Surgery and radiation therapy are currently the definitive curative approaches to head and neck cancers (HNCA); the hospital pharmacist can play an important part in supportive care during and after these treatments. The importance of incorporating the pharmacist into the multidisciplinary HNCA treatment team is often overlooked. For example, the 2005 HNCA practice guidelines issued by the National Comprehensive Cancer Network do not discuss the need for pharmacy support. The pharmacist can have a significant impact on the patient's quality of life (QOL) by helping to manage side effects, such as speech impairment, dysphagia, malnutrition, mucositis, and pain.

Treatment of the patient with HNCA is complex, and QOL is a major concern. Forty percent of patients are diagnosed with early-stage disease, for which single-modality treatment with surgery or radiation therapy is recommended; locally advanced HNCA is usually treated with combined modalities. The specific treatment strategy is determined by the anatomic disease site(s), extent or stage of disease, pathologic findings, and other patient-specific factors. The need for individualized treatment decisions and the importance of QOL issues present key opportunities for the pharmacist to help patients.

HEAD AND NECK CANCER SURGERY

Surgical resection of HNCA is determined by the anatomic site of the disease. HNCA is generally deemed unresectable if surgery would not be able to remove the entire gross tumor, local control would not be achieved postoperatively even with incorporation of radiation therapy, or the tumor could not be removed without imposing unacceptable morbidity. A cancer may be determined to be unresectable based on patient-specific comorbidities. It is important to realize that unresectable is not a standardized term and often is determined by the treatment team.

Head and neck cancer surgery is categorized as comprehensive or selective, depending on the approach to lymph node removal. Comprehensive neck dissection involves removal of all lymph node groups that would be included in a classic “radical” neck dissection. Selective neck dissection removes cer-
tain lymph nodes based on how the specific type of HNCA commonly spreads to the regional nodes. Selective dissection, often combined with adjuvant radiation therapy, is frequently used for small tumors, for which a small dissection may be able to control the disease.1 The side effects of surgery differ greatly depending on what type of surgery is done and which and how many lymph nodes are removed.

**POSTSURGICAL FUNCTION**

Resection of structures used in speaking and swallowing often results in some degree of functional deficit. Postsurgical function depends on the type and extent of surgery, postsurgical reconstruction, and amount of time that has elapsed since surgery. The functional deficits can cause challenging problems and must be weighed heavily in the treatment decision. However, surgery limits the amount of tissue exposed to treatment, is relatively fast, and avoids the complications of radiation therapy while still allowing postsurgical radiation therapy if necessary.

**RADIATION THERAPY FOR HEAD AND NECK CANCER**

Radiation therapy for HNCA is determined by the anatomic site and type of the tumor and the clinical circumstances. Cost also is a consideration. In some cases, radiation therapy is used because comorbidity renders surgery inappropriate. Postoperative radiation is recommended on the basis of tumor stage and histology and surgical findings, including tumor size, surgical margin status, and the degree of lymph node involvement and tissue invasion.1

Many advances have been made in optimizing radiation therapy procedures, but no single fractionation schedule has proved superior for all tumors. Hyperfractionation, or an accelerated schedule for administering radiation in an attempt to avoid tumor repair in early-responding tissues, has been shown to increase locoregional control of disease in some clinical studies but is associated with an increase in early and late toxicity. Brachytherapy, or using an implanted radioactive component, is the definitive treatment for early superficial lesions and is sometimes used with external radiation. Intensity-modulated radiation therapy uses beams of varied intensity that enter the body from many angles in a 3-dimensional approach to minimize damage to surrounding tissue without compromising doses to target tissue.1

**POSTTREATMENT FUNCTION**

Function after radiation therapy varies depending on the type of therapy used. Side effects, which can change over time, include pain, reduced salivary flow, edema, restricted movement, nausea and vomiting, reduced appetite, reduced senses of taste and smell, and dental problems. These problems must be weighed against the advantages of radiation therapy, which include fewer functional and cosmetic defects, the ability to treat lymph nodes, and the avoidance of surgical complications.

