# **Palliative and Hospice Care In dentistry**

Dr. K. Saraswathy Gopal<sup>1</sup>,: Dr.Kalaiselvi.R<sup>2</sup>

<sup>1.</sup>Head of the department, Department of oral medicine and Radiology, MADCH, chennai <sup>2.</sup>Post Graduate, Department of Oral medicine and Radiology, MADCH, Chennai Contact details: Dr.kalaiselvi.R Postgraduate student, Department Oralmedicine and Radiology MeenakshiAmmal dental College and Hospital, Chennai- 600095

## Abstract

Palliative care dentistry has been defined as the evaluation and management of patients with active, advanced, progressive disease in whom the oral cavity has been compromised either by the disease directly or by its treatment. The focus of care in these patients is on quality of life. Palliative care dentistry may play an important role in the general healthcare of terminally ill patients. Palliative care, also known as supportive care, helps people with serious illnesses feel more comfortable. Palliative care can help relieve pain and treat side effects as people go through disease treatment or hospice care at the end of life. Palliative dental care can be crucial for patients fighting cancer or other diseases because they can have unique and troublesome dental issues. The palliative doctor gives the 'touch of God' as he/she takes care of the terminally ill patient. The oncologist encounters great difficulties in managing oral cavity problems of these patients. So, a trained dental doctor can help other doctors in dealing with these situations.

Keywords: Dentistry, Oral cavity, Palliative care, Hospice care, Quality of life

\_\_\_\_\_

\_\_\_\_\_

Date of Submission: 11-09-2022

Date of Acceptance: 28-09-2022

## I. Introduction

While dying is a normal part of life, death is often treated as an illness. As a consequence, many people die in hospitals, alone and in pain. [1] Palliative care focuses primarily on anticipating, preventing, diagnosing, and treating symptoms experienced by patients with a serious or life-threatening illness and helping patients and their families make medically important decisions. The ultimate goal of palliative care is to improve quality of life for both the patient and the family, regardless of diagnosis. Although palliative care, unlike hospice care, does not depend on prognosis, as the end of life approaches, the role of palliative care intensifies and focuses on aggressive symptom management and psychosocial support.[2] The World Health Organization has defined *palliative care* as "an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual."<sup>[3].</sup>

Palliative team is a multidisciplinary approach where dental expression serves as 'healing hands' in pain control, social, psychological and spiritual problems. The palliative care team consists of specialists in various fields of medicine who provides care and treatment to the patients. A dentist can help to improve the quality of life of the patients. Mouth is the most important organ of expression and it is most often affected in later stages of diseases. Oral cavity is home for a great number of micro organisms which aggravates the disease process. The patients need the help of a dentist to alleviate his discomfort and to live a better life. He can help the patient right from the initial diagnosis of the condition up to the relief of pain in the terminal stages of the diseases. But many a times the general dentist is unaware of his responsibilities toward a terminally ill patient. The community is also unaware of the role that a nearby dentist can play. In this paper, a brief attempt is made to list a few areas in which a palliative care dentist can help other members of the palliative care team and also the patient in leading a better life.[4] As death approaches, a patient's symptoms may require more aggressive palliation. As comfort measures intensify, so should the support provided to the dying patient's family.

## THE CONCEPT OF TOTAL PAIN

The alleviation of suffering is an essential goal of medical care. To treat it, however, providers must first recognize pain and suffering.[6] Saunders first described the concept of total pain (Table 1)[7] and interaction among the various sources of pain and suffering.[8] Total pain is the sum of the patient's physical, psychological, social, and spiritual pain. This concept is central to the assessment and diagnosis of pain and

suffering. Because psychological distress, lack of social support, and physical pain are associated,[9] treating a patient's total pain is imperative, especially at the end of life. Optimal pain relief will not be possible unless all the elements of total pain are addressed. Clinicians should utilize other members of the multidisciplinary team, such as social workers and chaplains, to better treat suffering related to the different domains of total pain.

