

Head and Neck Cancer Management

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Head and Neck Cancer (HNC) is a broad category of cancer, comprises of cancer that origin into oral cavity, pharynx, larynx, sinuses and salivary gland. Majority of oral cancer cases reported in Pakistan are metastatic to Head and Neck and are with morphology of squamous cell carcinoma. Locally advance, un-resectable tumors are treated with systemic therapies. Commonly prescribe systemic therapies includes chemotherapy and targeted therapy. However, chemotherapy is the most prescribed systemic therapy because of advance presentation of cases with the morphology of Squamous cell carcinoma. Cisplatin and Carboplatin are drug of choice in HNC treatment. Chemotherapy treatment result in many toxicities such as nausea-vomiting, nephrotoxicity, cystitis, diarrhea, mucositis, ototoxicity, myelosuppression, allergic reaction and others. These side-effects could be overcome through pharmacological and non-pharmacological interventions.

Introduction

Head and Neck Cancer (HNC) is a broad category of cancer, comprises of cancer that origin in oral cavity, pharynx (naso, oro, and hypo), sinuses and salivary gland and larynx [1]. According to GLOBOCAN, 2020 report, age standardized rate, HNC incidences in males were 15.9 % and 4.8 % in females, leading to age standardized mortality of 7.9 % in males and 2.3 % in females [2]. Warnakulasuriya [3] reported that two third of oral and pharyngeal cancers are occurring in developing countries (Sri Lanka, India, Pakistan and Taiwan) [3]. In Pakistan, oral cancer incidences rank first in males with 12.9% and it ranked second most frequent cause of death among all other types of cancer occurring in both sexes [4]. Majority of oral cancer cases reported in Pakistan and worldwide are with the morphology of squamous cell carcinoma [3,5]. Oral cancer cases presented in Pakistan are metastatic to Head and Neck [5], creating need for systemic therapies. Hence, systemic therapies are used to treat tumors that are un-resectable, locally advance and for the purpose of organ preservation [6]. Commonly prescribed systemic therapies for treatment of HN squamous cell carcinoma in Pakistan could be further divided into two broad categories and those includes: chemotherapy, and targeted therapy.

Between two systemic therapies, chemotherapy is most widely used.

Systemic agents commonly prescribed in head and neck cancer treatment includes Cisplatin, Cetuximab and Carboplatin. Docetaxel, 5FU and other neoplastic drugs have also been used [6]. Cisplatin is a drug of choice, given either in a three weekly or weekly dose (in case of side effects develop with three weekly doses). However, if patient develops side effects because of cisplatin or patient overall health condition is not well at the start of treatment because of age factors and other co-morbid patients are prescribed cetuximab (targeted therapy) and last option is carboplatin (slightly less effective but cost-effective). According to Dasari et al. [7] "the clinical standard of dosage of carboplatin is usually a 4:1 ratio compared to cisplatin; that is, for a dose that usually requires a particular dose of cisplatin, four times more carboplatin is needed to achieve the same effectiveness" (p.193).

Article describes common systemic drugs for HNC treatment in term of their categories, their mechanism of action, side effects and care aspects.

Cisplatin

Cisplatin is a metallic (platinum) compound. Cisplatin was first synthesized by M. Peyrone in 1844 [7]. Beside platinum, other metals are now a day used in the treatment of cancer [8]. Cisplatin is used in variety of tumors including cancers of the ovaries, testes, and solid tumors of the head and neck. Several analogs of cisplatin have been synthesized such as carboplatin and oxiplatin. Cisplatin becomes activated once it enters the cell. In the cytoplasm, chloride atoms in cisplatin are displaced by water molecules making it hydrolyzed. This hydrolyzed product reacts with proteins and nitrogen donor atoms on nucleic acids. Hence, it causes deoxyribonucleic acid (DNA) damage in cancer cells, blocking cell division and resulting in apoptotic cell death. Cisplatin-induced oxidative stress and shifting of calcium from mitochondria to within the cell are another mechanism through which drug exerts its anti-cancerous effects [7].

Common side effects of Cisplatin are nausea/ vomiting, hearing loss (ototoxicity), renal toxicity, cystitis, hepatotoxicity, allergic reactions, myelosuppression and cardiotoxicity. Hence, drug should not be prescribed to older people, and patients with cardiac and chronic liver disease (CLD) problems.

Important care aspects with this drug include:

- Baseline monitoring of electrolyte sodium (NA⁺), potassium (K⁺), chloride (CL), renal function (BUN and creatinine) and complete blood count (CBC) prior chemotherapy infusion.
- Drug is contraindicated in patients with history of cardiac and renal issues.
- Intravenous fluid of 1-1.5 liters during chemotherapy treatment is infused to prevent renal toxicity and cystitis.
- Oral fluid intake of 2-3 liters post chemotherapy infusion is encouraged.
- Patient is asked to report any hematuria, dysuria, burning and urgency of urine, post chemotherapy dose.

Cetuximab

Cetuximab is a mono-clonal antibody used in treatment of head, neck and colorectal cancers. Cetuximab binds to epidermal growth factor receptor (EGFR) on both normal and tumor cells and competitively inhibits the binding of epidermal growth factor (EGF) and other ligands [9]. Drug is composed of anti-EGFR antibody with human IgG.

It is an expensive drug. However, side effects are less since it acts on pathways of cellular proliferation. Whereas chemotherapeutic agent previously discussed destroy DNA of cells. Hence, this is drug of choice in old age patients and in patients holding other co-morbidities.

Common side effect of cetuximab includes rash, malaise fever, and infusion reaction. These side effects can relate with drug composition "anti-EGFR antibody with human IgG". Administration of anti-allergic, anti-pyretic and corticosteroid drugs prior to cetuximab administration could prevent allergic reaction.

Carboplatin

Carboplatin is last drug of choice when patient can't receive cisplatin because of co-morbidities (renal or cardiac issues) and drug side effects. Second choice previously discussed cetuximab, is less preferred by patients because of high cost. Hence, most patients opt for carboplatin because it

is much cheaper than cetuximab. It also made up of platinum compound and belongs to alkylating agent class of anti-neoplastic drug. It is less effective than cisplatin because of its lower reactivity and slower DNA binding kinetics [6]. Major side effects are renal toxicity. Therefore, adequate hydration and renal monitoring is important.

HNC drugs, their mechanism of action, side effects and care are discussed above. Beside those, myelosuppression and mucositis are other common side effects. Use of mouth washes could prevent and treat mucositis. Percutaneous Esophageal Gastrostomy would be required to overcome nutrition deficits that occur in head and neck cancer cases that require multimodality treatment of chemotherapy and radiation therapy. Percutaneous Esophageal Gastrostomy (PEG) site infection could also occur, aseptic handling of PEG site 7-10 days post insertion could prevent infection.

Beside chemotherapy, other definitive treatment in head and neck cancer are surgery and radiation therapy. Awareness in public through education and media related to risk factors of Head and Neck cancer is needed.

Common risk factors include substance abuse (tobacco, betel nuts, tobacco, and others) and Human Papilloma Virus infection. Moreover, regular dental check for pre-cancerous lesion screening could be helpful strategy to identify high risk cases.

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