ABSTRACT

Introduction: One of the most important types of microorganisms in the oral cavity in both healthy and non-healthy individuals is Fusobacterium nucleatum. Although present as a normal resident in the oral cavity, this Gram-negative pathogen is dominant in periodontal disease and it is involved in many invasive infections in the population, acute and chronic inflammatory conditions, as well as many adverse events with a fatal outcome.

Aim: To determine the role of F. nucleatum in the development of polymicrobial biofilms thus pathogenic changes in and out of the oral media.

Material and method: A systematic review of the literature concerning the determination and role of F. nucleatum through available clinical trials, literature reviews, original research and articles published electronically at Pub Med and Google Scholar.

Conclusion: The presence of Fusobacterium nucleatum is commonly associated with the health status of individuals. These anaerobic bacteria plays a key role in oral pathological conditions and has been detected in many systemic disorders causing complex pathogenetic changes probably due to binding ability to various cells thus several virulence mechanisms.

Most common diseases and conditions in the oral cavity associated with F.nucleatum are gingivitis (G), chronic periodontitis (CH), aggressive periodontitis (AgP), endo-periodontal infections (E-P), chronic apical periodontitis (PCHA). The bacterium has been identified and detected in many systemic disorders such as coronary heart disease (CVD) pathological pregnancy (P); polycystic ovary syndrome (PCOS), high-risk pregnancy (HRP), colorectal cancer (CRC); pre-eclampsia (PE); rheumatoid arthritis (RA); osteoarthritis (OA).

Keywords: periodontitis, fusobacterium nucleatum, pathogenesis
INTRODUCTION

Periodontal disease is a multi-factorial inflammatory disease that has a progressive course, followed by damage to all periodontal structures, including bone destruction and consequently tooth loss. The initial inflammatory reaction occurs as a response of the host to colonizing periopathogenic bacteria. From the gingiva, the inflammatory process continues to spread deep into the tissues of the periodontium and causes loss of connective tissue and alveolar bone. Epidemiological data indicate that periodontal disease is widespread in the population and affect up to 90% of the world’s population. [1]

Periodontitis is an infectious disease of the tissues surrounding the tooth, with wide range of clinical, microbiological and immune disorders therefore is considered a consequence of the dynamic interaction between infectious agents, the host’s immune response, environmental exposure, and genetic predisposition. The prevalence and the relationship between bacterial species is particularly useful information in clarifying the biology of subgingival plaque. These findings may be useful in planning strategies of plaque control that are important in establishing a new approach to the diagnosis and treatment of periodontal diseases. Literature reports that more than 500 bacterial strains can be identified in a periodontal pocket. There are also findings claiming that all sub-gingival bacteria are equally important in the initiation and progression of periodontal disease. There is good evidence to support these facts that they are caused by certain inhabitants of normal oral flora, mainly gram-negative anaerobes. [2]

Defining the composition of the oral microbiological flora is crucial in clarifying its role in healthy and diseased periodontium. Many of these types of bacteria have pathogenic potential, but only a few can be true initiators of the disease. Others probably have an associate or supplementary role. Any changes from the usual composition of the interacting microorganisms in the symbiosis, which is normal oral flora, caused by internal (genetic) or external (diet, toxins, antibiotics, etc.) factors can enhance the pathogenic potential of microorganisms in the oral medium thus the continuation and progression of periodontal destruction. This is an important point to be seriously considered when evaluating the true role of bacteria with the help of diagnostic tests based on the detection of specific microorganisms. Members of the oral medium generally coexist and thrive by forming a complex polymicrobial community, i.e. “Biofilm”. Mutual communication of these species from their mutual co-evolution creates large structures known as dental plaque. With maturation of the plaque that is inevitably associated with periodontal disease, the number of gram-negative (predominantly aerobic) and anaerobic bacteria increases. [3-6]

Studies have shown that the prevalence of bacteria supra- or sub-gingival to one tooth surface can exceed 1x109 bacteria. By using chewing gum, the number of bacteria is reduced and ranges from 1x103 in the gingival sulcus to more than 1x108 in the periodontal pocket. [7]

