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TREATMENT OF PERIODONTITIS WITH INCLUSIVE ANTIFUNGAL DRUGS

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Abstract

Purpose: The aim of this study was the clinical testing of the paste with the antifungal drug "Narine" as a temporary therapeutic dressing (bandage) for endodontic treatment of chronic apical periodontitis.

Material and Methods: A total of 74 patients with chronic apical periodontitis were selected for the study. All patients underwent a thorough clinical and microbiological examination according to the generally accepted scheme. Periapical radiographs were taken to monitor treatment. Patients were divided into 2 groups to evaluate the effectiveness of using a probiotic for endodontic therapy of chronic periapical periodontitis.

Group I included 54 patients with whom the composition of the paste was used as an antibacterial and antifungal agent, based on the previously obtained positive results of their physicochemical properties: zinc oxide (ZnO) 2,5 parts, antifungal preparation 1.0 part ("Narine"), eugenol (clove oil) 1 part, which was left in the root canal for 7 days, followed by filling with zinc-eugenol paste; group II included 20 patients, whose root canals were treated according to the described method, followed by filling a sealant paste based on zinceugenol paste (without an antifungal component). The difference between the groups was that the main group was treated with temporary healing paste.

Results: The obtained results show that the antifungal drugs fluconazole, nystatin, "Narine" have antibacterial activity against Staphylolococcus aureus, Escherichia coli, Streptococcus Pseudomonas. Taking into account the beneficial effect on the periapical tissues and the obtained data of laboratory studies allowed us to use the above-mentioned drugs in the treatment of root canals and subsequent obturation with their introduction into the sealer (a patent for the invention of material for filling root canals N 3426A, dated 18.01.2021 was received).

Conclusion: Proposed Temporary endodontic paste is an effective addition to the traditional therapy of chronic apical periodontitis and is recommended for its use in endodontics.

Key words: *chronic forms of apical periodontitis, yeast fungi, antifungal therapeutic temporary root filling.*

Introduction

Microbiological studies using scanning electron microscopy of the contents of the root canals of the teeth indicate that in periapical lesions, the bacterial product stands out for its multiinfectious nature, the qualitative composition of which, in fact, remains in the process of medical interventions and in the post-treatment period [5, 10, 13]. Although the bacterial composition is mainly represented by the coccal flora, yeast fungi are also constantly present, the frequency of their detection according to various sources, is 17-20% [7, 9, 15]. Moreover, these fungi are able to form biofilms even in relatively clean and filled root canals.18 It should be noted that in apical periodontitis, Candida fungi are also common in pediatric practice [4, 11], and in primary purulent periodontitis of milk teeth [14].

Basing on experimental studies we can see that the presence of yeast fungi in the periapical focus significantly changes the bacterial product, which in its turn suggests the use of non-standard therapeutic treatment [16]. Very interesting results have been reported [9], based on the experimental data the most frequently detected pathogen in root canals, Enterococcus faecalis, remain viable for a long time alongside with other forms of bacteria, Candida fungi in particular. It was also revealed that after endodontic treatment, these two types of microorganisms retain their viability mainly due to the use of serum as a nutrient medium, which is very important in terms of post-treatment inflammatory complications [17]. There is also another view point stating that in cases of persistent chronic periapical lesions, yeast fungi are often found in the focus, among which, according to cell morphology characteristics, growth and absorption characteristics of hydrocarbons, about 20 strains of Candida fungi are distinguished: C. glabrata, C. albicans, C. guilliermondii, C. inconspicua, Geotrichum candidum, and etc[19]. To reveal the endodontic presence of Candida fungi in the development of subsequent complications and their absence after endodontic treatment, comparative studies were carried out [6], the results showed that with the development of complications, yeast fungi were found in 36.7% of cases, and in cases when there were no complications, this indicator was 13.3%. We can conclude that antifungal treatment should be of great importance in endodontic therapy.

The analysis of the scientific literature shows that Candida fungi are of pathogenic importance in the development of apical inflammatory processes, which requires the need to find out and include antifungal agents in the endodontic treatment of these lesions.

