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ORAL SQUAMOUS CELL CARCINOMA –AN UPDATE WITH REVIEW

Dental Science

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ABSTRACT

Oral and oropharyngeal cancer grouped together, forms the sixth most common cancer in the world.It constitutes approximately 5% of all cancers globally, with 60,000 new cases of oral cancer is reported every year in India. Oral cancer is a multifactorial disease, but tobacco is regarded as the most important attribute for its development. It canbe preventable by the intervention of risk factors. Its early detection can minimize its detrimental effects and can improve the quality of life of the patient. Various studies have revealed that there is a lack of awareness about oral cancer, its signs and symptoms among the general population across the globe.

KEYWORDS

Oral cancer, squamous cell carcinoma, treatment

Oral squamous cell carcinoma (OSCC) is the most common malignancy of the oral cavity. The rate of mortality and 5-year survival of patients with OSCC has not been improved markedly even though several diagnostic and therapeutic advances over the last decades occur. Oral squamous cell carcinoma (OSCC) comprises 94% of all malignant neoplasms of the oral cavity . In India, Oral squamous cell carcinoma (OSCC) ranks

among the top three cancers and worldwide it is the eighth most common cancer.

Squamous cell carcinoma is defined as a "malignant epithelial neoplasm exhibiting squamous differentiation as characterized byt he formation of keratin and/or the presence of intercellular bridges."[1-4]

OSCC is more common in age group of the sixth and the seventh decades of life and more commonly seen in male patients. The tongue, lip, and floor of the mouth are the most frequently affected sites of OSCC.[5]

OSCC has various clinical presentations such as exophytic, endophytic, leukoplakic and erythroplakic, which all of them show visible changes in the surface. Usually oral carcinomas are preceded by a preinvasive stage, that may last for many years. The majority of the initial alterations of precancerous and cancerous oral lesions are not readily recognizable, on clinical or histopathological examination. The basic biology of initiation and progression of these tumors is still obscure.[6-8]

Epidemiology

The incidence and mortality of oral squamous cell carcinoma (OSCC) is increasing, with approximately incidence and mortality of 6.6/100,000 and 3.1/100,000 in men and 2.9/100,000 and 1.4/100,000 in women, respectively. For the development of oral cancer tobacco and alcohol are the two most important known risk factors. Other factors which also contribute in occurrence of OSCC include dietary factors, immunodeficiency and viral infections like HPV16/18.[8-10]

Risk factors for oral cancer

These are intra-oral carcinogens, which may play a synergistic role in oral tumorigenesis. If people can avoid alcohol and tobacco, it has been estimated, that 75% of all oral cancers are preventable. Use of tobacco in various forms, consumption of alcohol, low socioeconomic condition related to poor hygiene, poor diet and rampant viral infections play a major role in higher incidence of carcinoma of the head-neck in relation to other malignancies in India .[8,.11,12]

Etiology[13-22]

(1) Betel and similar habits: In the betel quid, there are variety of ingredients, like betel vine leaf, betel (areca) nut, catechu, and, often, slaked lime together with tobacco. Some persons chew the betel nut only, and others prefer paan, which includes tobacco and sometimes lime and catechu. Betel quid chewing is an important risk factor, and the areca (betel) nut habit with or without tobacco use can cause cytogenetic changes in oral epithelium. Tobacco chewing, particularly when it is started early in life and is used frequently and for prolonged periods may predispose a person for OSSC. Studies from India have confirmed the paan tobacco chewing may leads to OSCC of the buccal and labial mucosa.

(2) Cigarette smoking: The risk of oral cancer in persons who smoke low/medium-tar cigarettes and high-tar cigarettes has high risk of developing oral cancer than the persons do not smoke.

(3) Alcoholic beverages may contain carcinogens or procarcinogens, including nitrosamine and urethane contaminants and ethanol. A frequency of 2–4 times greater of squamous carcinoma in smokers has been observed, and the risk is rising up to 6–15 times in association with chronic alcoholism

(4) Infective agents: Infective agents like *Candida albicans* and viruses, such as herpes viruses and papilloma viruses, may play a key role in incidence of OSCC.

(5) Diet: In persons who consume beta-carotene-rich vegetables and citric fruits, a significant protective effect against oral cancer have been reported.

(6) Others: associations also are apparent between oral cancer and other various oral conditions (e.g., oral submucous fibrosis, oral lichen planus, lupus erythematosus, dyskeratosis congenita, and Fanconi anemia). Epidemiological studies showed a high risk for this disease for the families with a history of head and neck cancers.

Diagnostic Aids for OSSC[23-26]

Noninvasive Diagnostic Aids

(1) Toluidine blue.
(2) Oral brush biopsy.
(3) Light-based detection systems: optical biopsy.
(a)Chemiluminescence(ViziLitePlus; Microlux/ DL, Orascoptic-DK).
(b)Tissue fluorescence imaging (VELscope).
(c) Tissue fluorescence spectroscopy.
(4). Saliva-based oral cancer diagnosis
(5) Biomarkers:
(a) DNA-analysis.
(6) Laser capture microdissection.

