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EFFECTS OF SMOKING TO THE LIPID PROFILE IN PATIENTS WITH PERIODONTAL DISEASE

ЕФЕКТИТЕ НА ПУШЕЊЕТО НА ЛИПИДНИОТ СТАТУС КАЈ ПАЦИЕНТИ СО ПАРОДОНТАЛНА БОЛЕСТ

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Abstract

The **aim** of this study was to determine the effects of smoking towards the lipid status in patients with periodontal disease through analyzing the serum dynamics of lipid parameters (triglycerides, total cholesterol, LDL and HDL cholesterol). The above aim was realized on the Clinic for Periodontology an Oral Medicine on examined group consisting of 45 patients diagnosed with periodontal disease, who were smokers; the control group was consisted of 45 patients diagnosed with periodontal disease, as well, but non-smokers. All the patients were in the age range from 40 to 60 years. According to the number of consumed cigarettes, the patients from the examined group were divided into three sub-groups, each consisting of 15 examinees. The first sub-group was consisted of patients who smoked up to 10 cigarettes in a day (light smokers); the second sub-group was consisted of patients who smoked from 10 to 20 cigarettes in a day (moderate smokers); the third sub-group consisted of patients who smoked more than 20 cigarettes in a day (passionate smokers). The values of Silness-Loe dental plaque index (DPI), index of gingival inflammation (IGI), Cowell gingival bleeding index (GBI) as well as the level of attachment loss (Ramfjord) were noted in both examined and control groups. The results of the total cholesterol and HDL cholesterol showed statistical significant difference between the mean values in the three sub-groups of the examined group, while the mean values of HDL cholesterol in the second and third examined sub-groups and control group are within the reference limits, and the value of the first sub-group is in higher range than the normal one. **Keywords:** TNF-α and IL1-β, periodontal indices, lipid status, smoking.

Апстракт

Целта на овој труд беше да се утврдат ефектите на пушењето на липидниот статус кај пациенти со пародонтална болест преку проследувсње на серумската динамика на липидните параметри(триглицериди,вкупен холестерол, ЛДЛ и ХДЛ холестерол). Реализација на поставената цел беше спроведена на Клиниката за болести на устата и пародонтот каде беше формирана испитувана група (45) сочинета од пациенти пушачи со дијагностицирана пародонтална болест и контролна група (45) непушачи со пародонтопатија (класифицирана според ААП од 1999 година) на возраст од 40-60 години. Според бројот на испушени цигари пациентите од испитуванат беа поделени во три подгрупи од 15 испитаници. Првата подгрупа ја сочинуваа пациенти кои пушат до 10 цигари на ден (лесни пушачи). Втората подгрупа ја сочинуваа пациенти кои пушат од 10 д0 20 цигари на ден (умерени пушачи). Третата подгрупа ја сочинуваа пациенти кои пушат над 20 цигари на (страсни пушачи). Кај двете групи на испитаници беа нотирани индексните вредности на дентален плак по Silness-Loe (IDP), гингивална инфламација по Loe Silnes (IGI), гингивално крвавење по Cowell (IGK) како и степенот на губиток на атачмент (Ramfjord). По извршениот клинички преглед и нотирање на индексните вредности кај двете групи на испитаници по пат на венепункција беа земани 5 мл на крв од v cubitali. Крвта беше земана во стерилни епрувети и дистрибуирана на Институтот за физиологија при Медицинскиот факултет во Скопје. Анализата на липидниот статус беше направена со колориметриска медода. Анализата на вкупниот холестерол и ХДЛ холестеролот регистрира разлика на просечните вредности кај трите испитувани подгрупи која е статистички сигнификантна, но просечните вредности на ХДЛ холестеролот кај втората и и третата подгрупа и контролната група се во граници на референтните, додека просечната вредност на првата подгрупа е повисока од референтната вредност. **Клучни зборови:** TNF-α и IL1-β, пародонтални индекси, липиден статус.