| Table 1. | Four | Components | of | Total | Pain |
|----------|------|------------|----|-------|------|
|----------|------|------------|----|-------|------|

| Р | Physical problems, often multiple, must be<br>specifically diagnosed and treated.   |
|---|---|
| Α | Anxiety, anger, and depression are critical<br>components of pain that must be addressed by<br>the physician in cooperation with other healthcare<br>professionals. |
| I | <b>Interpersonal</b> problems, including loneliness,<br>financial stress, and family tensions, are often<br>interwoven into the fabric of a patient's<br>symptoms.  |
| N | Not accepting approaching death, a sense of<br>hopelessness, and a desperate search for<br>meaning can cause severe suffering that is<br>unrelieved by medications. |

### MANAGING COMMON PHYSICAL SYMPTOMS

Patients near the end of life may experience extreme symptoms that include physical, spiritual, and psychosocial suffering. Preventing and managing these symptoms while optimizing the quality of life throughout the dying process is the goal of palliative medicine.[10]Factors important to seriously ill patients include adequately controlling pain and other symptoms, avoiding prolongation of the dying process, achieving a sense of self-control, finding meaning in life, and relieving the care burdens of family and loved ones while strengthening and completing those same relationships.[11]As death becomes nearer, the symptom burden increases while the patient and family tolerance of physical and emotional stress decreases. At this time, primary palliative care interventions should take precedence, and the focus on restorative care should decrease. The triggers for the shift to palliative care include the following four symptoms.

- ✓ Physical pain
- ✓ Dsypnoea
- ✓ Restlessness
- ✓ Death rattle

Dental expression in palliative care is defined as "the extended dental services with a central goal of providing pre-eminent feasible oral care to terminally-ill or patients with advanced disease, where oral lesions impact on quality of remaining life of patients whether they are as a result of their disease and/or therapy" (Mulk et al., 2014).

### ORAL CONSIDERATIONS IN PALLIATIVE PATIENTS – CAUSE AND CARE

The imperative and important problems faced by the palliative patients are discussed briefly. The symptoms that indicate terminal phase of life are categorized as [12]: 1) Bed-bound 2) Loss of appetite 3) Profound weakness 4) Trouble swallowing 5) Dry mouth 6) Weight loss 7) Becoming semiconscious, with lapses into unconsciousness 8) Experiencing day to day deterioration that is not reversible. Pain is one of the at most criteria which should be considered in palliative care. It remains a central feature of good palliative care. The common oral problems encountered in palliative patients include xerostomia, mucositis, candidiasis, dental caries, periodontal diseases, taste disorders, etc. [13]. Early clinical diagnosis of these oral lesions or conditions in palliative patients should be done to minimize pain and suffering. A thorough oral assessment based on a systematic approach is required for sound management of oral care and facilitate prevention or minimization of oral complications [14]. The most appropriate screening tool use with elderly is Geriatric Oral Health Assessment Index. (GOHAI) [15].

#### Mucositis and Stomatitis

Mucositis is a painful condition of oral cavity with ulceration of mucosal linings in the mouth, pharynx and digestive tract. It usually occurs as a result of toxic chemotherapy like 5-fluorouracil and methotrexate, which are potent mucositis agents, radiotherapy and stem cell transplantation [16]. 80% of patients with head and neck malignancies receiving radiotherapy and chemotherapy are prone to mucositis [17]. Clinically it may

present as red or white lesion in the mucosa, pseudo membrane formation and ulceration in the initial stages although late changes include fibrosis of connective tissue and hypovascularity [18]. Fractionated dose of 180-220 cGy/day results in mucositis within 1-2 weeks and increases throughout the course of therapy to maximum in 4 to 5 weeks [19]. The symptoms include severe pain, compromised oropharyngeal function and oral bleeding that effect quality of life.

The Severity of mucositis can be assessed by World health organization mucositis grading [14] Grade 0 – None

Grade 1 - Erythema, painful ulcers, mild sore throat

Grade 2 - Painful erythema and ulcers, oedema of oral mucosa, but able to eat solid food.

Grade 3 - Painful erythema and ulcers, painful oedema of oral mucosa that interferes with eating solid food

Grade 4 - Need for parenteral or enteric support due to severe stomatitis.

