Expert Consensus on the Detection and Screening of Oral Cancer and Precancer

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Oral cancer is an aggressive disease with a high incidence in both males and females in Asia and ranks as the first of all malignancies in India. The relatively high prevalence rate of oral cancer in Asia is mainly due to the fact that a high percentage of the population are smokers or chew betel nut. They comprised the so-called ‘high risk population’ of oral cancer. Meanwhile, epidemiological surveys showed a much lower 5-year survival rate in patients with advanced TNM stage III and IV oral cancer than those in the earlier stage I and II disease after treatment. Therefore, it is important to identify and treat precancerous lesions and oral cancer at early stages. In this article, we describe the expert consensus contributed by outstanding clinicians and scientists at the 11th Asian Congress of Oral & Maxillofacial Surgery (ACOMS) and we highlight the importance of oral cancer screening by various conventional and novel methods based on scientific research.

Key words: Asia, betel nut, oral cancer, screening, smoking

Oral cancer is the fifth most common cancer in the world, accounting for 412,000 new cases and 262,000 deaths annually since 1985, four-fifths of what occurred in the developing regions. In South Asia, oral cancer ranks as the first amongst all types of cancers in males and the third in females¹,². Oral cancer is associated with chronic irritating factors such as tobacco, smoking, alcohol and betel quid (BQ) use. While cigarette smoking and alcohol drinking are major risk factors in Western countries, betel quid use and smoking are major aetiologic factors of oral cancer in South Asia, Southeast Asia and Taiwan¹-³. Unfortunately, a higher rate of incidence of oral cancer and a higher mortality rate have been shown to correlate with the increasing prevalence rate of betel chewing in this area. For hundreds of years, betel chewing in Asia has been generally accepted as a social custom or behaviour. Previous epidemiological studies reported that the incidence of oral squamous cell carcinoma (OSCC) in BQ users and smokers was more than 100 times higher than the general population³,⁴. There is abundant literature clarifying the roles of ingredients of BQ-related carcinogenesis. It is generally agreed that BQ can potentially damage the oral mucosa to induce genotoxic or non-genotoxic effects, which may further contribute to initiation, promotion and progression of oral cancer. Various ingredients in BQ, including areca nuts, nitroso-derivatives, arecoline, safrole, lime and so on, have been extensively studied and linked to carcinogenic effects, co-carcinogenic effects and tumour promotion³,⁵-¹⁰.

In addition to oral cancer, other betel quid-associated diseases in the oral cavity such as mucositis, submucous fibrosis, severe tooth attrition and periodontitis have been difficult to manage, which has presented a great challenge for the general healthcare system. Currently,
in developing countries, more than 50% of oral cancer patients are diagnosed as stage III or IV during their first visit to a healthcare facility. Unfortunately, the overall 5-year survival rate of these patients will be poor despite recent advances in surgery, radiotherapy and chemotherapy. Furthermore, the cost of treatment in stage III or IV cases is far more than the cost of treatment in stage I or II cases. In the 11th Asian Congress of Oral & Maxillofacial Surgery (ACOMS) in Xi’an, China (Aug 22 to 25, 2014), an expert consensus on the detection and screening of oral cancer and precancer was conducted by outstanding clinicians and scientists from Asia and the United States. It was unanimously agreed that an efficient detection and screening programme allows the correct diagnosis of lesions at the pre-cancer stage or in early stages of oral cancer. Proper treatment can then be given to these patients to increase their survival. The Xi’an consensus highlights the importance of oral cancer and pre-cancer screening by various conventional and novel methods based on scientific research. This article reviews the related literature and discussions, which were addressed at the consensus meeting.

Screening the high risk population

Oral cancer is curable if it can be diagnosed and treated early enough. Amongst human cancers, oral cancer is one of few with a vast potential for early detection. Given the lack of successful strategies for oral cancer prevention so far, the priority should be focused on screening. The feasibility of oral cancer screening is largely based on the fact that the oral cavity can be easily accessed visually. Various programmes or policies have been supported by a number of governmental agencies worldwide for detecting oral cancer in the past decade. To cope with this, funding from these governmental agencies have been distributed to various organisations and healthcare professionals such as general health auxiliaries in the public first-line health care institute, dentists and ENT professionals such as general health auxiliaries in the public first-line health care institute, dentists and ENT professionals such as general health auxiliaries in the public first-line health care institute, dentists and ENT professionals such as general health auxiliaries in the public first-line health care institute, dentists and ENT professionals such as general health auxiliaries in the public first-line health care institute, dentists and ENT professionals such as general health auxiliaries in the public first-line health care institute, dentists and ENT professionals such as general health auxiliaries in the public first-line health care institute, dentists and ENT professionals. Therefore, other professions or specialties should also be included in the screening programme. Nevertheless, screening for oral cancer can be a simple and non-invasive procedure, which can be integrated into