The complexity of subgingival dental plaque composition has been identified and clarified long ago, with the first microscopic examination of this ecosystem by Van Leuwenhoek in 1683. [8] Since that time, numerous studies have examined and monitored the composition of the plaque using light and electronic microscopy, with numerous additional and auxiliary techniques explaining its variations supra- or sub-gingival and their role in the periodontium. All techniques support the initial findings of Van Leuwenhoek [8], that subgingival plaque consists of a large complex of heterogeneous bacterial species. Subgingival plaque bacteria are considered the primary etiological factor for the occurrence of periodontitis, but according to some authors, only a few species, such as: A. actinomycetemcomitans, F. nucleatum, and P. gingivalis, are highlighted as major periopathogens. [9]

FEATURES AND CHARACTERISTICS OF INDIVIDUAL PERIOPATHOGENS

P. gingivalis is a bacterial strain belonging to the red complex [10] that is most commonly associated with chronic periodontitis (CP) and progression of periodontal destruction. [11] These bacteria are considered to be an important etiologic factor in severe forms of periodontal disease, i.e. they are a prominent component of the oral media and at the same time a successful colonizer of the oral epithelium. [12] At this point, researchers are trying to find out exactly how symbiosis works among bacterial populations in the mouth, especially between P. gingivalis and F. nucleatum, as they are the main causes of gingival inflammation. Their specific role is based on interactivity with the host, although it has already been proven that neither bacterial species can survive without each other. [13] These bacteria are not only responsible for damaging the periodontium.
Therefore, Porphyromonas gingivalis is thought to be involved in the etiology of rheumatoid arthritis and Alzheimer's disease. [14]

P. gingivalis and F. nucleatum, thanks to their virulent components, manage to survive in complicated environments by selectively modulating the host's immune-inflammatory response. Studies reveal that bacterial infection and the host's immune response are involved in the induction and progression of the disease. [15]

By observing, monitoring and studying certain pathogens in the periodontal disease, current evidence suggests that the prevalence of periodontal pathogenic microorganisms, such as A. actinomyctemcomitans and P. gingivalis, differs between ethnic groups. Such differences appear to be related to host tropism (i.e., specific adaptation of subpopulations of bacterial subspecies to certain host genetic genera) rather than differences in geographic influence and living conditions. [16]

The importance of F. nucleatum in the development of polymicrobial biofilms has been fairly long researched, discussed, explained, and more recently partially proven. F. nucleatum acts as a bridge mediating the co-coherence of late disease-causing colonizers, including P. gingivalis, as a component of the dental biofilm. Co-infection with F. nucleatum may increase the potential for adhesion and invasion of P. gingivalis and A. actinomyctemcomitans on gingival epithelial cells. [17]

CHARACTERISTICS OF FUSOBACTERIUM NUCLEATUM

The greatest heterogeneity of bacteria (over 700 different species) and the proximity of numerous anatomical regions where they are present, characterize the oral microbiological flora as one of the most divergent microorganisms in the human body, according to colonized microorganisms. [18, 19]

F. nucleatum belongs to the family Bacteroidaceae, at the same time the dominant microorganism within the periodontium. It is a gram-negative anaerobic strain of Fusobacteria phylum, predominant in dental plaque biofilm and an important factor in biofilm ecology and human infectious diseases.

F. nucleatum is present in the oral cavity, absent or rarely detected elsewhere in the body under normal conditions. [20, 21] In medical conditions, however, F. nucleatum is one of the most abundant species found outside the oral cavity (in the intestine, ovaries, placenta, bronchi). F. nucleatum is a heterogeneous pathogen to which five subspecies (ss) are added, i.e. ss animalis, ss fusiforme, ss nucleatum, ss polymorphum and ss vincentii, whose prevalence in various diseases is quite heterogeneous and variable. [22, 25]

MANAGEMENT AND POSSIBLE TREATMENT MODALITIES

People become patients when they present some medical symptoms to the doctor. The prevalence of medically unexplained symptoms ranges from 5–65% in primary care, and to 37–66% in specialty clinics. However, the prevalence is approximate, because it is hard to define what constitutes these symptoms. As we mentioned previously, in the DSM-5, this group of disorders belong to the somatoform group, because there are no diagnostic biomarkers for any other psychiatric diagnosis. In the diagnostics an intensive, deep anamnesis for all important facts in early life, as well as socio-economic state of patient, relationships and family lives are important. It needs too much time and patience, which is a problem in the contemporary lifestyle. The evaluation comprises all available methods in dentistry even fMRI. As we said before, all clinical examinations in this group of patients remain negative. The psychological evaluation is most important.

