Int J Clin Exp Med 2015;8(4):6218-6223
www.ijcem.com /ISSN:1940-5901/IJCEM0005958

Original Article

Risk factors of recurrent aphthous ulceration among university students

LiuxiaShi[1*], Kuan Wan[2*], Mengmeng Tan[2], Guifang Yin[2], Mengkai Ge[2], Xiaoqian Rao[2], Lianping He[2], Yuelong Jin[2], Yingshui Yao[2]

[1]School of Stomatology, Wannan Medical College, Wuhu, Anhui 241002, China; [2]School of Public Health, Wannan Medical College, Wuhu, Anhui, 241002, China. [*]Equal contributors.

Received January 15, 2015; Accepted March 24, 2015; Epub April 15, 2015; Published April 30, 2015

Abstract: Recurrent aphthous ulceration (RAU) is a common oral mucosal disease. The etiological involves in genetics, vitamin deficiencies, trauma, immune dysfunction and stress. This study was to explore the related risk factors of recurrent aphthous ulceration (RAU) among college students, and provide basis for further research. We conducted a questionnaire survey among students from three colleges in Wuhu by stratified cluster sampling. The information collected includes general demographic characteristics, dietary habits and so on. The overall prevalence of RAU is 23.30% among college students (23.23% in male and 23.39% in female). There are statistical significance in prevalence of RAU between subjects with RAU and without RAU ($P<0.05$) the prevalence of RAU in different grade, age, adequate brushing time, good brushing habits, wear dentures or braces, other oral disease, eat barbecue, adequate exercise time is statistic difference. According to the result of multinomial logistic regression analysis, the risk of recurrent aphthous ulceration factors including grade, inadequate brushing time. Tempering was a protective factor of RAU. Some measure should be taken to control dental ulcer, which consist of promoting a correct way of living habits, paying attention to the health conscious diet, strengthen physical exercise, self-decompression and keeping good mentality.

Keywords: Recurrent aphthous ulceration, college students, influence factor

Introduction

Recurrent aphthous stomatitis (RAS) is character of chronic, inflammatory, ulcerative diseases of the oral mucosa [1, 2]. The prevalence of oral ulcers in worldwide is about 4%, with aphthous ulcers being the most common, affecting about 25% of the population worldwide [3]. Based on the clinical features, recurrent aphthous ulceration divide into three type: minor aphthae (Mikulicz's aphthae; MiRAS), major aphthae (Sutton's aphthae; MaRAS) and herpetiform aphthae (HeRAS) [4]. A common oral mucosal disorder is characterized by multiple, recurrent, small, round, or ovoid ulcers with circumscribed margins, erythematous haloes, and yellow or grey floors that present first in childhood or adolescence [5]. RAS is capable of causing severely painful and may interfere with eating, speaking, and swallowing. Predilection sites include the ventral surface of the tongue, floor of the mouth, and buccal, labial, soft palatal, and or pharyngeal mucosa [1, 6]. Thus, RAS can result in significant morbidity and quality of life [7, 8]. Although RAS is the most common disease affecting the oral mucosa, the etiology and pathogenesis of RAS remain unknown. previous study found that some factors of RAU, such as local, trauma, microbial, systemic, nutritional, immunological, and genetic factors [6, 9, 10].

Therefore, the aim of the study is to explore the risk factors of RAU among college students.

Subjects and methods

Subjects

This cross section study is conducted among college students from Wuhu (China) in November, 2013. A questionnaire was conducted among students from three college by clus-

Table 1. Characteristics of study population

Variable	Male		Female		Total
	N	%	N	%	
Grade					
Freshman class	312	61.18	198	38.82	510
Sophomore	232	61.21	147	38.79	399
Junior	203	51.00	195	40.00	398
Senior	286	50.09	285	49.91	571
Age					
<20	342	55.25	277	44.75	619
20-22	574	55.14	467	44.86	1041
>22	117	59.09	81	40.91	198
RAU					
Yes	240	55.43	193	44.57	433
No	793	55.65	632	44.35	1425

ter sampling method. Before the survey, the investigator must determine whether the object description meet the criteria of RAU.