The aim of this study was the clinical testing of the paste with the antifungal drug "Narine" as a temporary therapeutic dressing (bandage) for endodontic treatment of chronic apical periodontitis.

Material and methods

In this regard, studies were carried out on the physicochemical properties of temporary fillings at the laboratory "Obtaining agricultural pesticides and quality control" of the National Polytechnic University of Armenia (NPUA). Test methods are identical to those described in GOST R 51094-97 (ISO 3107-88) and GOST R 51744-200 (corresponds to international standards ISO 9917-91 and ISO 9917-298).

On the basis of zinc oxide, eugenol and antifungal additives, compositions of pastes for therapeutic temporary fillings of the following compositions (weight ratio) were made: zinc oxide (ZnO) 2.5 parts; antifungal drug 1.0 part; eugenol (clove oil) 1.0 part. As antifungal drugs nystatin, fluconazole, lyophilized lactic acid bacteria (Lactobacillus acidophilus Er-2 strain 317/402, probiotic "Narine" (produced in Armenia, "Nareks" company, RA) were used and some physicochemical properties of these compositions were studied, particularly pH, its solubility in distilled water and isotonic solution, drying time, surface structure.The studies carried out show that pastes based on zinc oxide and eugenol with antifungal agents (nystatin, fluconazole, "Narine") in terms of physicochemical properties (hardening time, disintegration, surface structure and degree of acidity) meet the requirements of GOST R 5109497 for temporary root filling materials [3].

In a comparative aspect, antibacterial and antifungal activity of some antifungal drugs (fluconazole, nystatin and "Narine" lactobacillus acidophilicus) was determined in the composition of pastes and the widely used antiseptic in endodontic practice (0.2% chlorhexidine) against the main pathogenic forms of bacteria in the apical area, namely Stahylococcus aureus, E. coli, Streptococcus, diphtheroids, acidophilus bacillus and Pseudomonas (Pseudomonas aeruginosa).

The latter stood out from the contents of the root canals when chronic periodontitis existed. In such cases, a root needle wrapped in cotton turunda was inserted into the root canal, then the contents were transferred into a Petri dish with an appropriate nutrient medium, afterwards they were taken to a thermostat and incubated at 37^0C. After the corresponding bacterial growth, a standard amount of tested pastes was placed in them and the antibacterial activity was determined after 1, 5, 10, 20 and 30 minutes. The studies were held in the laboratories of the Department of Epidemiology of the Yerevan State Medical University after M. Heratsi.

Clinical research

Conservative-endodontic treatment of chronic apical periodontitis was carried out. When making the diagnosis, we based on the WHO classification of periapical diseases,[20] and all the patients were diagnosed with Chronic apical periodontitis of pulpal origin. The method of treatment was as follows: after thorough mechanical treatment of the root canals (average expansion from 25-35 mm), opening the apical foramen by step-by-step evacuation of the root canal contents and putrid masses (in order to prevent its penetration behind the apex), constant antiseptic treatment of root canals on a thin root needle was carried out. Subsequently, drying was carried out with cotton or paper turundas, temporary filling of the root canals with a therapeutic paste with antifungal drug (for 7 days), followed by their filling with zinc-oxyeugenol paste (X-ray control required).

Herewith the patients were divided into 2 groups: group I included 54 patients with whom the composition of the paste was used as an antibacterial and antifungal agent, based on the previously obtained positive results of their physicochemical properties: zinc oxide (ZnO) 2,5 parts, antifungal preparation 1.0 part ("Narine"), eugenol (clove oil) 1 part, which was left in the root canal for 7 days, followed by filling with zinc-eugenol paste; group II included 20 patients, whose root canals were treated according to the described method, followed by filling a sealant paste based on zinc-eugenol paste (without an antifungal component). The difference between the groups was that the main group was treated with temporary healing paste. In both groups the following methods of paraclinical studies were used: anamnesis morbi, anamnesis vitae, status local is, dental status, radiography (targeted intraoral images, orthopantomography, CT scan (selectively), electroodontodiagnostics (using the OD-1 apparatus), thermometry, percussion. Post-treatment clinical observation was carried out on all the patients in course of 3 months.