The current approaches propose to measure stress with some psychometric instruments (Perceived stress scale) and measures of affect (Profile of moods state), measures of stressor exposure (Major life events stress scale) and lastly the stress biomarkers (Cortisol, C-Reactive protein and interleukins). In our practice, we used electrodermal activity as a fast and valuable measure for stress level [25-28].

The commonly used stress biomarkers include:

- Metabolic markers – cholesterol, high-density lipoprotein (HDL) cholesterol, total cholesterol-HDL ratio, albumin, glycosylated hemoglobin;
- Immunological markers – interleukin-6 (IL-6), tumour necrosis factor (TNF-α), C-re-
active protein (CRP), insulin-like growth factor (IGF-1);

- Neuroendocrine markers – cortisol, dehydroepiandrosterone (DHEA), and cortisol / DHEA ratio, adrenaline, noradrenaline, dopamine and aldosterone:
- Other parameters: i.e. arterial tension (systolic/diastolic), heart rate, electrodermal activity, brain spectral characteristics etc.

Recently, it has been shown that chronic stress alters ultrastructure of mitochondria of masticatory muscles in experimental animals. In some studies, anaerobic metabolism was shown increased, as well as the positive findings for oxidative stress. The fragmentation of mitochondria that is observed under chronic stress is due to unbalanced fission. A buccal swab can give enough cells to observe mitochondrial changes and the morphological changes of mitochondria could be used as biomarkers for chronic stress. Buccal swab collection is non-invasive and inexpensive, making ultrastructure changes in mitochondria easy to use for large epidemiological studies. The intensity of ultrastructure integrity loss can be related to the length of time under stress [29-33].

Many forms of psychotherapy can help these patients. Most frequently, the Cognitive–behavioural therapy, Self-observation, Relaxation training, Hypnotherapy, Biofeedback are used. Sometimes, the medication prescription is inevitable. As medication Antidepressants, Antianxiety drugs or even Antipsychotic drugs can be used [34-38]. Our results with biofeedback are very encouraging. For stress diminishing the peripheral biofeedback is extremely useful and has cost-beneficial effects.

THE ROLE OF F. NUCLEATUM IN THE PATHOGENESIS OF PERIODONTAL DISEASE

In clarifying the complexity of pathogenesis of periodontal disease and elucidating its role in periodontal disease, for F. nucleatum is believed to possess several virulence mechanisms that can be broadly classified into two groups: colonization and dissemination, and induction of host response. [26]

F. nucleatum is an adhesive bacterium. It co-aggregates with various microbiological species in the oral cavity, playing a key role in the formation of dental plaque. [27] It encodes several adhesins for interactions, including Fap2, RadD and aid1. [28-30] F. nucleatum also binds to various cells in the human population, including epithelial and endothelial cells, monocytes, erythrocytes, fibroblasts, and host molecules such as salivary macromolecules, extracellular matrix proteins, etc. [26-31]

So far only one adhesin has been identified, FadA which adheres to the host cells and is one of the strongest virulence factors. [26] FadA is not only adhesin but also invasive. [32] Also F. nucleatum elicits different host responses. [26] It stimulates the production and activity of human beta-defensin 2 from oral epithelial cells via FAD-I. [33] It stimulates atherosclerosis-inducing factors by GroEL [34], activates lymphocyte apoptosis by Fap2 and RadD [30], and is a potent stimulator of inflammatory cytokines, IL-6, IL-8 and TNF. [35, 36] Binding of F. nucleatum to NK cells (Natural killer cells) activates inflammatory reactions involved in periodontal disease. [37] In colorectal cancer (CRC), F. nucleatum activates not only inflammatory cells but also genes, especially oncogenes and Wnt genes which are markers of tumorigenesis. FadA plays a key role in the induction of these tumors where the gene response is absent. Synthetic peptide that prevents FadA binding to E-quadrant, blocks the activation of the inflammatory response but also affects oncogenes and Wnt gene expression. [38]

