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O. V. Pasechnyk <https://orcid.org/0000-0002-1350-0325>
A. O. Asmolova <https://orcid.org/0000-0001-7565-9094>
A. M. Pasechnik <https://orcid.org/0000-0002-6472-1494>
M. V. Rozumenko <https://orcid.org/0000-0003-2720-5009>

LOCAL APPLICATION OF A NEW HYGIENE AGENT FOR PREVENTION AND TREATMENT OF POST-IMPLANTATION INFLAMMATORY COMPLICATIONS

Odesa National Medical University, Odesa, Ukraine

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O. V. Pasechnyk, A. O. Asmolova, A. M. Pasechnik, M. V. Rozumenko

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Introduction. Dental implantation is widely developed in modern medicine. In order to obtain an early positive result of dental implantation, it is necessary to study and prevent early post-implantation inflammatory complications by means of local application of a new hygienic product – Apiprol dental elixir.

The aim of research is to study the changes in inflammatory reactions in the oral cavity with the local application of the new hygiene agent at the early postoperative period of dental implantation.

Material and methods. 28 patients (15 women and 13 men) with partial secondary adentia aged 32 to 60 years who underwent dental implantation. The effectiveness of the treatment was assessed by clinical and laboratory (biochemical, microbiological, immunological) examinations.

Results. The results showed that at the early postoperative stage of dental implantation in both study groups (with the local application of the new dental elixir and with the traditional use of herbal tinctures), local inflammatory processes occur in the tissues surrounding the implantation zone. At the early post-implantation period, the new dental elixir has a positive effect on the hygiene and microbiological status of the oral cavity decreasing the hygienic index on average from 3.8 to 0.5, quickly reduces the severity of edema and hyperemia of the peri-implant tissues with pain relief (on the 6th day in 91.6 % versus 72,9% in comparison group). At the early post-implantation stage, the dental elixir improves oral condition, inhibits free radical oxidation, activates enzyme components of antioxidant defence, which creates the basis for rapid recovery of peri-implant tissues compared to traditional local therapy.

Conclusion. The occurrence of early postoperative complications during dental implantation is reduced by local application of the dental elixir to the peri-implantation area during the first ten days of the post-implantation period.

Key words: dental implantation, oral fluid, markers of inflammation, dental elixir.

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О. В. Пасечник, А. О. Асмолова, А. М. Пасечник, М. В. Розуменко

ЛОКАЛЬНЕ ЗАСТОСУВАННЯ НОВОГО ГІГІЄНИЧНОГО ЗАСОБУ ДЛЯ ПРОФІЛАКТИКИ ТА ЛІКУВАННЯ ПОСТІМПЛАНТАЦІЙНИХ ЗАПАЛЬНИХ УСКЛАДНЕНЬ

Одеський національний медичний університет, Одеса, Україна

Мета дослідження – вивчення особливостей змін запальних реакцій у порожнині рота у разі місцевого застосування нового гігієнічного засобу у ранній післяопераційний період дентальної імплантації. Визначена ефективність лікування 28 пацієнтів у середньому віці 46 років з частковою вторинною адентією на основі оцінки клінічних і лабораторних досліджень. Отримані результати дають підставу вважати зменшення локального запального процесу в групі обстежених із використанням нового зубного еліксиру порівняно з групою із традиційним застосуванням настоянок трав. Висновок: виникнення ранніх післяопераційних ускладнень під час дентальної імплантації знижується у разі локального застосування на періімплантатну зону зубного еліксиру «Апіпрол» у перші десять днів постімплантаційного періоду.

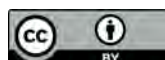
Ключові слова: дентальна імплантація, ротова рідина, маркери запалення, зубний еліксир.