To carry out the method of contact thermometry, a medical electronic thermometer Microlife model MT-1951 was used, with a range of 32.0 - 42.5 ^{0}C, the sensitivity of which is 0.1^{0}C, the contact area with the investigated surface is 2 mm^2, the measurement time is 10 seconds. The temperature in the room at the time of the measurement was 22 - 23 ^{0}C.

The body temperature of all the patients at the time of study was 36.5 - 36.7 ^{0}C. The temperature of the gingival mucosa was measured during nasal breathing at least three times, in the vestibular surface of the alveolar area of the projection of the apex of the roots of the treated teeth.

The study was approved by the Ethics Committee of the Yerevan State Medical University and was carried out during 2018-2019 at the University Dental Clinic № 1. In accordance with the Declaration of Helsinki 2008, all the patients who took part in these observations gave certified agreement to participate in the study. The study was carried out with the financial support of the State Committee of Science of the Ministry of Education and Science of Armenia within the framework of the scientific project № 18T-1F076 "Systemic influence of a chronic focus of infection of the periodontal complex on the body: diagnostic and preventive approaches."The results of clinical studies were statistically processed and analyzed by the student's method using the computer program SPSS Statistics 17.

Results

The indicators of the sensitivity of root canal microorganisms to chlorhexidine, nystatin, fluconazole, "Narine" are shown in Table 1.

The obtained results show that the antifungal drugs fluconazole, nystatin, "Narine" have antibacterial activity against Staphylolococcus aureus, Escherichia coli, Streptococcus Pseudomonas. Taking into account the beneficial effect on the periapical tissues and the obtained data of laboratory studies allowed us to use the above-mentioned drugs in the treatment of root canals and subsequent obturation with their introduction into the sealer (a patent for the invention of material for filling root canals N 3426A, dated 18.01.2021 was received). The development of inflammatory complications after endodontic treatment occurred as a result of the mistakes in mechanical processing of canals and in filling of root canals (Table 2).

As it can be seen in the table the most common causes of periapical inflammatory complications after endodontic dental treatment were insufficient filling or re-filling of root canals, which make up about 63% of all possible causes. Immediately after the constant filling of the root canals, some patients of the both groups experienced unpleasant feeling of discomfort in the area of the treated teeth. Comparative percussion showed weak sensitivity in 7 cases of group I (12.96%) and in 3 cases in group II (15.0%), which disappeared within 3-5 days of the post-treatment period. Yeast like Candida fungi were detected among 26 patients (35.1%) in the main and tested groups with indicators of biopsy sampling from root canals before the treatment for biological research. After 7 days following the disinfection of the previously filled with antifungal sealant and repeated sampling for microbiological examination, 4 cases (7.4%), and in 5 cases (25%) of fungal lesions were found among the patients of the main group. The comparative assessment of the obtained data indicates the beneficial effect of antifungal drugs in the composition of sealers used for obturation of root canals on periapical tissues.

Table 1. Comparative assessment of root canal microorganisms' resistance to chlorhexidine, nystatin, fluconazole, "Narine"

Exposure time in minutes	Aureus	E. Coli (11230)	Streptococcus	Diphtheroids	Acidophilus bacillus	Pseudomonas (Pseudomonas aeruginosa)	Drug name
1	-	-	-	-	-	-	Chlorhexidine 0.2%
5	+	-	-	+	-	-	
10	+	+	+	-	-	-	
20	+	+	+	-	-	-	
30	+	+	+	-	+	-	
1	-	-	-	-	-	-	Nystatin +ZnO (paste)
5	+	-	-	-	-	-	
10	+	-	+	-	+	-	
20	+	+	-	-	-	-	
30	+	+	+	-	+	-	
1	+	-	-	+	-	-	Fluconazole + ZnO (paste)
5	+	-	-	-	+	+	
10	+	+	+	-	+	+	
20	+	+	+	-	-		
30	+	+	+	-	+	+	
1	+	-	-	-		+	"Narine" (lactobacillus acidophilicus) + ZnO (paste)
5	+	+	-	-	-	-	
10	-	+	+	-	-	-	
20	+	+	+	-	-	-	
30	+	-	+	-	+	+	

