STOMATOLOGY EDU JOURNAL
stomaeduj
A WORLD OF EDUCATIONAL RESOURCES FOR EACH PRACTICE

SMOKING AND RECURRENT APHTHOUS STOMATITIS

Radmila Radisa Obradović[1a*], Marija LJ Igic[2a], Aleksandar D Mitic[3a], Ana S Pejcic[1a], Kosta M Todorovic[4b], Zana Popovic[5c]

[1]Department of Periodontology and Oral Medicine, Faculty of Medicine, Niš University, Serbia
[2]Department of Children and Preventive Dentistry, Faculty of Medicine, Niš University, Serbia
[3]Department of Dental Pathology and Endodontics, Faculty of Medicine, Niš University, Serbia
[4]Department of Oral Surgery, Faculty of Medicine, Niš University, Serbia
[5]Department of Dentistry, Faculty of Medical Sciences, Kragujevac University, Serbia

[a]DDS, PhD, Professor
[b]DDS, Assistant
[c]DDS, Postdoctoral Student

ABSTRACT **DOI: https://doi.org/10.25241/stomaeduj.2019.6(4).art.3**

Introduction: Recurrent aphthous stomatitis (RAS) is one of the most usual inflammatory diseases of the oral mucosa. The clinical characteristics of RAS are well defined, but the exact etiology and pathogenesis of the disease are not. Several investigations have noticed cigarette smoking to have a protective effect on RAS. The aim of the study is to investigate the association between cigarette smoking and RAS in order to improve the current knowledge on this issue.
Methodology: 68 patients with RAS participated in the study. A full mouth clinical examination was performed and a medical history was taken for each patient. Data were analyzed with χ^2 test.
Results: While 6 (8.9%) of patients with RAS were smokers, a significantly higher percentage (24.9%) among the subjects with RAS were not smokers (group II) ($\chi 2 = 70.4$; d.f. = 2, $P < 0.001$).
Conclusion: The negative association between smoking and RAS indicated by this investigation is not meant to encourage people to smoke nor to spare them from the intention to quit their habit. These conclusions should be used to clear up the cause and pathogenesis of the RAS and to identify better prevention and treatment.
Keywords: Oral Medicine; Aphthae; Recurrent Aphthous Stomatitis; Mouth; Smoking.

Peer-Reviewed Article

Citation: Obradović RR, Igic M, Mitic A, Pejcic A, Todorovic K, Popovic Z. Smoking and recurrent aphthous stomatitis. Stoma Edu J. 2019;6(4):237-240

Received: July 08, 2019
Revised: October 25, 2019
Accepted: October 28, 2019
Published: December 16, 2019

***Corresponding author:**
Professor Radmila Radisa Obradović, DDS, PhD
Department of Periodontology and Oral Medicine, Faculty of Medicine, Niš University 81, Dr Zoran Djindjic Blvd, 18000 Niš, Serbia
Tel: +381-64-235-9595,
Fax: +381-18-42-38-770,
e-mail: dr.rada@yahoo.com

1. Introduction

Recurrent aphthous stomatitis (RAS) is a very common disease of the oral mucosa. It is called minor aphthous ulcers, herpetiform ulcers, aphthosis and many other names. Aphthous ulcers can occur alone or as part of a syndrome [1]. RAS occurs only in non-keratinized mucosa as painful, shallow round ulcers with an erythematous halo covered by a membranous layer. The clinical ulcerative period for minor aphthous ulcers may last for 2 weeks and lesions usually heal without a scar [2]. The clinical characteristics of RAS are well known, but the exact etiology and patho-genesis of the disease are not complete. The etiology of RAS includes stress, microorganisms, food hyper-sensitivity, immune dysregulation, hormonal fac-tors and a genetic predisposition, usage of the toothpaste with sodium lauryl sulfate (SLS) [1,2]. Current investigations have focused on a possible immunopathogenesis of RAS [2,3]. The epithelial cell death and the creation of ulceration probably results from the activation of a cell-mediated immune response in which Tumor Necrosis Factor Alpha (TNFα) and other cytokines are produced [3]. Inheritance of HLA-B51 antigen, vitamin B12 deficiency, recurrent herpes labialis, Helicobacter pylori, hepatitis C and hypersensitivity to nickel are involved in the development of RAS [4,5]. It is necessary to better understand the pathogenesis and primary cause of RAS [2]. Previously, it is thought that approximately 0.89% of the adults over 17 years of age have at least one aphthous lesion and that males (1.13%) have almost twice the RAS than females (0.67%). It is noticed that reported prevalence of RAS varies according to patient selection, presence of lesions at the time of investigation or during a specified period and newer literature data show that the RAS prevalence is between 5 and 60%, depending on the population group studied [2].