#### MANAGEMENT OF MUCOSITIS

| Coating agents       | Kaolin-pectin, Aluminium chloride, Aluminium and<br>Magnesium Hydroxide, Hydroxypropyl cellulose,<br>Sucralfate |
|----------------------|---|
| Diluting agents      | Saline, Bicarbonate rinses, Frequent water rinses, Ice chips  |
| Lip lubricant        | Wax, Water based lubricants, Lanolin  |
| Topical anaesthetics | Dyclonine Hcl, Xylocaine Hcl, Benzocaine Hcl,<br>Diphenhydramine Hcl, Doxepin Hcl                               |

Oral mucositis is a prime complication which surpasses through various degrees of severity and accordingly the treatment focuses on palliation with administration of systemic opiate analgesics for moderate to severe mucositis pain, topical anesthetics and mucosal coating agents such as lidocaine, benzocaine, dyclonine, diphenhdramine,doxepin and benzydamine for moderate pain, and bland rinses for mild pain. Other agents like oral capsaicin, oral sulfasalazine and growth factor mouth washes. Olive leaf extracts and sedative hypnotics like ketamine in the form of mouth washes with its pronounced analgesic and anesthetic properties can also be given.

#### XEROSTOMIA

The subjective report of oral dryness is termed xerostomia, which is a symptom and not a diagnosis or disease. Xerostomia may not always be associated with hyposalivation. It is common in palliative patients mostly as a result of radiotherapy and medication [20].

Dry mouth is the most commonly reported oral problem (Delgado et al., 2018).

Might be as a result of medication and therapy (e.g. radiotherapy) but it may be subjective with no hyposalivation.

Negative effect on patient's life: diet, speech and incapacity to wear dentures

Clinical signs include: thick ropey saliva, lip stick, fissured tongue, candidiasis and high caries incidence.

#### ETIOLOGY OF XEROSTOMIA

| Developmental          | Salivary gland aplasia  |
|------------------------|---|
| Water/ metabolite loss | Impaired fluid intake, hemorrhage, vomiting/diarrhoea   |
| latrogenic origin      | Medications, radiation therapy to head and neck, chemotherapy   |
| Systemic diseases      | <u>Sjogren's</u> syndrome, diabetes mellitus, sarcoidosis, HIV,<br>hepatitis C infection, graft versus host disease, psychogenic<br>disorders |
| Local factors          | Decreased mastication, smoking, mouth breathing   |

#### MANAGEMENT OF XEROSTOMIA

Management include preventive, symptomatic and curative modalities. "Magic mouth wash" composed of antacids, diphenyhdramine and the topical antifungal nystatin and viscous lidocaine in various formulations has gained importance due to its pronounced therapeutic effect now days [21]. Preventive therapy includes maintenance of meticulous oral hygiene, frequent visits to dentist, supplemental fluoride, remineralizing solutions and noncariogenic diet [,22]. Nevertheless symptomatic therapy like water intake, oral rinses and gels, alcohol free mouthwashes, humidifiers, use of topical salivary stimulants like sugar free gums, artificial salivary substitutes, systemic secretogogues like bromohexine, anetholitrithione, pilocarpine Hcl and cevimelineHcl [23-25]. New modalities include electrical stimulation of salivary glands for salivary hypofunction which delivers low voltage electric charge to tongue and palate [26].

Curative treatment needs proper diagnosis of underlying pathology for hyposalivation which includes sialometry, sialochemistry, salivary gland imaging, etc. [27]. Based on investigative procedures and accurate diagnosis, treatment plan should be done accordingly.

Certain Novel approaches like trans cutaneous electric nerve stimulation (TENS) and acupuncture can be used which increases the salivary flow. To treat any damaged salivary parenchyma, techniques like Gene transfer(Recombinant technology) and GTR (guided tissue regeneration) can be used. .Artificial type of salivary glands with use of irradiated NIH 3T3 fibroblasts which serve as feeding layer are also in process.