Table 2. Reasons for the development of inflammatory complications in the periapical area

The reason for the development of complications after treatment	Occurrence frequency (amount /%)
Incomplete root pulp removal	3/4,05
Root wall perforation	7 / 9,46
Anatomical constriction destruction	7 / 9,46
Endodontic instrument fracture	5/6,77
Insufficient canal filling	27 / 36,49
Removal of material beyond the apical foramen	19 / 25,67
Unknown cause (presence of undiagnosed additional tubules)	6/8,10
Total number of patients	74

Table 3. Dynamic indicators of electrical excitability and thermometry in the observed (researched, tested) groups

Patient groupsand forms of periodontitis	Indicators					
	EDI (mA)		t	thermometry (t^0C)		t
	before	after 3 months		before	after 3 months	
I group *(n=54)*	145,02±1,56	140,28±1,47	2,21	33,51±0,06	34,07±0,06	7,00
II group *(n=20)*	145,13±2,19	145,33±2,44	0,06	33,53±0,07	33,59±0,05	0,67
t	0,04	1,77	-	0,22	5,58	-

Dynamic observation of the patients of the both groups based on the data of electrical excitability and thermometry, the results of which are displayed in Table 3, show the following comparison: it should be noted that before treatment, the average EDI values in the groups did not differ significantly (the coefficient of reliability t <2).We can observe significant difference of the EDI indicator between the average values of I group, and in II group, by this time (3 months) a slight decrease in tissue electrical excitability was observed when comparing the average EDI indicators in this group.

Thermometry of the mucous membrane in the area of the projection of the tops of the treated teeth revealed the following dynamic changes: before the treatment, the values of the thermometry index between the groups did not differ significantly with average values, and the results of thermometry in group I before treatment were the most distant from the norm (when interpreting the results of thermometry, we followed the data of Manuilov EA and the co-author [1] that the normal temperature of the mucous membrane in this area is 34.6°C); 3 months after the treatment, both groups showed a positive dynamics of the thermometric indicator, however, in group I, this dynamics was more distinct, which affected the statistical significance of the difference between the average values of this indicator, and in group II, this positive dynamics was so insignificant that it did not affect the reliability of the results. Our data on thermometry are generally consistent with literature data, which indicate that in destructive forms of chronic apical periodontitis, there is a decrease in the local temperature of the gingival mucosa in the projection of the root apex to 33.8 ± 0.2°C [2].

X-ray examination of the treatment results also show the positive use of temporary endodontic paste with the prefungal drug "Narine", namely, in group I, (3 months after the treatment), in all cases, there was either stabilization of the pathological process in the area of the tops of the teeth (42.59%), or some restoration of periapical tissues (57.41%) (Fig. 1, 2, 3, 4).

