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Opium Usage as an Etiologic Factor of Oral Cavity Cancer

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Purposes: The aim of this study was to evaluate the role of opium in causing oral cancer.

Patients and Methods: Eighty patients and 80 selected matched controls who were referred to the ear-nose-throat department of an academic hospital were included in this study between October 2008 and September 2010. In addition to demographic data, information regarding alcohol, tobacco, and opium use was documented in the subjects. Finally, the effect of each risk factor was assessed.

Results: There was no significant difference in patient demographics between the 2 groups. Smoking ($P = 0.042$) and poor oral hygiene ($P = 0.016$) significantly correlated with cancer.

Finally, opium addiction showed a significant relationship with oral cavity cancer with an odds ratio of 4 (95% confidence interval, 1.2–13.6).

Conclusion: Opium use is among the possible risk factors for oral cancer.

Key Words: Oral cancer, opium, epidemiology, risk factor, addiction, smoking, head and neck cancer

Oral cancer is one of the most common head and neck malignancies.^{1,2} Moreover, the site of involvement may enable physicians to detect them in early stages, which would significantly lower morbidity. On the other hand, identifying and eliminating risk factors significantly affects development. In an attempt to identify the risk factors of oral cancer, researchers have found that smoking

and alcohol consumption are the most notorious factors.^{1–9} However, oral cancer, like similar cancers, has multifactorial etiology.¹ Genetic factors and tobacco chewing also play an important role.^{1,2,4,6,7,10,11} These factors work together additively or synergistically.

Despite, the relatively well-documented risk factors, there are other less established risk factors involved in the pathophysiology carcinogenicity of the oral cavity cancer, like the human papilloma virus, dental and oral diseases, diet, and nutrition.¹ Accordingly, the effect of opium usage, as a probable etiologic factor, is still a debatable topic. Although oral cancer is rather prevalent in different parts of the world, there is great variation in different geographical locations.¹ The effect of opium consumption on inducing some cancers, such as laryngeal or esophageal cancer, has been assessed by some researchers.^{11,12} The development of oral cancer in opium users is a notable theory.¹³ Opium addiction is a concerning issue in the Iranian society. We assess the role of opium in causing oral cancer.

MATERIALS AND METHODS

Study Subjects

The study subjects were selected among 80 consecutive patients who were referred to the ear-nose-throat department of an academic hospital (Imam Khomeini Hospital Complex) between October 2008 and September 2010. All patients' condition was diagnosed as squamous cell carcinoma of the oral cavity as the primary disease. Moreover, all pathology specimens were evaluated by the same pathologist. Additionally, 80 similar age- and sex-matched subjects with the same socioeconomic status were selected among normal individuals in the same period. Most of them belonged to patients' families. The protocol of this study was approved by the institutional review board of the Tehran University of Medical Sciences. Detailed information about the study was given to the participants, and a written informed consent was obtained from each one. All aspects of the study were conducted according to the Declaration of Helsinki.

Subjects' Variables

In addition to demographic data, information regarding personal and family history of head and neck cancer, use of dentures, and immune deficiency were recorded. Furthermore, individuals were categorized according to use of alcohol, tobacco, and opium; and the history and amount of using tobacco and alcohol were recorded. Opium dependency was defined for one who was opium dependent for at least 5 years. The duration of opium use was documented. Data collection was conducted with the same method under the supervision of the senior author, using face-to-face interview.

Statistical Method

Data were analyzed using SPSS 11.5 for Windows (SPSS Inc, Chicago, IL); χ^2 test was used to evaluate ratios and t test was used to compare mean values. Multiple logistic regressions and the Fisher exact test were also used. Values were evaluated using descriptive statistical methods (mean \pm SD), and results were significant if $P < 0.05$.