Malignant transformation of precancerous lesions

Attention should specifically be focused on patients with precancerous lesions. Although the potential of malignant transformation for patients with erythroplakia is higher than patients with leukoplakia, oral leukoplakia is far more common. Some of the patients are idiopathic while the others exhibited habits such as smoking tobacco, drinking alcohol or using BQ. About 80% of patients with leukoplakias are in fact at low risk of developing OSCC with no evidence of dysplasia in the lesions, whereas others may eventually transform into OSCC. Unfortunately, there is currently no histological or alternative means which can reliably predict which leukoplakia is indeed premalignant. Overall the rate of malignant transformation of oral leukoplakia is about 3% to 6% over 10 years, although much higher rates have been reported, which is largely dependent on the populations surveyed and the rigour of follow-up care performed. Medical management of leukoplakia includes reducing or quitting habits related to risk factors, increasing the intake of fruit and vegetables in the diet, lesion removal and possibly the use of active agents. Retinoids, carotenoids and topical cytotoxic agents have been tried to treat oral leukoplakia and to prevent OSCC development with limited success. Newer therapies developed from frontier and novel research are still on the horizon.

Roles of healthcare workers

Healthcare workers or auxiliaries need to clearly understand their roles in cancer screening. One may argue that oral cancer screening is not necessary because routine dental examinations already include a full oral mucosa examination. However, apart from the fact that more than 50% of the adult population do not visit a dentist annually in many developing countries, there is evidence which suggests that many oral cancer cases are missed by healthcare professionals including dental practitioners. Many reasons may contribute to this outcome including the inability to recognise early lesions, the innocuous appearance of the lesions or lesions without morphological changes before the development of invasive cancers, plus a lack of experience from clinicians. Therefore, other professions or specialties should also be included in the screening programme.
advocate the use of an alternative method for screening, by collecting exfoliated cells through tissue scraping. However, exfoliated cell cytology in the screening for oral cancer has never achieved the same success as it has for diagnosing cancer of the uterine cervix. Oral exfoliated cell cytology enjoyed much attention in the 1960s, eventually falling out of favour, due largely to the subjective nature of its interpretation. Yet the application of quantitative and immunocytochemical techniques has, to some extent, refined its potential role. However, the absence of a validated marker, present in all malignant lesions but never seen in benign lesions, limits its clinical utility. The other drawback of exfoliated cell cytology for screening oral cancer is that the location of cancerous lesions may be difficult to identify, and to allow biopsy and pathological confirmation. Technical problems may also be easily encountered in cases with field cancerisation in the BQ chewers. Saliva being secreted from the major or minor salivary glands without cellular content was considered to have no value for cancer detection. However, saliva containing the exfoliated cells from scraping or natural exfoliation combined with cytospin may improve its value in oral cancer detection. Utilising cytospin preparation from the saliva may potentially increase the collected cellular content for analysis. However, unlike alpha-fetoprotein (AFP) for hepatoma, protein specific antigen (PSA) for the prostate or specific biomarkers for other cancers, no specific marker, which has received universal acceptance from the scientific community, are available for the detection of oral cancer. It may well be accepted that a more scientific and efficient way of oral exfoliated cell cytology might offer greater success, based on the understanding of the molecular mechanism and characteristics of cancer development. The future role for oral exfoliated cell cytology – bleak or bright – remains to be determined.

Mechanisms of oral cancer formation

Analogous to a well-established colorectal carcinoma model, oral cancer is also considered to be a multi-hit process involving a number of aberrant genetic and epigenetic events culminating during the tumorigenic process. It is well known that following the action of various carcinogens (chemical, physical, biological) on normal cells, a long period (latency) of several months to years (10 months to 30 years) in humans occur between the development of precancerous cells and their transformation into cancer cells. However, the molecular and biological events that take place within the precancerous cells during this quiescent stage are not yet fully understand-
New markers and tools for oral cancer detection

Over the past four decades, given that the 5-year survival rate has not improved for oral cancer patients, we believe the research priorities should explore the mechanism to find out new approaches for early diagnosis and novel therapy. With improved understanding of the underlying molecular features and biology in oral tumorigenesis, new biomarkers and molecular targets for oral cancer have been identified in the last decade. Significant momentum has been devoted to the exploration in Ras oncoproteins, p53, p16 tumour suppressor genes, abnormal expression of other genes such as cyclin-D1, retinoic acid nuclear receptors, telomerase, and more. These effects act on DNA, RNA and protein synthesis, as well as on cell replication, cell cycles, cell surfaces and intercellular communications. Therefore, these abnormal DNA, oncogenes or tumour suppressor genes, and ultrastructural intracellular or cell surface antigenic determinants as potential biomarkers are essential for the early detection of preneoplastic cells and cancer cells. Although, a universal tumour marker might still be lacking, a combination of several markers may be useful and more accurate than ever. In particular, the last 20 years has seen a shift in diagnostic methods from the histopathological to the molecular level. It is expected that oral exfoliated cell cytology may not only assume a greater role by providing samples of DNA for genetic analysis but also can provide a useful tool for screening.

References