The pathogenicity of F. nucleatum is attributed, in part, to its function as a “bridge in the organism” that supports the integration of periopathogens into oral biofilms. [39,40] With this unique skill they have the ability to merge to early and the late colonizers. F. nucleatum is thought to play a central role in environmental change from predominantly gram-positive flora to predominantly gram-negative, and thus to a pathogenically transformed biofilm community that tends to initiate a progressive periodontal disease. [39]

Despite extensive research on F. nucleatum, its interspecies, interactions, and identification of a large number of binding partners, to date, only two fusobacterial large outer membrane proteins (NMPs), RadD and Fap2, are important at the molecular level as binding adhesins for different gram-positive bacterial strains, [28,29] among which most commonly Porphyromonas gingivalis. [41] RadD and
DETERMINATION OF THE ROLE OF FUSOBACTERIUM NUCLEATUM IN THE PATHOGENESIS IN AND OUT THE MOUTH

Fap2 are members of the protein family, which are the most well-known autotransporter family and have a strong influence as virulence factors that may originate from gram-negative bacteria. [42] Auto-transporters have numerous biological functions including adhesion [43,44] cell aggregation, biofilm formation [45-48] and their invasion. [49] It is therefore not surprising that despite their role in interspecies, i.e. binding, fusobacterial auto-transporters are multifunctional and actively involved in induction of apoptosis in lymphocytes [29,30] and adherence to placental cells (demonstrated by mouse studies). [41]

There is evidence that the prevalence of F. nucleatum increases with the worsening of disease, progression of inflammation and deepening of pockets. [50-52] Among the five so far verified subspecies most commonly fusiforme and virulentii are most often associated with healthy status, while nucleatum with non-healthy state in the organism. [53].In the context of this explanation it is worth emphasizing that the serum titers of F. nucleatum antibodies are elevated in the sick patients. [54]

The presence of F. nucleatum to a greater or lesser extent is influenced by certain factors that come from the environment e.g. smoking increases the prevalence of this anaerob in both healthy and sick individuals. [54,55] In patients with chronic periodontitis, those with uncontrolled type 2 diabetes have higher levels of F. nucleatum. [56] When F. nucleatum has the role of co-infection with other oral bacterial species, e.g. Tannerella forsythia, Porphyromonas gingivalis and Streptococci, it’s evident the synergy of virulence with the indicated bacterial species as evidenced by increased bone loss and creation of abscess. [57-61]

F. nucleatum is one of the most prevalent species in the oral cavity. It is involved in all forms of periodontal disease, emphasizing mild reversible forms of gingivitis or advanced irreversible forms of periodontal disease, chronic periodontal disease, localized aggressive periodontal disease, generalized aggressive periodontal disease and others. [50,51]

Moore and Moore [50] concluded that F. nucleatum is the most common cause of gingival inflammation that initiates periodontal disease and is the most dominant pathogen in periodontal destruction. The importance of F. nucleatum in the development of polymicrobial biofilms has long been proven. F. nucleatum binds to early colonizers and acts as a bridge mediating the cohesion of late colonizers that cause disease, including P. gingivalis, in the dental biofilm. Most gram-negative bacteria are associated with various forms of periodontal disease. They are asaharolytic species, but unlike them F.nucleatum can obtain energy by fermenting simple sugars such as glucose or fructose, but not sucrose; or by fermenting certain amino acids, free or in the form of small peptides. This metabolic versatility probably explains why it is found in supra and subgingival dental plaque. [62]

ASSOCIATION OF FUSOBACTERIUM NUCLEATUM WITH OTHER SYSTEMIC DISEASES

It is one of the most common oral isolated types from and beyond oral infections, including blood, brain, chest, lungs, liver, joints, abdominal, obstetric and gynecological infections.