It is estimated that tobacco use is the major cause of more than 5 million deaths every year [6]. Smoking is a common risk factor in a number of chronic diseases like lung diseases, cancer, cardiovascular diseases; and a major risk factor in the prevalence of

Table 1. Relationship between RAS and smoking.

	RAS	(no RAS or RAS history)	Total
Smoking (group I)	6 (8.9%)	68 (91.9%)	74
Nonsmoking (group II)	62 (24.9%)	202 (76.5%)	264
Total	68 (20.1%)	270 (79.9%)	338

periodontal diseases [6-10]. Cigarette smoke contains approximately 4800 chemicals, with over 60 of them known to have 3 damaging effects on human cells [11]. Cigarette smoking could camouflage signs of periodontal disease like gingival bleeding or redness, by suppressing the immune response which could cause a problem in the diagnosis of the disease. Several studies have noticed cigarette smoking to have a protective effect on RAS [12-15]. It is not clear how cigarette smoking can reduce RAS prevalence but it is thought that immunological mechanisms are involved and that the cytokine (TNF) plays an important role in the pathogenesis. Nicotine has been shown to influence the immune response in inflammatory conditions [16,17]. It acts through the central nervous system inducing the production of glucocorticoids and activating the autonomic nervous system and consequently reducing the level of inflammation [16]. Nicotine can activate the nicotinic acetylcholine receptors on macrophages and reduce the production of TNF1and interleukins [17].

2. The aim of the study

The aim of the study is to investigate the association between cigarette smoking and RAS in order to increase current knowledge on this issue.

3. Methodology

The study was conducted on 338 patients who came at the Department of Oral Medicine and Periodontology of the Dental Clinic of Faculty of Medicine, Niš University, for one year. The Ethics Committee of the Faculty of Medicine Niš approved the study protocol (evidential number 01-2800-7). After the medical history was taken, the patients who had undergone antibiotic and corticosteroid therapy in the last three months, were not included in the study. A full mouth clinical examination was performed and the patients with active aphthous lesions and who per medical history had suffered from oral ulcers at least once within a period of 5 months were considered to suffer from RAS. The patients with other oral diseases who came at the Dental Clinic of the Medical Faculty Niš for other medical reasons were also included in this study. Out of 338 examined patients, 68 patients had RAS and 270 had no RAS or RAS history. Patients who smoked over 10 cigarettes per day (per medical history) were considered to be "smokers" and they constituted group I (74 patients). The nonsmoking patients constituted group II (264 patients).

4. Results

There were 68 participants with RAS, out of which 31 (46.92%) were men and 37 (53.1%) were women. The average age was 29.7± 8.8 years. 66 (97.1%) had the minor type of the disease, 2 (2.9%) had both minor and major RAS.

The relationship between RAS and smoking is shown in Table 1. While 6 (8.9%) of patients with RAS were active smokers (group I), a significantly higher percentage (24.9%) among the subjects with RAS were not smokers (group II) ($\chi 2 = 70.4$; d. f. = 2, $P < 0.001$).