Today, dental implantation dominates in complex approaches to the replacement of lost teeth. Despite the improvement of the dental implantation technique and prescription of drug therapy, the frequency of inflammatory complications at the early post-implantation period remains high [1; 2]. Many clinical studies by Ukrainian and foreign specialists confirm the great risk of inflammatory reactions

associated with dental implants at the early postoperative period, which is caused by the postoperative tissue damage, stress, and a low immune response to microflora invasion [3; 4]. Therefore, at the stage of post-implantation treatment it is most important to create a background that would facilitate the recovery of affected tissues and protect against inflammatory complications. A routine therapeutic management includes antibacterial, anti-inflammatory drugs, vitamins. However, the incidence of inflammatory reactions at the peri-implantation area remains high today. So, in order to prevent and remove post-implantation compli-

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cations, anti-inflammatory, regenerative, and immuno-activating drugs are included in the management protocols for patients who have undergone dental implantation. That is why the search and development of means of prevention and treatment of the inflammatory process at the postoperative period of dental implantation is of great relevance.

The aim of the study is to analyse changes in inflammatory reactions in the oral cavity with the topical application of a hygiene product at the early postoperative period of dental implantation.

Material and methods. The study included 28 patients aged on average 46 years selected for dental implantation. Among them were 15 (53.5%) women and 13 (46.4%) men with partial adentia without concomitant diseases. All patients were informed and consented to participate in the research process and use their clinical information in accordance with the World Medical Association (WMA) Declaration of Helsinki “Ethical Principles for Medical Research Involving Human Subjects, 2013”.

The patients were examined in accordance with the protocol for treatment with dental implants, which includes questioning, medical history and clinical examination of the oral cavity. X-rays were taken for all patients as part of the initial examination before intraosseous implantation. The follow-up was carried out: at the operation day, after its completion before the 2-nd stage – replacement of the cover screw with the gingival former in order to confirm the diagnosis and monitor the results. Dental implantation was planned after an X-ray examination of the jaws and teeth, primarily at the area of implantation. With a diagnosed alveolar process atrophy, the open sinus lifting surgery was performed.

The clinical examination determined the dental status of the patients, including the assessment of the hygienic condition of the oral cavity and peri-implant tissues by the Green–Vermillion index, Russell’s periodontal index [5].

All the patients who underwent intraosseous dental implantation were divided into 2 groups: the main group (14 persons) and the comparison group (14 persons). The control group (8 persons) had no dental pathology and concomitant diseases. The technique of dental implantation in the main and comparison groups was the same. If no more than 3–4 implants were installed through 1–2 surgical accesses, only anaesthetic agents for 1–2 days and rinsing the mouth with herbal tinctures for 3–8 days were recommended at the postoperative period in the comparison group. If the implantation of a greater volume and complexity was performed, anaesthetic, anti-inflammatory and hyposensitization agents were prescribed for 2–3 days, as well as antibiotics for 3–5 days.

In addition to routine postoperative therapy, patients in the main group were recommended to rinse the mouth with Apiprol dental elixir (5–8 ml) with a delay of 30–60 seconds on the wound surface [6]. The dental elixir is a newly created agent based on honey products and plant adaptogens. The patients were instructed about the need to use the dental elixir 2–3 times a day beginning from the next day after the operation for 5–8 days (depending on the type and severity of the process). The effectiveness of the treatment was evaluated by the general condition of the patients, clinical and laboratory (biochemical, microbiological) examinations. The object of the study was oral fluid collected in half an hour after rinsing the mouth daily after surgery in the course

of 12 days. In the oral fluid, lysozyme activity (including relative activity) was determined by the bacteriological method [7], urease activity (including relative activity) and the level of oral dysbiosis were determined by the enzymatic method [8]. The state of the pro-oxidant system was determined by the level of malondialdehyde (MDA) [9]. The state of the antioxidant system (AOS) was studied by the activity of catalase [9] and superoxide dismutase (SOD) [9]. The material taken from the peri-implant area on an empty stomach after rinsing the mouth with distilled water from day 1 to day 12 after dental implantation was examined according to the traditional method of processing the results in a microbiological laboratory using a molecular biological method based on the polymerase chain reaction (PCR) [10].

The data were statistically processed by the method of variation statistics using the Student’s t-test with the help of Microsoft Excel 2000. The difference was considered significant at $p < 0.05$.

