

Renata Chalas

# Koncentracija kalcija i kalija u slini pacijenata s multiplom sklerozom

## *Calcium and Potassium Saliva Concentration in Patients with Multiple Sclerosis*

Stomatološki odjel Medicinskog fakulteta u Lublinu, Poljska  
*Department of Conservative Dentistry, Medical University of Lublin, Poland*

### Sažetak

**Svrha:** Ovom se studijom željelo procijeniti kolika je koncentracija kalcija i kalija u slini pacijenata s multiplom sklerozom. **Ispitanici i postupci:** Ispitano je 86 pacijenata s multiplom sklerozom (MS-om) i 54 zdrave osobe. Koncentracije kalcija i kalija bile su određene kolorimetrijski. Nakon toga su dobiveni podaci statistički obrađeni testovima t-student i hi-kvadrat. **Rezultati:** Razine kalcija u slini pacijenata s MS-om bile su statistički znatno niže od onih kod zdravih osoba, a koncentracije kalija mnogo manje. **Zaključak:** Ustanovljeni poremećaj u koncentraciji elektrolita može se povezati s neurološkim i imunološkim poremećajima svojstvenima multiploj sklerozi.

**Zaprimljen:** 12. listopada 2008.  
**Prihvaćen:** 20. veljače 2009.

### Adresa za dopisivanje

Dr n. med. Renata Chalas  
Department of Conservative Dentistry  
Medical University of Lublin  
Karmelicka 7  
20-081 Lublin, Poland  
tel: 0 048 81 528 79 20  
renata.chalas@gmail.com

### Ključne riječi

multipla skleroza; kalcij; kalij; slina; elektroliti

### Uvod

Multipla skleroza (MS) kronična je upalna bolest središnjega živčanog sustava kod koje se posredstvom T stanica uništavaju mijelinske ovojnice. Posljedica su sve češći i sve lošiji simptomi bolesti i znakovi rasprostranjenih lezija u mozgu i leđnoj moždini (1). Određene kliničke manifestacije javljaju se i u orofacijalnoj regiji (2,3). Pacijenti s MS-om mogu imati biokemijske biljege u perifernoj krvi i cerebrospinalnom likvoru (CSF-u) te u slini (4,5). Ona sadržava prihvatljive uzorke za ispitivanje kemijskih promjena kod oboljelih od MS-a (6). Naime, za razliku od CSF-a, uzorci se mogu dobiti neinvazivno, jednostavno i uvijek ponovno (7).

Kalcij (Ca) i kalij (K) glavni su elektroliti u ljudskom tijelu. Razine kalcija u miješanoj slini iznose od 5,15 do 10,68 mg%. U usporedbi s parotidnim

### Introduction

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system characterized by T-cell mediated destruction of the myelin sheath. As a result, relapsing and remitting symptoms and signs with evidence of disseminated lesions in the brain and spinal cord were observed (1). Certain clinical manifestations affect also the oro-facial region (2,3). MS patients may display biochemical abnormalities in the peripheral blood, cerebrospinal fluid (CSF), and in saliva (4,5). Saliva offers attractive samples for the investigation of chemical changes in MS (6). That is because in contrast to CSF it can be gained noninvasively, easily and repeatedly (7).

Calcium (Ca) and potassium (K) are the main electrolytes in the human body. The calcium level

žlijezdama više razine nalaze se u slini submandibularnih žlijezda. Kalcij se u slini nalazi u koloidnoj otopini u obliku kalcijeva fosfata, djelomice u spoju s ugljičnim dioksidom. Kalcijeve soli mogu se također nalaziti u slini i sudjelovati u nastanku tvrdih zubnih naslaga (8). Pacijenti s parodontitisom imaju više razine kalcija nego zdravi ljudi (9).