Include criteria: Based on clinical examination, students with suspected malignant ulcers were excluded from the study, which follow the WHO guidelines [11]. We divide the subjects into two groups: RAU group and non-RAU group. Recurrent oral ulcers questionnaire includes general demographic characteristics (age, gender, nationality, height, weight, etc.), behavior and dietary habits (smoking, drinking, genetics, diet, oral hygiene, types of fruits and vegetables intake and psychological factors).

Methods

In order to make students well understand the aim of the study, we introduce the purpose of the survey, requirements and considerations, as well as described the survey voluntary and confidential before the investigation. The questionnaires also are checked when we collect the data.

Quality control: Quality controller are arranged to answer investigators' questions on-site and responsible for collecting, reviewing the questionnaire. The questionnaires need to be returned to the investigators until the omissions and logic errors filling out completely or modifying correctly. Following the investigations, quality controller would sort out and unify all the questionnaires to data custodian.

Data collection and analysis: Establish a database for data entry by Epidata 3.0 software. Import the data to SPSS16 for data analysis. We describe the characteristics of study population. Relationships between general information and dependent variable RAU were assessed using multivariate logistic regression. Adjusted odds ratios (OR) and their 95% confidence intervals (CI) were calculated. A value of $P<0.05$ was considered statistically significant.

Ethical approval: This study is approved by local Ethical Committee. A written informed consent was obtained from the respondents.

Results

General demographic characteristics

This study enrolled 1858 subjects, including 1033 males and 825 females, their age was ranged from 16 to 26 years. The characteristics of study population are showed in **Table 1**.

Related factors

Of 1858 respondents, the overall prevalence of RAU is 23.30% (23.23% in male and 23.39% in female); the risk factors which may affect recurrent aphthous ulcers as following: grade, age, adequate brushing time, good brushing habits, wear dentures or braces, other oral diseases, eating barbecue, adequate exercise time, parental illness, physical symptoms, etc. The difference was statistically significant ($P<0.001$). Factors associated with recurrent aphthous ulcers analysis are showed in **Table 2**.

Multivariate logistic regression analysis

All relevant variables into multinomial logistic regression models are showed in **Table 3**. the results reveals that un-adequate brushing time and un-adequate exercise time students are more likely to suffer from RAU, OR (95% CI) values were 1.334 and 1.438, respectively; students whose parent with RAU have higher prevalence of recurrent aphthous ulceration than those of students whose both parents without RAU (OR=3.945; 95% CI=2.252, 6.908; OR=2.783; 95% CI=2.143, 3.615); Grade is a risk factor of RAU, the students from freshman year and third-year suffering lower recurrent

Table 2. The related factors of recurrent aphthous ulceration

Variable	Non-RAU Object		RAU Object		χ^2	*P*
	n	%	n	%		
Grade					20.007	<0.001
Freshman class	421	82.55	89	17.45		
Sophomore	289	76.25	90	23.75		
Junior	309	77.64	89	22.36		
Senior	406	71.10	165	28.90		
Age					6.770	0.034
<20	497	80.29	122	19.71		
20~22	781	75.02	260	24.98		
>22	147	74.24	51	25.76		
Adequate brushing time					8.034	0.005
No	524	73.18	192	26.82		
Yes	901	78.90	241	21.10		
Good brushing habits					4.245	0.039
On	719	78.75	194	21.25		
Yes	706	74.71	239	25.29		
Wear dentures or braces					4.109	0.043
On	1353	77.18	400	22.82		
Yes	72	68.57	33	31.43		
Other oral disease					5.849	0.016
On	1018	78.25	283	21.75		
Yes	407	73.07	150	26.93		
Eat barbecue					3.959	0.047
On	1347	77.19	398	22.81		
Yes	78	69.03	35	30.97		
Adequate exercise time					7.652	0.006
No	1092	75.26	359	24.74		
Yes	333	81.82	74	18.18		
The prevalence of Parents					85.785	<0.001
All	30	53.57	26	46.43		
One party	225	61.14	143	38.86		
All no	1170	81.59	264	18.41		
Physical symptoms					7.649	0.022
The heavier	18	75.00	6	25.00		
General	284	71.54	113	28.46		
Normal	1123	78.15	314	21.85		