Figure 1. Rentgen picters before endodontic treatment

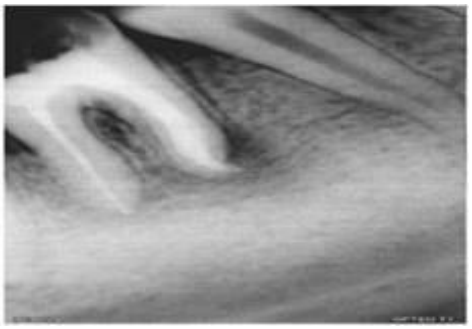

Figure 2. Tooth canal wasf filled

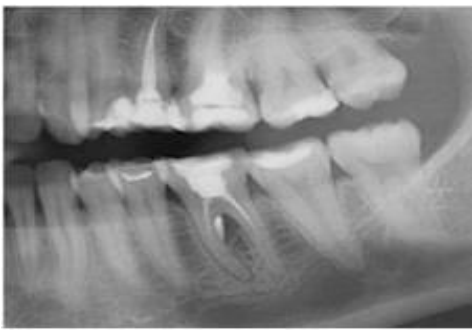

Figure 3. Rentgen picters before endodontic treatment

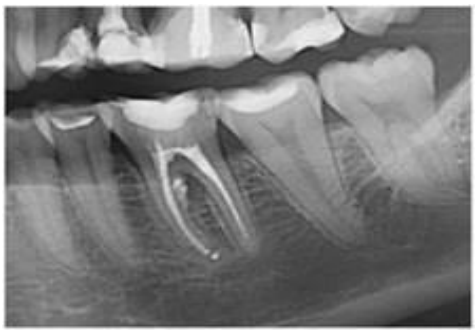

Figure 4. Tooth canal was filled

In group II, 4 patients (20%) had an X-ray deterioration of the pathological process (an increase in the volume of destructive changes in the area of the apex of the teeth), and in other cases (80%) only stabilization of the pathological process was observed.

Conclusion

After careful clinical studies we can conclude that the use of the antifungal drug "Narine" in the form of a paste for temporary filling of root canals shows positive results in the treatment of chronic forms of periodontitis, which results in stabilization of the pathological process or some restoration of periapical area tissues; basing on the results of microbiological (suppression growth of fungi), electrodontometric (lowering the threshold of electrical excitability of tissues), thermometric (a tendency for the indicator to come to a norm) and X-ray (restoration of periapical tissues) studies. The results obtained allowus to recommend a temporary endodontic paste with antifungal drug "Narine" for widespread use in clinical practice in the treatment of chronic forms of apical periodontitis as an innovative method.

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Conflict of Interest

The author declares that he has no conflict of interest and there was no external source of fundingfor the presentstudy.

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None of the authors have any relevant financial relationship(s) with a commercial interest. The work was notfunded.

Ethical approval

The study was reviewed and approved by the local Ethical Committee (Approval number N14, Date 17.11.19) and in accordance with those of the World Medical Association and the Helsinki Declaration. Informed consent Patients were informed verbally and in writing about the study andgave written informed consent.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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ՊԵՐԻՈԴՕՆՏԻՏԻ ԲՈՒԺՈՒՄԸ ՀԱՄԱԼԻՐ ՀԱԿԱՍՆԿԱՅԻՆ ԴԵՂԱՄԻՋՈՑՆԵՐՈՎ

Տատինցյան Լ.Վ. [1], Խաչատրյան Ժ.Ռ. [2], Համբարձումյան Ս.Գ. [1], Միքայելյան Ա.Ռ. [3], Տատինցյան Վ.Գ. [1], Պողոսյան Մ.Ա. [1], Հակոբյան Ա.Գ. [1], Կուպելյան Ա.Գ. [1], ՇահինյանԱ.Գ. [1]

1. Մ. Հերացու Երևանի պետական բժշկական համալսարան Մ. Հերացի
2. «Փայլ Դենտ» ստոմատոլոգիական կլինինկա Երևան, Հայաստան
3. Հայաստանի ազգային պոլիտեխնիկական համալսարան (ՀԱՊՀ)