Intracelularno, dakle u stanicama, nalazi se 98% ukupne količine kalija (4000 mmol), a samo 60 mmola je u izvanstaničnom fluidu. Prisutnost kalija u slini povezana je sa sekrecijom tekućine i regulacijom osmotskog tlaka. Glavna aktivna sekrecija kalijevih iona u slinu i reapsorpcija obavlja se u odvodnim kanalićima žlijezda slinovnica. Taj se proces nadzire mineralokortikoidima. Viša razina kalija u slini zabilježena je kod pacijenata s aktivnim karijesom te se smatra da je taj proces povezan s promjenama u razinama elektrolita u slini (K, Ca, Cl, Na), (10).

Svrha studije bila je odrediti koncentracije kalcija i kalija u slini pacijenata s multiplom sklerozom i usporediti ih s kontrolnom skupinom.

## Ispitanici i postupci

Ujutro su uzeti uzorci nestimulirane, miješane sline od 140 ispitanika (84 s multiplom sklerozom i 54 klinički zdravih) u dobi između 22 i 56 godina. Nakon toga slina je ohlađena i 15 minuta centrifugirana na 5000 rpma. Zatim su do početka analize uzorci bili pohranjeni u hladnjaku. Koncentracija kalcija bila je određena kolorimetrijski reagensom Chiron Diagnostic Calcium Reagent®. Koncentracija kalija izmjerena je Chironovim koanalizatorom 614, nakon što je slina četiri puta bila razrijeđena u redestiliranoj vodi.

Dobivene vrijednosti raščlanjene su statistički. Prikazani su: broj (n), raspon vrijednosti (min-maks.), aritmetička sredina (X), median (Me), standardna devijacija (SD) i varijanca (V%). Usporedba vrijednosti koncentracije kalcija između muških i ženskih sudionika u pokusu te oboljelih od MS-a i zdravih ispitanika, obavljena je usporedbom aritmetičkih sredina i korištenjem testova: t-Student (t), ANOVA (F) i U test. Zbog velike osobne varijabilnosti (V%>50,0) za razine kalija, utjecaja spola i multiple skleroze na ispitane parametre, rabljen je test Hi-kvadrat te uspoređen postotak slučajeva iznad i ispod medijana (Me). Uzeta je razina statističke znatnosti od  $p \leq 0,05$ .

in the mixed saliva is from 5,15 to 10,68 mg%. The higher level of Ca is observed in the saliva from submandibular glands comparing with parotid glands. Calcium in the saliva exists as a colloid form of calcium phosphate, partially in a complex with carbon dioxide. Calcium salts may precipitate in the saliva and form a tartar (8). Patients with periodontitis have higher level of Ca than healthy people (9).

98% of total amount of potassium (4000 mmol) is present in intracellular fluid and only 60 mmol in extracellular fluid. Potassium prevalence in the saliva is connected with the mechanism of fluid secretion and regulation of the osmotic pressure. The main active secretion of potassium ions into saliva and reabsorption of sodium ions take place in the ducts of the salivary glands. This process is controlled by mineralocorticoides. The higher level of saliva potassium is observed in patients with active caries. It can suggest that decay process is probably associated with changes of saliva electrolytes levels (K, Ca, Cl, Na) (10).

The aim of the study was an assessment of the concentration of calcium and potassium in the saliva of patients with multiple sclerosis and to correlate their levels with those of the control group.

## Material and Methods

140 people (84 multiple sclerosis and 54 adults clinically healthy) aged between 22 and 56 years, from whom samples of unstimulated, mixed saliva were taken in the morning. After that saliva was cooled and centrifuged during 15 minutes with 5000 rotations. Next, samples with diagnostic material were stored in the fridge until estimation. The calcium concentration was assessed by colorimetric method with a use of Chiron Diagnostic Calcium Reagent. Potassium level was estimated with a use of 614 Na/K Analyzer by Chiron after four times dilution of saliva sample in redistilled water.