### CANDIDIASIS

The incidence of candidiasis in palliative care has been estimated to be 70-85% [28]. Candida albicans is the most common infectious organism encountered in candidiasis.In most cases, candidiasis is associated with dry mouth . Most common type of candidiasis in terminal end-stage immunocompromised patients is pseudomembranous . Predisposing factors: immunosuppression, dry mouth, poor oral hygiene, denture wearers, poor nutrition and medications (e.g. corticosteroids, broad spectrum antibiotics)

| Drug           | Form   | Dosage  |
|----------------|--|---|
| Amphotericin B | 1. Lozenge 10mg<br>2. Oral suspension 100mg/ml | Dissolve in mouth slowly 3-4 per day or 2 weeks   |
| Nystatin       | 1. Cream<br>2. Oral suspension 100,000 U       | 1. Apply to affected areas 3-4 times per day<br>2. Apply after meals 4 times per day for 7days  |
| Clotrimazole   | 1. Cream<br>2. Solution                        | 1. Apply to affected areas 2-3 times daily for 3-4 weeks<br>2. 2.5ml 3-4times daily for 2 weeks.  |
| Ketoconazole   | Tablets  | 200-400mg tablets twice daily with food for 2weeks.   |
| Fluconazole    | Capsules                                       | 50-100mg once daily for 2-3 weeks.  |
| Itraconazole   | Capsules                                       | 100mg capsules daily taken immediately after meals for 2 weeks  |
| Miconazole     | 1. Oral gel<br>2. Cream                        | <ol> <li>Apply to the affected area 3-4times daily</li> <li>Apply twice per day and continue for 10 to 14 days after the lesion heals.</li> </ol> |

#### MANAGEMENT OF CANDIDIASIS

Presently Caspofungin, micafungin and anidulafungin are echinocandins which have been used extensively.

#### NUTRITION AND TASTE DISORDERS

Nutrition is the most important aspect of health and well being. Nutrition is required for physical and alert active mental status. However it is most commonly compromised in people suffering from end stage disease and patients undergoing treatment for the same. The role of dental professional is to assess nutritional status, oral implications causes of complaints provide guidelines and refer to appropriate provider [29]. Taste is very important for life; it manages food intake and provides pleasure feeling from eating. The taste regulates digestion, absorption, and storage of nutrient perception by activation neuronal pathways [30]. Alteration or taste dysfunction (dysgeusia) may decrease the quality of life by affecting and psychological well-being, appetite, and body weight.

**Zinc supplements** can be useful for patients receiving chemotherapy. Zinc protected the cancer patients from taste alteration [31] other form, a zinc containing polaprezinc that can also protect against taste disorder [32]. Amifostine, protect salivary gland normal tissues from damage by chemotherapy and radiation [33]] thus leading to improvement of xerostomia that may cause taste alterations [34].

Dental caries and Periodontitis Patients with terminal end stage are usually prone to caries and periodontitis, with most common reasons being radiation therapy which in turn causes changes in salivary flow, decreased pH, reduced buffering capacity, increased viscosity, reduced cleansing action and debris accumulation leading to increased rate of caries and periodontitis [Table/Fig-6] The best method of reducing caries is by combination of restorative dental procedures, proper oral hygiene and topical application of sodium fluoride. Avoidance of dietary sucrose further reduces concentration of streptococcal mutants and lactobacillus [35]. Teeth which are grossly decayed and severely periodontally compromised should be extracted based on patients health status, as it improves patients comfort for intake of food.

#### OSTEORADIONECROSIS

Osteoradionecrosis is a complication result from radiation therapy to the head and neck that results in bone death, its side effect includes neuropathic pain [36]. Hyperbaric oxygen (HBO) therapy companied surgery can be used in the management of osteoradionecrosis, HBO enhances tissue oxygenation through control of

infection, angiogenesis, predominantly through stimulate bacterial killing fungi, macrophages, and production of bactericidal free radicals [37,38]. Other treatment modalities—Ultrasound has reported to stimulate tissue regeneration by enhancing blood flow in chronically ischemic muscles, protein synthesis and cure of ischaemic varicose ulcers. Pentoxifylline and calcitonin also have been used successfully to treat ORN [39].