**QUALITY-OF-LIFE MEASUREMENTS**

Given the importance of short-term and long-term QOL issues in HNCA, the use of methods to assess QOL should be considered to determine the impact of treatment for individual patients and in clinical trials as an aspect of the comprehensive evaluation of new treatment approaches. Optimally, these measures should be multidimensional, sensitive to changes in the patient’s needs during and after treatment, appropriate to disease type, and sensitive to the perspective of the patient. In addition, the methods must be easy to administer and practical for their use to be incorporated into clinical practice.

Validated measures of QOL in HNCA include a range of methods, such as the University of Washington Quality of Life Scale, the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Head and Neck Cancer Module (QLQ-H&N35), and the Functional Assessment of Cancer Therapy Head and Neck Module.2 Some methods focus on issues specific to HNCA, such as the QLQ-H&N35, which asks patients about pain, swallowing, senses, speech, social eating, social contact, sexuality, teeth, opening the mouth, dry mouth, sticky saliva, coughing, and feeling ill.2 Other measures incorporate a broader evaluation of issues related to QOL; the EORTC Core Questionnaire (QLQ-C30) evaluates aspects of QOL, such as physical functioning, role functioning, emotional functioning, cognitive functioning, social functioning, fatigue, nausea and vomiting, general QOL, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial problems.2 Perhaps the best determination of QOL is provided by using a combination of these assessments, but the use of 2 questionnaires may be time consuming and impractical.
Sherman et al evaluated the reliability and validity of QOL measures in 120 ambulatory patients with advanced HNCA before treatment, during treatment, within 6 months of completing treatment, and more than 6 months after treatment by using the QLQ-C30, QLQ-H&N35, Profile of Mood States, and Impact of Events Scale. The QLQ-H&N35 demonstrated acceptable reliability and was shown to discriminate among subgroups of patients at different phases of treatment and to be sensitive to the effects of radiation treatment and the site of disease. El-Deiry et al compared long-term health-related QOL outcomes in 27 matched pairs of patients with advanced HNCA who received surgery followed by radiation therapy or concurrent chemotherapy and radiation therapy. The investigators used the University of Iowa Head and Neck Cancer Inventory and the Beck Depression Inventory to evaluate QOL at least 12 months after treatment. The results showed that the 2 treatment combinations resulted in a similar QOL (Table 1).

**DIFFICULTIES EXPERIENCED BY PATIENTS WITH HEAD AND NECK CANCER**

The many difficulties encountered by patients with HNCA as a result of the disease and its treatment represent an opportunity for the pharmacist to substantially improve care and optimize their response to issues that affect patients’ QOL. Many symptoms and toxicities associated with therapies can be managed and at times alleviated with pharmacologic intervention. The incorporation of a pharmacist into the healthcare team during all phases of treatment should be considered to optimize the pharmaceutical care associated with treatment and disease-related complications.

**SPEECH IMPAIRMENT**

Speech impairment is one of the primary difficulties experienced by patients with HNCA as a result of surgery and radiation therapy. Surgical removal, rearrangement, and reconstruction of tissue in the lips, tongue, and jaw may affect speech and voice. Radiation may cause mucosal changes that lead to oral mucositis, muscle changes that lead to atrophy and fibrosis, and other effects that impair speech, including xerostomia, peripheral nerve deficits, and dental problems. Speech dysfunction after radiation may be transient. Although normal function may return as early as 3 months after radiation therapy, patients may continue to perceive postradiation voice changes for years after such therapy has ended.

Speech impairment has a large impact on the management of HNCA and treatment-related symptoms. Rodriguez and VanCott have shown that patients with HNCA tend to be undertreated for disease-related and treatment-related pain because patients cannot communicate easily with the healthcare team about their pain symptoms. QOL was greatly affected by the availability of voice and communication rehabilitation in this study. A potential role of the pharmacist is to minimize problems that contribute to speech impairment, particularly mucositis and xerostomia. In addition, the pharmacist should consider issues and strategies to optimize communication about drug-related issues and assessment of complications. A tremendous opportunity exists for the pharmacist to work with speech-impaired patients to implement communication techniques to enable their symptoms to be better understood and eventually better managed.

