Original Research

Risk factors associated with oral and maxillofacial benign tumors: A case-control study

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Abstract: This study aimed to investigate the risk factors for oral and maxillofacial benign tumors (OMFBTs). A total of 138 patients diagnosed with OMFBTs between September 2010 and September 2015 were retrospectively analyzed. Clinical data including demographic characteristics, smoking and drinking status, dietary habit, oral hygiene and tumor related family history were collected and compared with 134 cases of healthy people who visited the hospital for physical examination during the same time. Logistic regression analysis was performed for multivariable regression analysis. OMFBTs was associated with smoking more than 20 cigarettes per day, accumulated cigarette consumption more than 30, accumulated cigarette package consumption more than 1000, present smoking and drinking, passive smoking before 18 years old, initial smoking age more than 20 years old and alcohol consumption more than 50 g/d ($P < 0.05$). Consumption of meat, fish, seafood, fruits and vitamin tablets were associated with lower risk of OMFBTs. Non-conditional logistic regression analyses indicated that the independent risk factors of OMFBTs included accumulated cigarette consumption, passive smoking before the age of 18, meat-free, fish-free, fruit-free, vitamin tablets-free, frequency of tooth brushing lower than once a day, not routinely attending oral examination, wearing denture and drinking alcohol ($P < 0.05$). Smoking and drinking should be discouraged in dental patients. Keeping a good dietary habit and routinely attending oral examination are highly encouraged.

Key words: Oral and maxillofacial benign tumors; Risk factor; Case-control study.

Introduction

Oral and maxillofacial benign tumors (OMFBTs) mostly affect gums, oral cavity, maxillofacial regions. Benign tumors usually seen in clinic include ameloblastoma, pleomorphic adenoma, osteofibroma. An epidemiology study showed the incidence of OMFBTs was estimated at 0.4-12.4 persons per 100,000 persons[1]. In recent years, the incidence was noticed to be increased due to environmental pollution and diet changes. Treatment for OMFBTs may lead to changes in appearance, swallowing difficulty and language dysfunction because of the site of origin for these lesions. These obvious alterations may lower patients' self-esteem in social occasions, bring up inferiority, anxiety and other negative emotions, and even cause psychological malfunction, especially in younger ones. Thus, it is more important to reduce the possible risk factors for OMFBTs, to prevent the onset of the disease in an early stage, in order to lower the incidence rather than to narrow down the focus on treatment. By far, researches related to OMFBTs still concentrate on the surgical approach, while few has discussed the etiology of OMFBTs. This study was designed to analyze the risk factors of OMFBTs, in order to reduce the incidence in a long term.

Materials and Methods

Patients

A total of 138 patients diagnosed with OMFBTs between September 2010 and September 2015 were retrospectively analyzed, while 134 cases of healthy visitors to the hospital for physical examination at the same time were chosen as control. All participants were long-term residence of the study area. OMFBTs were diagnosed histopathologically. Exclusion criteria included oral and maxillofacial inflammation, malignant tumors, severe cases which cannot complete the study, etc. This study was approved by the Ethics Committee of Zhejiang Provincial Hospital of Traditional Chinese Medicine.

Clinical data collection

All subjects were given lifestyle questionnaire by well-trained investigators. The questionnaire was drawn on basis of a former example from one of the references[2], including general situation (such as age, gender, nationality, occupation, residence, education level, marital status, height, weight etc.), smoking and drinking history, diet habit, oral hygiene, cancer related family history. Smoking was defined if the subject had smoked more than 100 cigarettes. Accumulated cigarette consumption referred to a daily consumption of cigarettes × smoking years, and accumulated cigarette package consumption referred to a daily consumption of cigarette package × smoking years. Drinking (alcohol) was defined as a consumption of alcohol × alcohol content × 0.8 (density of alcohol).

Statistical analysis

SPSS 17.0 was used for statistical analysis. The t-test was applied to compare the difference of measurement data, and chi-square $\chi2$ test for categorical data. Non-conditional Logistic regression analysis was performed

for multivariable regression analysis. A *P* value< 0.05 indicated statistical significance.

Results

Demographic characteristics

No significant difference was found in age, occupation, gender, marital status, education level and residence between OMFBTs group and healthy control group (Table 1).

Association between smoking and drinking factors and OMFBTs

Risk factors for OMFBTs included smoking more than 20 cigarettes per day, accumulated cigarette

consumption more than 30, accumulated cigarette package consumption more than 1000, present smoking and drinking, passive smoking before 18 years old, initial smoking age more than 20 years old and alcohol consumption more than 50 g/d ($P<0.05$) (Table 2).

Association between dietary factors and OMFBTs

Long term regular consumption of meat, fish and seafood, fruit, vitamin tablets reduced the risk of OMFBTs ($p<0.05$).Poultry, green vegetables, dietary supplements seemed to have no influence ($p>0.05$) (Table 3).