| Radiation dose < 3000 cGy      | Mucositis, Candidiasis, Xerostomia & Dysgeusia begins                                   |
|--------------------------------|---|
| Radiation dose > 3000 cGy      | Xerostomia (permanent) and<br>Dysgeusia, saliva is thick, more<br>acidic, altered flora |
| Radiation dose > 5000 cGy      | Trismus,Concerns for Osteo<br>radionecrosis   |
| Radiation dose > 6000-6500 cGy | Significant concerns for<br>Osteoradionecrosis  |

## EFFECTS OF RADIATION PERTAINING TO DAMAGE

## PAIN MANAGEMENT FOR ORAL CANCER PATIENTS

Cancer pain may result from direct invasion cell of cancer into the nerve or bone tissue in the end stages of oral cancer and its management is critical issue [40]. Opioid analgesics are usually prescribed for controlling oral cancer-related pain. In spite of high dosages of opioids are prescribed, high level of cancer pain is usually poorly controlled. Switching is often necessary due to different side effects or tolerance of opioids. Methadone has been widely prescribed to manage oral pain because of its exclusive properties (e.g., long duration of action strong, high bioavailability, and analgesic effect) [41].

### ROLE OF A DENTIST IN PALLIATIVE CARE

Palliative dental care is a novel emerging branch, which provides symptomatic relief to the terminal end stage patients. The key role of dentist in palliative team was enlightened only since 2006.[29]

The role of dentist in the management of oral complications either due to progressive far advanced disease or by its treatment can be managed through various modalities. Comprehensive clinical examination of the extra and intra oral soft tissues, periodontium and dentition is essential. High patient awareness and motivation are essential to minimize potentially devasting dental complications. Oral care protocols should strive to maintain the integrity of oral mucosa and lips, prevent caries and periodontal disease, alleviate oral pain and discomfort and prevent or treat infectious complications [42,43].

Diet modification forecasts an important role in palliative care. Reduction of sugar intake, replacement of refined carbohydrates with substances such as sorbitol, xylitol, aspartame and saccharine further reduces incidence of dental caries. Dry spicy and acidic foods, alcohol, alcohol containing mouth washes and tobacco products should be avoided [44]. The overall sequel of complications like caries, periodontitis and osteoradionecrosis can be avoided with maintenance of meticulous oral hygiene [45] A dental practitioner should spotlight the patient suffering and navigate the minefield of potentially devastating legacies of pain caused due to various conditions.

#### II. Conclusion

Patients in end stage diseases and life need special care and treatment which involves a group of specialists to render it, and oral physicians are a definitive inclusion in this team. As a usual protocol of management, much importance is given to the disease and its treatment and in this scenario oral cavity is often neglected. Various adverse/side effects of such diseases and their treatments often has lots of effects on the oral cavity, causing a lot of discomfort and disturbance in the day to day routine and diet effecting the nutrition and general well-being. Along with the physical disabilities and chronic pain these patients suffer from many psychological effects like depression and social stigma. Oral cavity is the most common site of abuse of all such direct and indirect effects. Definitive diagnosis and management of such oral conditions in these patients is proficiently done by oral medicine specialists, which calls for the inclusion of them in the palliative care team. Adequate training programs have to be conducted and awareness has to be created. A trained oral physician will be a good team mate for the oncologist or radiotherapist or other doctors of the palliative care team.