Նյութեր և մեթոդներ: Հետազոտության համար ընտրվել են քրոնիկ գագաթային պերոդոնտիտով 74 հիվանդ: Բոլոր հիվանդները ենթարկվել են մանրակրկիտ կլինիկական և մանրէաբանական հետազոտության՝ ընդհանուր ընդունված սխեմայի համաձայն: Բուժումը վերահսկելու համար կատարվել են ներբերանային ռադիոգրաֆիա: Հիվանդները բաժանվել են 2 խմբի՝ գնահատելու քրոնիկ գագաթային պերիոդոնտիտի էնդոդոնտիկ թերապիայի համար պրոբիոտիկների օգտագործման արդյունավետությունը: I խումբը ներառում էր 54 հիվանդ, որոնցում մածուկի բաղադրությունը օգտագործվել է որպես հակաբակտերիալ և հակասնկային միջոց՝ հիմնվելով նրանց ֆիզիկաքիմիական հատկությունների նախկինում ստացված դրական արդյունքների վրա՝ ցինկի օքսիդ (ZnO)՝ 2,5 մաս, հակասնկային դեղամիջոց՝ 1,0 մաս «Նարինե», էվգենոլ (մեխակի յուղ) 1 բաժին, որը 7 օր մնացել է արմատախողովակում, որին հաջորդում է ցինկ-էվգենոլի մածուկով լցնում; II խումբը ներառում էր 20 հիվանդ, որոնց մոտ իրականացվել է արմատախողովակի բուժում ըստ նկարագրված մեթոդի, որին հաջորդել է արմատալիցք ցինկ-էվգենոլ մածուկի վրա հիմնված հերմետիկ մածուկով (առանց հակասնկային բաղադրիչի): Խմբերի տարբերությունն այն էր, որ հիմնական խումբը բուժվել է ժամանակավոր բժշկական մածուկով:
Արդյունքները: Ստացված արդյունքները ցույց են տալիս, որ ֆլուկոնազոլ, նիստատին, «Նարինե» հակասնկային դեղամիջոցները հակաբակտերիալ ակտիվություն ունեն Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa-ի դեմ: Հաշվի առնելով հարարմատային հյուսվածքների վրա ունեցած բարենպաստ ազդեցությունը և լաբորատոր հետազոտություններից ստացված տվյալները՝ հնարավոր եղավ օգտագործել վերը նշված դեղամիջոցները արմատախողովակների բուժման և հետագա արամատալիցքի համար:
Եզրակացություն: Առաջարկվող ժամանակավոր էնդոդոնտիկ մածուկը արդյունավետ հավելում է քրոնիկ գագաթային պերոդոնտիտի ավանդական բուժմանը և խորհուրդ ՝ տրվում օգտագործել էնդոդոնտիայում:

ЛЕЧЕНИЕ ПАРОДОНТИТА КОМПЛЕКСНЫМИПРОТИВОГРИБКОВЫМИ ПРЕПАРАТАМИ

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Материалы и методы: Для исследования были отобраны 74 пациента с хроническим верхушечным периодонтитом. Всем больным проведено тщательное клиническое и микробиологическое обследование по общепринятой схеме. Делали периапикальные рентгенограммы для контроля лечения. Пациенты были разделены на 2 группы для оценки эффективности применения пробиотика для эндодонтической терапии хронического периапикального периодонтита. В I группу вошли 54 больных, у которых в качестве антибактериального и противогрибкового средства использовали состав пасты, исходя из полученных ранее положительных результатов их физико-химических свойств: оксид цинка (ZnO) 2,5 части, противогрибковый препарат 1,0 часть («Наринэ»), эвгенол (гвоздичное масло) – 1 часть, которую оставляли в корневом канале на 7 дней с последующим пломбированием цинк-эвгеноловой пастой; во II группу вошли 20 пациентов, у которых лечение корневых каналов проводилось по описанной методике с последующим пломбированием герметизирующей пастой на основе цинкэвгеноловой пасты (без противогрибкового компонента). Разница между группами заключалась в том, что основную группу лечили временной лечебной пастой.
Результаты: Полученные результаты свидетельствуют о том, что противогрибковые препараты флуконазол, нистатин, «Наринэ» обладают антибактериальной активностью в отношении золотистого стафилококка, кишечной палочки, синегнойного стрептококка. Учет благоприятного действия на периапикальные ткани и полученные данные лабораторных исследований позволили использовать вышеперечисленные препараты при лечении корневых каналов и последующей обтурации с введением их в силер (патент на изобретение материала для пломбирования корневых каналов получен № 3426A от 18.01.2021).
Заключение: Предлагаемая временная эндодонтическая паста является эффективным дополнением к традиционной терапии хронического апикального периодонтита и рекомендована к применению в эндодонтии.

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