5. Discussion

Smoking is a known risk factor in a number of chronic diseases and major risk factor of periodontal disease [2-6]. Cigarette smoking suppresses the immune host response, masks early signs of periodontal disease and has as reported by some authors a beneficial protective effect on RAS. It has also been noticed that the incidence of RAS is higher among young individuals and that adults younger than 40 years of age have more than twice higher RAS rate than those older than 40 years [12-15]. We noticed similar results in our study where the average age of the patients with RAS was 29.7±8.8 years. It could be suspected that stress could be an aphthae provoking factor. Previously, lifestyle could induce stress and social conditions and self-management are important determinants of health. The effects of living exposed to many stress factors may cause poorer health and more frequent occurrence of RAS [18,19]. Literature data reveal a significant reduction of RAS in individuals who smoke. The prevalence and odds ratios for number of cigarettes smoked is significant and suggest a dose response effect [14,15]. A reduction in RAS prevalence with higher blood levels of nicotine is found to be significant [20]. Our study noticed a similar situation. where 8.9% of patients with RAS were active smokers and a significantly higher percentage (24.9%) among the subjects with RAS were not smokers (group II) ($\chi 2 = 70.4$; d. f. = 2, $P < 0.001$). Kalpana [13] noticed that significant differences exist in the prevalence of RAS among cigarette smokers, which could be related to the number of cigarettes smoked per day and the duration of the habit. The "protective effect"

on RAS was noticed only when the persons were heavy smokers or had smoked for longer periods of time. Cigarette non-smokers have far greater odds of RAS than individuals who smoked >1 pack per day. It was concluded that the associations of RAS with cigarette smoking and with cotinine levels were significant. Our study noticed similar results, namely that a higher number of individuals with RAS were nonsmokers (24.9%). RAS is characterized by recurrences of short-lived lesions. The lesions are not always noticed at the time of examination and the diagnosis is often based on the patient's clinical history. The statistical evaluation of RAS is hampered because lesions cannot be evaluated by the investigator at any time and is usually based on a self-reported history of RAS. Such a diagnosis is less reliable that one based upon the observation of present lesions by a practitioner. It is to be noticed that many of the studies which found a negative correlation between RAS and smoking were based on a self-reported history of RAS [21]. Information should be carefully interpreted, especially where there is some basis to suspect response bias. The findings in this study were based on anamnesis and clinical examination conducted by an experienced practitioner and provide data on the general prevalence of RAS in smokers. There is a small number of studies in which patients were diagnosed by direct detection of present lesions by a practitioner. Queiroz et al [22] evaluated 4895 cases of recurrent aphthous ulcerations with a focus on treatment, diagnosis and etiology. Data such as sex, age, race, location, smoking habits, types of treatment, relapsing episodes, laboratory test results and clinical characteristics were collected. Regarding smoking habits, in the majority of 59 patients (77.6%) smoking was not recorded. The investigators did not consider the percentages of smoking notifications because they are influenced by a bias of selection of the sample. Other researchers have found a lower incidence of RAS in smokers on the basis of the disease history but not by direct detection of present lesions by a practitioner [12-14]. A similar negative correlation between smoking and RAS was noticed in our study. The treatment and, many times, the diagnosis of RAS are a challenge in the daily life of the clinician. Dental professionals and otorhinolaryngologists are usually responsible for the first contact with the patients who have RAS. These professionals should be alert to the clinical aspects of this condition since each patient will be treated in an individualized manner, because treatment is usually palliative and not curative.

6. Conclusion

On the basis of the aim of the study, its applied methodology and the results obtained it can be concluded that the incidence of RAS is higher among young individuals and among subjects who do not smoke. The negative association between smoking and RAS in our study is not indeed meant to encourage people to smoke nor to sway them in the decision to quit their habit. Smoking cessation is the main option to remove the harmful tobacco effects on oral tissues and to improve the quality of life.

Author Contributions

All authors (RO, MI, AM, AP, KT, and ZP) contributed in data collection and analysis, and manuscript writing. All authors agree to be accountable for the content of the work.