Introduction

The risk of periodontal disease and its prognosis is associated with a number of factors like: age, stress, presence of specific microorganisms, genetics, diabetes and smoking[1]. Historically, it was believed that all individuals are uniformly susceptible to development of periodontal disease and that the accumulation of the dental plaque, bad oral hygiene and possible occlusal trauma are enough to initiate the periodontal disease. During the last four decades it has been accepted that the periodontitis is caused by specific bacterial infection and the individuals are equally susceptible to these infections as from the damage they cause. This understanding made the clini-

cians and researches to focus their efforts on developing markers which will help in identifying the susceptible individuals, prior to the initiation of the disease, as well as the risk factors which can be modified in order to prevent the periodontal disease or to change its course[2]. Smoking is the best confirmed modifying risk factor in the developing and progress of periodontal disease[3]. Smoking can be involved in the aetiopathogenesis of the periodontal disease through releasing pro-inflammatory cytokines and inflammatory mediators which can be able to initiate cascade of biochemical reactions and to cause periodontal and endothelial damage[4]. Thus, smokers can be systemically affected even in absence of clear clinical symptoms of the disease[5].

Aim of the study

Taking into consideration the literary data associated to the influence of smoking on the systemic health, as well as to the pathogenic mechanisms of the periodontal disease, the aim of the study was set: to determine the effects of smoking in patients with periodontal disease, through analyzing the serum dynamics of the lipid parameters (triglycerides, total cholesterol, LDL cholesterol and HDL cholesterol)

Materials and methods

In order to achieve the set aim, an examined group consisted of 45 patients - smokers diagnosed with periodontal disease, and a control group consisted of 45 patients - non-smokers with diagnosed periodontal disease were formed at the Clinic for Periodontology and Oral Medicine. All the patients were in the age range 40-60 years. The present periodontal disease was classified according to the American Association of Periodontology from 1999. The diagnosis was established on the basis of anamnesis, clinical evaluation and x-ray findings. Great attention was paid to the anamnesis, in order to gain detailed data for verification of absence of any systemic disease. All the patients signed an informed consent and agreed that the collected data and materials would be used only for scientific and research purposes. According to the number of cigarettes, the patients from the examined group were divided in three sub-groups, each consisting of 15 examinees, as follows:

- first sub-group, consisted of patients who smoked up to 10 cigarettes in a day (light smokers)
- second sub-group, consisted of patients who smoked from 10 to 20 cigarettes in a day (moderate smokers)
- third sub-group, consisted of patients who smoked more than 20 cigarettes in a day (passionate smokers)

The values of Silness-Loe dental plaque index (DPI), gingival inflammation index (IGI), Cowell gingival bleeding index (GBI) as well as the level of attachment loss (Ramfjord) were noted in both examined and control groups. After the clinical evaluation and index values determination, a venepuncture of the cubital vein was performed in all the examinees from both groups and 5 ml of blood were collected from each of them. The blood was collected in sterile test-tubes and transported to the Institute of Physiology in the Medical Faculty in Skopje. The samples were remained still for 2 hours, at room temperature. After the coagulum retraction, the remained serum was centrifuged using Becman centrifuge in 5000 rotations per minute. The analysis of the lipid status was performed using the colorimetric method (Merck diagnostics).

Results and discussion

Smoking and its duration lead to increased concentration of total serum cholesterol, triglycerides, LDL cholesterol, but to lower anti-atherogenic HDL cholesterol[6], which plays a key role in atherosclerosis process. The combination of nicotine and lipopolysaccharide (LPS) can result in releasing inflammatory cytokines such as IL-1β and TNF-α, which influence to the lipid metabolism and promote hyperlipidemia[7]. Related to the potential association between smoking, hyperlipidemia and periodontal disease, today it is thought that smoking may induce changes in the immunocellular function, resulting in impaired metabolic regulation of the lipids, through mechanisms which involve proinflammatory cytokines[8].

A considerable number of cytokines, like IL-1β and TNF-α are produced as a result of the presence of periodontal pathogenic gram negative bacteria[9,10]. These cytokines have a great influence on the lipid metabolism[11], either through provoking production of other cytokines and changing the chemodynamics (utilization of aminoacids) from different tissues which participate in the lipid metabolism, or through modifying the hypothalamus-hypophysis-adrenal axis and increasing the concentration of adrenocorticotropic hormones, cortisol, adrenalin, noradrenalin and glucagon in the plasma[12]. Therefore, the activity of IL-1β and TNF-α, microbial exposure and action of nicotine enable the increasing of the level of free fatty acids, cholesterol and triglycerides occur.[13]