There is evidence that F. nucleatum and Porphyromonas gingivalis synergistically increase the progression of oral cancer. [72] Studies concerning the impact of these two periodontal pathogenic bacteria indicate several virulence mechanisms that promote carcinogenesis. [73] The specific properties of virulence suggest their potent invasion into the subcutaneous and intestinal epithelium, blocking oncogene signaling, blocking their adhesion, inflammation induction, and inhibition of natural killer cells and cytotoxic T-cells, promoting tumor proliferation and progression. [73,74]

Gastrointestinal disorders have a particular role on this anaerobic, which is believed to contribute to the development of colorectal cancer (CRC), inflammatory bowel disease (IBD) and appendicitis. F. nucleatum is regularly identified in studies of colorectal cancer (CRC) present in the tumor microbiome, often as an adjunct to other oral microorganisms. [75] F. nucleatum was first detected in cancers and rectal swabs of patients with CRC. [76,77] Several studies have reported an association of F. nucleatum with the appendicitis. [78-80]

There is evidence that the finding of this anaerob is associated with certain complicated conditions in the body. Complication of pregnancy is essentially a broad term, which includes preterm delivery, chorioamnionitis, premature rupture of
Table 1. Incidence and association of fusobacterium nucleatum in oral cavity diseases

<table>
<thead>
<tr>
<th>Sample taken from</th>
<th>Method</th>
<th>Total number of patients</th>
<th>Related to</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subgingival biofilm</td>
<td>PCR</td>
<td>70</td>
<td>G</td>
<td>[63]</td>
</tr>
<tr>
<td>Subgingival biofilm</td>
<td>PCR</td>
<td>70</td>
<td>CH</td>
<td>[63]</td>
</tr>
<tr>
<td>Subgingival biofilm and saliva</td>
<td>PCR</td>
<td>81</td>
<td>AgP</td>
<td>[64]</td>
</tr>
<tr>
<td>Supragingival dental plaque</td>
<td>Cultivation</td>
<td>30</td>
<td>CH</td>
<td>[65]</td>
</tr>
<tr>
<td>Subgingival dental plaque</td>
<td>Cultivation</td>
<td>30</td>
<td>CH</td>
<td>[65]</td>
</tr>
<tr>
<td>Endoperiodontal lesion</td>
<td>PCR</td>
<td>46</td>
<td>EP</td>
<td>[66]</td>
</tr>
<tr>
<td>Saliva</td>
<td>PCR</td>
<td>31</td>
<td>G</td>
<td>[67]</td>
</tr>
<tr>
<td>Saliva</td>
<td>PCR</td>
<td>46</td>
<td>CH</td>
<td>[67]</td>
</tr>
<tr>
<td>Saliva</td>
<td>PCR</td>
<td>36</td>
<td>Ag</td>
<td>[67]</td>
</tr>
<tr>
<td>Periapical lesion</td>
<td>r16S rDNA</td>
<td>20</td>
<td>PCHA</td>
<td>[68]</td>
</tr>
<tr>
<td>isolate from root infected canals</td>
<td>16S rRNA (rRNA)</td>
<td>87</td>
<td>PCHA</td>
<td>[69]</td>
</tr>
<tr>
<td>isolate from root infected canals</td>
<td>DNA-DNA hybridization</td>
<td>24</td>
<td>PCHA</td>
<td>[70]</td>
</tr>
<tr>
<td>isolate from root canals</td>
<td>PCR</td>
<td>55</td>
<td>G</td>
<td>[71]</td>
</tr>
</tbody>
</table>

Legend: G--gingivitis; AgP--aggressive periodontitis; CH--chronic periodontitis; EP--endo-periodontitis; PCHA--chronic apical periodontitis.

membranes, preeclampsia, miscarriage, low birth weight, premature birth, neonatal sepsis, etc. In all these states, F. nucleatum is one of the most widespread species and one of the most frequently detected microorganisms. [81] It is assumed that F. nucleatum is transmitted from the mother’s oral cavity to the intrauterine bed through hematogenous transmission. [81,83] Of the five subspecies, only two were detected in intrauterine infection, in the majority the subspecies animalis and less the polymorphum.

