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Integrative medicine in head and neck cancer

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Abstract

Objective—Complementary and alternative medicine (CAM), or integrative medicine, has become increasingly popular among patients with head and neck cancer. Despite its increasing prevalence, many patients feel uncomfortable discussing such therapies with their physicians, and many physicians are unaware and underequipped to evaluate or discuss their use with patients. The aim of this manuscript is to use recent data to outline the decision-making inherent to integrative medicine utilization among patients with head and neck cancer, to discuss the ethical implications inherent to balancing integrative and conventional approaches to treatment, and to highlight available resources to enhance head and neck cancer providers' understanding of integrative medicine.

Data Sources—Randomized controlled trials involving integrative medicine or CAM treatment for cancer patients.

Review Methods—Trials were drawn from a systematic PubMed database search categorized into cancer prevention, treatment, and symptom management.

Conclusions—Integrative medicine is gaining popularity for the management of cancer and is most commonly used for symptom management. A number of randomized controlled trials provide data to support integrative therapies, yet physicians who treat head and neck cancer may be faced with ethical dilemmas and practical barriers surrounding incorporation of integrative medicine.

Implications for Practice—In the management of head and neck cancer, there is an increasing demand for awareness of, dialogue about, and research evaluating integrative medicine therapies. It is important for otolaryngologists to become aware of integrative therapy options, their risks and benefits, and resources for further information in order to effectively counsel their patients.

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Introduction

Complementary and alternative medicine (CAM) encompasses “a group of diverse medical and health care interventions, practices, products, or disciplines that are not generally considered part of conventional medicine”.¹ These modalities are used by 38% of adult patients in the United States and prevalence continues to increase.² In recent years, “integrative medicine” has replaced “complementary and alternative medicine” as the preferred terminology. Integrative medicine focuses on a collaborative approach to patient care that involves “bringing conventional and complementary approaches together in a coordinated way”³ and suggests a more cohesive and patient-centered treatment.

As the use of integrative therapies is becoming increasingly common among patients with cancer, physicians must become adept at helping patients navigate these therapies. However, despite its increasing popularity among patients, integrative medicine has been slow to gain acceptance in the mainstream healthcare system, in part due to a lack of awareness among clinicians of research and clinical trials demonstrating the efficacy of integrative therapies⁴, the barriers to paying for integrative therapies, and a paucity of resources to guide clinicians in finding integrative medicine resources and providers.

Despite its overall growing presence in Western medicine, a role for integrative medicine has not been fully established among head and neck cancer providers. For patients and providers alike, key considerations in using integrative therapies include assessing the potential risks and benefits of the therapy, available evidence for specific therapies, and whether patients intend to use such therapy as an alternative treatment or in a complementary/integrative manner.⁵⁻⁷ Given this complex and challenging landscape, clinicians may benefit from an increased awareness of how integrative medicine can enhance the patient-doctor interaction and potentially improve patient experiences. Herein we present index patients with head and neck cancer who used integrative medicine in order to guide a discussion of how clinicians might better understand the types of and rationale for integrative medicine as they navigate the inherent practical and ethical challenges. We also offer resources clinicians can use to help guide them in determining the evidence for as well as the potential harms, interactions, and contraindications of integrative therapies.

Methods

Articles were identified via a formal PubMed database search specifying all randomized controlled trials published within the past ten years investigating integrative medicine or CAM for cancer patients and/or head and neck cancer patients. Trials were assessed by the authors and sorted into categories of cancer prevention, cancer treatment, or symptom management.

Illustrative deidentified case examples were chosen to exemplify the inherent issues. The University of Michigan Institutional Review Board has determined that publication of deidentified case studies does not require formal review or approval.