#### References

- A controlled trial to improve care for seriously ill hospitalized patients. The study to understand prognoses and preferences for outcomes and risks of treatments (SUPPORT). The SUPPORT Principal Investigators. JAMA. 1995 Nov 22-29;274(20): 1591-1598; Erratum in: JAMA. 1996 Apr 24;275(16):1232.
- [2]. Robin B. Rome, MSN, FNP-C, Hillary H. Luminais, RN, Deborah A. Bourgeois, MN, APRN, ACNS-BC, Christopher M. Blais, MD, MPH, FACP, FAAHPM, The Role of Palliative Care at the End of LifEe.
- [3]. Adina C. Jucan, DDS; Ralph H. Saunders, DDS, MS, Maintaining Oral Health in Palliative Care Patients
- [4]. Rani P Mol, The Role of Dentist in Palliative Care Team.
- [5]. Robin B. Rome, MSN, FNP-C, Hillary H. Luminais, RN, Deborah A. Bourgeois, MN, APRN, ACNS-BC, Christopher M. Blais, MD, MPH, FACP, FAAHPM, The Role of Palliative Care at the End of Life.
- [6]. Cassell EJ. Diagnosing suffering: a perspective. Ann Intern Med. 1999 Oct 5;131(7):531-534.
- [7]. Bial A, Levine S. The assessment and treatment of physical pain associated with life-limiting illness. Hospice/Palliative Care Training for Physicians: UNIPAC. Vol 3. 3rd ed. Glenview, IL: American Academy of Hospice and Palliative Medicine; 2007.
   [8]. Saunders C. A personal therapeutic journey. BMJ. 1996 Dec 21-28;313(7072):1599-1601.
- [9]. Zaza C, Baine N. Cancer pain and psychosocial factors: a critical review of the literature. J Pain Symptom Manage. 2002 Nov; 24(5):526-542.
- [10]. Kuebler KK, Heidrich DE, Esper P. Palliative & End-of-Life Care: Clinical Practice Guidelines. St. Louis, MO: Saunders/Elsevier; 2007
- [11]. . Singer PA, Martin DK, Kelner M. Quality end-of-life care: patients' perspectives. JAMA. 1999 Jan 13;281(2):163-168
- [12]. Hall-Lord ML, Larsson G, and Steen B. Chronic pain and distress in older people: A cluster analysis. International Journal of Nursing Practice. 1999; 5(2):78-85.
- [13]. Dickinson JA .Symptom control in palliative care. Australian Prescriber. 1988; 11(4):78-82.
- [14]. Holmes S, Mountain E. Assessment of oral status: evaluation of three oral assessment guides. Journal of Clinical Nursing. 1993;2:35-40.
- [15]. Jones JA, Spiro A, Miller DR, Garcia RI, Kressin NR. Need for dental care in older veterans: Assessment of patient based measures. Journal of the American Geriatrics Society. 2002; 50(1): 163-8.
- [16]. Pazdur R, Wagman LD, Camphausen KA, Hoskins WJ. Cancer management a multi disciplinary approach. 11th ed Journal Oncology. USA.
- [17]. [12] Rubenstein EB, Peterson DE, Schubert M, Keefe D, McGuire D, et al. Clinical practice guide lines for the prevention and treatment of cancer therapy induced oral and gastrointestinal mucositis. Cancer. 2004;100:2026-46.
- [18]. [13] Epstein JB, Stevenson-Moore P, Jackson S, et al. Prevention of oral mucositis in radiation therapy: A controlled study with benzydamine hydrochloride rinse. Int J Radiation OncolBiol Phys. 1989; 16:1571-5.
- [19]. [14] Sonis ST, Eilers JP, Epstein JB, et al. Validation of a new scoring system for the assessment of clinical trial research of oral mucositis induced by radiation or chemotherapy. Cancer. 1999;85:2103-13.
- [20]. ] Wiseman MA. Palliative care dentistry. Gerodontontology. 2000; 17:49-51.
- [21]. Rosental DI, Trotti A. Strategies for managing radiation induced mucositis in head and neck cancer. Seminars in radiation oncol. 2009;19:29-34.
- [22]. [22] Zero DT. Dentifrices, mouthwashes and remineralization caries arrestment stratagies. BMC Oral health. 2006;(6)1:Suppl:S9.
- [23]. [23] Cohen-Brown G, Ship JA. Diagnosis and treatment of salivary gland disorders. Quintissence Int. 2004; 3:108-23.
