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ScienceDirect
European Journal of Integrative Medicine 3 (2011) 11–16
European Journal of INTEGRATIVE MEDICINE
www.elsevier.com/eujim

Mini-review article

Complementary therapies for side effects of chemotherapy and radiotherapy in the upper gastrointestinal system

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Received 22 November 2010; received in revised form 7 December 2010; accepted 4 February 2011

Abstract

Introduction: Chemotherapy and radiotherapy remain the mainstay of treatment for patients with advanced malignant disease that is incurable by local surgery. However, effective use of these therapies is limited by toxic effects. Serious side effects in the upper GI system include mucositis, xerostomia, nausea and vomiting. Standard care for these side effects is suboptimal. Recent studies suggest complementary and alternative medicine (CAM) may have a role in supportive care for people with cancer. We therefore reviewed the literature to assess the potential role of CAM in upper GI toxicities of chemo/radiotherapy.
Methods: We conducted a Medline term-combination search for articles in English that included: stomatitis, mucositis, xerostomia, nausea, vomiting, chemotherapy, radiotherapy, complimentary/alternative therapies, amino acids, antioxidants, vitamins, minerals, plant extracts, herbs, mind–body, guided imagery, hypnosis, acupuncture, massage and yoga.
Results: The initial search identified a total of 217 articles. Of these, 36 were selected and reviewed. Recommendations for integration of some CAM therapies in supportive cancer care can be made.
Conclusion: CAM therapies can be effective and safe in treating upper GI toxicities of chemo/radiotherapy. Guidelines in supportive cancer care should include appropriate CAM therapies, and patients need to be informed of such treatment options.

Keywords: Stomatitis; Mucositis; Xerostomia; Nausea; Vomiting; Chemotherapy; Radiotherapy; Complementary and alternative medicine

Introduction

Upper alimentary tract toxicity can be a serious complication of chemotherapy and radiotherapy [1], mucositis, xerostomia, nausea and vomiting being the most common of them. Current supportive care does not offer optimal treatment for these side effects. In recent years there has been a growing body of literature that documents the benefits of several complementary and alternative medicine (CAM) therapies in supportive cancer care. In this article we will summarize our findings from a literature review on CAM therapies with positive outcomes for upper GI side effects of radio/chemotherapy.

Methods

The authors independently searched Pubmed for keywords (alone and in various combinations) in the following categories:

a. Oncology-related keywords (cancer; oncology; palliative; chemotherapy; radiation).
b. CAM-related keywords (CAM, complementary/alternative/integrative medicine, integrative oncology, traditional medicine, herbs, herbal, mind–body, relaxation, meditation, guided imagery, hypnosis, homeopathy, acupuncture, nutritional/dietary supplements, naturopathy, energy, healing, manual healing, massage, reflexology, yoga, Alexander, Feldenkreis, and anthroposophic medicine).
c. Keywords related to upper gastro-intestinal symptoms: nausea, vomiting, xerostomia, mucositis, and aphtous stomatitis.

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doi:10.1016/j.eujim.2011.02.006

The initial search identified a total of 217 articles. Of these, 36 articles focusing on the clinical practice of CAM in gastrointestinal symptoms during active oncology treatment were selected and reviewed.

Chemotherapy and radiotherapy induced mucositis

Cytotoxic chemotherapies and radiotherapies are most effective against rapidly dividing cells. However, a negative consequence of this mechanism is that host tissues containing rapidly dividing cells may be damaged. The cells of the GI tract are the most rapidly proliferating cells in the human body; hence they are prone to such toxicity. Oral mucositis, i.e. inflammation of the mucous membrane lining the mouth, is a common dose-limiting toxic effect of chemotherapy, especially fluoropyrimidines, anthracyclines, and folate-based drugs such as methotrexate [2]. Oral mucositis is associated with a higher risk of infection, pain, chemotherapy-dose reduction, and infection-related death. Furthermore, severe mucositis commonly results in compromised nutritional intake and quality of life. At present, there is no standard therapy to prevent mucositis [1]. Treatment is mostly supportive, consisting of good oral hygiene, mouthwashes, and analgesia [3].