The results of this study regarding the total cholesterol show statistically significant differences between the mean values of the groups ($p = 0{,}018072$) (Table 1), but the mean values are higher within the second and third sub-group in the examined group (Table 2). Post hoc Tukey's test showed predominant difference between the third sub-group and the other sub-groups and the control group (Table 3), which confirms the

Table 1. Mean values of total cholesterol within the examined group with its sub-groups and the control group.

group	Mean value	Number	St. Dev	minimum	maximum
I	5,107143	15	0,523985	4,6	6,7
II	6,080000	15	1,044851	4,9	8,4
II	7,033333	15	2,859987	4,0	13,5
IV	6,270732	45	1,379718	3,5	9,0

This table shows the mean values of total cholesterol which are in normal ranges (3,1-5,5 mmol/l) within the first sub-group, while the mean values in the other two sub-groups and within the control group are higher than the normal values.

Table 2. Analysis of variance of the mean values of total cholesterol

SS	df	MS	SS	df	MS	F	p
27,52450	3	9,174834	209,5115	81	2,586562	3,547116	0,018072

Analysis of variance of the mean values of total cholesterol in the examined group with its sub-groups which are statistically significant for p=0,018072.

Table 3. Post hoc Tukey HSD test for total cholesterol

group	I	II	III	IV
I		0,369058	0,009796	0,098171
II	0,369058		0,371497	0,979334
II	0,009796	0,371497		0,400672
IV	0,098171	0,979334	0,400672	

There is statistical significance regarding the total cholesterol mainly between the third sub-group and other groups.

influence of the higher number of smoked cigarettes daily to the systemic and periodontal health. The results regarding to the level of total cholesterol in smokers and non-smokers with periodontal disease are in accordance with the results reported by Katz et al.[12] and Loeshe et al.[14], but opposite to those reported by Kenney et al.[16]

Smoking, poor nutrition and high-fat meals result in prolonged impairment of the antibacterial function of the polymorphonuclear leukocytes[16], i.e. hyperreactivity and increased production of oxygen species[17], which is associated with periodontal disease progression in adults.

The concentrations of pro-inflammatory cytokines TNF-α, IL-1β, prostaglandin E2 (PGE-2) reach high levels in individuals with periodontal disease.[18] Inflamed periodontal tissues may act as a permanent renewable container for releasing of TNF-aα, IL-1β and PGE-2 in circulation, thus evoking extended systemic effects, as well as influencing the lipid metabolism[19]. The increase of serum lipids occurs due to the higher synthesis or lower degradation of triglycerides[9], as well as reduced elimination of LDL cholesterol.

The results regarding to LDL cholesterol show higher values compared to the referent values in the three sub-groups and control group (Table 4). The difference between mean values of the examined groups is not statistically significant for p=0,090300 (Table 5). These results about the level of LDL cholesterol in smokers and non-smokers with periodontal disease are in accordance with the results reported by Katz et al.[12] and Loeshe et al.[14], but opposite to those reported by Kenney et al.[16] Nutrition can influence the host inflammatory response, i.e. to participate in the activation of the inflammatory cytokines that affect the immune function and probably have effect on the periodontal health and the condition of some specific systems in the body[20]. The nutrition with higher intake of saturated fats, but lower intake of cellulose and fruits can lead to changes of the lipid status.

The mean values of HDL cholesterol are within the referent ranges in the second and third sub-group and in the control group, while the mean value in the first sub-group is higher than the referent values (Table 6). The dif-

Table 4. Mean values of LDL cholesterol within the examined group with its sub-groups and within the control group.

group	Mean value	Number	St. Dev	minimum	maximum
I	4,071429	15	1,188036	1,7	5,2
II	4,620000	15	0,829113	2,4	5,7
II	4,900000	15	2,592572	0,7	9,6
IV	3,821951	45	1,343040	1,3	6,1

This table shows the mean values of LDL cholesterol within the examined group with its sub-groups and within control groups which are higher than the referent values (2,2 - 3,5 mmol/l).

Table 5. Analysis of variance of mean values of LDL cholesterol

SS	df	MS	SS	df	MS	F	p
16,08424	3	5,361414	194,2228	81	2,397813	2,235961	0,090300

This table shows the difference between the mean values within the examined groups which is statistically significant for p=0,090300.