Research results and discussion. The early postoperative period during intraosseous dental implantation was characterized by pain syndrome, edema of muscular tissues and mucous membranes, and hyperemia at the area of the intervention. Hyperemia and edema were the most pronounced on the 3rd day after dental implantation, but decreased already on the 4th post-implantation day in the main group, on the 6th day – in the comparison group. In the main group hyperemia and edema were completely absent on the 6th day (91.6% of cases), in the comparison group – on the 8th day (72.9% of cases) respectively. Signs of residual hyperemia and edema remained on the 10th day after implantation in 2.1% in the main group, which was 18.8% (20.9%) less than in the comparison group ($p < 0.05$).

The clinical picture of inflammatory changes in the oral cavity of patients of the main group after treatment with the new hygiene agent in local therapy had more pronounced significant positive dynamics; inflammation and edema were removed faster than in the comparison group with a standard drug therapy.

The rate of the post-implantation wound epithelization was different in the main and comparison groups. The first signs of the wound’s initial epithelization in most patients were observed 2 days earlier in the main group than in the comparison group (on 3rd and 5th day, respectively), with the number of patients in the main group being 18.2% higher than in the comparison group. Complete epithelization of the post-implantation mucosal lesion occurred on average 2.7 days earlier in the main group than in the comparison group (by 10.10 ± 0.10 and 12.8 ± 0.20 days, respectively) ($P < 0.05$).

The oral condition before the operation was the same in all the patients, because before implantation they had professional oral hygiene. On the 2nd day after dental implantation, the oral condition worsened due to formation of plaques. A comparative analysis of the oral condition according to the Green–Vermillion index revealed differences in patients of the investigated groups: patients receiving standard therapy had worse level of hygiene compared to the main group whose patients received the new tooth elixir. Rapid positive dynamics (in points) was determined in the main group from an average of 3.80 ± 0.01 before treatment to 0.50 ± 0.08 on 8th day of treatment against 3.40 ± 0.02 from the baseline to 1.80 ± 0.12 in the comparison group ($P < 0.05$). More than half

of the patients in the comparison group had the plaque spread to the dental neck, while in patients of the main group it was observed only in 8.2%. It proves that the local application of the dental elixir having antimicrobial properties in the complex treatment in the main group improves clinical outcomes compared to the use of a traditional local therapy alone.

The study of oral microbiocenosis during dental implantation revealed changes in the level of microbial contamination and antimicrobial protection of the oral cavity in the patients of the study groups (Table 1). So, after treatment with the dental elixir, urease activity in the oral fluid increased on the 3rd day after surgery, then returned to the baseline level on the 8th day after implantation. At the same time, with a traditional therapy the urease activity exceeds the baseline data 1.22 and 1.16 times, respectively.

This dynamic is more pronounced in the presented data of relative urease activity. Changes in the absolute and relative activity of urease of the oral fluid in the main group, which determine the decrease in the oral microbial contamination level with usage of the dental elixir, indicate its negative effect on the oral microbiota activity, as a result of which dysbiosis decreases.

According to the data on lysozyme activity, there is a tendency to increase the level of local antimicrobial protection in the oral fluid of patients in the main group compared to patients in the comparison group.

The analysis of the oral ecosystem according to the dysbiosis index revealed normalisation of the oral microbiocenosis in the main group. In contrast to the main group, the patients of the comparison group had insignificant changes in indicators of impaired oral biocenosis, which was reflected in the level of dysbiosis [11].

A biochemical study of the oral fluid showed that after dental implantation on the 3rd day, all patients had increased levels of MDA, indicating activation of free radical oxidation processes compared to healthy individuals. With the use of the dental elixir, the MDA level in the patients' oral fluid returned to the baseline values on the 8th day after surgery, in the comparison group it remained elevated (16% higher than the baseline).

