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ULOGA KARBOANHIDRAZE U NASTANKU KARIJESA

THE ROLE OF CARBOANHYDRASE IN THE OCCURENCE OF CARIES

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Kratak sadržaj

Jedan od osnovnih preduslova za efikasno sistematsko smanjenje prevalence karijesa kao i kvalitetnu profilaksu jeste determinacija rizika za nastanak ovog kompleksnog oboljenja. Cilj ovog rada je dokazivanje značaja uvođenja karboanhidraze kao validnog biomarkera u proceni rizika za nastanak karijesa kod dece.
U radu je objašnjen značaj aktivnosti karboanhidraze u pljuvačci u smanjenju lokalne kiselosti.

Ključne reči:

Abstract

One of the basic preconditions for systematic monitoring of caries prevalescence, as well as its efficient profilaxis, is the determination of risk for this complex disease incidence. The aim of the investigation is to prove the importance of carbonic anhydrase as valid biomarkers for the estimation of risk for caries incidence in children. This paper is going to examine the mentioned parameter values in saliva of children

Key words:

Opšte napomene

Karboanhidraza (CA) je cink metaloenzim čija je aktivnost u ljudskoj pljuvačci poznata skoro 70 godina.[1] Do pre nekoliko godina veoma mali broj studija se bavio fiziološkom ulogom CA.[2,3,4,5,6] Goveđi salivarni CA izoenzim u parotidnoj pljuvačnoj žlezdi je opisao Fernley[7] 1979. godine. Ovaj enzim su prvi put izolovali iz humane pljuvačke Murakami i Sly[8] 1987 godine. Njegova molekularna težina je 43 kDa. Molekul enzima ima dva N – oligosaharidna lanca, koji mogu biti razgrađeni endo-*β*-*N*-acetzilglukozaminidazom F, ali ne i endo-*β*-*N*-acetzilglukozaminidazom H, što ukazuje da su oligosaharidi kompleksnog tipa.[8]

Kod ljudi, imunohistohemijske studije ukazuju na lokaciju sekrecije CA isključivo u sekretornim granulama acinusnih ćelija parotidne i submandibularne žlezde.[9]

General remarks

Carboanhydrase (CA) is a zinc metalloenzyme the activity of which in the human saliva has been known for almost 70 years.[1] Until recently, there were very few studies dealing with the physiologic role of CA.[2,3,4,5,6] Bovine salivary CA isoenzyme in the parotid salivary gland was first described by Fernley[7] in 1979. The enzyme was first isolated from the human saliva by Murakami and Sly[8] in 1987. Its molecular weight is 43 kDa. Its molecule has two N-oligosaccharide chains, degradable by endo-β-N-acetylglucosaminidase F, but not by endo-β-N-acetylglucosaminidase H, which suggests that these oligosaccharide are of a complex type.[8]

In humans, immunohistochemical studies demonstrate that the exclusive CA secretion site are secretory granulas of acinar cells of the parotid and submandibular gland.[9]

Sekrecija CA, posebno izoenzima CA VI u pljuvačku, prati cirkadijalni periodicitet. Shodno tome, njegova koncentracija je veoma mala tokom perioda sna i rapidno raste tokom dana, pogotovu nakon buđenja i doručka.[10] Cirkadijalni periodicitet karboanhidraze je veoma sličan periodicitetu pljuvačne α-amilaze. Treba istaći da je uočena i signifikantna pozitivna korelacija između aktivnosti pljuvačne amilaze i concentracije CA VI.[10] Istraživanja ukazuju da se ova dva enzima sekretuju putem sličnog mehanizma i da mogu biti prisutni u istim sekretornim granulama. Ako se zna da je uloga autonomnog nervnog sistema u sekreciji amilaze dobro poznata,[11] može se anticipirati da autonomni nervni sistem takođe kontroliše i sekreciju karboanhidraze. Ovu pretpostavku potkrepljuje i istraživanje Fernley-a i saradnika[12] koji su demonstrirali, koristeći nervnu stimulaciju i holinergičke supstance, da parasimpatički i simpatički nervni putevi mogu regulisati koncentraciju CA VI u salivi ovce.