Table 6. Mean values of HDL cholesterol.

group	Mean value	Number	St. Dev	minimum	maximum
I	3,215385	15	1,302463	1,1	4,9
II	1,446667	15	0,417247	0,5	2,0
II	1,400000	15	0,311677	0,8	1,9
IV	1,368293	45	0,329726	0,7	1,9

This table shows the mean values of HDL cholesterol within the examined groups with its sub-groups and within the control group which are in normal ranges (2,2-3,5 mmol/l) in the second and third sub-group, while the mean values in the first sub-group are higher than the referent values.

Table 7. Analysis of Variance of mean values of HDL cholesterol

SS	df	MS	SS	df	MS	F	p
36,61934	3	12,20645	28,50304	80	0,356288	34,26006	0,000000

This table shows the difference between the mean values of HDL cholesterol in examined groups and control group, which is statistically significant (p=0,000000).

ference between the mean values in the examined groups is statistically different for p=0,000000. According to post hoc Tukey's test, the difference is mainly significant between the first and other groups (Table 7).

Higher levels of HDL cholesterol show anti-inflammatory action and lower the adhesion of the endothelial cells, with this lowering the risk of cardiovascular diseases. The results regarding to the HDL cholesterol levels in smokers and non smokers with periodontal disease are in accordance with the results reported by Cutler at al.[6], but opposite to those reported by Buhlin et al.[15]

Different mechanisms that lead to lipid alteration due to smoking include the action of nicotine which stimulates the sympathetic adrenal system, which results in higher secretion of catecholamines, higher lipase levels and higher concentration of plasm fatty acids and thus, higher secretion of hepatal fatty acids and triglycerides[11]. The mean values of triglycerides in the three sub-groups and control group were higher than the referent ones (Table 8). The difference which can be noted between the mean values in the examined groups (smokers) is not statistically significant (p=0,345041) (Table 9). The bio-

Table 8. Post hoc Tukey HSD test

group	I	II	III	IV
I		0,000147	0,000147	0,000147
II	0,000147		0,996576	0,972293
II	0,000147	0,996576		0,998116
IV	0,000147	0,972293	0,998116	

This table shows the post hoc Tukey HSD test which shows significance mainly between the first sub-group and other groups.

Table 9. Mean values of triglycerides

group	Mean value	Number	St. Dev	minimum	maximum
I	2,585714	14	0,799863	1,9	4,5
II	2,453333	15	0,604586	1,2	3,2
II	3,106667	15	1,007448	1,6	5,0
IV	2,521951	41	1,393828	0,9	4,7

This table shows the mean values of triglycerides within the examined group with its subgroups and at the control group which are higher than the referent ones (0,1-2,2 mmol/l).

Table 10. Analysis of variance of mean values of triglycerides

SS	df	MS	SS	df	MS	F	p
4,378888	3	1,459629	105,3541	81	1,300667	1,122216	0,345041

This table shows the difference in the mean values of triglycerides between the examined groups and the control group which is statistically significant (p=0,345041).

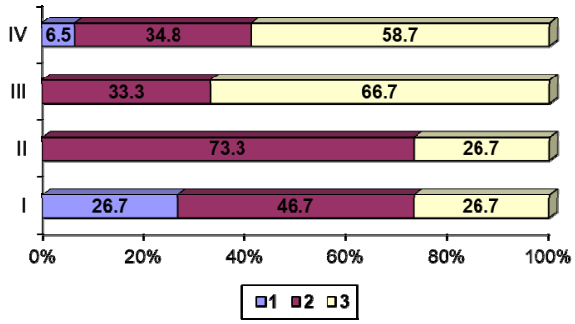
logic signal molecules from the local inflamed tissue has physiologic effects to the stimulation of lipogenesis, increasing the lipolysis and decreasing the lipid clearness, resulting in hyperlipidemia or accumulation of free fatty acids (FFA) and triglycerides[21].

The results regarding to the level of triglycerides in smokers and non-smokers with periodontal disease are in accordance to those reported by Loeshe et al.,[14] but opposite to those reported by Buhlin et al.[15] The analysis of the lipid status in both examined groups showed higher values in both examined groups, thus confirming our results[22] on the dependence between the hyperlipidemia and periodontal disease.

