



UDC 616.314-17-008.1-084-085

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## FEATURES OF INFLUENCE OF NEW APGEL IN THE LOCAL THERAPY TISSUES OF ORAL CAVITY IN PATIENTS WITH DISEASES OF ORAL MUCOSA

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ОСОБЕННОСТИ ВЛИЯНИЯ НОВОГО АПИГЕЛЯ ПРИ МЕСТНОЙ ТЕРАПИИ ТКАНЕЙ РОТОВОЙ ПОЛОСТИ У ПАЦИЕНТОВ С ЗАБОЛЕВАНИЯМИ СЛИЗИСТОЙ ОБОЛОЧКИ

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В клинических обследованиях и биохимических исследованиях ротовой жидкости пациентов с заболеваниями слизистой оболочки определена эффективность использования гигиенического средства — апигеля на течение заболеваний по данным маркеров воспаления (белка и протеазы), бактериального обсеменения (уреазы), содержания свободнорадикального окисления липидов, за степенью дисбиоза, активностью лизоцима и антиоксидантной системы (каталазы, СОД) с положительным влиянием на неспецифическую резистентность ротовой полости в сравнении со стандартной терапией.

**Ключевые слова:** ротовая жидкость, воспаление, дисбиоз, ферменты, лизоцим.

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On the base of clinical observations and biochemical study of oral fluid in patients with diseases of oral mucous membrane the efficiency of use the hygienic agent — apigel is proved by decrease of the level of the markers of inflammation (protein and protease), bacterial insemiation (urease), inhibition of free-radical oxidation and the degree of dysbiosis, stimulate lysozyme secretion and activity of anti-oxidant system (catalase, SOD), has positive influence on nonspecific resistance in oral cavity in comparison with a standard therapy.

**Key words:** oral liquid, inflammation, disbiosis, enzymes, lysozyme.

Diseases of the oral mucosa (OM), periodontal disease occupy a leading place in the structure of dental diseases, to this day remain unresolved problem of dentistry, which is associated with the multifactorial origin of them.

The low efficacy of traditional therapy for OM and periodontal disease induces the search for new means and

methods of their treatment. Taking into account the pathogenesis of inflammatory diseases of OM, periodontal disease, prophylactic and therapy should be aimed at the restoration of impaired homeostasis of the oral cavity, the removal of local factors that initiate metabolic and immunological shifts in the oral fluid. Therefore, development and study of new means of lo-

cal therapy of OM lesions that possess anti-inflammatory, antibacterial, anti-edema, pain-relieving, hemostatic, wound healing properties, which will allow them to be used in cases of pathology periodontal diseases, ММОС, is an actual problem of modern dentistry.

The purpose of this work is evaluation of efficiency of local application of developed oral care gel in the combination therapy of the OM diseases.



## Materials and Methods of Research

42 persons (15–30 years old) had complex dental exam, and were divided into 3 groups. The basic group and group of comparison included 27 patients with the OM diseases. The diagnosis was established on the basis of objective examination, anamnesis, clinical, clinical and laboratory and biochemical examinations. In order to obtain objective results all examined patients in these groups were comparable by age, sex, disease course and level of injury. 15 patients had mechanical trauma of OM (8 patients with the chronic traumatic erythema, 7 — with the chronic traumatic erosion), 12 patients had toxic stomatitis as a result of mechanical, chemical-toxic irritation while using removable denture. The basic group included 14 patients, who were treated with local application of a new hygienic agent in the combination therapy — the gel on the basis of apiproducs and other biologically active matters [1] as applications, layer thickness 0.5–0.8 mm 2–3 times per a day during 5–7 days (depending on type and severity of inflammatory process). The group of comparison consisted of 13 patients with OM, which had a standard therapy, without application of gel. The group of control consisted of 15 persons of the same age without dental pathology. All examined patients had no serious concomitant diseases.

Efficiency of treatment was evaluated taking into account the common condition of patients, clinical and laboratory data. Therapy was evaluated by the next parameters: level of oral hygiene by dynamics of OHI-S (oral hygiene index); presence of inflammatory process by PMA index; bleeding by PBI (papilla

bleeding index) Muhlemann-Saxer index; pain severity by the visual-analog ten-point scale [2]. In the oral fluid sampled in fasting state [3] there was determined protein level by O. H. Lowry et al., total proteolytic activity (TPA) [4], malonic dialdehyde (MDA) concentration by tiobarbituric method [5], urease activity and dysbiosis level in oral cavity by fermentation method [6], activity of antioxidant defence by catalase (K) [7] and superoxide dismutase (SOD) activity [8] antioxidant-prooxidant index (API) in relation of K to MDA, lysozyme activity by bacteriologic technique [9].

The statistical analysis of obtained data was conducted with Student's t-test.