Prema nekim istraživačima, CA bi mogla biti ključni enzim u oralnoj fiziologiji. Kadoya i saradnici[13] ističu da CA reguliše pH i puferski kapacitet pljuvačke. Međutim, druga grupa autora,[4,14] dolazi do rezultata koji ove varijabile ne dovodi u direktnu vezu sa koncentracijom CA u pljuvačci. Novija istraživanja otkrivaju korelaciju koncentracije gustina i CA u pljuvačci, inače dva veoma slična proteina po svojim proteinskim sekvencama i drugim fizičko-hemijskim parametrima.[15]

Uloga CA u zaštiti tvrdih zubnih tkiva

Karboanhidraza (CA) učestvuje u održavanju pH homeostaze u različitim tkivima i biološkim fluidima ljudskog organizma katalizujući proces reverzibilne hidratacije ugljen dioksida, po formuli:

$$CO_2 + H_2O <=> HCO_3^- + H^+$$

Do sada je izolovano jedanaest izoenzima sa CA aktivnošću kod sisara, i svi se lociraju u alimentarnom traktu. Od jedanaest izoenzima dva su značajna za salivarnu fiziologiju.[13]

CA II je citoplazmatski izoenzim visoke aktivnosti prisutan u seroznim acinusnim ćelijama parotidne i submandibularne žlezde. Smatra se i da ima ulogu u produkciji bicarbonata u pljuvačci.

CA secretion is circadian, which especially relates to the secretion of CA VI isoenzyme into the saliva. Accordingly, its concentration is very low during sleep and rapidly rises during daytime, especially after the awakening and breakfast.[10] Circadian rhythm of CA resembles very closely the rhythm of salivary α-amylase. It should be pointed out that a significant positive correlation was noticed between the activity of salivary amylase and CA VI concentration.[10] Studies indicate that these two enzymes are secreted via a similar mechanism and that they can be present in the same secretory granulas. The role of autonomous nerve system in the secretion of amylase is well known and the similar controlling role of this system in the secretion of CA should be expected. This assumption is further supported by the investigation of Fernley et al., who demonstrated, utilizing nerve stimulation and cholinergic substances, that parasympathetic and sympathetic nerve pathways could regulate CA VI concentration in the sheep saliva.

Some authors suggest that CA could be the key enzyme in oral physiology. Kadoya et al.[13] point out that CA regulates pH and buffer capacity of the saliva. However, other authors[4,14] have got results which could not directly correlate these variables with CA concentration in the saliva. Some recent investigations elucidated the correlation of gustin and CA concentrations in the saliva; by their protein sequences and other physical/chemical characteristics, these are two very similar proteins.[15]

The role of CA in the protection of dental hard tissues

Carboanhydrase (CA) takes part in the maintenance of pH homeostasis in various tissues and biologic fluids in humans catalyzing the process of reversible hydration of carbon dioxide, which is described by the formula:

$$CO_2 + H_2O <=> HCO_3^- + H^+$$

Up to the present, eleven isoenzymes with CA activity have been isolated in mammals, all of them within the alimentary tract; out of these eleven, two enzymes are of significance for salivary physiology.[13]

CA II is a very active cytoplasmic isoenzyme present in the serous acinar cells in the parotid and submandibular glands. It is believed that CA II has a role in the production of bicarbonates in the saliva.

CA VI je jedini poznati sekretorni CA izoenzim. Lokalizovan je takođe u seroznim acinusnim ćelijama parotidne i submandibularne žlezde, odakle se sekretuje u pljuvačku.[16]

Fiziološka uloga pljuvačne karboanhidraze VI (CA VI) je u potpunosti razjašnjena. Niska salivarna koncentracija CA VI je u vezi sa povećanom prevalencom karijesa.[16] Szabo[3] je 1974. godine, u do sada jedinom radu u svetskoj literaturi koji se bavi analizom CA kod dece, uočio visoku CA aktivnost kod dece bez karijesa nego kod dece sa aktivnim karijesom. Ako se uzme u obzir pozitivna korelacija koncentracije CA VI i lučenja pljuvačke i negativna korelacija CA sa KIPs indexom, skorašnja istraživanja ukazuju da salivarna CA igra ulogu u zaštiti zuba od karijesa[17].

Kao što je već istaknuto, izgleda da CA nije direktno uključena u regulaciju pljuvačne pH i njenog puferskog kapaciteta. Takođe, nije uočena ni korelacija koncentracije CA i nivoa mutans streptokoka ili laktobacila (Lenander-Lumikari., Loimaranta 2000).

