



Professional article

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THE ROLE OF NITRIC OXIDE IN SALIVA IN REDUCTION OF CARIES

SUMMARY

One of the basic preconditions for effective systemic decrease of caries prevalence, as well as for qualitative profilaxis, is to determine the risk of this complex disease onset. There is a large number of salivary substances exerting direct or indirect role in caries onset. In this study, the role of nitric oxide during this pathological process is presented. Numerous authors have proven the ability of salivary nitrites to have an inhibitory effect on growth and survival of cariogenic bacteria in acid environment. It is believed that NO expresses its antibacterial effect in two ways – by inhibition of bacterial growth and/or by increase of macrophages-mediated cytotoxicity from saliva. Definitely, nitric oxide can be considered as one of possible biomarkers in etiology of onset, as well as in development of caries lesions.

Key words: caries, nitric oxide, saliva

INTRODUCTION

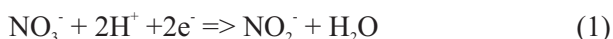
One of the basic preconditions for effective systemic decrease of caries prevalence, as well as for qualitative profilaxis, is to determine the risk of this complex disease onset. The tendency to determine high-risk caries subjects in order to improve oral health leads to the final goal – population without caries. Developing possibilities to predict caries onset in children, who have not been affected by caries yet, is the future of prevention programmes in dentistry. Many parameters are used for that – methods and individual or group analysis, such as: prior caries experience (level of caries experience and/or caries activity); nutrition (quality features, frequency of refined carbohydrate intake); level of colonisation of caries associated microorganisms (including their acidic potential, as well); quantity and quality of saliva: secretion level, buffer capacity, pH values, mineral content, enzyme and other biological marker levels; exposure to fluorides

(drinking water, tablets, paste, rinses...); level of oral hygiene; genetic predisposition (1,2).

A special place in caries onset risk assessment belongs to saliva. This oral fluid is undoubtedly the most important component of oral environment and an integral component of oral health. Besides tissue lubrication, saliva keeps neutral pH environment, making teeth remineralisation by mineral ions present in its solution possible. Saliva also helps antimicrobial function by the effects of immunoglobulins and proteins present in fluid (3). A large number of salivary substances have direct or indirect role in caries onset. In this study, the role of nitric oxide during this pathological process is presented.

The origin of nitric oxide (NO) in oral cavity appears in two ways. It can occur chemically, by physiological reduction of nitrates from food and enzymatically from L-arginine by inducible nitric oxide synthase (iNOS), an enzyme expressed in salivary glands (4,5).

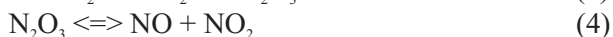
In humans, dietary nitrates are absorbed in duodenum and upper parts of ileum in blood circulation, and then concentrated in salivary glands by the mechanisms of active transport, reaching the concentration up to ten times higher than the concentration in plasma (6). After secretion into oral cavity, its fast reduction into nitrites occurs (Equation 1):



This reaction happens due to activities of nitrate-reducing microorganisms, present on tongue surface, in fact their enzyme – nitrate reductase. Nitrites acidification occurs in acid environment of teeth tissues. Acid surrounding is obtained by existing microflora including *Lactobacillus*, *Streptococcus mutans*, *Actinomyces*, microorganisms implied in dental caries (7), as well as *Staphylococcus Aureus* and *Staphylococcus Epidermidis* (8). Nitrite acidification leads to the formation of nitrous oxide and nitrous acid mixture (Equations 2,3,4):



Nitrous acid is unstable and spontaneously converted into nitric oxide (NO) and nitric dioxide (NO₂) (equations 3 i 4) (9).



Low pH value, inevitable for previously mentioned reactions, is obtained in caries lesion, where pH value can decrease even to 3,6. These local sites of extreme pH depression make nitrite conversion to antimicrobial components possible

(Equations 3 i 4), resulting in autoinhibition of acidogenic bacteria, such as *S. Mutans* (8).

It is well-known that NO has strong antibacterial effect (5). Nitric oxide is a highly reactive radical, taking part in nonspecific natural defense mechanisms of oral cavity, aiming to prevent bacteria growth and development. Numerous authors (8,10) prove the ability of salivary nitrites to have an inhibitory effect on growth and survival of cariogenic bacteria in acid environment. It is believed that NO expresses its antibacterial effect in two ways – by inhibition of bacterial growth and/or by increase of macrophages-mediated cytotoxicity from saliva. Nitric oxide easily passes cell membranes and can provoke damage of microorganisms by different mechanisms, such as impairment of biological oxidation in mitochondria (11), DNA damage (12) and formation of highly toxic peroxynitrite (13).

Despite the fact that some researches indicate that caries incidence is lower in subjects with high level of NO in saliva (10,14), there are some contradictory data, reporting that caries incidence is not decreased in patients with high concentration of NO in saliva (15).

Continuous plaque deposition (plaque maturity) makes nitrite conversion with pH level below 7 and iNOS induction possible, leading to the conversion of *L*-arginine into NO (10). Bayindir et al. (15) indicate positive correlation of high NO level and high plaque index. The same authors conclude that caries incidence in subjects with high level of NO is not reduced. It is explained by the fact that poor oral hygiene enables high level of NO (by plaque maturity), but high caries incidence indicates that high concentration of NO is not enough to inhibit the cariogenicity of plaque.

Nitric oxide can definitely be considered as one of the possible biomarkers in etiology of onset, as well as the development of caries lesions.

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ULOGA AZOT MONOKSIDA IZ PLJUVAČKE U REDUKCIJI KARIJESA

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SAŽETAK

Jedan od osnovnih preduslova za efikasno sistematsko smanjenje prevalencije karijesa kao i kvalitetnu profilaksu jeste determinacija rizika za nastanak ovog kompleksnog oboljenja. Veliki broj supstanci iz pljuvačke ima posrednu ili neposrednu ulogu u nastanku karijesa. U ovom radu će biti predstavljena uloga azot monoksida tokom ovog patološkog procesa. Brojna istraživanja dokazuju sposobnost salivarnih nitrita da u kiselj sredini imaju inhibični efekat na rast i preživljavanje kariogenih bakterija. Smatra se da svoje antibakterijsko dejstvo NO ispoljava na dva načina – inhibicijom rasta bakterija i/ili povećanjem citotoksičnosti posredovane makrofagima iz pljuvačke. Azot monoksid, tačnije njegova koncentracija u pljuvački, može se definitivno svrstati u jedan od mogućih biomarkera kako u etiologiji tako i u razvoju karijesne lezije.

***Ključne reči:* karijes, azot oksid, pljuvačka**