**DYSPHAGIA**

Dysphagia is another possible effect of HNCA surgery and radiation therapy and results from disruption of the structure or function of the oral cavity, pharynx, and esophagus. The pharmacist can help the healthcare team address this impairment by working with the team and patient to determine the most appropriate and cost-effective methods to optimize Table 1. Head and Neck Cancer QOL Outcomes by Treatment

<table>
<thead>
<tr>
<th>QOL Measure</th>
<th>CRT</th>
<th>SRT</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eating</td>
<td>37.8</td>
<td>40.8</td>
<td>.69</td>
</tr>
<tr>
<td>Speech</td>
<td>65.1</td>
<td>56.0</td>
<td>.23</td>
</tr>
<tr>
<td>Aesthetics</td>
<td>80.3</td>
<td>69.2</td>
<td>.14</td>
</tr>
<tr>
<td>Social disruption</td>
<td>69.7</td>
<td>70.6</td>
<td>.9</td>
</tr>
<tr>
<td>Overall QOL</td>
<td>55.5</td>
<td>64.0</td>
<td>.14</td>
</tr>
<tr>
<td>Depressive symptom</td>
<td>11.6</td>
<td>9.6</td>
<td>.42</td>
</tr>
</tbody>
</table>

*≥12 months after treatment.

nutrition and drug therapy. Developing a patient-specific drug-therapy plan may involve the use of innovative dosage strategies to optimize care.

**Malnutrition**

Patients with HNCA often find it difficult to ingest enough calories, and malnutrition is commonly associated with HNCA, especially in patients receiving radiation therapy. Weight loss during radiotherapy is an early indicator of nutritional decline. A proactive approach to this issue is beneficial. By comparing the benefits of dietary counseling, enteral feeding through a feeding tube, and oral alimentary supplementation, Ravasco et al showed that providing dietary counseling when radiotherapy is initiated can increase caloric intake.5

**Metabolic Abnormalities**

Nutritional problems can result in metabolic abnormalities in patients with HNCA, particularly in patients receiving radiation therapy. In a retrospective analysis, Lin et al studied the metabolic impact of chemotherapy and radiation therapy on patients with HNCA who received induction chemotherapy followed by concurrent chemotherapy and radiation.4 Body weight and metabolism were evaluated before and during induction chemotherapy and chemoradiation. The results showed that patients receiving radiation therapy were subject to greater metabolic disturbances, primarily because mucositis prevented patients from eating.6

**Oral Mucositis**

Patients with HNCA are at risk for oral mucositis from surgery and radiation therapy. Patient-related risk factors include advanced age, male sex, chronic periodontal disease, xerostomia, poor nutritional status, and lack of oral care during therapy; treatment-related factors include radiation dose and schedule.7 Whereas mucositis tends to heal rapidly after each course of treatment in patients receiving chemotherapy, patients receiving radiation therapy may experience it continually. Radiation-induced mucosal thinning leads to ulcers, inflammation, and depletion of epithelial basal layers followed by bacterial infection, and continual radiation exposure can damage the germinal epithelial tissue, which prevents healing.8

Mucositis can range in severity from mild mouth soreness to soreness that results in the need for parenteral support (Table 2).9,10 Complications include pain; inability to eat, drink, swallow, and talk because of impaired oropharyngeal function; hemorrhagic complications; taste alterations; and fungal, viral, and bacterial infection. These complications can extend hospital stays, increase hospital and home care costs, prevent the patient and caregiver from working, and interrupt treatment, which increases the risk of death. Other problems include experiencing halitosis, completely losing the appetite, needing to restrain oneself to eat, being sick, having to use distasteful mouthwashes regularly, feeling tired, having to make a special effort to talk, and being socially isolated.11 The pharmacist can have a substantial effect on patient care and patient QOL by working with the healthcare team to implement strategies to prevent and manage mucositis.