## Results of Research and Discussion

As a result of dental examination all patients were revealed clinical signs of the inflammatory diseases of OM. Clinical examination detected that all persons with injured OM had change in color of oral mucosa (hyper-

emia of different intensity — from slight reddening to bright red coloration). These changes were accompanied by edema in 25%, by burning and dry mouth in 50%; 3 (11.1%) patients had increase in *Candida* fungi. The application of apigel in the combination therapy of patients with the OM diseases improved basic clinical symptoms.

Gel applications with professional hygiene improved the oral hygiene level dramatically (Table 1). So, oral hygiene index decreased from  $2.56 \pm 0.14$  to  $0.15 \pm 0.03$ , i. e. 17 times after the administered treatment. In case of a standard therapy there was a rise of oral hygiene index: the index of hygiene decreased from  $2.42 \pm 0.16$  to  $0.53 \pm 0.05$  after the treatment, i. e. only 4.5 times.

The application of apigel resulted in reduction of gingival bleeding on average from  $2.92 \pm 0.09$  to  $0.76 \pm 0.04$ , in the group of comparison decrease is less pronounced — on average from  $2.74 \pm 0.11$  to  $1.25 \pm 0.14$ .

Stable subsided inflammation was confirmed by positive dy-

Table 1  
Dynamics of Clinical Signs of Oral Cavity in Patients at the Background of Administered Therapy

Data	Control group	Groups of patients			
		Basic group		Group of comparison	
		Before treatment	After treatment	Before treatment	After treatment
Oral hygiene index OHI-S	$0.12 \pm 0.03$	$2.56 \pm 0.14$ P<0.05	$0.15 \pm 0.03$ P>0.05 P <sub>1</sub> <0.05	$2.46 \pm 0.16$ P<0.05	$0.53 \pm 0.05$ P<0.05 P <sub>1</sub> <0.05
PMA	$2.40 \pm 1.04$	$45.30 \pm 2.40$ P<0.05	$3.10 \pm 1.31$ P>0.05 P <sub>1</sub> <0.05	$43.25 \pm 1.65$ P<0.05	$9.10 \pm 1.28$ P<0.05 P <sub>1</sub> <0.05
Bleeding index PBI	$0.64 \pm 0.06$	$2.92 \pm 0.09$ P<0.05	$0.76 \pm 0.04$ P>0.05 P <sub>1</sub> <0.05	$2.74 \pm 0.11$ P<0.05	$1.25 \pm 0.14$ P<0.05 P <sub>1</sub> <0.05
Evaluation of pain severity by 10-point score	0	$7.10 \pm 0.20$ P<0.05	$1.68 \pm 0.11$ P<0.05 P <sub>1</sub> <0.05	$6.40 \pm 0.28$ P<0.05	$3.30 \pm 0.18$ P<0.05 P <sub>1</sub> <0.05

Note. P — statistical significance with the control group; P<sub>1</sub> — statistical significance with group "before treatment".



namics of PMA index in both groups of the OM patients, the more intensive anti-inflammatory reaction was observed in the basic group. By the end of treatment the PMA index in patients with common therapy fell down from  $43.25 \pm 1.65$  to  $9.10 \pm 1.28$ , while in basic group of patients — from  $45.3 \pm 2.4$  to  $3.10 \pm 1.31$ .

As the inflammatory diseases of OM are accompanied by pain, great attention was attached to the analysis of anaesthetic effect of the new hygienic agent. Pain severity in patients of the basic group on 3rd–5th day of apigel applications decreased on average from  $7.10 \pm 0.20$  to  $1.68 \pm 0.11$ . The patients of comparison group had pain relief from  $6.40 \pm 0.28$  to  $3.30 \pm 0.18$ , remaining at the same level up to 7th day of treatment.

The pronounced improvement of clinical symptoms in patients with the OM diseases in case of apigel applications is conditioned by its anti-inflammatory and anesthetic properties.

The conducted biochemical analysis of oral fluid in patients with the OM diseases revealed the increase of inflammation markers — TPA and MDA (1.6 and 2.2 times correspondingly). The local application of apigel in the combination therapy of these patients allowed to lower the TPA level in 7 days, level of protein and MDA came to the norm. The Table 2 demonstrates that the comparison group patients had higher indices which did not reach the norm.

