

Advanced Head & Neck Cancer: Care Beyond Cure

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Abstract

Head and neck cancer patients have some premorbid features which make them a more challenging group compared to those with cancers in other anatomic regions. They have a tendency to abuse or have abused alcohol, tobacco or both; they may be less meticulous in personal habits, especially oral care, tend towards poor nutrition and have a higher incidence of personality and character disorders. They are also less successful socio-economic group. Most of those who succumb to head and neck cancer have uncontrolled local disease irrespective of the presence of metastasis. Distant metastasis arises in lung, liver and bone in a small number of patients particularly if there is involvement of multiple lymph nodes. The recent cancer estimates show that out of 10 million new cancer cases diagnosed annually 0.675 million patients suffer from head and neck cancer and 60% of all head and neck cancer occur in less developed countries 1. The 5-year survival rates of multimodal chemo-radiotherapy is below 20%, with a median survival of 12 months or less 2,3,4.

According to WHO (2002) 'Palliative Care' is an approach that improves the quality of life of patients and their families facing the problems 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. Palliative care is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life such as chemo therapy or radiation therapy and includes those investigations needed to understand better and manage distressing clinical complications. It is usually apparent that palliative treatment may differ from curative treatment but in certain situations the borderline between the two may be blurred and a clear-cut distinction may not always be possible in many T3 and T4 primary lesions in recurrent disease.

Accompanying the great expansion of ablative and reparative cure in head and neck cancer over the past three decades, the scope for palliation has also improved substantially and perhaps over a broader field than curative therapy. These are the following symptoms from which Head & Neck cancer (HNC) patient suffers.

SWALLOWING

An intact anatomy and an effective cough reflex offer important protection to the airway during swallowing, without which, aspiration of oropharyngeal or gastric contents into the larynx and lower respiratory tract can occur. The clues of aspiration includes (a) choking after feeding (b) noisy breathing, cough or dyspnoea at night as oropharyngeal secretions accumulated due to suppressed cough reflex by sedatives, hypnotics opioids c) chest x-ray showing infiltrations in posterior segment of the upper lobes, apical basal or basal segments of lower lobes. Patients who aspirate are at the risk for pneumonia. In the stroke population, aspiration results in 40,000 deaths per year 5. Lundy et al 6 reported on 166 consecutive patients referred for swallowing evaluation of which 80 patients had neurologic problems, 38 medical problems and 33 HNC. HNC patients had the greatest rate of aspiration with a total

of 76% versus 49% for patients with a neurologic diagnosis and 43% for patients with a medical diagnosis. The most commonly used technique for swallowing assessment is the videofluoroscopy, also referred to as the modified barium swallow study. The "3-Ounce Water Swallow Test" is a bedside screening test for assessment of risk of aspiration performed by asking the patients to drink 3 ounces of water. This test correctly detects 80% of those who aspirates on videofluoroscopy 7. Stenson et al 8 undertook an analysis of HNC patients prior to treatment to provide baseline swallowing abnormalities. The tools were the modified barium swallow study (MBSS) and the swallowing performance status scale (SPSS) which is the global assessment tool for reporting the results of a MBSS. It is rated on a scale of 1 to 7. The degree of swallowing impairment was site specific with hypopharyngeal and laryngeal patients experiencing the most impaired swallowing with a SPSS score 4.1 and 3.7 respectively.