RESULTS

During the study period, 80 patients with a diagnosis of oral cancer and 80 healthy subjects were selected. The characteristics of the 2 groups are summarized in Table 1. Among the subjects who consumed alcohol, all were social drinkers (none were alcoholics) and they predominantly drank wine and beer. Additionally, there were no reports of human papilloma virus infection in the patients or the controls. The site distribution of the oral tumor is depicted in

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TABLE 1. Characteristics of Patients and Controls

| Variable | Case | Control | P |
|--|---------------------|---------------------|-----------------------|
| Age, yr | 58.2 ± 16.2 | 58.4 ± 16.3 | t test (0.99) |
| Sex (male/female) | 51/29 (63.8%/36.2%) | 50/30 (62.5%/37.5%) | χ ² (0.87) |
| Family history of head and neck cancer | 2 (2.5%) | 1 (1.3%) | Fisher (0.5) |
| Alcohol consumption | 3 (3.8%) | 2 (2.5%) | χ ² (0.63) |
| Education (>12 yrs) | 28 (35%) | 25 (31.2%) | χ ² (0.32) |
| Immune deficiency | 3 (3.7%) | 5 (6.2%) | χ ² (0.33) |

Figure 1. We could not find any significant relationships between the site of involvement and evaluated risk factors. Another evaluated factor was the history of smoking, and, as Table 2 shows, there was a significant difference in this regard between the patients and the controls (χ², P = 0.042) The mean number of smoked cigarettes per day was 11.2 ± 2 in the patients and 7.3 ± 2.7 in the controls, which showed a significant difference (t test, P = 0.002). Furthermore, the mean duration of smoking was 27 ± 12 years in the patients and 26 ± 13 year in the controls (t test, P = 0.858). Moreover, poor oral hygiene, as another probable causative factor, was seen in 49 patients (70%) and 40 (50%) controls, showing a significant difference (χ², P = 0.016). Ultimately, the ratio of opium consumption in the patients and the controls is summarized in Figure 2. As Figure 2 shows, there was a significant difference in the ratio of opium consumption with an odds ratio of 4 (95% confidence interval, 1.2–13.6). However, the duration of abuse was not significantly different between the 2 groups. All participants in both groups stated that the traditional way of opium usage (water pipe) was their predominant way of use. Additionally, for better evaluation of the independent role of opium, logistic regression of the variables was performed, which showed significant relationships, as shown in Table 3. Moreover, the logistic regression was repeated by using the pack-year instead of the history of smoking itself, and there was still a significant relationship between smoking, opium abuse, and the development of oral cancer (Table 4).

DISCUSSION

The etiology of oral cancer remains elusive despite the efforts of many researchers over the years. Among different factors, opium consumption in drug abusers is an attractive theory.¹⁴ To investigate

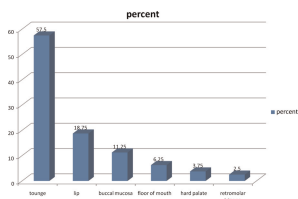


FIGURE 1. The site distribution of oral cavity cancer.

TABLE 2. History of Smoking in Patients and Controls

| Groups | Never Smoked | Smoker | Quit Smoking |
|----------|--------------|------------|--------------|
| Patients | 59 (73.8%) | 15 (18.8%) | 6 (7.4%) |
| Control | 63 (78.8%) | 17 (21.2%) | 0 (0%) |

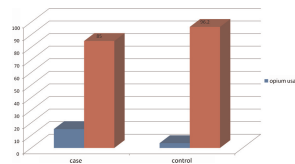


FIGURE 2. Opium usage in patients and controls.

TABLE 3. Relationship Between Risk Factors and the Development of Oral Cavity Cancer

| Variable | Standard Coefficient | T | P |
|----------|----------------------|-------|--------|
| Age | -0.003 | 0.039 | 0.969 |
| Sex | 0.061 | 0.673 | 0.502 |
| Alcohol | -0.014 | 0.162 | 0.871 |
| Smoking | -0.061 | 0.662 | 0.009* |
| Opium | -0.150 | 1.69 | 0.043* |

*Significant.