Along with intensification of lipid peroxidation and inflammation in the oral cavity in case of the OM diseases there was a great rise in conditioned pathogenic and pathogenic bacterial flora, which is confirmed by growing activity of urease in the oral fluid. The level of this enzyme in the oral fluid of patients

**Influence of Combination Therapy on the Biochemical Indexes of Oral Fluid in Patients with Traumatic Injuries of Oral Mucosa**

Table 2

Data	Control (norm) p=15	Patients with OM diseases			
		Basic group		Group of comparison	
		Before treatment	After treatment	Before treatment	After treatment
TPA, ncat/l	$1.74 \pm 0.20$	$2.87 \pm 0.38$ P<0.05	$1.82 \pm 0.28$ P>0.05 P <sub>1</sub> <0.05	$2.99 \pm 0.40$ P<0.05	$2.27 \pm 0.46$ P>0.05 P <sub>1</sub> >0.05
Level of protein, g/l	$1.68 \pm 0.06$	$2.19 \pm 0.10$ P<0.05	$1.84 \pm 0.08$ P<0.05 P <sub>1</sub> >0.05	$2.42 \pm 0.12$ P<0.05	$2.12 \pm 0.12$ P<0.05 P <sub>1</sub> >0.05
MDA, mcmol/l	$0.27 \pm 0.02$	$0.40 \pm 0.02$ P<0.05	$0.30 \pm 0.03$ P>0.05 P <sub>1</sub> <0.05	$0.46 \pm 0.05$ P<0.05	$0.40 \pm 0.03$ P<0.05 P <sub>1</sub> >0.05
Activity of catalase, mlcat/l	$0.42 \pm 0.06$	$0.28 \pm 0.03$ P<0.05	$0.38 \pm 0.02$ P>0.05 P <sub>1</sub> >0.05	$0.22 \pm 0.02$ P<0.05	$0.30 \pm 0.03$ P<0.05 P <sub>1</sub> <0.05
Activity of SOD, RU/l	$0.50 \pm 0.05$	$0.32 \pm 0.03$ P<0.05	$0.40 \pm 0.06$ P>0.05 P <sub>1</sub> <0.05	$0.28 \pm 0.03$ P<0.05	$0.38 \pm 0.04$ P>0.05 P <sub>1</sub> <0.05
API	1.55	0.70	1.26	0.48	0.75
Urease, mccat/l	$0.050 \pm 0.006$	$0.140 \pm 0.040$ P<0.05	$0.087 \pm 0.030$ P<0.05 P <sub>1</sub> <0.05	$0.154 \pm 0.040$ P<0.05	$0.120 \pm 0.040$ P<0.05 P <sub>1</sub> >0.05
Lysozyme, mcg/ml	$0.28 \pm 0.05$	$0.14 \pm 0.06$ P>0.05	$0.26 \pm 0.04$ P>0.05 P <sub>1</sub> >0.05	$0.16 \pm 0.03$ P>0.05	$0.20 \pm 0.04$ P>0.05 P <sub>1</sub> >0.05
Level of dysbiosis	0.17	1	0.33	0.96	0.60

Note: P — statistical significance with the control group; P<sub>1</sub> — statistical significance with group “before treatment”.

increased 3 times as much. Urease activity in patients who were administered standard therapy was at the definite high level as compared with the control group and exceeded the corresponding values in the basic group. During treatment in the basic group of patients the activity of urease fell down by 38%, in the group of comparison only by 22%, 3 times decrease of oral disbiosis level in the patients of the basic group, 1.6 times in the group of comparison, which proves antimicrobial local action of the new gel.

Growth of pathogenic bacterial flora in the oral cavity is connected with decrease of lys-

ozyme activity in case of the OM diseases. Prescription of gel for patients of the basic group contributed to rise of lysozyme activity up to the normal level, while it was only a tendency to rise in the group of comparison.

Analysis of oral fluid in patients with the OM diseases revealed significant decrease of basic enzymes activity of antioxidant defense: catalase on average by 66.6% and SOD — by 64%, correspondingly the antioxidant-prooxidant index decreased too. The local application of apigel, lowering inflammatory phenomena, activated AOS protective enzymes in the oral



fluid. Level of K and SOD activity in patients of the basic group rose by the end of treatment up to the norm, which proves antioxidant properties of the new gel. The activity of given enzymes had a less pronounced dynamics in the group of comparison.

So, the conducted examination revealed positive action of local application of the new oral care agent in the combination therapy of the OM diseases on the dynamics of clinical symptoms due to its anti-inflammatory and anesthetic properties. Biochemical analysis of oral fluid in patients with the OM diseases showed that the use of apigel prevents from growth of pathogenic bacterial flora, and rise in inflammation and lipid peroxidation, stimulates activity of lysozyme and enzymes of the antioxidant system, which improves nonspecific resistance in the oral cavity.

### Conclusions

1. Local application in the combination therapy of the new hygienic agent on the basis of apiproducs positively affects on dynamics of clinical symptoms of the OM diseases, improving oral hygienic condition, rendering antiinflammatory and anaesthetic action.

2. New apigel with OM diseases lowers level of inflammation and oral disbiosis, having an antimicrobial effect.

3. Use of developed hygienic agent increases nonspecific reactivity in the oral cavity due to antioxidant defence enzymes activation.