The obtained laboratory data were statistically analyzed. The following was shown: number of examined persons (n), range of values (min-max), arithmetical mean (X), median (Me), standard deviation (SD) and variation coefficient (V%). The differences analysis of calcium levels between men and women and between MS and healthy people was performed with a comparison of arithmetical means by following tests: t-Student (t), ANOVA (F) and test U. Because of the big personal variation (V%>50,0) for the potassium levels, the influence of gender and multiple sclerosis on the examined parameter was checked by Chi-square test and

the percentage of cases with above or below median (Me) was compared. A value of  $p \leq 0,05$  was considered to be significant.

## Rezultati

Dobiveni rezultati koncentracija kalcija i kalija iz sline ispitanika prikazani su u Tablicama 1. i 2. te na Grafikonima 1. i 2.

## Results

The obtained results of the calcium and potassium concentration in saliva of examined persons are shown in tables 1-2 and on graphs 1-2.

**Tablica 1.** Koncentracija kalcija (Ca) u slini pacijenata s multiplom sklerozom i u kontrolnoj skupini (mmol/l).

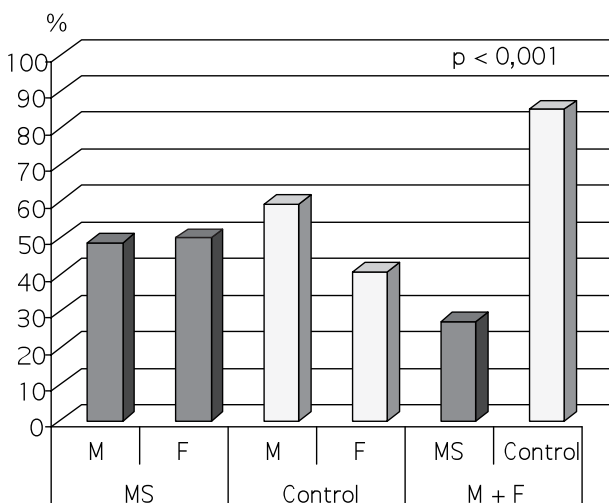
**Table 1** The calcium concentration (Ca) in saliva of patients with multiple sclerosis and in the control group (mmol/l).

Skupina • Group	Spol • Gender	Me	n	Br. ispitanika s Ca-om • No. of persons with Ca		% ispitanika s Ca > Me • % of persons with Ca > Me	Znatnost razlike • Significance of differences	
				< Me	> Me		$\chi^2$	p
MS	M	0,420	37	19	18	48,6	0,02	> 0,90
	Ž • F		48	24	24	50,0		
Kontrola • Control	M	0,935	27	11	16	59,3	1,85	> 0,17
	Ž • F		27	16	11	40,7		
MS	M + Ž • M + F	0,650	85	62	23	27,1	44,63	< 0,001
Kontrola • Control	M + F		54	8	46	85,2		

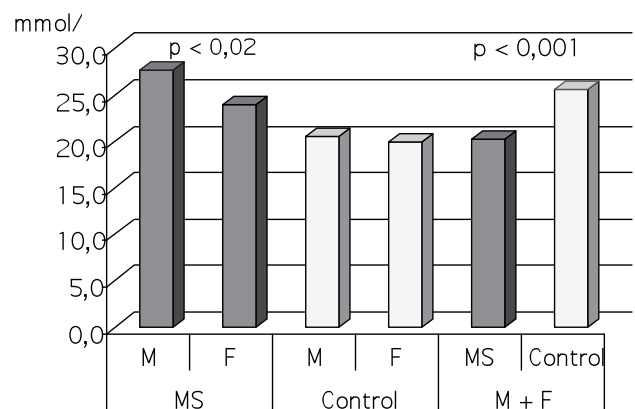
**Tablica 2.** Koncentracija kalija (K) u slini pacijenata s multiplom sklerozom i u kontrolnoj skupini (mmol/l).

**Table 2** The potassium concentration (K) in saliva of patients with multiple sclerosis and in the control group (mmol/l).