These patients were the most likely to experience aspiration (80 and 67% respectively), but there was no association between T-stage or overall stage and swallowing dysfunction. In post-treatment swallowing abnormalities the degree of functional deficit is largely dependant on the extent of surgery. McConnel et al ⁹ evaluated 30 patients who underwent resection of oral cavity cancers. The percentage of oral and tongue base resected were the only parameters prognostic for swallowing outcome. This has been confirmed by other investigators ¹⁰. In addition to the extent of resection, Logemann and Bytell ¹¹ demonstrated that patients undergoing floor of mouth(FOM) or tongue base(TB) resection had more swallowing difficulty than those undergoing supraglottic laryngectomies. Adjuvant radiation may worsen swallowing by increasing oedema, fibrosis and xerostomia. Kendall et al ¹² conducted a study of swallowing function in patients who received 12 months primary radiotherapy and they demonstrated abnormal swallowing in all patients of which tongue base tumours were found to have a high incidence of aspiration. Murry et al ¹³ identified disease site as a predictor for swallowing outcome after aggressive treatment with intra-arterial chemoradiation for organ preservation. Logmaal et al ¹⁴ evaluated that patients with zerostomia had swallowing deficits. Dejonckere reported the results of retrospective analysis of swallowing function in 88 patients who had completed therapy: 87% were treated with surgery with or without post operative radiation and 13% were treated with radiation only. Post treatment, all patients underwent evaluation of swallowing function followed by rehabilitation. Rehabilitation lasted less than 12 weeks for 45% of patients and less than 24weeks for 78% of patients. 9 of 82 patients had significant swallowing abnormalities which show that there was an improvement in swallowing function post-treatment. Specific swallowing strategies include feeding patients at an upright position ,dividing therapy food into small boluses, feeding slowly etc. In patients with immobile hemipharynx it is helpful to tilt or turn the head towards the paralysed side to open the contralateral normally functioning lateral food channel. Other modifications such as food of pasty consistency may reduce risk of aspiration.

VOICE

The abnormalities in the voice or resonance of voice may be due to disorder of speech. Speech abnormalities are either from the lesion in the lip, tongue, teeth or hard palate. Disorder resonance is due to the soft palate which is unable

to contact with the posterior pharyngeal wall to separate the nasal and oral cavities and allow for normal articulation of plosive consonants. The palatal paralysis can lead to hypernasal speech which is unintelligible. When a malignancy requires surgical resection of soft palate the resulting tissue deficit creates velopharyngeal insufficiency. Treatment for such lesion ranges from behavioural therapy, pharyngeal flap and pharyngeal wall implant. In case of palatal paralysis, a palatal adhesion effectively eliminates hypernasality and nasal regurgitation. Alternatively, a palatal lift prosthesis or a speech bulb/obturator can be fitted.

The voice disorder resulting from laryngeal paralysis is extremely debilitating. Most patients present with a very soft, breathy voice quality or even a whisper. Attempts to force enough volume to be heard results in rapid fatigue of laryngeal and respiratory muscles, and patients may avoid communication because of the effort required. In patients with unilateral vocal fold paralysis, medialization laryngoplasty is performed to reposition the immobile vocal fold into a more favourable partner ¹⁵. A small silastic implant is placed lateral to the paralysed vocal fold, which pushes the muscle towards the laryngeal midline. Improved vocal fold contact restores voice and prevents aspiration. Studies have documented that voice quality is normal or better following phonosurgery (^{16, 17}). Injection of collagen has been recommended for vocal fold immobility ¹⁸. Numerous other materials have been evaluated for vocal fold immobility. New concern over potential bioreaction has prompted testing of autologous material. Injection of fat tissue has been found to improve glottal closure in case of laryngeal paresis, ^{19,20} however, its abbreviated life span of less than 12 months has been corroborated histologically.

Operative procedures which spare some glottic structures and mobility yield varying voice results. Vocal cordectomy or cordotomy remove a portion of the sound source of phonation, and create a breathy dysphonia. When a malignancy involves one vocal fold and surrounding structures, a vertical hemilaryngectomy may provide a mechanism for voicing; the uninvolved vocal fold vibrates against the tissue of the neolarynx, preserving a functional voice. In the case of supraglottic tumour the entire laryngeal vestibule may be excised, with membranous folds left intact to provide for phonation ²¹. When laryngeal cancer requires a supracricoid laryngectomy all laryngeal structures above the level of the glottis are removed as well as the membranous vocal folds. Usually one or both mobile arytenoids cartilages are spared ²². In near total

laryngectomy a tracheopharyngeal tract is created for sound production. The total laryngectomy patients communicate either through an artificial larynx (electro larynx) or by oesophageal speech, which requires a long commitment to therapy but allows greatest communicative independence. Prosthetic speech, which is created by inserting a one-way valve in the tracheo-oesophageal tract, is advantageous over oesophageal speech because the patient can remove the device periodically for cleaning. Speech therapist can help the patients to develop general strategies during speaking, e.g. to lower the speed of speech, to break the word into syllables, to maintain face to face contact and to reduce the background noises. Other helpful technique is compensatory movements of tongue during speaking.