Discussion

Integrative Medicine Use in Head and Neck Cancer

Several types of integrative therapies, including natural products, mind-body practices, naturopathy, and Ayurveda, are commonly used among patients³. Biologically-based therapies such as herbal medicines, medicinal teas, and vitamins/minerals are the most common integrative therapies used by patients with head and neck cancer, followed by mind-body interventions such as visualization.^{6,8} Patients tend to use integrative medicine in regard to cancer in one of three separate paradigms: 1) prevention of cancer, 2) intended treatment of cancer, and 3) mitigation of side effects associated with cancer and conventional treatments.^{8,9} While scientific evidence is generally limited with regard to the efficacy of integrative therapies for cancer prevention and treatment, there is a wealth of data supporting integrative therapies for symptom management. In fact, there are over 200 randomized controlled trials focusing on integrative therapies for symptom management of breast cancer alone.¹⁰

While prevalence of integrative medicine usage varies greatly across studies, systematic reviews suggest that approximately one-third to one-half of cancer patients are using some form of integrative therapy^{11,12}. Specifically in head and neck cancer, rates of use are more varied, ranging from 6–79%.^{6,9,13} This variation may be a function of methodology of data collection as well as timing; notably, integrative medicine use in head and neck cancer patients may increase dramatically after diagnosis and initiation of treatment.⁸

It may be difficult for patients and physicians to know where to find reliable information regarding the efficacy of these therapies, especially because the preponderance of internet-based information is of questionable veracity and accuracy.¹³ There is an increasing demand for rigorous integrative medicine data and clinical trials in cancer in order for physicians to provide better recommendations to their patients.¹⁴

Cancer Prevention

A 45-year old woman is referred to the head and neck oncology clinic for worsening white lesions in the oral buccal mucosa. She has no previous tobacco or alcohol use. Her past medical history is otherwise unremarkable, but she does have an uncle who was a heavy smoker and developed larynx cancer. On exam she appears to have benign oral leukoplakia. She is relieved, but asks about any data for dietary supplements that may help in preventing oral cancer.

Integrative therapies for cancer prevention have generated interest from patients and researchers alike. A number of natural compounds commonly used for cancer prevention have demonstrable anti-cancer effects in both *in vitro* and *in vivo* translational studies, while others are backed by testimonials or individual case studies. Curcumin, an active compound in turmeric, has been shown to have anti-cancer properties in both *in vitro* and *in vivo* studies.^{15–17} A number of antioxidants have been shown to display cancer preventive properties as well by reducing oxidative free radical production in cells.^{18,19} Common antioxidants utilized include green tea (active agent: EGCG), grape seed extract

(resveratrol), and pomegranates (polyphenols), which have been shown to have anti-cancer properties.²⁰

Other dietary factors may play a role in cancer prevention. Prospective epidemiologic studies have identified that pretreatment low fruit intake predicts worse survival in head and neck cancer patients²¹ while diets rich in whole foods such as fruits, vegetables, whole grains, fish, and poultry are associated with better prognosis.²² Diets rich in soy may also aid in head and neck cancer prevention: soy isoflavones, particularly genistein, have been shown to inhibit proliferation of head and neck cancer cells *in vitro*, and may act as a chemopreventive agent in various human carcinomas.^{23,24} Additionally, an epidemiologic study suggested a possible decreased thyroid cancer risk associated with consumption of soy-based foods.²⁵

There have been some early phase clinical trials which have demonstrated modest efficacy of agents in premalignant oral cavity lesions, including retinoic acid and green/black tea (Table I).²⁶ However, despite encouraging preclinical data, demonstrating a clinically significant and durable preventative intervention in patients has been difficult. The challenges of such studies in regards to head and neck cancer prevention are the relatively low overall incidence of head and neck cancer (necessitating an extremely large cohort) and the high potential of confounding patient dietary and lifestyle factors. Specific patient populations at significantly elevated risk for head and neck cancers (e.g. patients with Fanconi anemia or BRCA2 mutations) may prove to be ideal populations in which to validate chemoprevention agents. However, such studies have not been performed to date. As such, currently there are no clear evidence-based recommendations for head and neck cancer chemoprevention (dietary or otherwise).

Cancer Treatment

A 53 year-old male smoker with advanced stage laryngeal squamous cell carcinoma is treated with concurrent chemoradiotherapy with curative intent. He presents for follow-up shortly after completion of treatment with persistent/recurrent cancer. The patient is counseled that a salvage laryngectomy represents his only option for curative intent. He is hesitant to lose his voice box and wants to explore other options, including a trip to Central America for alternative therapy with a traditional healer. He is counseled about the risks of disease progression and mortality associated with delay of standard treatment, but is not ready to consider surgery until he has explored his alternatives.