Skupina • Group	Spol • Gender	n	$\bar{X}$	SD	V %	Usporedbe • Comparisons			
						Razlika arit. sredina • Means' difference	T	p	
MS	M	38	27,66	7,82	28,3	+ 3,76	F	6,690	< 0,02
	Ž • F	48	23,90	5,67	23,7				
Kontrola • Control	M	27	20,48	4,41	21,5	+ 0,52	t	0,430	> 0,60
	Ž • F	27	19,96	4,45	22,3				
MS	M + Ž • M + F	86	25,56	6,92	27,1	+ 5,34	u	5,578	< 0,001
Kontrola • Control	M + F	54	20,22	4,40	21,8				



**Slika 1.** Postotak ispitanih osoba (s MS-om i zdravih) sa sadržajem iznad medijana  
**Figure 1** Percentage of examined persons (MS and healthy) with calcium contents above median.



**Slika 2.** Razine kalija u slini ispitanika s multiplom sklerozom (MS-om) i zdravih (kontrola).  
**Figure 2** The level of potassium in the saliva of patients with multiple sclerosis (MS) and healthy persons (Control).

Rezultati u Tablici 1. ne pokazuju statistički veliku razliku u koncentracijama kalcija između muških i ženskih ispitanika, ni kod oboljelih od MS-a ni u kontrolnoj skupini. Točno 48,6 % muškaraca i 50,00 % žena s multiplom sklerozom imali su razine kalcija iznad medijana ( $Me=0,42$  mmol/l) –  $p>0,90$ , kao i 59,3 % sudionika i 40,7 % sudionica iz kontrolne skupine ( $Me=0,935$  mmol/l). Razlika između oboljelih od MS-a i kontrolne skupine bila je statistički znatna - 27,1 % ispitanik s multiplom sklerozom i 85,2% iz kontrolne imali su koncentracije kalcija iznad 0,65 mmol/l ( $p<0,001$ ).

Srednja vrijednost kalija u slini oboljelih od MS-a bila je  $25,56 \pm 6,92$  mmol/l te  $20,22 \pm 4,40$  mmol/l u kontrolnoj skupini. Ta zabilježena razlika statistički je velika ( $p<0,001$ ). Skupina s pacijentima oboljelima od MS-a imala je više koncentracije kalija u slini nego oboljele pacijentice ( $p<0,02$ ). U kontrolnoj skupini muškarci su imali gotovo istu koncentraciju kalija u slini kao i žene ( $p>0,60$ ).

## Rasprava

U jednoj od hipoteza o etiologiji multiple skleroze ističe se pomanjkanje kalcija i vitamina D<sub>3</sub> povezano sa zemljopisnom lokacijom MS-a. U južnoj i zapadnoj Finskoj, u područjima sa smanjenom količinom kalcija u tlu, veća je incidencija MS-a (11,12). Yasui i Ota tvrde da kalcij ima glavnu zadaću u imunološkom sustavu, jer aktivira T limfocite. Uočili su manji sadržaj kalcija u bijeloj tvari pacijenata oboljelih od MS-a (13). Naime, manjak kalcija može se povezati s autoimunom bolešću kao što je MS (14,15). Kod pacijenata s astmom – dakle, drugačijom autoimunom bolesti - finski znanstvenici su također uočili manji sadržaj kalcija u slini (16). I u ovoj studiji istaknuta je niža razina kalcija u slini pacijenata s multiplom sklerozom u usporedbi s kontrolnom skupinom. Razlika je statistički jako velika. Elektroliti u žlijezdama slinovnicama, poput kalija, odgovorni su za lučenje i regulaciju osmotskog tlaka. Količina kalija u slini uvijek je viša od njegove koncentracije u krvi (17). U ovoj studiji ispitanici s multiplom sklerozom imali su više kalija u slini nego oni iz kontrolne skupine. Prema mišljenju Traczyka, veća količina kalija u izvanstaničnoj tekućini, što je i slina, može uzrokovati manjak živčane podražljivosti (18). Zbog oštećenja mijelinske ovojnice kod multiple skleroze, često su spori impulsi koji stimuliraju optički živac, mozak i leđnu moždinu (1).