The decreased activity of the key enzymes of antiradical protection – SOD and catalase – was observed at the 3rd day after dental implantation. Hypofunction of the catalase and superoxide dismutase systems causes AOS insufficiency within the first days after surgery. In the oral fluid of the main group patients, the parameters of AOS did not change significantly with a tendency to increase, at the end of treatment they were identical to the control data, while in the comparison group they differed from the control data (catalase was lower by 25% on the 3rd day, by 17% – on the 8th day. The changes in SOD activity was insignificant, on average 5%).

So, the application of the dental elixir in the complex treatment of the wound process at the postoperative period after dental implantation provided the restoration of the lost protective functions of AOS, which was reflected in the clinical picture of implant integration, reducing the average duration of inflammation in peri-implant tissues.

On the 7th day after the dental implantation, examination of periodontopathogenic anaerobic microbes on the implant's surface was carried out using a molecular biological method based on the polymerase chain reaction (PCR). In the com-

parison group, genetic markers of two periodontal pathogenic species of the 1st order were determined: *Porphyromonas gingivalis* and *Tannerella forsythia* – in 15% and 18% of samples, respectively, but these species were not detected in the patients of the main group. Another periodontopathogenic species of the 1st order *Aggregatibacter actinomycetemcomitans* was found in 14% of samples in the comparison group and only in 5% – in the main group ($P < 0.05$). Among periodontal pathogenic species of the 2nd order, the frequency of revealed genetic markers in patients on the 7th day after dental implantation was different. So, *Micromonas micros* and *Prevotella intermedia* markers occurred in 20% and 12% in the comparison group, and only in 8% and 5% in the main group, that is 2.5 times lower ($P < 0.05$). Genetic markers of *Fusobacterium nucleatum* were determined equally often in all patients, coinciding with the frequency of detection of the second type of periodontopathogens of the 2nd order – *Treponema denticola* (in 50% of patients in both groups). In our opinion, the obtained data indicate that species of the 2nd order periodontopathogens, which are equally detected in material samples of all patients after dental implantation, behave like normal resident species without causing inflammation and aggression.

Thus, the dental elixir affects the composition of the oral microbiocenosis (primarily periodontal pathogenic), preventing the persistence of pathogenic microorganisms in the peri-implantation zone, which reduces the risk of complications.

The number of patients with pain syndrome on the 1st day of the post-implantation period after the end of anesthesia in patients of both groups had no difference. Pain relief in the main group occurred 1 day faster than in the comparison group (on the 3rd day in the main group and on the 4th day in the comparison group). At the same time, the number of patients in the main group (on the 3rd day) who experienced earlier pain relief exceeded the number of similar patients in the comparison group (on the 4th day) by 37% ($P < 0.05$). On the 8th day, the number of patients with pain relief in the main group exceeded the number of patients in the comparison group by 29.5% ($P < 0.05$). By the 10th day, the pain syndrome was absent in all the patients of the main group, whereas almost a third of patients in the comparison group perceived pain as insignificant.

The obtained results demonstrated that during dental implantation the oral epithelium is injured, which leads to violation of the isolation of the internal environment and leads to entering microorganisms into the tissues. Some authors believe that inflammation of tissues around the implant is caused by microflora that is normally present in the oral cavity [12; 13]. However, the causes of these complications, the role of oral microflora species and the signs of their clinical course are not yet fully understood [14; 15]. The use of the new dental elixir significantly improved the clinical course of the postoperative period of dental implantation. Its local usage demonstrated a pronounced tendency to normalise microbiocenosis and hygiene in comparison with the use of herbal tinctures. The dental elixir accelerated removal of hyperemia and edema in peri-implant tissues, reduced pain syndrome. The biochemical studies have shown inhibition of MDA with simultaneous potentiation of stress-stabilising mechanisms in the oral cavity under the influence of local therapy with the dental elixir at the early stage of dental implantation, which forms a favourable basis for the rehabilitation period after implantation and

Changes in biochemical indicators of oral fluid during the treatment at the early period after dental intraosseous implantation

