0.26	7.86	0.00
Greasy face look	2.53	1.00	9.28	28.00	0.00	15.00	15.00	0.64	0.00	0.00	1.00
Erythema	1.73	0.27	8.77	28.00	0.00	15.00	15.00	0.46	0.46	1.00	1.00
Desquamation	1.73	0.40	7.56	28.00	0.00	15.00	15.00	0.46	0.51	1.23	0.71
Sensation of pulling	1.27	0.20	5.06	28.00	0.00	15.00	15.00	0.70	0.41	2.89	0.06



Graph 2. Number of erythemas, desquamation and sensation of pulling as undesirable effects.

Table 3. t test of SG2 (adapalene), between initial state and seventh week of treatment

Variables	Second sub-group (SG <sub>2</sub> ) - adapalene										
	Mean G 1:0	Mean G 2:7	t-value	df	p	Valid N G 1:0	Valid N G 2:7	Std.Dev. G 1:0	Std.Dev. G 2:7	F-ratio variances	p variances
Comedone	2.50	1.00	13.08	38.00	0.00	20.00	20.00	0.51	0.00	0.00	1.00
Papula	2.05	1.25	3.61	38.00	0.00	20.00	20.00	0.89	0.44	3.99	0.00
Greasy face look	2.50	1.20	8.85	38.00	0.00	20.00	20.00	0.51	0.41	1.56	0.34
Erythema	1.60	1.25	1.93	38.00	0.06	20.00	20.00	0.68	0.44	2.35	0.07
Desquamation	0.70	1.30	-3.08	38.00	0.00	20.00	20.00	0.73	0.47	2.43	0.06
Sensation of pulling	0.90	1.30	-1.95	38.00	0.06	20.00	20.00	0.79	0.47	2.81	0.03

## Discussion

Effective acne management should be targeted toward these factors which are implicated in the pathogenesis of the disease. The goal was to reduce or eliminate the primary clinical lesion—the microcomedo, which is the precursor of almost all other acne lesions (9). Since the microcomedo is invisible, topical treatment should be applied not just to the obvious lesions, but also to the acne prone area, to prevent the development of new lesions (4,10). Topical retinoids, as monotherapy, are mainly used in patients with non-inflammatory comedones, in combination with other topical and systemic drugs in mild, moderate, and severe inflammatory

acne (14,15,16). Adapalene is characterized by very low percutaneous absorption once the drug has penetrated the stratum corneum, and becomes trapped in the epidermis and the hair follicle, which is the targeted area (17). The most significant positive effects in the treatment of mild to moderate acne by reducing the number of lesions (non-inflamed and inflamed), were obtained in the subjects of first sub-group who used AHA 40%. Obtained results of this research are in accordance with the results of clinical trials by Yu & Van Scot (18) and Vićentić et al (19), conducted with the aim of monitoring and evaluating the efficiency and tolerance of AHA and others clinical trials, e.g., trials of Perić et al (20), Wolf (21), Czerniewsky et al (22),

Milikan (23), Shalita (24), conducted with the aim of monitoring and evaluating the efficiency and tolerance of adapalene in the treatment of acne vulgaris.

### Conclusion

Topical AHA and topical adapalene had overall efficiency and superior therapeutic dimension. Undesirable

effects appeared during the treatment and were present until the end of the therapy, but they did not significantly affect the positive results. As a conclusion of actual research, topical AHA and topical adapalene are well tolerated, safe and effective procedures that can be used with patients in the treatment of acne vulgaris.

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## KORISNI EFEKTI LOKALNO PRIMENJENIH SUPSTANCI U LEČENJU BLAŽIH DO UMERENIH OBLIKA AKNI

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Kratak sadržaj: *Uvod: α-hidroksi kiseline (AHAs) predstavljaju posebnu grupu organskih kiselina koje su prisutne u mnogim prirodnim proizvodima. Ove kiseline se u literaturi pominju u tretmanima u kojima abnormalna keratinizacija doprinosi stalnim patološkim procesima, koji uključuju ihtioze, pojavu bradavica, psorijazu, ekcem i akne. Adapalene menja ćelijsku keratinizaciju i inflamatorne procese, a takođe ima i komedolitičko i protiv zapaljensko dejstvo. Ovi efekti nastaju kao posledica inhibicije aktivnosti lipooksigenaze, kao i oksidativnog metabolizma arahidonske kiseline. Ciljevi: Cilj istraživanja je bio poređenje efikasnosti i tolerancije kože na primenu preparata sa alfa-hidroksi kiselinama i retinoidom*

*adapalenom, kod blažih do umerenih oblika akni, a sve u cilju smanjenja akni. Eksperimentalni deo: Uzorak je sačinjavalo 35 ispitanika, podeljenih u dva subuzorka. U okviru prvog subuzorka, svim ispitanicima (Nsg1=15), aplikovano je 2ml 40%-nog rastvora  $\alpha$ -hidroksi kiselina (Dr Murad voćne kiseline 40%) jednom nedeljno. U okviru drugog subuzorka, svim ispitanicima (Nsg2=20), aplikovan je 0.05%-tni Adapalen (Ainol krema), jednom dnevno. Testirane površine kože levog i desnog obraza, bile su 5x5 cm, paralelno. Terapija je trajala 7 nedelja. Za statističku analizu podataka i interpretaciju rezultata u upotrebi je bio softver "SPSS verzija 13". Rezultati su izraženi putem deskriptivne statistike u vidu učestalosti, dok je za utvrđivanje statistički značajnih razlika korišćen t test značajnosti. Rezultati: Rezultati ovog istraživanja su pokazali da  $\alpha$ -hidroksi kiseline i adapalen imaju veliku ulogu u tretmanu, kojim se smanjuju akne redukcijom broja lezija (neinficiranih i inficiranih). Šta više, manje neželjenih efekata, imali su ispitanici tretirani  $\alpha$ -hidroksi kiselinama u poređenju sa ispitanicima tretiranim adapalenom. Zaključak: Topikalna  $\alpha$ -hidroksi kiselina i topikalni adapalen pokazali su ukupnu efikasnost i superiornu terapeutsku dimenziju.*

**Ključne reči:** *akne vulgaris, adapalen,  $\alpha$ -hidroksi kiseline*