4. Obtained results prove gel application perspective during treatment of the OM diseases for improvement of rehabilitation and quality of life of patients.

**Ключові слова:** ротова дінина, запалення, дисбіоз, ферменти, лізоцим.

### ЛІТЕРАТУРА

1. Kravchenko L.S. (patentee) Patent of Ukraine 119715 MPK (2017.01) A61K36/00, A61K36/00, A61K8/42. Gel "Apisan" for prophylaxis and treatment of traumatic defects of oral mucosa Bulletin, 19. 2017.

2. Golovko N. V., Babenko A. D. Evaluation of state of hygiene of oral cavity and parodontal tissues in patients suffering from chronic hypertrophic gingivitis against a background of treatment of non-removable technique. *Ukrainsky stomatologichnyy almanakh*. 2010. № 1. P. 8–10.

3. Levitskiy A. P., Makarenko O. A., Rossakhanova L. N. Salivation in healthy persons of different age and in dental patients. *Visnyk stomatologii: Spets. Vypusk*. 2005. № 2. P. 7–8.

4. Barabash R. D., Levitskiy A. P. Casein-lytic and BAEE-esterase activity of saliva and salivary glands at rats in the postnatal ontogenesis. *Bulleten eksperimentalnoi biologii*. 1973. № 8. P. 65–67.

5. Stalnaya I. D., Garishvili T. G. *Metod opredeleniya malonovogo dialdegida s pomoshchyu tiobarbiturovoi kisloty* [Method of malonic dialdehyde detection with tiobarbituric acid]. Modern methods in biochemistry. Moscow: Medicine, 1977. P. 66–68.

6. Levitskiy A. P. *Fermentativnyi metod opredeleniya disbioza polosti rta dlya skringa proprebiotikov. Metodicheskiye rekomendatsii* [Fermentation method of oral disbiosis detection for screening propebiotics. Methodical recommendations]. Kiev, 2007. 20 p.

7. Korolyuk M. A., Ivanova D. I., Mayrova I. G. Method of catalase activity. *Laboratornoye delo*. 1988. № 1. P. 16–18.

8. Cheviri S., Chaba I., Sekey I. Role of superoxide dismutase in oxidizing processes and method of its evaluation in biological material. *Laboratornoye delo*. 1985. № 11. P. 678–681.

9. Levitskiy A. P. *Lizotsym vmesto antibiotikov* [Lysozyme instead of antibiotics]. Odessa: KPOGT, 2005. 74 p.

### REFERENCES

1. Kravchenko L.S. (patentee) Patent of Ukraine 119715 MPK (2017.01) A61K36/00, A61K36/00, A61K8/42. Gel "Apisan" for prophylaxis and treatment of traumatic defects of oral mucosa Bulletin, 19. 2017.

2. Golovko N.V., Babenko A.D. Evaluation of state of hygiene of oral cavity and parodontal tissues in patients suffering from chronic hypertrophic gingivitis against a background

of treatment of non-removable technique. *Ukrainsky stomatologichnyy almanakh* 2010; 1: 8–10.

3. Levitskiy A.P., Makarenko O.A., Rossakhanova L.N. Salivation in healthy persons of different age and in dental patients. *Visnyk stomatologii: Spets. Vypusk* 2005; 2: 7–8.

4. Barabash R.D., Levitskiy A.P. Casein-lytic and BAEE-esterase activity of saliva and salivary glands at rats in the postnatal ontogenesis. *Bulleten eksperimentalnoi biologii* 1973; 8: 65–67.

5. Stalnaya I.D., Garishvili T.G. *Metod opredeleniya malonovogo dialdegida s pomoshchyu tiobarbiturovoi kisloty* [Method of malonic dialdehyde detection with tiobarbituric acid]. Modern methods in biochemistry. Moscow, Medicine, 1977. p. 66–68.

6. Levitskiy A.P. *Fermentativnyi metod opredeleniya disbioza polosti rta dlya skringa proprebiotikov. Metodicheskiye rekomendatsii* [Fermentation method of oral disbiosis detection for screening propebiotics. Methodical recommendations]. Kiev, 2007. 20 p.

7. Korolyuk M.A., Ivanova D.I., Mayrova I.G. Method of catalase activity. *Laboratornoye delo* 1988; 1: 16–18.

8. Cheviri S., Chaba I., Sekey I. Role of superoxide dismutase in oxidizing processes and method of its evaluation in biological material. *Laboratornoye delo* 1985; 11: 678–681.

9. Levitskiy A.P. *Lizotsym vmesto antibiotikov* [Lysozyme instead of antibiotics]. Odessa, KPOGT, 2005. 74 p.

Submitted 14.11.2019

Reviewer MD,

prof. R. S. Vastyanov,  
date of review 16.11.2019