- [24]. [24] Ship JA. Diagnosing, managing and preventing salivary gland disorders. Oral diseases. 2002; 8:77-81.
- [25]. [25] Jedel E. Acupuncture in xerostomia-A systemic review. J Oral Rehabiltation. 2005;32:392-6.
- [26] [26] Steller M, Chou L, Daniels TE. Electric stimulation of salivary flow in patients with S'jogrens syndrome. Journal of Dental research. 1988; 67:1334-7.
- [27]. Ettinger RL. Changing dietary patterns with changing dentition: how do people cope? Special care Dent. 1988; 18(1):33-9.
- [28]. Wiseman MA. Palliative care dentistry. Gerodontontology. 2000; 17:49-51.
- [29]. Bhavanasujana mulk1 , raja lakshmi chintamaneni2 , prabhat mpv3 , sarat gummadapu4 , shyamsundarsalvadhi, Palliative Dental Care A Boon for Debilitating
- [30]. Brondel L, Jacquin A, Meillon S, Pénicaud L. Le goût: Physiologie, rôlesetdysfonctionnements. Nutrition Clinique etMétabolisme. 2013;27(3):123-133
- [31]. Halyard MY, Jatoi A, Sloan JA, Bearden JD III, Vora SA, Atherton PJ, et al. Does zinc sulfate prevent therapyinduced taste alterations in head and neck cancer patients? Results of phase III double-blind, placebo-controlled trial from the North Central Cancer Treatment Group (N01C4). International Journal of Radiation Oncology, Biology, Physics. 2007;67(5):1318-1322
- [32]. Mizukami Y, Sato J, Nihei S, Kashiwaba M, Kudo K, Okuyama H, et al. The effectiveness of polaprezinc preparation for taste alteration in cancer chemotherapy. Gan to Kagaku Ryoho. Cancer & Chemotherapy. 2016;43(8):979-983
- [33]. Kouvaris JR, Kouloulias VE, Vlahos LJ. Amifostine: The first selective-target and broad-spectrum radioprotector. The Oncologist. 2007;12(6):738-747
- [34]. Shokohi T, Bandalizadeh Z, Hedayati MT, Mayahi S. In vitro antifungal susceptibility of Candida species isolated from oropharyngeal lesions of patients with cancer to some antifungal agents. Jundishapur Journal of Microbiology. 2011;4(1):S19-S26
- [35]. Holmes S. Nursing management of oral care in older patients. Nursing Times. 1996; 92(9): 37-9.
- [36]. WI W. Scarborough je osteoradionecrosis in intra-oral cancer. American Journal of Roentgenology. 1938;40:524-534
- [37]. Silvestre-Rangil J, Silvest F-J. Clinico-theraper-rtic management of osteoradionecrosis: A literature review and update. Medicina Oral, Patología Oral y CirugíaBucal. 2011;16(7):E900-E904
- [38]. Re M. A new concept in treatment of osteoradionecrosis. Journal of Oral and Maxillofacial Surgery. 1983;41:351-357 [
- [39]. Adam SJ et al. Paradigm shifts In the management of osteoradionecrosis of mandible. Oral Oncology. 2010;46:95-801
- [40]. McDermott JD, Eguchi M, Stokes WA, Amini A, Hararah M, Ding D, et al. Short-and long-term opioid use in patients with oral and oropharynx cancer. Otolaryngology Head and Neck Surgery. 2019;160(3):409-419
  [41]. Sekido K, Tomihara K, Horikawa H, Tachinami H, Murakami N, Noguchi M. Successful control of opioid-refractory cancer pain
- [41]. Sekido K, Tomihara K, Horikawa H, Tachinami H, Murakami N, Noguchi M. Successful control of opioid-refractory cancer pain with methadone in a patient with advanced oral squamous cell carcinoma: A case report. Oral Science International. 2018;15(2):78-80
- [42]. Andrews N, Griffiths C. Dental complications of head and neck radiotherapy: Part 2. Australian dental journal. 2001; 46(3):174-82.
- [43]. Miaskowski C. Management of mucositis during therapy. NCI Monographs 1990;9:95-8.
- [44]. Wind DA. Management of xerostomia: an overview. Practical Hygeine. 1996;5:23-7.
- [45]. Pochanugool L, Manomaiudom W, Im –Ersbin T. Dental management in irradiated head and neck cancers. Journal of medical association Thai. 1994; 77:261-5