Herbal and nutritional approaches to mucositis

Honey was a traditional remedy used to treat wounds until the introduction of antibiotics. Honey has been shown to inhibit bacterial growth and enhance wound healing [4]. Three trials have evaluated the role of honey for the prevention of chemo/radiotherapy induced mucositis. In a double blind randomized clinical trial from Iran, patients took 20 ml of honey (swish & swallow) 15 min before, 15 min after, and 6 h after radiotherapy [5]. Compared to saline rinse a significant reduction in mucositis severity was observed among patients in the honey-treated group. In another randomized trial from Egypt, honey rinse prophylaxis was also shown to significantly reduce mucositis severity in head and neck cancer patients receiving either chemotherapy or radiotherapy [6]. In another trial from Malaysia, a significant reduction in mucositis was observed among prophylactic honey-treated patients compared to controls. In addition, 55% of patients treated with topical honey showed no change or a positive gain in body weight compared to 25% in the control arm, the majority of whom lost weight [7].

Chinese herbs are an essential part of the healthcare system in several Asian countries, and are considered to be CAM in most Western countries. Although Chinese herb consumption is becoming increasingly popular the evidence base of this field is still in its infancy. Moreover, issues of safety are significant, especially in terms of herb-drug interactions. Two RCT's reported the efficacy of Chinese herbal formulas for prevention of chemo/radiotherapy-induced mucositis in 395 patients with head and neck cancer. The herbal formulas were individualized according to traditional Chinese medical diagnosis. Each formula contained a mixture of more than five herbs. Patients in the control group received Dobell's solution (an antiseptic mouthwash solution) [8,9]. Chinese herbs showed a benefit at all mucosal injury levels with risk reduction values ranging between 0.16 and 0.59. A Cochrane review concluded that Chinese herbs were found to have some benefit in preventing or reducing the severity of mucositis associated with cancer treatment [3].

Syousaikotou, a Japanese herbal preparation was compared to gargling with providone-iodine and amphotericin B, in patients undergoing chemotherapy [10]. Syousaikotou significantly reduced both the incidence of mucositis and the pain associated with such lesions. The analgesic effects of Syousaikotou gargle lasted for about 2 h. No major adverse effects were noted in the herbal preparation group.

Dietary and homeopathic supplements in the treatment of mucositis

L-Glutamine is a conditionally essential amino acid that has multiple well-defined functions in human biological processes. Several studies have evaluated the role of glutamine for the prevention and treatment of chemo/radiotherapy-induced mucositis. Although trials vary in methodology, glutamine formulation and dosing, there is sufficient evidence for effectiveness and safety to support its use in the treatment of stomatitis [11,12].

Saforis is a proprietary oral glutamine formula that facilitates delivery of glutamine into oral mucosal cells. In a double blind randomized control trial, Saforis significantly reduced the incidence of oral mucositis in breast cancer patients receiving anthracycline-based chemotherapy [13]. No significant adverse effects occurred in the Saforis group. Further trials are needed to establish the role of glutamine for prevention of oral mucositis.

Alpha-Tocopherol, a form of the antioxidant vitamin E, was assessed for the prevention of mucositis. Patients receiving radiotherapy for cancer of the orpharynx were randomized to Alpha-Tocopherol mouth rinse or placebo. Patients rinsed their mouths before each radiation treatment, and again 8–12 h later. Alpha-Tocopherol was associated with a 12.9% reduction in mucositis incidence as well as a 41.1% reduction in mucositis severity [14]. Although the issue of antioxidant consumption during radiotherapy remains controversial, in this trial no survival difference was observed between groups.

Traumeel is a homeopathic-complex remedy. In one laboratory study, Traumeel was shown to inhibit the secretion of pro-inflammatory mediators from gut epithelial cells in an inversely dose-related manner. Interestingly, these mediators are considered to play a role in generating mucosal inflammation [15]. In a double-blind controlled trial, 32 patients undergoing allogeneic or autologous stem cell transplantation were randomized to receive either Traumeel or placebo as a mouth rinse for the prevention and treatment of stomatitis. In the Traumeel group patients developed significantly less stomatitis, and lesions were less severe [16]. However, in a trial that ended only recently, Traumeel was not superior to placebo in preventing or treating mucositis in young patients undergoing stem cell transplantation [17]. Another trial for assessing Traumeel for radiation-induced mucositis is currently being conducted.