Integrative medicine has long been considered for curative treatment of cancer, both as a monotherapy and as an adjuvant therapy. It is important to note that patients who seek out alternative therapy and forego conventional treatment comprise a small minority (<5%) of patients using integrative medicine. This small cohort is often motivated to use alternative medicine due to distrust of and/or dissatisfaction with the conventional healthcare system as well as a strong desire for control.²⁷ For physicians, awareness of this underlying distrust for conventional medicine may allow for a useful starting point for discussions with such patients.

More commonly, patients seek out integrative therapy as a supplement to standard medical care. Indeed, current NIH-funded clinical studies are investigating integrative medical therapies in a variety of cancer treatment paradigms to supplement current standard of care.²⁸

Interestingly, many chemotherapeutic agents currently being used in Western medicine for cancer treatment are derived from natural compounds.²⁹ For example, (–)-gossypol, a therapeutic derived from cottonseeds and previously used as an herbal Chinese compound, has been shown to enhance radiation sensitivity *in vitro*³⁰ as well as inhibit tumor growth in *in vivo* models of head and neck cancer.³¹ Mistletoe extract historically has been used as an adjuvant cancer therapeutic in many European countries, with *in vitro* studies demonstrating cytotoxic effects on cancer cells and anecdotal evidence of a clinical effect in laryngeal cancer.^{32,33} Other commonly used natural compounds have been demonstrated to have potential as anti-cancer agents in *in vitro* studies, including curcumin (turmeric) and genistein (soy).^{24,34,35}

Clinical trials studying integrative products as treatment for head and neck cancer have been limited (Table II). The most robust study to date involved mistletoe extract as an adjuvant therapy after surgery/radiotherapy, which did not demonstrate an effect on survival.³⁶ Notably, our institution is currently conducting a clinical trial examining the potential benefit of adding (–)-gossypol (AT101) to chemoradiation for advanced larynx cancer.³⁷ Further clinical trials advancing promising agents from *in vitro/in vivo* studies may uncover novel adjuvant therapeutic agents in the near future.

Symptom Management

A 62 year-old woman with tonsil cancer is treated with trans-oral robotic resection and neck dissection. Postoperative adjuvant radiation therapy is recommended. She develops local treatment toxicity, including neck pain, stiffness and xerostomia. She is committed to finishing her course of radiation, but asks if any additional options exist for helping her with her troublesome symptoms.

Patients most often use integrative medicine to counteract side effects of cancer and/or conventional treatment. Frequent thematic responses from a survey of head and neck cancer patients pursuing integrative medicine therapies at MD Anderson included to “improve emotional well-being, hope, and optimism”; and to do “everything to fight the disease”.³⁸ Head and neck cancer therapies are often associated with significant local and systemic morbidity; thus, patients may be drawn to integrative therapies that may ameliorate or temporize bothersome side effects.¹⁴

A variety of studies support the efficacy of various integrative therapies for symptom management during chemotherapy and radiation for head and neck cancer, including honey for mucositis and calendula cream for skin toxicity after radiotherapy for head and neck cancer.^{39,40} While encouraging, many of these studies are limited by small sample sizes.

Acupuncture has repeatedly been shown to effectively manage numerous cancer- and radiation-related symptoms, including xerostomia, pain, nausea/vomiting, pain after neck

dissection for head and neck cancer, as well as provide pain relief from cancer symptoms (Table III).^{41–45} These promising results show that acupuncture may provide significant symptom relief for patients with head and neck cancer and can be considered as a therapeutic option. Additionally, an ongoing Phase III clinical trial is studying the effect of acupuncture on radiation-induced xerostomia, although the results of this study are not yet available.⁴⁶

Additional integrative interventions, including visualization, meditation, and prayer may increase quality of life for patients with head and neck cancer by reducing psychological distress in cancer patients.⁴⁷ In addition, yoga and meditation are routinely recommended for anxiety and mood disorders related to cancer.¹⁰ These mind-body practices are unlikely to interfere with conventional treatments and have the potential to provide comfort. In sum, there is robust evidence validated from reliable clinical trials supporting acupuncture and other integrative modalities in alleviating symptoms from cancer pain and treatment-associated toxicities.