AIRWAY CONTROL

Obstruction can occur in any area along the airway and the symptoms and treatment defer depending on the level of obstruction. Mouth breathing with normal inspiratory-expiratory duration and without noise may be indicative of purely nasal obstruction; whereas, sonorous mouth breathing without stridor would suggest obstruction at the tongue base or oral cavity that can be immediately palliated with a nasal trumpet and upright positioning. Inspiratory or biphasic stridor is more indicative of a fixed laryngotracheal obstruction which will likely require bypass in the form of a tracheostomy. Additional factors such trismus and neck immobility from prior radiation or direct tumour involvement may complicate intubation and a tracheotomy under LA may be a fair choice. In tracheostomy, the trachea is generally entered between tracheal rings 2 and 3, however, it may be entered lower, if necessary to bypass any sub glottic extension of tumour. The initial tracheostomy change should be performed by the surgeon, but after 1 to 2 weeks when a mature tract has formed, it may be done with ease by the patient or caregiver. Patients are encouraged to cough to maintain patency while additional saline lavage and deep suctioning are to be done routinely, initially every 4 hour and as needed. Humidifier and addition of mucolytics such guaifenesin or nebulized mucomyst helps to clear thick secretions. Cuffed tracheostomy tubes are usually needed initially and for patients requiring positive pressure ventilation, but after a mature tract has formed a cuffless tube can be used in the cancer patient. This will permit enough collateral flow around the tube, if appropriately sized, to allow a patient to occlude the lumen with a finger or a passy-muir valve and steel speak. The tracheostomy tube can be modified by adding a fenestrated opening in the cannula to improve speech but this can incite granulation

tissue formation and can cause problems.

NUTRITION

Clinical trials have demonstrated that weight loss at the time of diagnosis is prognostic for survival and ability to tolerate treatment^{23,24,25}. Further studies have demonstrated that aggressive nutritional intervention can minimise weight loss and decrease treatment related toxicity. Prior to instituting therapy the causes of weight loss should be identified and treatable causes must be attended to quickly. Decreased oral intake may be due to oral pain, difficulty swallowing or mechanical obstruction caused by the tumour. The presence of infected, necrotic material also leads to unpleasant taste & breath which spoils the enjoyment of food and suppress appetite. Patients with mild to moderate swallowing deficits, soft, pureed foods and liquid supplements can stabilize weight loss. Severe swallowing difficulties require more aggressive therapy such as placement of a PEG feeding tube. Patients undergoing primary radiation therapy or combined chemo radiation may develop severe mucositis which results in a profoundly diminished oral intake. Newman et al²⁶ reported that patients undergoing aggressive chemo radiotherapy lost an average of 10% body weight during therapy. Tyldesley et al²⁷ reported that patients who received an elective PEG tube prior to radiation therapy had a 3% stabilized weight loss at week-6 of therapy versus 9% in control group. The difference is maintained at 3 months (3% versus 12%)²⁷. The use of nasogastric tube should be avoided since patients with head and neck cancers usually require prolonged nutritional support and it exacerbates radiation induced mucositis. Factors that contribute to decreased food intake with or without restriction in the consistencies and types of food include swallowing abnormalities due to tumour or treatment, xerostomia from salivary gland radiation, dental extractions, alteration in the ability to chew solid food, alterations in taste cause food aversions and mucosal sensitivity. In addition to the functional and treatment related causes of weight loss, patients with locally advanced, metastatic, or recurrent disease may also have cancer cachexia. The anoxia of terminal disease is poorly understood but may be hypothalamic in origin. Kutscher et al²⁸ have suggested that in most terminal disease, other than oropharynx or oesophageogastric tumours, there is little physical obstruction to eating, but rather a generalized lack of appetite and disinterest to food and nutrition. It has been realized recently that trace elements (e.g. manganese or zinc) may be severely depleted as well as vitamins; however, serum levels may not reflect a cellular lack. Where nausea or

vomiting is a problem the phenothiazine group are still the most useful medications in such group of patients.