Association between oral hygiene and OMFBTs

Oral hygiene-related risk factors associated with OMFBTs included not routinely attending oral ex-

Table 1. Demographic characteristics.

Characteristics		Control (n = 134)		OMFBTs (n = 138)		χ2	*P* value
		case	percentage	case	percentage		
Age	<35	34	25.37	37	26.81	0.843	> 0.05
	35-45	41	30.60	40	28.99		
	45-55	32	23.88	30	21.74		
	≥55	27	20.15	31	22.46		
Occupation	Farmer	51	38.06	55	39.86	0.674	> 0.05
	Labor	38	28.36	40	28.99		
	Others	45	33.58	43	31.15		
Gender	Male	71	52.99	73	52.90	0.962	> 0.05
	Female	63	47.01	65	47.10		
Marital status	Married	116	86.57	122	88.41	0.789	> 0.05
	Unmarried or others	18	13.43	16	11.59		
Education level	Illiteracy	57	42.54	60	43.48	0.841	> 0.05
	Below high school	43	32.09	41	29.71		
	High school or above	34	25.37	37	26.81		
Residence	Countryside	87	64.93	91	65.94	0.894	> 0.05
	City	47	35.07	47	34.06		

OMFBTs: Oral and maxillofacial benign tumors.

Table 2. Effects of smoking and drinking on the prevalence of OMFBTs.

Smoking and drinking		Control (n=134)		OMFBTs (n=138)		χ2	*P*value
		Case	Percentage	Case	Percentage		
Smoking	Yes	24	17.91	46	34.33	8.934	<0.05
	No	110	82.09	92	65.67		
Daily cigarettes consumption	None	110	82.09	92	66.67	10.146	<0.05
	≥20	5	3.73	34	24.63		
	<20	19	14.18	12	8.70		
Accumulated cigarette package consumption	None	110	82.09	92	66.67	12.341	<0.05
	≥30	7	5.22	37	26.81		
	<30	17	12.69	9	6.52		
Accumulated cigarette consumption	None	110	82.09	92	66.67	9.357	<0.05
	≥1000	6	4.48	39	28.26		
	<1000	18	13.43	7	5.07		
Passive smoking (before 18 years old)	Yes	39	29.10	59	42.75	7.825	<0.05
	No	95	70.90	79	57.25		
Drinking	Yes	29	21.64	57	41.30	8.793	<0.05
	No	105	78.36	817	58.70		
Initial drinking age	None	98	73.12	78	56.52	7.823	<0.05
	≥20	18	13.44	19	13.77		
	<20	18	13.44	41	29.71		
Alcohol consumption (g/d)	None	98	73.13	78	56.52	8.568	<0.05
	≥50	23	17.16	51	36.96		
	<50	13	9.71	9	6.52		

OMFBTs: Oral and maxillofacial benign tumors.

amination, starting wearing dentures at early age, low frequency of tooth brushing (<1 /d) (p<0.05).Sub-standard dental prostheses was not associated with OMFBT(p>0.05) (Table 4).

Multivariable logistic regression analysisof the risk factorsfor OMFBTs

Non-conditional logistic regression analyses indicated that the independent risk factors of OMFBTs included accumulated cigarette consumption, passive smoking before the age of 18, meat-free, fish-free, fruit-free, vitamin tablets-free, frequency of tooth brushing lower than once a day, not routinely attending oral examination, wearing denture and drinking alcohol (P <0.05) (Table 5).

Discussion

Our study demonstrated that the independent risk factors of OMFBTs included accumulated cigarette consumption, passive smoking before the age of 18, meat-free, fish-free, fruit-free, vitamin tablets-free, frequency of tooth brushing lower than once a day,

not routinely attending oral examination, wearing denture and drinking alcohol. This was consistent with the conclusion which has been reported in other studies(3-4). It indicated that the risk of OMFBTs is influenced by multiple factors, mainly related to smoking, drinking and other activity through the oral cavity.

It was reported that long-term smoking was associated with the onset of oral and pharyngeal cancer(5). The risk is proportional to the amount and length of smoking, which was also proven by our results. Cigarettes contain nicotine, carcinogenic nitrosamine, aromatic amines and other harmful substances, which may lead to mitochondrial DNA lesions, abnormal protein conformation, thus affect the chromosomes in the structure, function and gene expression. It was pointed out by a previous study that about 40%-50% patients in clinic with oral tumors were found mutated with p53 gene, the expression of which was positively correlated with the patient's smoking status(6). The mechanism is that benzene contained in cigarettes was a strong inducer in p53 gene mutation. Once it is inhaled into human body, activated broparoestrol is generated as final

Table 3. Effects of dietary factors on the prevalence of OMFBTs.