this theory further, 80 patients and 80 controls were selected for this study. The distribution of oral cancers in various subunits in our patients was similar to other studies; for example, the tongue was the most common site of involvement in this series. Cigarette smoking, like other series,^{1,3,6,15} was the most effective carcinogen in this study; however, the duration of consumption did not show a significant difference, maybe due to the long duration of smoking in most patients and normal subjects. Moreover, we evaluated chronic irritation caused by dentures as another risk factor of oral cancer. Similar to other studies, it was found to have a significant relationship with this type of cancer.⁸ On the contrary,^{4,16,17} tobacco chewing was not reported by any of the patients or the controls in this series since it is not a common habit in Iran. Alcohol consumption showed no significant relationship with cancer in our patients. The possible explanation for this contradictory finding¹ is that its consumption is not as common in Iran as it is in other countries because of religious beliefs. Opium usage was significantly correlated with oral cancer, and this effect was independent of the confounding factors with an odds ratio of 4 (95% confidence interval, 1.2–13.6); it can be considered as a possible cancer risk factor. The proposed mechanism of the carcinogenicity of opium is exposure to residues from the opium pipe.^{11,18} Moreover, the other possible mechanism of carcinogenicity is reduction in the first pass clearance of nitrosodimethylamine by the liver, which can substantially increase carcinoma rate in animal studies.¹¹ Malaveille et al¹⁹ evaluated the opium carcinogenicity as promutagens, producing frame shift mutations after activation in metabolism. Opium addiction is a social

TABLE 4. Relationship Between Risk Factors (Pack-Year) and the Development of Oral Cavity Cancer

| Variable | Standard Coefficient | T | P |
|----------|----------------------|--------|--------|
| Age | -0.003 | -0.039 | 0.969 |
| Sex | 0.061 | -0.673 | 0.50 |
| Alcohol | -0.014 | -1.045 | 0.87 |
| Tobacco | -0.061 | -0.662 | 0.026* |
| Opium | -0.150 | -1.69 | 0.043* |

*Significant.

problem in Iran, and several studies that have evaluated its role in head and neck cancers have proposed that it plays a role in inducing esophageal and laryngeal cancers.^{12,18}

CONCLUSIONS

Appropriate precaution measures should be taken to reduce addiction rate in such societies as Iran, as an effective action to diminish social and health problems. Although the exact mechanism of opium carcinogenicity is unclear, it should be considered a risk factor of oral cavity cancers. However, further research is warranted to elucidate better this relationship and the mechanism of opium carcinogenicity.

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Cervical Necrotizing Fasciitis Resulting in Acupuncture and Herbal Injection for Submental Lipoplasty

Hwan Jun Choi, MD, PhD

Abstract: Acupuncture is used for some conditions as an alternative to medication or surgical intervention. Several complications had been reported, and they are generally due to physical injury by the needle or transmission of diseases. Necrotizing fasciitis is an uncommon infection, but potentially lethal, especially when associated with systemic disorders such as diabetes. The authors report a case of serious cervical necrotizing fasciitis that developed after acupuncture and herbal injection treatment of fat accumulation of the submental area in a 32-year-old healthy woman. She presented with discharging wound over the submental area. The initial diagnosis was based on clinical information, in which localized necrosis areas in the cervical and chin regions were observed. Wide antibiotic therapy was applied, followed by surgical drainage, debridement, and negative pressure wound therapy. Culture was positive for *Serratia liquefaciens* and *Staphylococcus intermedius*. She made a good recovery.

Key Words: Acupuncture, complication, necrotizing fasciitis, wound infection, trauma

Acupuncture is an important alternative medical treatment that has been used in China and other Asian countries for thousands of years to treat a variety of diseases and symptoms, most commonly for chronic pain. Although most acupuncturists consider the procedure to be noninvasive, many complications, including physical injuries due to acupuncture needles, and problems related to wounds or systemic infections have been reported.¹ These included physical injuries due to the acupuncture needles and problems related to wound or systemic infection.² Necrotizing fasciitis (NF) is a life-threatening infection involving the fascia and subcutaneous tissue.² The authors report a case where this condition developed in a patient who had acupuncture and herbal treatment of fat accumulation of the chin.

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