Istraživanje Leinonen-a i saradnika[18] ukazuje na vezivanje CA VI za gleđnu pelikulu, uz prisutnu enzimsku aktivnost na površini zuba (slika 1). U gleđnoj pelikuli CA VI katalizuje konverzaciju salivarnog bikarbonata i vodonikovih jona (poreklom iz aktivnosti mikroba) u ugljen monoksid i vodu.

Na taj način dolazi do smanjenja kiselosti i povećanja lokalne pH vrednosti na površini zuba što deluje povoljno na redukciju karijesa.

Karboanhidraza, tačnije njena koncentracija u pljuvačci, može se definitivno svrstati u jedan od važnih biomarkera u etiologiji nastanka i razvoja karijesne lezije.

CA VI is the only known secretory CA isoenzyme which has been detected in the saliva secreted by the serous acinar cells of the parotid and submandibular glands[16].

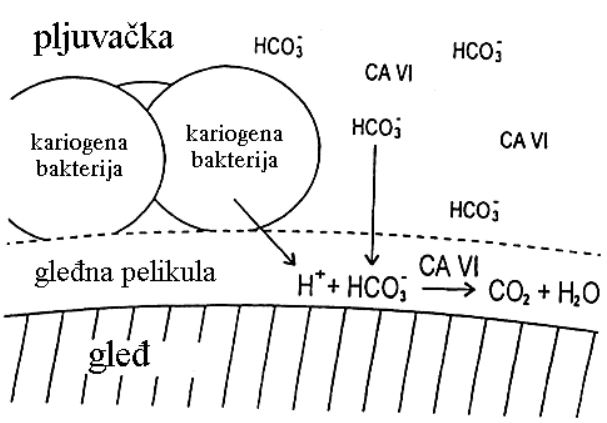
Physiologic role of salivary carboanhydrase VI (CA VI) has now been completely elucidated. Low salivary concentration of CA VI has been related to increased caries prevalence[16]. In his paper from 1974, the only one in the literature worldwide dealing with CA in children, Szabo[3] noted high CA activity in children without caries compared to those with active caries. If we take into account positive correlation of CA VI concentration and saliva secretion and negative correlation of CA with the DMF index, recent papers have indicated that salivary CA has a role in the protection of teeth from caries[17].

As already mentioned, it looks as if CA cannot be directly implicated into the regulation of salivary pH and its buffer capacity. Also, there has not been any correlation between CA concentration and the level of streptococcus mutans or lactobacillus (Lenander-Lumikari, Loimaranta 2000).

The study conducted by Leinonen et al[18], points out the binding of CA VI to the enamel pellicula, with enzymatic activity on the tooth surface (Figure 1). Within the pellicula, CA VI catalyzes the conversion of salivary bicarbonate and hydrogen ions (originating from microbial activity) into carbon dioxide and water.

That results in acidity reduction and elevation of local pH value on the tooth surface, which acts favorably regarding caries reduction.

Carboanhydrase, i.e. its salivary concentration (activity), can definitely be classified among the important biomarkers in caries etiopathogenesis.



Slika 1. Model mehanizma delovanja CA VI na površini zuba (Lenander-Lumikari., Loimaranta 2000).

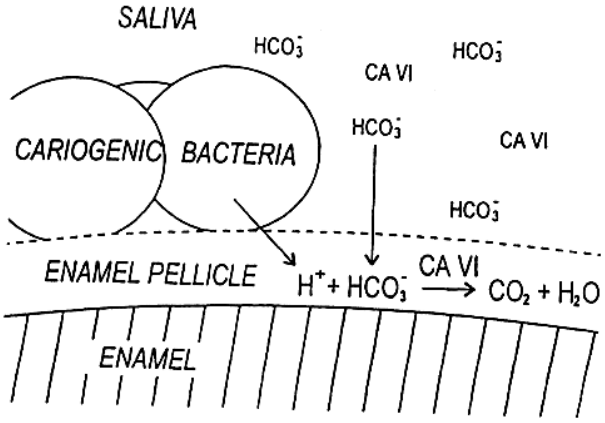


Figure 1. Model of the CA VI mechanism of action at the tooth surface

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