Shared Decision-Making

As awareness and use of integrative medicine continues to increase, head and neck cancer providers may struggle to balance their ethical obligations while safely advising their patients about their options. Despite being used for centuries, integrative therapies remain poorly understood and underutilized in the modern Western healthcare system. This lack of awareness of integrative medicine research combined with a historical deficiency of educational material in most medical school curricula creates a population of physicians with little knowledge about or confidence in such therapies, despite a globally increasing interest in these therapies.⁴⁸ This sets a difficult stage for the patient-physician interaction with regard to discussions about integrative medicine. For example, many patients feel that their physicians are unequipped or unwilling to discuss integrative medicine and therefore avoid disclosing their plans or behaviors to medical professionals.⁴⁸ Not only does such nondisclosure create potential for patient harm through unintended therapeutic interactions, potential adverse side effects, and lack of regulated production or dosing, but it can also create an atmosphere of distrust in the patient-physician relationship.

An overriding theme in all venues of cancer care involves a strong patient-physician relationship with an emphasis on conversation and shared decision-making. As such, when patients with head and neck cancer show interest in integrative medicine, it is crucial that physicians take time to discuss these options. Physicians should consider screening for and opening dialogue in regard to integrative medicine use, as this can build trust between patient and physician as well as create an atmosphere of open-mindedness to integrative therapies.

Patients may have a variety of philosophical motivations for pursuing integrative medicine. For example, many patients use integrative medicine not because of a dissatisfaction with conventional medicine, but because the ideas behind integrative medicine are more aligned with their philosophical beliefs about health.²⁷ By discussing goals of care with patients, physicians can create a more individualized treatment regimen.

When discussing integrative medicine with patients, physicians must be careful to avoid acting in a paternalistic manner. Since knowledge about these therapies is generally limited among conventional healthcare providers and patients, education and evidence-based research or appropriate referral to an integrative medicine provider is vital before beginning an integrative medicine regimen. Disclosing any physician bias regarding alternative therapies to patients is important⁶; however, physicians should refrain from passing judgment on patients for using these therapies and instead focus on having a clear discussion that leaves room for both patient and physician education.

The ultimate obligation of any physician is to avoid and mitigate patient harm. However, this ethical obligation becomes complicated when physicians and patients disagree about what constitutes the proper course of treatment. Since there is limited awareness about integrative therapies for head and neck cancer, a patient's desire to use integrative medicine can provide a unique opportunity for physicians and patients to collaboratively explore these therapies and develop a treatment plan that is safe, effective, and patient-centered. In order to safeguard the health of patients, physicians are obliged to ensure that their patient's use of integrative medicine is safe and monitored.

Despite the potential benefits of integrative therapies, it is imperative that physicians consider potential unintended effects that these therapies may have on standard treatment/cancer prognoses and advise their patients appropriately. A common patient misconception about herbal medicine is that natural compounds are always safe. If physicians believe that an integrative therapy has the potential to negatively impact patient health, they are obliged to discuss this with patients and possibly recommend a safer/more effective therapy. Rather than attempt to discredit or steer patients away from integrative therapies altogether, physicians might recommend treatments that are known to be safe and effective, as well as advise patients about harmful therapies that should be avoided.⁴⁹ For example, cytochrome P450 inhibitors/activators such as St. John's Wort have significant effects drug metabolism, and thus effects on chemotherapy response.⁵⁰ Additionally, some agents generally considered to be safe in most circumstances, may be deleterious in specific instances. As a case in point, high-dose antioxidants have been shown to reduce tumor control during radiation and decrease survival¹⁸.