The results presented in Table 1 didn't show significant differences in Ca concentration between men and women, both in MS and control group. 48,6% of men and 50,0% of women with multiple sclerosis had calcium values above median ( $Me = 0,42$  mmol/l) –  $p>0,90$  and 59,3% of men and 40,7% of women from the control group ( $Me = 0,935$  mmol/l). But there were observed highly significant differences between MS and control group. 27,1% of patients with multiple sclerosis and 85,2% of healthy persons had the calcium concentration above 0,65 mmol/l ( $p<0,001$ ).

The mean level of potassium in saliva of MS patients was  $25,56 \pm 6,92$  mmol/l, and  $20,22 \pm 4,40$  mmol/l in the control group. The observed difference was statistically highly significant ( $p<0,001$ ). MS group of men had higher potassium concentration in saliva than women with MS –  $p<0,02$ . In the control group men had almost the same level of potassium in saliva like women ( $p>0,60$ ).

## Discussion

One of hypothesis of the etiology of multiple sclerosis tells about role of lack of calcium and Vitamin D<sub>3</sub> which is connected with a geographical location of MS. In southern and western Finland, where the presence of calcium in soil is decreased, the frequency of MS incidence is increased (11,12). According to Yasui and Ota, calcium plays a pivotal role in an immunological system activating lymphocytes T. They observed the lowered calcium content in white matter of patients with multiple sclerosis (13). The lack of calcium can be associated with an autoimmune disease which MS is (14,15). In patients with asthma, a different autoimmune disease, the Finnish researchers noticed the reduced calcium saliva concentration, too (16). In my study I observed the lower level of calcium in the saliva of patients with multiple sclerosis compared with a control group. The difference was highly statistically significant.

Electrolyte like potassium present in the salivary glands is responsible for fluid secretion and regulation of osmotic pressure. The saliva concentration of potassium is always higher than its blood concentration (17). In the conducted study patients with multiple sclerosis had higher level of saliva potassium than people from the control group. According to Traczyk, the increase of potassium in an extracellular fluid which saliva is, can cause the lack of nervous excitability (18). Because of a damage of myelin sheet in multiple sclerosis, the slowness of impulses stimulation in optic nerve, brain and spinal cord (1) is often observed.

**Zaključci**

- Promjene elektrolita u slini uočene kod pacijenata s multiplom sklerozom:
  - razine kalcija u slini ispitanika s MS-om znatno su niže od kontrolne skupine sa zdravim ljudima;
  - razine kalija u slini ispitanika s MS-om mnogo su više nego u kontrolnoj skupini sa zdravim ljudima.
- Zabilježeni poremećaji kod elektrolita mogu se povezati s neurološkim i imunološkim promjenama svojstvenima multiploj sklerozi.

**Conclusions**

- Electrolytes changes in saliva were noticed in patients with multiple sclerosis:
  - Calcium levels in the saliva of MS patients were statistically lower than in healthy persons.
  - Potassium saliva concentrations of MS patients were statistically higher than in the control group.
- The observed electrolytes disorders can be associated with the neurological and immunological disturbances which are characteristic for multiple sclerosis.

**Abstract**

**Objective:** The aim of the study was an assessment of the calcium and potassium saliva concentration in patients with multiple sclerosis. **Material and Methods:** 86 patients with multiple sclerosis and 54 healthy persons were examined. Saliva levels of calcium and potassium were estimated with the use of the colorimetric method. The obtained data were statistically analyzed using t-Student and Chi-square tests. **Results:** Calcium levels in the saliva of MS patients were statistically lower than in healthy persons. Potassium saliva concentrations of MS patients were statistically higher than in the control group. **Conclusion:** The observed electrolytes disorders can be associated with the neurological and immunological disturbances which are characteristic for multiple sclerosis.