F. nucleatum is associated with a wide range of infections and abscesses, including head and neck infections (Lemier syndrome, acute and chronic mastoiditis, chronic otitis and sinusitis, periodontitis, tonsillitis, peritonsillar and retropharyngeal absces, prolonged cervical lymphadenitis) brain, lungs, abdomen, pelvis, bones and joints. [84-86]

The frequency of F. nucleatum detection in atherosclerotic plaques and blood vessels is directly related to the severity of periodontal disease. [87] Additional diseases involving F. nucleatum include rheumatoid arthritis and Alzheimer’s disease. [88,89] Periodontal treatment has been shown to improve the clinical outcome of rheumatoid arthritis. [89]

RESULTS AND DISCUSSION

Studies emphasise the prevalence and association of F. nucleatum with the most common diseases and conditions of the oral cavity: gingi-
DETERMINATION OF THE ROLE OF FUSOBACTERIUM NUCLEATUM IN THE PATHOGENESIS IN AND OUT THE MOUTH

Table 2. Prevalence and association of fusobacterium nucleatum with certain systemic diseases

<table>
<thead>
<tr>
<th>Sample taken from</th>
<th>Method</th>
<th>Total number of patients</th>
<th>Related to</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atheromatous plaques</td>
<td>PCR</td>
<td>44</td>
<td>CAD</td>
<td>[90]</td>
</tr>
<tr>
<td>Supragingival biofilm</td>
<td>qPCR</td>
<td>23</td>
<td>P</td>
<td>[91]</td>
</tr>
<tr>
<td>Saliva</td>
<td>qPCR</td>
<td>35</td>
<td>PCOS</td>
<td>[92]</td>
</tr>
<tr>
<td>Amniotic fluid</td>
<td>16S rRNA</td>
<td>46</td>
<td>PTB</td>
<td>[93]</td>
</tr>
<tr>
<td>Oral mucosa</td>
<td>PCR</td>
<td>24</td>
<td>HRP</td>
<td>[94]</td>
</tr>
<tr>
<td>Chorionic tissue</td>
<td>PCR</td>
<td>24</td>
<td>HRP</td>
<td>[94]</td>
</tr>
<tr>
<td>Colon tissue</td>
<td>PCR</td>
<td>130</td>
<td>CRC</td>
<td>[95]</td>
</tr>
<tr>
<td>Feces</td>
<td>ddPCR</td>
<td>184</td>
<td>CRC</td>
<td>[96]</td>
</tr>
<tr>
<td>Placenta</td>
<td>PCR</td>
<td>16</td>
<td>Preeclampsia</td>
<td>[97]</td>
</tr>
<tr>
<td>Fetal membrane</td>
<td>16S rRNA</td>
<td>15</td>
<td>PTB</td>
<td>[98]</td>
</tr>
<tr>
<td>Fetal membrane</td>
<td>PCR</td>
<td>43</td>
<td>PTB</td>
<td>[98]</td>
</tr>
<tr>
<td>Abscesses content</td>
<td>cultivation</td>
<td>226</td>
<td>Abscessus</td>
<td>[99]</td>
</tr>
<tr>
<td>Lung aspirate</td>
<td>cultivation</td>
<td>226</td>
<td>Aspirational pneumonia</td>
<td></td>
</tr>
<tr>
<td>Nail</td>
<td>cultivation</td>
<td>226</td>
<td>Paronychia</td>
<td>[99]</td>
</tr>
<tr>
<td>Material from the middle ear</td>
<td>cultivation</td>
<td>226</td>
<td>Otitis media</td>
<td>[99]</td>
</tr>
<tr>
<td>Bone</td>
<td>cultivation</td>
<td>226</td>
<td>Osteomyelitis</td>
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</tr>
<tr>
<td>Synovial fluid</td>
<td>16S-23S rRNA</td>
<td>11</td>
<td>RA</td>
<td>[100]</td>
</tr>
<tr>
<td>Synovial fluid</td>
<td>16S-23S rRNA</td>
<td>25</td>
<td>OA</td>
<td>[100]</td>
</tr>
<tr>
<td>Dental plaque</td>
<td>16S-23S rRNA</td>
<td>36</td>
<td>RA+ OA</td>
<td>[100]</td>
</tr>
</tbody>
</table>

Legend: CAD- coronary artery disease; P-pregnancy; PCOS - polycystic ovary syndrome; PTB- preterm birth; HRP - high-risk pregnancy; CRC- colorectal cancer; PE-preeclampsia; RA-rheumatoid arthritis; OA-osteoarthritis.

vitis (G), chronic periodontitis (CH), aggressive periodontitis (AgP), endo-periodontal infections (EP), chronic apical periodontitis (PCHA) in a variety of media: subgingival and supragingival dental plaque, fluid, saliva, tissue. The presence of this anaerobe is commonly associated with the health status of individuals.