Eisenberg⁵¹ proposes a step-by-step strategy for physicians to advise patients who are interested in integrative medicine that emphasizes communication and teamwork between doctor and patient, as well as patient safety. His strategy involves questioning patients about current symptoms and closely monitoring these symptoms throughout the course of treatment. Next, physicians should discuss patients' expectations and motivations for using integrative medicine and work together to research the safety and efficacy of each therapy. If patients still show interest, physicians should work with them to identify a licensed integrative medicine provider and brainstorm questions to ask during the initial visit. Many tertiary care centers are establishing departments of integrative medicine in general, and for cancer patients specifically. Finally, Eisenberg recommends carefully documenting patient visits and scheduling follow-ups to monitor the patient's well-being throughout the course of integrative medicine treatments.

In order to integrate such therapeutic modalities into head and neck cancer management, physician and patient education must increase synergistically (Figure 1). Furthermore, the incorporation of research-based integrative medicine programs into oncology departments can optimize patient access to safe and effective integrative medicine.⁵² Open discussion between physician and patient is key in the joint effort to treat cancer in a more interdisciplinary, holistic manner.

National Positions on Integrative Medicine

Integrative medicine is undeniably beginning to play a more important role in Western medicine. As such the Institute of Medicine has stated that “integrating CAM into traditional systems should be a high priority for research.”⁵³ In 1998, the National Cancer Institute founded the Office of Cancer Complementary and Alternative Medicine (OCCAM) specifically to fund robust basic and clinical research into the potential for integrative medicine therapies for cancer. Additionally, the National Institute of Health (NIH) established the National Center for Complementary and Integrative Health (NCCIH; formerly known as the National Center for Complementary and Alternative Medicine).⁵⁴ Both of these organizations conduct and fund a multitude of integrative medicine research, but also represent the necessity of increased clinically sound research about such therapies.

Integrative medicine programs have been or are being established in hospitals throughout the country and are frequently incorporated into cancer centers. Indeed, there has been a movement toward involving integrative medicine counselors as part of comprehensive cancer treatment planning and delivery.⁵² Additionally, there has been an expansion of interest in integrative medicine by private institutions as well as national organizations, which will aid in the assimilation of integrative medicine into the mainstream.⁵⁴

Integrative Medicine Resources

The array of potential integrative therapy options can be daunting for both physicians and patients. Fortunately, there are publically available resources that can provide lists of commonly used integrative medicines, peer-reviewed research investigating their therapeutic effects, and potential drug side effects and drug interactions. Among those providing such resources are the NIH (NCCIH division), Memorial Sloan Kettering Cancer Center, and the Natural Medicines (Table IV).

Implications for Practice

The use of integrative medicine is prevalent among patients with head and neck cancer and is employed in three main paradigms: cancer prevention, cancer treatment, and management of side effects associated with cancer treatment. Patients most frequently seek out integrative medicine for hope, a sense of control in the treatment of their cancer, and symptom management. Using integrative medicine for cancer prevention and symptom management generally does not impose a significant risk to patient health, but awareness of potential interactions and risks are necessary for both the provider and patient. Barriers to care include patient discomfort in disclosing integrative medicine use, physician discomfort in discussing and providing recommendations on integrative therapies, and the relative lack of randomized clinical trials regarding the efficacy of integrative therapies in HNSCC. Although only a

small cohort of patients choose to forego recommended clinical cancer-directed therapies in favor of alternative cancer treatments, such cases engender ethical dilemmas that are difficult for patients and clinicians alike. There is a need for greater awareness of, dialogue about, and research evaluating integrative medicine therapies for head and neck cancer management.