Received: October 12, 2008

Accepted: February 10, 2009

**Address for correspondence**

Dr n. med. Renata Chalas  
Department of Conservative Dentistry  
Medical University of Lublin  
7 Karmelicka Street  
20-081 Lublin, Poland  
Tel: 0 048 81 528 79 20  
renata.chalas@gmail.com

**Key words**

Multiple Sclerosis; Calcium; Potassium;  
Saliva; Water-Electrolyte

**References**

- Tourbah A, Clapin A, Gout O, Fontaine B, Liblau R, Batteux F, et al. Systemic autoimmune features and multiple sclerosis: a 5-year follow-up study. *Arch Neurol.* 1998;55(4):517-21.
- Kovac Z, Uhač I, Buković D, Cabov T, Kovacević D, Grzić R. Oral health status and temporomandibular disorders in multiple sclerosis patients. *Coll Antropol.* 2005;29(2):441-4.
- Hefti AF, Eshenaur AE, Hassell TM, Stone C. Gingival overgrowth in cyclosporine A treated multiple sclerosis patients. *J Periodontol.* 1994;65(8):744-9.
- Craelius W. Comparative epidemiology of multiple sclerosis and dental caries. *J Epidemiol Community Health.* 1978;32(3):155-65.
- van de Beek MT, Taal W, Veldkamp RF, Vecht CJ. A woman with multiple sclerosis and pink saliva. *Lancet Neurol.* 2003;2(4):254-5.
- Minagar A, Adamashvili I, Kelley RE, Gonzalez-Toledo E, McLarty J, Smith SJ. Saliva soluble HLA as a potential marker of response to interferon-beta 1a in multiple sclerosis: a preliminary study. *J Neuroinflammation.* 2007;4:16.
- Fischer HP, Eich W, Russell IJ. A possible role for saliva as a diagnostic fluid in patients with chronic pain. *Semin Arthritis Rheum.* 1998;27(6):348-59.
- Shaw L, Murray JJ, Burchell CK, Best JS. Calcium and phosphorus content of plaque and saliva in relation to dental caries. *Caries Res.* 1983;17(6):543-8.
- Sewón L, Mäkelä M. A study of the possible correlation of high salivary calcium levels with periodontal and dental conditions in young adults. *Arch Oral Biol.* 1990;35 Suppl:211S-212S.
- Halperin ML, Kamel KS. Potassium. *Lancet.* 1998;352(9122):135-40.
- Bauer HJ. Concluding remarks in multiple sclerosis in Europe: an epidemiological update. Darmstadt: Leuchtturm - Verlag/ LTV Press; 1993. p. 340-2.
- Lauer K. Multiple sclerosis in the Old World: the new old map. In: Firnhaber W, Lauer K, editors. Multiple sclerosis in Europe: an epidemiological update. Darmstadt: Leuchtturm - Verlag/ LTV Press; 1993. p. 14-27.
- Yasui M, Ota K. Experimental and clinical studies on dysregulation of magnesium metabolism and the aetiopathogenesis of multiple sclerosis. *Magnes Res.* 1992;5(4):295-302.
- Liblau RS, Fontaine B. Recent advances in immunology in multiple sclerosis. *Curr Opin Neurol.* 1998;11(4):293-8.
- Podojil JR, Miller SD. Cross-linking of CD80 on CD4+ T cells activates a calcium-dependent signaling pathway. *J Immunol.* 2009;182(2):766-73.
- Lenander-Lumikari M, Laurikainen K, Kuusisto P, Vilja P. Stimulated salivary flow rate and composition in asthmatic and non-asthmatic adults. *Arch Oral Biol.* 1998;43(2):151-6.
- Schenkels LC, Veerman EC, Nieuw Amerongen AV. Biochemical composition of human saliva in relation to other mucosal fluids. *Crit Rev Oral Biol Med.* 1995;6(2):161-75.
- Traczyk WZ. *Fizjologia człowieka w zarysie.* Warszawa: PZWL; 1989.