aphthous ulceration than that of the four-year (OR=0.572; 95% CI=0.419, 0.782; OR=0.638; 95% CI=0.465, 0.875). After adjusted the gender and age, a statistically significant association also was observed.

Discussion

Recurrent aphthous ulcers represent a very common but poorly understood mucosal disorder, which occur in men and women of all ages, races and geographic regions [1].

Present study reveal that students whose parents suffer from RAU more more prone to RAU. Multivariate logistic regression analysis showed that genetic factors are risk factors of recurrent oral ulcers, which are similar to the findings of Koybasi et al. [12], family history was the most important factor for RAU among the investigated ones. Occur among sibling may be parents' RAU status [13] with increased risk in children of two affected parents (67-90%), and correlation between the incidence of RAU and identical twins was found [14].

The brushing time is a protective factor of RAU. Several studies demonstrated that microorganisms' including bacteria and viruses plays an important role in the development of RAU [15-17]. In addition, Helicobacter pylori has been detected in the dental plaque and saliva of healthy persons with gastric disease [18, 19]. Oral cavity may be an alternative reservoir for the organism. Thus, the way to inhibit the growth of helicobacter pylori infection is brushing teeth in correct way.

The studies demonstrate that un-exercise students are 1.466 times compare to those who do exercise usually, doing exercise was a protective factor of RAU. Physical exercise could improve the body's immune system, which has been recognized by the fact of the medical profession. Several studies show that the cytokines of human, including IL-2, IL-10, IL-12, IFN-γ, TNF-β, TGF-α, play an important role in the development of RAU [20-22]. The secretion of anti-inflammatory cytokines TGF-α IL-10 was significantly decreased in RAS patients compared to the healthy controls. Albanidou-Farmaki [23] found increasing of T lymphocytes can produce pro-

Table 3. Related factors of recurrent aphthous ulceration

Variable	Unadjusted OR (95% CI)		*P*	Adjusted OR[#] (95% CI)		*P*
Adequate brushing time						
No	1.334	(1.060, 1.680)	0.014	1.353	(1.073, 1.705)	0.011
Yes	1			1		
Adequate exercise time						
No	1.438	(1.072, 1.928)	0.015	1.466	(1.091, 1.970)	0.011
Yes	1			1		
Anxiety levels						
The heavier	0.419	(0.172, 1.022)	0.056	0.429	(0.176, 1.048)	0.063
General	0.892	(0.638, 1.247)	0.503	0.896	(0.640, 1.253)	0.520
Normal	1			1		
The prevalence of Parents						
All	3.945	(2.252, 6.908)	<0.001	3.922	(2.280, 6.922)	<0.001
One party	2.783	(2.143, 3.615)	<0.001	2.802	(2.125, 3.641)	<0.001
All no	1			1		
Grade						
Freshman Class	0.572	(0.419, 0.782)	<0.001	0.526	(0.346, 0.799)	0.003
Sophomore	0.781	(0.570, 1.070)	0.124	0.732	(0.509, 1.053)	0.093
Junior	0.638	(0.465, 0.875)	0.005	0.625	(0.451, 0.866)	0.005
Senior	1			1		

[#]Adjusted for gender, age.

inflammatory cytokines (IL-2, IL-12 and IFN-γ) and reduce IL-10-level in peripheral blood of the RAS patients in comparison to the healthy controls. Modern college students spend much time in the dormitory to play games and learn knowledge, and ignore the importance of exercise. Epidemiology study of sport find that the during time and frequent of the exercise failure to meet the reference of our national [24].