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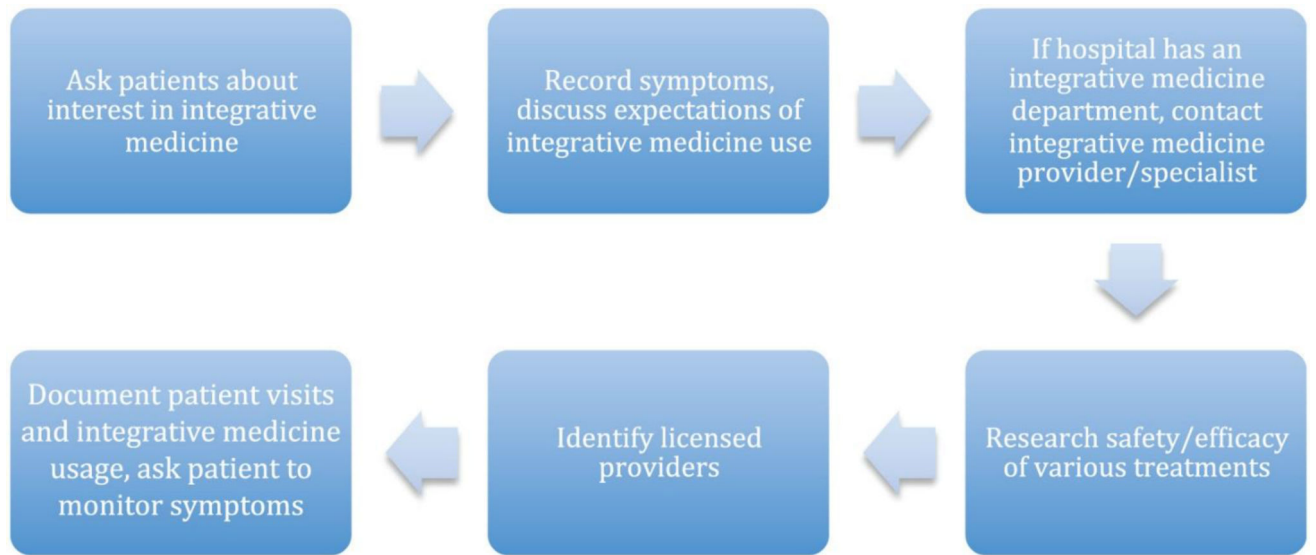


Figure 1. Approach to discussion of integrative medicine with head and neck cancer patients.

Table I

Selected Randomized Controlled Trials for Integrative Medicine for Head and Neck Cancer Prevention

| Study | Intervention | Outcome measured | Findings |
|---------------------------------------|---|---|---|
| Sankaranarayanan (1997) ⁵⁵ | Vitamin A extract vs. β -carotene | Chemoprevention of oral premalignant lesions | Vitamin A and β -carotene administration both induced regression of oral premalignant lesions more effectively than placebo |
| Hong (1986) ⁵⁶ | 13-cRA vs. placebo | Chemoprevention of oral premalignant lesions | 13-cRA significantly decreased size of oral premalignant lesions |
| Hong (1990) ⁵⁷ | 13-cRA vs. placebo | Chemoprevention of second primary tumors | 13-cRA prevents second primary tumor development |
| Tsao (2009) ²⁶ | Green tea extract vs. placebo | Chemoprevention of oral premalignant lesions | No significant difference between groups |
| Mayne (2001) ⁵⁸ | B-carotene vs. placebo | Chemoprevention of second primary tumors | No decrease or delay in second primary tumor development |
| Dash (2012) ⁵⁹ | Tea | Chemoprevention | Inconclusive, high dropout rate |
| Halder (2005) ⁶⁰ | Black tea | Chemoprevention of oral premalignant lesions | Clinical improvement shown among group administered black tea |
| Li (1999) ⁶¹ | Tea | Chemoprevention of oral premalignant lesions | Tea consumption led to a decrease in size of premalignant lesions as well as pathological differences |
| Mallery (2014) ⁶² | Black raspberry gel | Chemoprevention of oral premalignant lesions (OPL) | Topical application of black raspberry gel is effective in decreasing size and histologic grade of oral premalignant lesions. |
| Shin (2015) ⁶³ | Green tea polyphenon E | Maximum tolerated dose of green tea polyphenon E with erlotinib for chemoprevention of premalignant lesions | Ongoing clinical trial |
| Goodin (2009) ⁶⁴ | Green tea | Efficacy of green tea lozenge on prevalence, size, and severity of oral leukoplakia | No study results posted |