The clinical and radiological findings of the periodontal condition indicate that it is worse for smokers compared to non-smokers, while the clinical condition is presented with presence of deep periodontal pockets, higher attachment loss, gingival recession, increased alveolar bone loss and higher values of dental plaque[23]. Smoking influences the composition of the subgingival bacterial flora as well, with that increasing the subgingival infection. Smoking also has effects to the oxidative-reduction potential of the dental biofilm, creating anaerobic conditions and predomination of gram negative anaerobic bacteria[24]. The decreased protective and reparatory capability of the periodontium and the presence of aggressive bacteria in the dental plaque lead to increased damaging of the periodontium in smokers, compared to non-smokers[25,26]. The analysis of dental plaque index (DPI) showed percentual difference between the first and second, compared to the third subgroup which is statistically significant (p=0,0353); the difference between the first and second sub-group compared to the control group is statistically significant (p=0,0354)(Graph 1). The results regarding to the values of the dental plaque index are in accordance with those reported by Machuca et al.,[23] but opposite to those reported by Baab and Qberg[27].

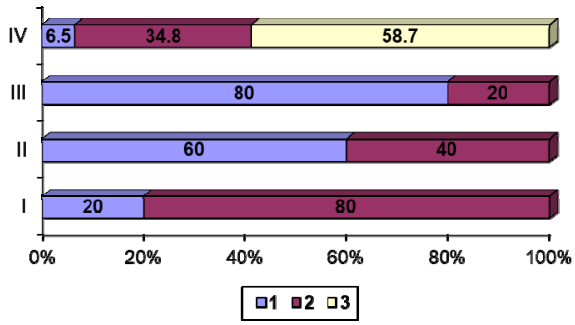
It is our opinion that the higher volume of dental plaque in smokers is a result of bad oral hygiene and for-

Graph 1. Distribution of Silness-Loe dental plaque index



Graph 1 shows the distribution of dental plaque index within the examined group with its sub-groups and control group. There is percentual difference between the first and the second, compared to the third sub-group which is statistically significant (p=0,0353) and between the the first and the second sub-group compared to the control group (p=0,354).

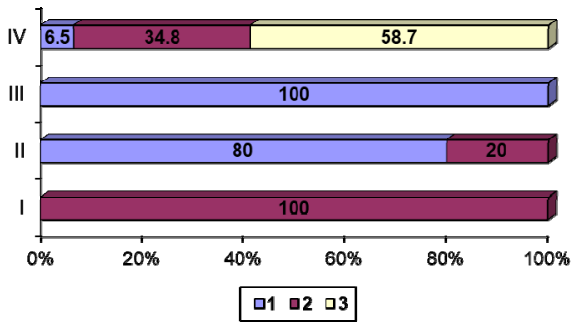
Graph 2. Distribution of Silness-Loe index of gingival inflammation



Graph 2 shows the distribution of the index of gingival inflammation within the examined group with its sub-groups and within the control group. A clear percentual difference can be noted between the control group and the second and the third sub-groups which is statistically significant (p=0,0000) and between the control group and third sub-group (p=0,0036).

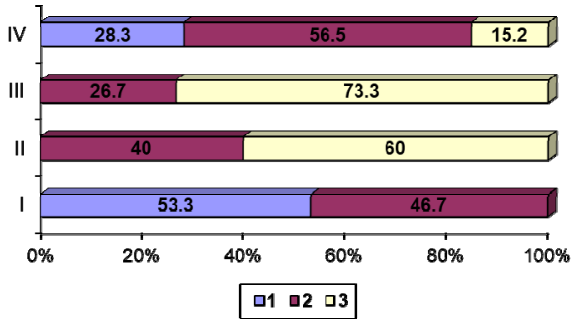
mation of nicotine pigmentations which increase the plaque accumulation[25,26]. The inflammatory response induced by the accumulation of dental plaque may be modified by the secondary products of the tobacco, like the cotinine[27], a secondary product of the nicotine which has effect of peripheral vasoconstriction and reduces the clinical signs of gingival inflammation, the redness and swelling[28]. The reduced intensity of the gingival response is probably due to vascular changes; the thickness of the marginal gingival epithelium is damaged by smoking. The local vasoconstriction effect of the nicotine leads to lower blood flow in the gingival tissue, hypoxia and decreased capability in elimination of the products of the tissue metabolism[29]. All these events have an effect of decreasing the reparatory capability of the periodontium, which is clinically manifested as delayed tissue healing. The analysis of the index of gingival inflammation (IGI) and gingival bleeding index (GBI) indicates clear percentual difference between the control group and second and third sub-group, which is statistically significant (p=0,0000), and between the control group and third sub-group, where a statistically significance is present (p=0,0036)(Graph 2). This confirms the peripheral vasoconstriction effect of the nicotine, which reflects with low clinical signs of inflammation in smokers.