Meanwhile, the prevalence of RAU in grade one, grade three students is lower than that of the students from grade four. The possible reason is that with students from higher grade have more pressure for seeking job. An increasing number of studies suggest that anxiety, depression, and psychological stress are associated with symptoms of RAS [25-27]. Laura B, recorded 160 cases of patients with RAU daily stress of events through telephone follow-up [28], which find that stressful events may involved in initiation of new RAS episodes.

Conclusions

Genetic, brushing time, exercise, grades and other factors have an impact on the incidence of RAU. Thus, learn self-buck, maintain a good attitude, a positive and optimistic approach to life; focus on healthy eating, balanced diet nutrition; promote healthy living, good habits; long-term exercise can better reduce risk of RAU.

Acknowledgements

We grateful thank Yanjiao Fang and Zhengdong Dou from Centers for Disease Control and Prevention (Wuhu, China) for their help. This study was supported by Provincial Training Programs of Innovation and Entrepreneurship for Undergraduates (AH201310368116), Provincial Natural Science Research Project of Anhui Colleges (No. KJ2012B205).

Disclosure of conflict of interest

None.

Address correspondence to: Yuelong Jin and Yingshui Yao, School of Public Health, Wannan Medical College, No. 22 Road Wenchangxi, Yijiang District, Wuhu, Anhui, 241002, China. Tel: 86-553-3932031; E-mail: jinyl0803@163.com (YLJ); Tel: 86-553-3932651; Fax: +86-553-3932651; E-mail: yingshuiyao@163.com (YSY)

References

[1] Natah SS, Konttinen YT, Enattah NS, Ashammakhi N, Sharkey KA and Hayrinen-Immonen R. Recurrent aphthous ulcers today:

a review of the growing knowledge. Int J Oral Maxillofac Surg 2004; 33: 221-234.
[2] McCullough MJ, Abdel-Hafeth S and Scully C. Recurrent aphthous stomatitis revisited; clinical features, associations, and new association with infant feeding practices? J Oral Pathol Med 2007; 36: 615-620.
[3] Shulman JD, Beach MM and Rivera-Hidalgo F. The prevalence of oral mucosal lesions in U.S. adults: data from the Third National Health and Nutrition Examination Survey, 1988-1994. J Am Dent Assoc 2004; 135: 1279-1286.
[4] Wardhana and Datau EA. Recurrent aphthous stomatitis caused by food allergy. Acta Med Indones 2010; 42: 236-240.
[5] Jurge S, Kuffer R, Scully C and Porter SR. Mucosal disease series. Number VI. Recurrent aphthous stomatitis. Oral Dis 2006; 12: 1-21.
[6] Scully C and Porter S. Oral mucosal disease: recurrent aphthous stomatitis. Br J Oral Maxillofac Surg 2008; 46: 198-206.
[7] Tabolli S, Bergamo F, Alessandroni L, Di Pietro C, Sampogna F and Abeni D. Quality of life and psychological problems of patients with oral mucosal disease in dermatological practice. Dermatology 2009; 218: 314-320.
[8] Hapa A, Aksoy B, Polat M, Aslan U and Atakan N. Does recurrent aphthous stomatitis affect quality of life? A prospective study with 128 patients evaluating different treatment modalities. J Dermatolog Treat 2011; 22: 215-220.
[9] Ship JA, Chavez EM, Doerr PA, Henson BS and Sarmadi M. Recurrent aphthous stomatitis. Quintessence Int 2000; 31: 95-112.
[10] Jenerowicz D, Silny W, Danczak-Pazdrowska A, Polanska A, Osmola-Mankowska A and Olek-Hrab K. Environmental factors and allergic diseases. Ann Agric Environ Med 2012; 19: 475-481.
[11] Kramer IR, Pindborg JJ, Bezroukov V and Infirri JS. Guide to epidemiology and diagnosis of oral mucosal diseases and conditions. World Health Organization. Community Dent Oral Epidemiol 1980; 8: 1-26.
[12] Koybasi S, Parlak AH, Serin E, Yilmaz F and Serin D. Recurrent aphthous stomatitis: investigation of possible etiologic factors. Am J Otolaryngol 2006; 27: 229-232.
[13] Ship II. Epidemiologic aspects of recurrent aphthous ulcerations. Oral Surg Oral Med Oral Pathol 1972; 33: 400-406.
[14] Miller MF, Garfunkel AA, Ram C and Ship II. Inheritance patterns in recurrent aphthous ulcers: twin and pedigree data. Oral Surg Oral Med Oral Pathol 1977; 43: 886-891.
[15] Scully C and Porter S. Recurrent aphthous stomatitis: current concepts of etiology, pathogenesis and management. J Oral Pathol Med 1989; 18: 21-27.
[16] Scully C. Are viruses associated with aphthae and oral vesiculo-erosive disorders? Br J Oral Maxillofac Surg 1993; 31: 173-177.
[17] Cohen L. Etiology, pathogenesis and classification of aphthous stomatitis and Behcet's syndrome. J Oral Pathol 1978; 7: 347-352.
[18] El-Mekki A, Kumar A, Alknawy B, Al-Ammari O, Moosa R, Quli S and Ahmed M. Comparison of enzyme immunoassays detecting Helicobacter pylori specific IgG in serum and saliva with endoscopic and biopsy findings in patients with dyspepsia. Indian J Med Microbiol 2011; 29: 136-140.
[19] Jia CL, Jiang GS, Li CH and Li CR. Effect of dental plaque control on infection of Helicobacter pylori in gastric mucosa. J Periodontol 2009; 80: 1606-1609.
[20] Borra RC, Andrade PM, Silva ID, Morgun A, Weckx LL, Smirnova AS and Franco M. The Th1/Th2 immune-type response of the recurrent aphthous ulceration analyzed by cDNA microarray. J Oral Pathol Med 2004; 33: 140-146.
[21] Buno IJ, Huff JC, Weston WL, Cook DT and Brice SL. Elevated levels of interferon gamma, tumor necrosis factor alpha, interleukins 2, 4, and 5, but not interleukin 10, are present in recurrent aphthous stomatitis. Arch Dermatol 1998; 134: 827-831.
[22] Lewkowicz N, Kur B, Kurnatowska A, Tchorzewski H and Lewkowicz P. Expression of Th1/Th2/Th3/Th17-related genes in recurrent aphthous ulcers. Arch Immunol Ther Exp (Warsz) 2011; 59: 399-406.
[23] Albanidou-Farmaki E, Markopoulos AK, Kalogerakou F and Antoniades DZ. Detection, enumeration and characterization of T helper cells secreting type 1 and type 2 cytokines in patients with recurrent aphthous stomatitis. Tohoku J Exp Med 2007; 212: 101-105.
[24] Zhou CG. The investigation and analysis: Wuhu college students' sports present situation. Anhui Normal University (Natural Science) 2011; 34: 98-102.
[25] Gavic L, Cigic L, Biocina Lukenda D, Gruden V and Gruden Pokupec JS. The role of anxiety, depression, and psychological stress on the clinical status of recurrent aphthous stomatitis and oral lichen planus. J Oral Pathol Med 2014; 43: 410-417.
[26] Miller MF and Ship II. A retrospective study of the prevalence and incidence of recurrent aphthous ulcers in a professional population, 1958-1971. Oral Surg Oral Med Oral Pathol 1977; 43: 532-537.

[27] Ship II, Brightman VJ and Laster LL. The patient with recurrent aphthous ulcers and the patient with recurrent herpes labialis: a study of two population samples. J Am Dent Assoc 1967; 75: 645-654.
[28] Huling LB, Baccaglini L, Choquette L, Feinn RS and Lalla RV. Effect of stressful life events on the onset and duration of recurrent aphthous stomatitis. J Oral Pathol Med 2012; 41: 149-152.