Indicator of oral liquid examination	Control group n=8	Experimental groups					
		Main group			Comparison group		
		Before operation, n=14	3rd day after operation	8th day after operation	Before operation, n=14	3rd day after operation	8th day after operation
Activity of urease, $\mu\text{mol/l}$	2.26±0.12	2.18±0.11	2.68±0.09	2.24±0.09	2.22±0.10	2.72±0.11	2.58±0.09
P_1	–	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
P_2	–	–	>0.05	>0.05	–	>0.05	>0.05
Relative activity of urease	–	0.96±0.04	1.18±0.07	0.99±0.03	0.98±0.03	1.20±0.06	1.14±0.07
P_2	–	–	<0.05	>0.05	–	<0.05	<0.05
Activity of lysozyme, unit/l	82.40±1.60	79.30±1.40	80.20±2.14	81.30±1.90	78.40±1.60	79.20±2.10	79.60±1.80
P_1	–	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
P_2	–	–	>0.05	>0.05	–	>0.05	>0.05
Relative activity of lysozyme	–	0.96±0.02	0.97±0.02	0.98±0.02	0.95±0.02	0.96±0.02	0.96±0.02
P_2	–	–	>0.05	>0.05	–	>0.05	>0.05
Level of Dysbiosis	–	1	1.2	1.01	1.03	1.25	1.18
MDA, $\mu\text{mol/l}$	0.48±0.02	0.46±0.02	0.54±0.02	0.48±0.02	0.50±0.02	0.60±0.03	0.58±0.03
P_1	–	>0.05	<0.05	>0.05	>0.05	<0.05	<0.05
P_2	–	–	<0.05	>0.05	–	<0.05	<0.05
Catalase, mkat/l	0.12±0.01	0.11±0.01	0.10±0.01	0.13±0.02	0.12±0.02	0.09±0.01	0.10±0.03
P_1	–	>0.05	>0.05	>0.05	>0.05	<0.05	>0.05
P_2	–	–	>0.05	>0.05	–	>0.05	>0.05
SOD, CU/l	0.50±0.04	0.48±0.03	0.47±0.02	0.48±0.02	0.47±0.02	0.45±0.03	0.45±0.03
P_1	–	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
P_2	–	–	>0.05	>0.05	–	>0.05	>0.05

Note. P_1 – the probability of the difference of indicators of the control and experimental groups; P_2 – the probability of the difference of indicators of the main group and the comparison group before treatment.

reduces inflammatory reactions. Stimulating the production of antioxidants prevents excessive cell damage and stabilises the mechanisms of stress-induced cell death [16; 17].

The above-mentioned proves that the dental elixir in combination with a standard therapy is effective at the early post-implantation period. Its local application helps to quickly relieve a nonspecific inflammatory reaction to surgery, reduce swelling, hyperaemia and pain. Thus, the dental elixir prevents the occurrence of unfavourable conditions for secondary infection and impaired healing, and creates optimal conditions for normal recovery.

Conclusions. Local application of Apiprol dental elixir in the complex treatment of tissues in the postoperative period of dental implantation can reduce or prevent inflammatory complications.

In the early post-implantation period of dental implantation, Apiprol significantly reduces the severity of edema and hyperaemia, achieving their relief 1–2 days faster than in patients in the comparison group who used herbal tinctures, and reduces the duration of the pain syndrome. The dental

elixir renders a positive effect on hygiene and microbiological status in the oral cavity after dental implantation: leads to early epithelization on the 2nd day, reduces microbial contamination and normalizes biochemical indicators of oral fluid.

The use of the dental elixir at an early stage of dental implantation helps to improve the condition of the oral cavity, inhibit free radical oxidation, activate the enzyme components of antioxidant defence, creating favourable conditions for tissue renewal in the peri-implantation zone.

The results of the study prove that dental elixir can be recommended for local use to prevent destructive and inflammatory processes during dental implantation.

Conflict of interests. The authors declare that they have no conflict of interest in relation to this research, including functional, personal, authorship or other nature, which could affect the research and its result presented in this article.

Findings. The study was conducted without financial support.

Availability of data. The manuscript has data included as electronic supplementary material

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Електронна адреса для листування pasechnykalla@gmail.com