Graph 3. Distribution of Cowell index of gingival bleeding



Graph 3 shows the distribution of the Cowell index of gingival bleeding within the examined group with its sub-groups and at the control group. A clear percentual difference can be noted between the control group and the first, second and third sub-groups which is statistically significant (p=0,0000)

Graph 4. Distribution of Ramfjord attachment loss index



Graph 4 shows the distribution of Ramfjord attachment loss index withinthe examined group with its sub-groups and at the control group. Next findings should be noted:

1. *attachment loss up to 3 mm. Percentual difference is not statistically significant (p=0,082).*
2. *attachment loss from 3-6 mm. Percentual difference is statistically significant only between the control group and third sub-group (p=0,0496).*
3. *attachment loss higher than 6 mm. Percentual difference is statistically significant between the control group and second and third sub-group (p=0,00).*

The results regarding to the values of IGI and GBI are in accordance to those reported by Johnson et al.[30], but there is no literature data which decline this finding. The effect of smoking to the periodontium is cumulative, t.e. the negative effects depend on the duration of smoking and on the number of smoked cigarettes[31]. The alveolar bone loss and attachment loss in smokers are increased, and the correlation depends on the dose of nicotine taken by smoking and the effect showed years later[26,31]. The analysis of the attachment loss within the range of 3-6 mm showed percentual difference between the control group and third sub-group which is statistically significant (p=0,0496); statistically significance was found between the control, second and third sub-group for the attachment loss higher than 6 mm (p=0,0496). The percentual difference was not statistically significant (p=0,082)(Graph 4) in the first sub-group and control group for attachment loss up to 3 mm. These results regarding to the index of attachment loss are in accordance with those reported by Rivera-Hidalgo[26] and Tanur et al. [31], but opposite to those reported by Baab and Qberg[27].

We consider that nicotine stimulates the osteoclast differentiation, with that increasing the resorption of calcium phosphate, the major structure of bones. Higher concentrations of nicotine lead to increased number of osteoclasts, cells responsible for resorption and remodelation during the periodontal disease.

Conclusions

The investigation of the role of smoking as a risk factor in etiopathogenetic events in periodontal disease, with verification of the lipid status and clinical parameters, leaded to these conclusions:

1. The parameters of the lipid status detected difference between the mean values in the examined groups which are not statistically significant for LDL cholesterol (p=0,090300) and for triglycerides (p=0,345041), with mean values higher than the referent ones at the examined sub-groups and at the control group, with exception of the values of triglycerides in the first sub-group which are in normal range.
2. The analysis of total cholesterol and HDL cholesterol showed difference of the mean values for HDL in the three examined sub-groups, which is statistically significant (p=0,018072); statistical significance was found between the same groups for the total cholesterol, as well (p=0,000000); mean values of HDL in second and third sub-group and control group are in normal ranges, while the mean value in the first sub-group is higher than the referent values.
3. Results from the analysis of the dental plaque index (DPI) showed percentual difference in the first and second, compared to the third sub-group, which is statistically significant (p=0,0353) as well as at the first and second sub-group, compared to the control group (p=0,0354).
4. Analysis of the index of gingival inflammation (IGI) indicates clear percentual difference between the control group and second and the third sub-group, which is statistically significant (p=0,0000), as well as between the control group and the third sub-group (p=0,0036).
5. Analysis of the gingival bleeding index (GBI) indicates clear percentual difference between the control group and first, second and third sub-group, which is statistically significant (p=0,0000).
6. Attachment loss at smokers is increased, with the loss level depending on the nicotine dose taken by smoking (number of smoked cigarettes daily) and effect is evident years later.
7. It can be concluded that very serious approach in the treatment of periodontal disease is necessary. It should include frequent check-ups of patients and comprehensive instructions for maintaining oral hygiene in the event of existence of a predisposing factor.

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