Table II

Selected Randomized Controlled Trials for Integrative Medicine for Head and Neck Cancer Treatment

| Study | Intervention | Outcome measured | Findings |
|----------------------------------|-----------------------|---|---|
| Pisters (2001) ⁶⁵ | Green tea extract | Maximum-tolerated dose of green tea extract (Phase I Trial) | Maximum-tolerated dose was 4.2 g/m ² once daily or 1.0 g/m ² three times a day. |
| Steuer-Vogt (2001) ³⁶ | Mistletoe extract | Efficacy of mistletoe preparation as adjuvant therapy after surgery/radiation | Mistletoe had no effect on survival rates, cellular immune response, or quality of life |
| Worden (2015) ³⁷ | (-)-gossypol (AT-101) | Efficacy of AT-101 and chemotherapy for organ preservation in advanced laryngeal cancer | Ongoing clinical trial |

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Table III

Selected Randomized Controlled Trials for Integrative Medicine for Symptom Management in Head and Neck Cancer

| Study | Intervention | Outcome measured | Findings |
|-----------------------------------|---|---|---|
| Barton (2010) ⁶⁶ | Ginseng | Symptom management – fatigue, toxicity | No calculable results, only high doses of ginseng showed some improvements |
| Alimi (2003) ⁴² | Acupuncture | Symptom management – cancer pain | Pain intensity after 2 months significantly decreased for patients in acupuncture group |
| Chen (2008) ⁶⁷ | Acupuncture vs. orally-administered pain medication | Symptom management – cancer pain | Both methods effectively controlled pain; total effective rate of acupuncture group was better than medication group ($p < 0.05$) |
| Jayachandran (2012) ⁶⁸ | Honey | Symptom management – oral mucositis | Significant reduction in mucositis in group with honey treatment |
| Simcock (2012) ⁴⁵ | Acupuncture | Symptom management – radiation-induced xerostomia | Significant reduction in symptoms of dry mouth in acupuncture treatment group |
| Pfister (2010) ⁴¹ | Acupuncture | Symptom management – pain and dysfunction after neck dissection, xerostomia | Significant reduction in pain, dysfunction, and xerostomia in acupuncture treatment group |
| Sahebamee (2015) ⁶⁹ | Aloe vera | Symptom management – radiation-induced mucositis | Aloe vera was equally effective as the control mouthwash and could be used as an alternative |
| Tsujimoto (2015) ⁷⁰ | L-glutamine | Symptom management – chemoradiotherapy-induced mucositis | L-glutamine decreased severity of mucositis |
| Palatty (2014) ⁷¹ | Sandalwood oil and turmeric-based cream | Symptom management – prevention of radiodermatitis after radiation therapy | Sandalwood oil/turmeric-based cream effective in preventing radiodermatitis |
| Lu (2012) ⁷² | Acupuncture | Symptom management – dysphagia after chemoradiation | Inconclusive results |
| Meng (2012) ⁷³ | Acupuncture | Symptom management – radiation-induced xerostomia | Acupuncture led to significant reduction of xerostomia and improved quality of life |
| You (2009) ⁷⁴ | Indigowood root extract | Symptom management – radiation-induced mucositis | Extract reduced severity of mucositis, anorexia, and difficulty swallowing |
| Su (2004) ⁷⁵ | Aloe vera | Symptom management – prevention of radiation-related mucositis | No significant improvement after aloe vera treatment |

Table IV

Integrative Medicine Resources

| Source | Site | Overview of CAM? | Herbal Information? | Other CAM Information? | Provider Information? | Links to new research? |
|-------------------|---|------------------|---------------------|------------------------|-----------------------|------------------------|
| NIH | https://nccih.nih.gov/ | Yes | Yes | Yes | Yes | Yes |
| MSKCC | https://www.mskcc.org/cancer-care/treatments/symptom-management/integrative-medicine | Yes | Yes | Yes | Yes | Yes |
| Natural Medicines | https://naturalmedicines.therapeuticresearch.com | No | Yes | No | No | Yes |
| Consumer Lab | https://www.consumerlab.com | No | Yes | No | Yes | Yes |
| OCCAM | http://cam.cancer.gov/health_camaz.html | Yes | Yes | Yes | Yes | Yes |
| NCI CAM PDQ | http://www.cancer.gov/about-cancer/treatment/cam/hp | Yes | Yes | Yes | No | Yes |