PAIN

Pain in HNC is a multi-dimensional symptom complex with physical, emotional, psychosocial and cultural factors contributing to the overall pain experience. Twycross^{29,30,31,32} has pioneered the pharmacological control of cancer pain. Analgesics can be prescribed according to WHO analgesic ladder. All these factors must be addressed in order to provide adequate palliation. Grond³³ reported on the type of pain experienced by HNC patients prior to, during and after treatment. Of 167 patients studied, 138 (38 %) patients had pain due to tumour. Of 138 patients with tumour-related pain, 80% had soft tissue pain, 20% bone pain and 35% neuropathic pain. In head and neck cancer somatic pain is due to deeply ulcerative lesions. Tumour invasion into nerves either peripherally or at the level of the base of the skull can lead to refractory pain syndromes and neurologic deficits. Tumours such as adenoid cystic carcinoma may track along peripheral nerve and into nerve roots resulting in painful peripheral neuropathies³⁴. Sometimes benign processes such as sinusitis, temporo-mandibular joint dysfunction or maxillofacial neuralgias can be the first manifestation of carcinomas producing maxillofacial pain^{35,36,37,38,39,40,41}. Sometimes postoperative pain assessment is difficult due to tracheostomy tube placement, loss of speech function or severe oral pain causing difficulty in communication. Chronic postoperative pain is common in HNC patients. Chaplin and Morton,⁴² reported that 26% of patients had pain 2 years after completing therapy. Pain was described as moderate or severe in 14% of patients. Predictors for chronic pain are due to pain at 3 months post treatment and neck dissection. Other causes include peripheral nerve damage during resection (neuropathic pain) and contracture and tissue scarring in the neck and shoulders. Short et al demonstrated that⁴³ sparing of the spinal accessory nerve resulted in diminished shoulder pain. Other modes of therapy are heat, massage and relaxation techniques to decrease musculoskeletal pain. Steroids in the dosage commonly prescribed can cause euphoria, stimulate appetite, create a sense of wellbeing and may even be instrumental in decreasing narcotic requirements and helping to control pain^{44,45}. They are more effective when pain is associated with inflammation and oedema and may have antiemetic effect as well. The effect of 8mg dose is usually manifested within 2-3days. Patients, who receive radiation therapy as a primary treatment or an adjuvant in the post

operative setting, develop severe debilitating mucositis and radiation dermatitis which produced pain. During the first 2-3 weeks of radiation therapy there is a mild oral discomfort which can be relieved by topical lignocaine solution and mixed opioid/non-opioid tablets. By week 4 or 5, oral and dermal pain begins to increase and patients' ability to swallow decrease substantially. Fentanyl patches are very convenient in this population and short acting intravenous narcotics or subcutaneous route may be used for breakthrough pain. This radiation mucositis pain takes weeks to months to dissolve. Pain due to local recurrence is a major palliative issue in terminal head and neck cancer patients and at times it may be the first symptom indicating recurrent disease. Smit et al⁴⁶ reported pain as the first symptom indicative of recurrence in 70% of patients with a median lag time of 4 months between the onset of pain and the diagnosis of recurrent disease. In case of intractable HNC pain, intrathecal or intraventricular infusion of morphine is recommended^{47,48,49}. Surgical interruption of pain conducting nerves contributing to intractable HNC pain is another option⁽⁵⁰⁾. If nerve block is not feasible⁵¹, cranial nerve division, medullary tractotomy and cordotomy are possibilities that lead to good results^{50,52}. Percutaneous thermal rhizotomy of the trigeminal nerve is another proposed procedure⁽⁵¹⁾. Electrical treatment of severe HNC pain has also been advocated⁵³.

MUCOSITIS

It is an acute complication of radiotherapy resulting due to mitotic death in the basal layer and an inability to replace the naturally exfoliated apical layer of cells at the mucosal surface. It usually begins 10 to 14 days after radiation therapy with a transient patchy white discoloration of the mucosa initially, followed by a confluent deep erythema and pseudo membrane formation⁵⁴. Mucositis may be exacerbated by accelerated radiation fractionation,⁵⁵ concurrent chemotherapy⁵⁶, superinfection with *Candida albicans* or abnormal bacterial flora⁵⁷. In addition to causing pain mucositis impairs eating, swallowing and speech.