Acknowledgment

This research was supported by a grant from the Internal project number 11, Medical Faculty, University of Niš, Niš, Serbia.

References

1. Cui RZ, Bruce AJ, Rogers RS. Recurrent aphthous stomatitis. *Clin Dermatol.* 2016;34(4):475-481.
2. Edgar NR, Saleh D, Miller RA. Recurrent aphthous stomatitis: a review. *J Clin Aesthetic Dermatol. 2017*;10(3):26-36.
Scopus
3. Manthiram K, Lapidus S, Edwards K. Unraveling the pathogenesis of periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis through genetic, immunologic, and microbiologic discoveries: an update. *Curr Opinion Rheumatol.* 2017;29(5):493-499.
[Full text links] [CrossRef] [PubMed] Google Scholar Scopus
4. Najafi S, Mohammadzadeh M, Zare Bidoki A, et al. HLA-DRB and HLA-DQB allele and haplotype frequencies in Iranian patients with recurrent aphthous stomatitis. *Iran J Allergy Asthma Immunol.* 15(4):289-295.
[Full text links] [PubMed] Google Scholar Scopus
5. Kuo YS, Chang JYF, Wang YP, et al. Significantly higher frequencies of hemoglobin, iron, vitamin B12, and folic acid deficiencies and of hyperhomocysteinemia in patients with Behcet's disease. *J Formos Med Assoc.* 2018;117(10):932-938.
[Full text links] [CrossRef] [PubMed] Google Scholar Scopus
6. *Britton J. Death, disease and tobacco*. Lancet 2017;389(10082): 1861-1862.
[Full text links] [CrossRef] [PubMed] Google Scholar
7. Holde GE, Baker SR, Jönson B. Periodontitis and quality of life: What is the role of socioeconomic status, sense of coherence, dental service use and oral health practices? An exploratory theory-guided analysis on a Norweigan population. *J Clin Periodontol.* 2018;45(7):768-779.
[CrossRef] Google Scholar
8. Waziry R, Jawad M, Ballout RA, AlAkel M, Akl EA. The effects of waterpipe tobacco smoking on health outcomes: an updated systematic review and meta-analysis. *Int J Epidemiol.* 2017;46(1): 32-43.
[Full text links] [CrossRef] [PubMed] Google Scholar Scopus
9. Chaffee BW, Couch ET, Ryder MI. The tobacco-using periodontal patient: role of the dental practitioner in tobacco cessation and periodontal disease management. *Periodontol 2000.* 2016;71(1): 52-64.
[Full text links] [Free PMC Article] [CrossRef] [PubMed] Google Scholar Scopus
10. Mahmud SZ, Amin MS. Association between tobacco consumption and periodontal diseases among type 2 diabetes mellitus patients. *Saudi J Oral Sci.* 2016;3:90-96.
[CrossRef] Google Scholar
11. Jeong M, Noar SM, Zhang D, et al. Public understanding of cigarette smoke chemicals: Longitudional study of US adults and adolescents. *Nicotine Tob Res.* 2019;pii:ntz035
[Full text links] [CrossRef] [PubMed] Google Scholar