Typical interventions to alleviate mucosal changes caused by radiation include using salivary supplements, drinking water liberally, taking analgesics, using mouthwashes, topical gels, and mechanical cleansing, and eliminating drying substances, such as alcohol-based mouthwashes and decongestants. To help preserve mucosa and mouth function, muscle interventions, such as cold stimulation, stretching, and strengthening exercises, ensure that the muscles are still being used even if the patient is not eating.

Many agents for treating mucositis have been tried, including vitamins, sucralfate, allopurinol, topical chlorhexidine, topical sodium bicarbonate, topical saline, topical gentian violet, antibiotic lozenges, anesthetic cocktails, topical nonsteroidal anti-inflammatory agents, topical hydrogen peroxide, prostaglandins, antiprostaglandins, and growth factors. In addition, the keratinocyte growth factor palifermin, which was approved by the US Food and Drug Administration in 2004 to treat mucositis in patients with hematologic malignancies, is currently being investigated for use in HNCA treatment.

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**Table 2. Mucositis Grading**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Signs and Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No ulcers</td>
</tr>
<tr>
<td>1</td>
<td>Painless ulcers, erythema, or mild soreness in the absence of lesions</td>
</tr>
<tr>
<td>2</td>
<td>Painful erythema, edema, or ulcers; patient is able to eat</td>
</tr>
<tr>
<td>3</td>
<td>Painful erythema, edema, or ulcers; patient is unable to eat</td>
</tr>
<tr>
<td>4</td>
<td>Requires parenteral or enteral support</td>
</tr>
</tbody>
</table>

Data from World Health Organization9 and National Cancer Institute.10
One simple but effective approach to care is to address mucositis proactively by keeping the area as clean as possible and managing pain on an individualized basis. Initially, pain medication is generally best given as needed but, in patients with continual mucositis, may need to be scheduled for administration around the clock for some length of time. It is important to assess the need to schedule opiates and to determine when opiate administration should be changed back to an as-needed schedule. Pain management options include topical anesthetics, systemic anesthetics, and opiates. The route of administration of opiates, the dose, and the schedule should be determined on an individualized basis. However, the adverse effects of chronic opiate use should be kept in mind. Modifying the regimen as the patient heals also is important. One example is the use of transdermal fentanyl. These patches often are considered because the patient does not need to worry about frequent dosing or oral administration of an opiate, but the dose of pain medication provided by transdermal patches may be difficult to titrate down after healing begins. Ingesting oral medications is an issue in patients who cannot swallow. Although not always a first-line or appropriate choice, patient-controlled analgesia can give patients the flexibility to use medication only when they have more pain, such as while eating. This approach can be very helpful in end-stage HNCA.

**DISEASE-RELATED PAIN**

Beyond the pain related to treatment, such as radiation-induced mucositis and postsurgical pain, another focus for pharmaceutical care is the management of disease-related pain in individuals with HNCA. As HNCA advances, the disease often enlarges locally, which can result in considerable nerve, bone, and tissue pain. Therefore, pain management in this patient population must be constantly reassessed and treatment approaches modified. A mixed-pain syndrome requires aggressive management that is modified as the patient’s description of the pain changes; it is not a matter of simply increasing the dose of the opiate. Appropriate management strategies should be constantly reevaluated and guided by the type and presentation of pain. Disease-related pain is another area in which the pharmacist can play a vital role.

**CONCLUSIONS**

Although the definitive treatment of HNCA is nonpharmacologic, such treatment presents many often unrecognized opportunities for the pharmacist to help improve patient outcomes and QOL. The side effects of surgery and radiation, such as speech impairment, dysphagia, malnutrition, mucositis, and pain, often require pharmacologic treatment, and the patient may benefit from the involvement of the pharmacist to facilitate optimal care, communication, and patient education. As new agents are developed to help treat HNCA and the side effects of its treatment, the pharmacist will take on an even more important role.

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**REFERENCES**