Dietary factors		Control (n = 134)		OMFBTs (n = 138)		χ^2	*P*value
		Case	Percentage	Case	Percentage		
Meat	None	26	19.40	66	47.83		
	<1 meal/d	33	24.63	38	27.54	8.985	< 0.05
	>1 meal/d	75	55.97	34	24.63		
Poultry	None	30	22.39	29	21.01		
	<1meal/d	30	22.39	48	34.78	0.121	> 0.05
	>1meal/d	74	55.22	61	44.20		
Fish and seafood	None	32	23.88	70	50.72		
	<1meal/d	35	26.12	28	20.29	9.582	< 0.05
	>1meal/d	67	50.00	40	28.99		
Green vegetables	None	58	43.28	64	46.38		
	<1meal/d	40	29.84	41	29.71	0.956	> 0.05
	>1meal/d	36	26.87	33	23.91		
Fruits	None	33	24.63	64	46.38		
	<1meal/d	35	26.12	32	23.19	9.235	< 0.05
	>1meal/d	66	49.25	42	30.43		
Dietary supplements	No	85	63.43	71	51.45	1.345	> 0.05
	Yes	49	36.57	67	48.55		
Vitamin tablets	No	44	32.84	81	58.70	9.682	< 0.05
	Yes	90	67.16	57	41.30		

OMFBTs: Oral and maxillofacial benign tumors.

Table 3. Effects of oral hygiene on the incidence of OMFBTs.

Oral hygiene		Control (n=134)		OMFBTs (n=138)		χ^2	*P*value
		Case	Percentage	Case	Percentage		
Frequency of oral examination	Never	41	30.60	71	51.45		
	less thanonce/5 year	61	45.52	21	15.22	8.356	<0.05
	more than once/5 year	32	23.88	46	33.33		
Age start wearing dentures	None	67	50.00	35	25.36		
	≥55 yrs	23	17.16	56	40.58	7.824	<0.05
	<55 yrs.	44	32.84	47	34.06		
Frequency of tooth brushing	≥1/d	81	60.45	49	35.51	8.672	<0.05
	<1/d	53	39.55	89	64.49		
Sub-standard dental prostheses	Yes	93	69.40	87	63.04	0.415	>0.05
	No	41	30.60	51	36.96		

product, leading to p53 gene mutation and neoplastic lesion. When the DNA repair mechanism cannot compensate the accumulated DNA damage caused by p53 mutation, carcinogenesis usually occurs(7). Alcohol is also one of the important risk factors in the pathogenesis of OMFBTs. Alcohol promotes the absorption of carcinogenic substances in the oral mucosa, resulting in molecular structure change. In addition, alcohol causes liver damage, leading to malfunction of carcinogen metabolism(8). It has been reported that long-term drinking caused oral and maxillofacial mucosa injury and rupture(9). Reiterative drinking further aggravates these mucosal thinning, swelling and erosion. Combined with mucosa burn caused by high temperature from smoking, the permeability of cell membrane is increased, leading to aggravation of external factors inducing tumorigenesis. Therefore, more damage is done to cell membrane, resulting in benign tumorigenesis.

A number of studies have confirmed large consumption of fruits, vitamin tablets, and green vegetables reduced the incidence of cancer. This conclusion also can be applied to oral and maxillofacial tumors. The mechanism may be due to the high concentration of protective antioxidants in these foods including carotene, vitamin C, vitamin E and dietary fiber, which neutralize the free radical damage caused by metabolites and external factors such as smoking and drinking(10). Meat, fish and seafood are rich in protein and calories, which increase the level of free radicals, lower plasma antioxidant concentrations and reduce oxide stress reaction. It is reported that a large intake of saturated fatty acid foods reduced the prevalence of OMFBTs . Epidemiology studies showed vitamin E, vitamin C, vitamin A, nicotinic acid, flavonoids, potassium and magnesium were all negatively correlated with OMFBTs(11).

Oral hygiene is one of the risk factors for OMFBTs, which has been clinically confirmed. Chronic stimulation developed ulcers in tongue, cheek, floor of mouth, gums and other oral sites, followed by tissue hyperplasia before the onset of OMFBTs eventually(12,13). OMFBTs mostly occur in middle-aged or senior people, who have experienced long-term chronic local tissue inflammation in oral cavity as they are at the age of needing repair for loose or missing teeth, or they do not care about oral cleaning enough. Ultimately, chronic inflammation induces oral tumorigenesis. One of the studies claimed that, the younger the initial age of wearing denture, the greater the risk of OMFBTs(14). Another study indicated that, long-term neglect in oral cleaning and examining was an independent risk factor for OMFBTs, which is in accordance with our results(15). This supports the idea that oral cleaning can lower the risk of OMFBTs.

In summary, smoking should be discouraged in dental patients. Reducing alcohol consumption, keeping a good dietary habit like regular consumption of fruit, meat, fish and vitamin tablets are recommended. Routinely attending oral examination, keeping oral hygiene and treating inflammation in an early stage are highly encouraged. Lowering these risk factors is quite helpful in lowering the risk of OMFBTs.

Conflict of interest
The authors have declared that no competing interests exist.

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