Invasive Diagnostic Aid

1. Surgical Biopsy.

The staging of OSCC, which is based on the TNM system, has been used for several years to estimate both the clinical response to therapy and survival outcome. The histopathological grading of OSCC is based on the proportion of the neoplasm resembling normal squamous epithelium and the amount of keratin production. Lesion are classified into three distinct grades of well, moderately, and poorly differentiated.[27]

TNM classification of carcinomas of the lip and oral cavity)[28]
T—Primary Tumour

TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma in situ
T1	Tumour 2 cm or less in greatest dimension
T2	Tumour more than 2 cm but not more than 4 cm in greatest dimension
T3	Tumour more than 4 cm in greatest dimension
T4a (oral cavity)	Tumour invades through cortical bone, into deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), maxillary sinus, or skin of face
T4b (oral cavity)	Tumour invades masticator space, pterygoid plates, or skull base or encases internal carotid artery

N—Regional Lymph Nodes

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension
N2	Metastasis as specified in N2a, 2b, 2c below
N2a	Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension
N2b	Metastasis in multiple ipsilateral lymph nodes, none more than 6cm in greatest dimension
N2c	Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
N3	Metastasis in a lymph node more than 6 cm in greatest dimension

M—Distant Metastasis

MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

Stage grouping

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T1, T2, T3	N1 N0, N1	M0 M0
Stage IVA	T1, T2, T3 T4a	N2 N0, N1, N2	M0 M0
Stage IVB	Any T	N3	M0
Stage IVC	Any T	Any N	M1

Treatment of Oral Cancer
Surgery and Neck Dissection[29-32]

The most common treatment modality for oral cancer is surgery. The aim of surgery is to completely remove cancerous tissue, leaving behind histologically normal tissue. Larger tumors often require an approach from outside the oral cavity and the removal of both soft tissue and bone. Surgical removal of involve the lymph nodes may be required in more advanced oral cancers. Positive lymph node involvement might necessitate a radical neck dissection. Elective neck dissections are undertaken when the lymph nodes are negative in order to prevent the risk of metastasis. The level of neck dissection depends on the number, size, and site of the lymph nodes involved. The efforts to minimize extensive surgery have resulted in the invention of newer advanced surgical techniques, which decreased the morbidity and provided an overall benefit to rehabilitate of the patient.

Different forms of surgery for the cure of oral cancer[29-32]

1. Fluorescence visualization (FV) guided surgery
2. Reconstructive surgery
3. Laser microsurgery
4. Sentinel node mapping
5. Cyber knife robotic radiosurgery system
6. Transoral robotic surgery (TORS)
7. Osseointegrated implant surgery

Radiotherapy [33-35]

Ionizing radiation is used to treat OSCC- may be as an external radiation beam targeting the tumor (external beam radiotherapy), or by directly implanting radioactive sources within the tumor (brachytherapy). Total dose is delivered over time in smaller doses or fractions in external radiation beam therapy. Usually it is given as single daily fractions of 1.8-2 Gy, 5 days/week, resulting in dose accumulation of approximately 10 Gy/week. Radiotherapy is given in nearly 50% of the patients with OSCC. Advancement in radiation oncology have helped to improve outlook for patients and found more effective treatment with less side-effects.

Different forms of radiotherapy for the cure of oral cancer

1. Particle radiation therapy
2. Intra operative electron radiation therapy (IOERT)
3. Stereotactic radiotherapy
4. Intensity-modulated radiotherapy (IMRT)
5. Image guided radiotherapy (IGRT)
6. 3D conformal radiation therapy
7. Radioimmunotherapy

Chemotherapy

With the invention of new drugs, chemotherapy has very important role in treatment of OSCC. Combination of chemotherapy and radiotherapy is one of the accepted methods for the treatment of advanced oral and oropharyngeal cancers. The main goal of chemotherapy is to destroy dividing cancer cells and thereby restricting invasion and metastasis. There are three different modes of chemotherapy:

1) Induction chemotherapy which is given before surgery.
2) Concurrent chemoradiotherapy which is in conjunction with radiation treatment
3) Adjuvant chemotherapy, which is given after surgery.

Chemotherapeutic agents can be classified into: platinum compounds (cisplatin and carboplatin) ,Antimetabolites (methotrexate and 5-fl uorouracil), and taxanes (docetaxel). Platinum containing agents are regarded as the major drugs forming the foundation of most chemotherapy schedules.[27,28]

Forms of chemotherapy that are used for the treatment of OSCC:

1. Targeted therapy

Other Recent Developments in OSCC Management [35]

1. Gene therapy
2. Nutraceuticals

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