12. Peruzzo DC, Gimenes JH, Taiete T, et al. Impact of smoking on experimental gingivitis. A clinical, microbiological and immunological prospective study. *J Periodontal Res.* 2016;51(6):800-811.
[Full text links] [CrossRef] [PubMed] Google Scholar Scopus
13. Kalpana R. Relation between smoking and recurrent aphthous stomatitis. *Oral Maxillofac Pathol J.* 2016;7(2):761-762.
Google Scholar
14. Oliveira MJ, Coimbra F, Mesquita P, Carvalho J, Pereira-Lopes O. Characterization of recurrent aphthous stomatitis in a young population. *Rev Port Estomatol Med Dent Cir Maxilofac.* 2018;59(1):10-17.
Scopus
15. Souza PRM, Doquia RP, Breunig JA, Almeida JRHL. Recurrent aphthous stomatitis in 18-year-old adolescents - Prevalence and associated factors: a population-based study. *An Bras Dermatol.* 2017;92(5):626-629.
[Full text links] [Free PMC Article] [CrossRef] [PubMed] Google Scholar Scopus
16. Rothbard JB, Rothbard JJ, Soares L, Fathman G, steinman L. Identification of a common immune regulatory pathaway induced by small heat shock proteins, amyloid fibrils, and nicotine. *PNAS* 2018;115(27):7081-7086.
[Full text links] [Free PMC Article] [CrossRef] [PubMed] Google Scholar
17. Hosseinzadeh A, Thompson PR, Segal BH, Urban CF. Nicotine induces neutrophil extracellular traps. *JLB* 2016;100(5):1105-1112.
[Full text links] [CrossRef] [PubMed] Google Scholar Scopus
18. Chaudry A, Wimer C. Poverty is not just an indicator: The relationship between income, poverty, and child well-being. *Acad Pediatr.* 2016;16(3):23-29.
[CrossRef] Google Scholar Scopus
19. Ismayilova L, Karimli L, Sanson J, et al. Improving mental health among ultra-poor children: Two-year outcomes of a cluster-randomized trial in Burkina Faso. *Soc Sci Med.* 2018; 208:180-189.
[Full text links] [CrossRef] [PubMed] Google Scholar Scopus
20. Zakaria M, El-Meshad A. Clinical efficacy of nicotine replacement therapy in the treatment of minor recurrent aphthous stomatitis. *J Arab Society Medical Res.* 2018;13(2):106-112.
[CrossRef] Google Scholar
21. Namrata M, Abilasha R. Recurrent aphthous stomatitis. *Int J Orofacial Biol.* 2017;1(2):43-47.
22. Queiroz SIML, Silva MVA, Medeiros AMC, et al. Reccurrent aphthous ulceration: an epidemiological study of etiological factors, treatment and differential diagnosis. *An Bras Dermatol.* 2018;93(3):341-346.
[Full text links] [Free PMC Article] [CrossRef] [PubMed] Google Scholar

Radmila Radisa OBRADOVIĆ
DDS, PhD, Professor
Department of Oral Medicine and Periodontology
Dental Clinic
Faculty of Medicine
Niš University
Niš, Serbia

CV

Doctor Radmila Radisa Obradović is a Professor at the Department of Oral Medicine and Periodontology, Dental Clinic, Faculty of Medicine, Niš University and at the Department of Oral Medicine and Periodontology, Faculty of Medical Sciences, Kragujevac, Serbia. She is also a member of the Niš Dental Clinic's Ethical Committee, Serbian Medical Society, Serbian Anthropological Society and Serbian Oral Laser Society (SOLAS).
She participates in national projects, and delivers many dental courses and conferences as a lecturer.
She has many scientific publications in international and Serbian medical and dental journals.

Questions

1. Recurrent aphthous stomatitis (RAS) is very common disease of the oral mucosa. It is called:

❑a. Minor aphthous ulcers;
❑b. Herpetiform ulcers;
❑c. Simple aphthosis;
❑d. All of the above answers are correct.

2. Cigarette smoking could influence signs of periodontal disease like:

❑a. Provoking bleeding;
❑b. Provoking gingival redness;
❑c. Camouflage gingival bleeding or redness;
❑d. Provoking gingival swelling.

3. The etiology of RAS includes:

❑a. Stress and immune dysregulation;
❑b. Microorganisms and food hypersensitivity;
❑c. Hormonal factors and a genetic predisposition;
❑d. All of the above answers are correct.

4. The patients were divided into:

❑a. Two groups: smokers and nonsmoking patients;
❑b. Three groups: smokers, nonsmoking patients and patients with RAS;
❑c. Two groups: smokers and patients with RAS;
❑d. Two groups: nonsmoking patients and patients with RAS.