XEROSTOMIA

It is a severe and permanent complication of external beam radiotherapy resulting from damage to the acinar cells and stromal matrix of the major and minor salivary glands. The degree is related to the amount of salivary gland tissue and the radiation dose delivered. salivary gland function, both stimulated and unstimulated, drops rapidly to 5-30% of normal within the first 2-3 weeks of therapy and remains low

(< 10% of normal) following completion of radiation for a prolonged period of time^{58,59,60,61}. In mild xerostomia the problems are deglutition difficulty, dental caries, speech, swallowing, weight loss, mucosal irritation and pain. Severe xerostomia patients may drink litres of fluid daily for comfort purposes and rinse mouth with sodium bicarbonate to maintain dental hygiene and to sooth the mucosal surface. Pilocarpine at the dose of 5mg t.i.d. or q.i.d. has been used for the treatment of radiation induced xerostomia with minimal side-effects. Its peak effect is after 1 hour, duration of action is between 3-5 hours and symptom relief is maximal at 4 months. Amifostine, a free radical scavenger, can also be used for reduction in xerostomia at a dose of 200mg/m² 15-30 minutes prior to each fractionation of radiation in post operative radiation therapy.

AUDITORY FUNCTION

HNC patients may experience sensorineural hearing loss from therapy with radiation or systemic chemotherapy agents like cisplatin. In a longitudinal study of hearing loss in patients treated with radiation or radiochemotherapy for nasopharyngeal carcinoma,⁶² 31% of patients had a measurable sensorineural hearing loss 3 months after completing therapy. Hearing deficit improved over time in only 40% of patients. Older patients (>50 years of age) and patients with pre-treatment hearing deficit were more likely to develop measurable sensorineural hearing loss. Concomitant chemotherapy did not worsen hearing outcome. Middle ear effusions are a common cause of non-sensorineural hearing loss and should be identified and treated appropriately.

TASTE ALTERATION

Loss of taste may be caused by a wide variety of medical illness and pharmaceutical agents including many chemotherapy drugs⁶³. Radiation therapy, which is an integral part of treatment for all patients with locally advanced disease, may result in severe and permanent alteration in taste sensation. Taste alteration may begin 2-3 days after initiating therapy and taste bud degeneration may be seen 6-7 days after starting radiation therapy. Accumulated doses over 600 cGy may be associated with permanent damage. It results in nausea and vomiting and has profound effect in nutrition and quality of life. Taste slowly returns within weeks or months after completion of therapy.

WOUND CARE, FISTULA AND CAROTID RUPTURE

Regional and distant tissue transfer techniques have

expanded the ability to cover vital organs such as the carotid artery and bring well vascularized tissue into a contaminated operative field that can resist infection and postoperative radiation therapy. In all cases, the reconstruction, particularly in the immediate postoperative period, is solely dependent on its blood supply and careful attention must be given to placing any dressings around neck, which may compress the pedicle vessels. Patients who have undergone prior radiation therapy or combined chemo radiation therapy are at greater risk for wound breakdown as a result of the small vessel arteritis that reduces oxygen tissue exchange in the area. Additionally, patients' preoperative nutritional status and smoking history complicate their wound healing capacity. Pharyngocutaneous fistula may result from wound breakdown if a watertight seal of the pharynx cannot be maintained. Patients who have had a breach of pharynx during their resection are often maintained with nasogastric feedings to limit the contamination of suture lines for 1-2 weeks. Fistula formations are usually heralded by erythema of the neck, tenderness and low grade fever. The saliva of the neck must be drained and the path away from the carotid artery exposure of the neck vessels lead to carotid rupture, lead to an acute emergency. The vessel should be covered with saline soaked gauze and any leaky carotid should be taken seriously and explored if needed. If a fistula does not form, the wound should be covered with wet or dry gauze twice a day or more, if contamination excessive. In unresectable disease of the neck there is ulceration and necrosis. Tumour hygiene can be achieved by debridement by hydrogen peroxide and antibiotics. Oral hygiene is maintained with saline or soda mouth rinse.