In the body this bacteria has been identified and detected in synovial fluid, placenta, fetal membrane, lung fluid, abscess content and in many systemic disorders such as: coronary artery disease (CAD) pathological pregnancy (P); polycystic ovary syndrome (PCOS); high-risk pregnancy (HRP); colorectal cancer (CRC); pre-eclampsia (PE); rheumatoid arthritis (RA); osteoarthritis (OA). F. nucleatum is an oral commensal involved in oral infections, and in most diseases even with a fatal end. This anaerobe with quite pathogenic effects can be distributed systemically from the oral cavity by colonizing different sites in the body, or vice versa. However, the path of eradication is an issue that has not been clarified and is still open.

From the available literature it can be understood that F. nucleatum initiates a full spectrum of host responses, ranging from immune, bacteriological, toxic, enzymatic and inflammatory processes. Most authors share the opinion that
adenine FadA of F. nucleatum and is a key virulence factor. Relying on the abundance of highly processed literature, it is clear that F. nucleatum has a rather important role in the pathogenesis of diseases of the oral cavity. Whether its role is predominant or it is secondary, it is the subject of additional research, analysis and reporting.

CONCLUSION

F. nucleatum predominates in various pathological conditions in biofilms in and out of the mouth, since its involvement in the pathogenesis of these diseases.

The presence of Fusobacterium nucleatum is commonly associated with the health status of individuals. This anaerob plays a key role in oral pathological conditions and has been detected in many systemic disorders causing complex pathogenesis probably due to binding ability to various cells thus several virulence mechanisms.

REFERENCES

DETERMINATION OF THE ROLE OF FUSOBACTERIUM NUCLEATUM IN THE PATHOGENESIS IN AND OUT THE MOUTH


DETERMINATION OF THE ROLE OF FUSOBACTERIUM NUCLEATUM IN THE PATHOGENESIS IN AND OUT THE MOUTH


90. Gaetti-Jardim E Jr, Marcelino SL, Feitosa AC, Romito GA, Avila-Campos MJ. Quantitative de-


Резиме

ПРИСУСТВО И УЛОГА НА FUSOBACTERIUM NUCLEATUM ВО УСТАТА И НАДВОР ОД НЕА

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Вовед: Еден од најважните видови микроорганизми во усната празнина и кај здрави и кај болни индивиду е Fusobacterium nucleatum. Иако е присутен како нормален жител, овој грам-негативен патоген е доминантен во пародонталната болест и е вклучен во многу инвазивни инфекции кај популацијата, акутни и хронични воспалителни состојби, како и многу несакани дејства со фатален завршеток.

Цел: Да се утврди улогата на F. nucleatum во развојот на полимикробни биофилм во оралнот медиум преку следење на литературата и надвор од неа.

Материјал и метод: Систематски преглед на литературата во врска со застапеноста и улогата на F. nucleatum преку достапните клинички испитувања, прегледи на литература, оригинални истражувања и статии објавени по електронски пат во Pub Med и Google Scholar.

Заклучок: Присуството на Fusobacterium nucleatum е најчесто поврзано со здравствената состојба на поединците. Овие анаеробни бактерии играат клучна улога во оралните патолошки состојби и се откривени кај многу системски нарушувања, предизвикувачки комплексен патогенетски промени веројатно поради случувањата во различни клетки и преку различни механизми за вирулентност. Најчесто забележувања и состојби во усната празнина поврзани со F.nucleatum се гингивитис (G), хронична пародонтопатија (CH), агресивна пародонтопатија (AgP), ендо-периондонтална инфекција (E-P), хроничен апикален периодонтитис (PCHA). Исто така, бактеријата е идентификувана и откривена кај многу системски нарушувања, како што се коронарната срцева болест (CVD), патолошката бременост (P); синдромот на полицистични јајници (PCOS), високоризичната бременост (HRP), колоректалниот карцином (CRC); прееклампсијата (PE); ревматоидниот артритис (RA); и остеоартритисот (OA).

Ключни зборови: пародонтопатија, Fusobacterium nucleatum, патогенеза