Carotid rupture is a catastrophic complication of HNC and its therapy. It may occur in patients undergoing extensive resection, external beam radiotherapy, brachytherapy or those with recurrent / advanced cancers of the neck. The investigators at MSKCC reviewed the data of 2346 patients undergoing head and neck surgical procedures between 1994-1995 but only one case of carotid rupture was identified⁶⁴. The carotid rupture can be investigated with angiography and may be treated by balloon occlusion and embolisation.

OSTEORADIONECROSIS

Mandibular osteoradionecrosis is one of the most serious complications from head and neck radiation. The incidence varies depending upon total radiation dose⁶⁵, fractionation, volume irradiated⁶⁶, follow up time, the status of dentition and reporting institution^{67,68,69}. The pathogenesis of

osteoradionecrosis includes a decrease in cellularity, suppressed osteoblastic activity, altered bone remodelling, avascularity and fibrosis that leads to poor wound healing after dental trauma and increased risk of secondary infection from bacterial flora. It can ultimately result in exposure of bone, fistula formation and pathological fracture. Antibiotic prophylaxis should be used, grossly diseased maxillary and mandibular tissue should be extracted and a minimum of 14 days should be allowed for healing prior to onset of radiation⁷⁰. Apart from improving oral hygiene and removing local irritants like alcohol and tobacco, pentoxifylline can be used to promote healing of the radiated soft tissue. In severe cases surgical reconstruction has to be done.

DERMATITIS AND SOFT TISSUE DAMAGE

Acute radiation dermatitis usually begins 2 to 3 weeks after external beam radiation therapy. Initially there is erythema with mild oedema followed by ulceration, blistering and sloughing that heals within 2 to 4 weeks after radiation is completed. Long term sequella develop 2 to 4 months after completion of therapy as fibrous soft tissue mass in the anterior neck or submental region. Sometimes there is facial oedema and swelling due to blockage of lymphatic and vascular drainage of the neck. Use of steroids, diuretics or massage may diminish symptoms.

PSYCHOLOGICAL SUPPORT

Good communication is the key to psychological support. Imparting information must be undertaken with honesty and openness, in an atmosphere of sensitivity and compassion, with adequate emotional support⁷¹. The level of information and pace at which it is given should be appropriate for an individual's ability, needs and culture. Usually patients want information on their illness^{72,73}, but, in many parts of the world, information with ominous portent is withheld from patients. While this practice is based on compassion and family concern, a 'conspiracy of silence' and a 'conspiracy of words', may add to a patient's suffering. Progressive acceptance by the patient of what is happening often occurs naturally and slowly, in a truly supportive environment. Unless patients are enabled to unburden themselves and share their anxieties and fears, pain and other symptoms may become the intractable avenue through which psychological distress is expressed⁷⁴.

Although it may be impossible to offer hope of a cure, it is always possible to offer pain relief, psychological support, improved quality of life, and comfort in dying. However, as with pain management, there is a need for specific training

in communication skills⁷⁵.

In the last few years several new therapeutic procedures for advanced head and neck cancer, which are not included in the generally accepted methods, such as immunotherapy, gene therapy, intratumoral cisplatin gel therapy as well as selective intra-arterial chemotherapy, were developed and applied^{76,77,78}. Intra-arterial chemotherapy is more effective with decreased toxicity than intravenous and the effect can even be increased by an accompanying therapy with thiosulphates⁷⁹.

CONCLUSION

The advanced HNC presents with difficult and unique problems to patients, carers, and health care professional's. Living with advanced HNC is often emotionally traumatic for both patient and carer. The HNC patient has to cope with a terminal disease, impact and complications of treatment, and psychological consequences of disfigurement. Health care professionals often find caring for HNC patients difficult and stressful, especially in the presence of communication difficulties and bad smelling wounds. Carers need access to support and advice. Lastly, multidisciplinary approach to management of advanced HNC is necessary along with the development of palliative care approach to pain and symptom management in this group of patients.

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