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Analytical Review: Systematic Search

Exploring the Usefulness of Botanicals as an Adjunctive Treatment for Lymphedema: A Systematic Search and Review

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Abstract

Objectives: To provide a critical analysis of the current published research regarding the use, risks, and benefits of botanicals in the treatment of lymphedema and to provide health professionals with current knowledge of safe, appropriate use of botanicals for treatment of lymphedema.

Type: This systematic search and review addresses the use of botanicals in the treatment of lymphedema in order to develop a best evidence synthesis of the research.

Literature Survey: Articles were identified from 11 major medical indices published from 2004-2012 using search terms for lymphedema and management. Eighty-five articles met the inclusion criteria of evidence-based lymphedema therapies for the category "complementary and alternative methods for lymphedema therapy."

Methodology: Two clinical lymphedema experts reviewed the studies according to level of evidence guidelines established by the Oncology Nursing Society, *Putting Evidence into Practice*, and subdivided the methods into subcategories that included Botanical, Pharmaceutical, Physical Agent Modalities, and Modalities of Contemporary Value. The pharmaceutical articles were excluded (5) because they fell outside the inclusion criteria. Twenty-two articles were used in a separate review of physical agent modalities and modalities of contemporary value for lymphedema. Botanicals generated substantial research (11) and warranted its own independent review.

Synthesis: The levels of evidence are weak, because research conclusions were limited by size, dose, and study design. A limited number of randomized controlled trials have been performed, and reliability is not always evident, particularly in the context of large systematic reviews where evidence was bundled.

Conclusions: Evidence supporting the use of botanicals for the treatment of lymphedema is insufficient. Some evidence suggests benefits for the treatment of chronic venous insufficiency. Development of specific and sensitive measurement methods may change how botanicals are studied and establish a body of evidence for their use.

Introduction

Lymphedema is a progressive, chronic disease caused by an impairment of the transport capacity of the lymphatic system, a mechanical failure that results in the accumulation and congestion of protein-rich interstitial fluid within the affected body region [1]. Rockson and Rivera [2] estimate the population prevalence of lymphedema to be 1.3 to 1.4 per 1000. Lymphedema leads to significant secondary health issues and loss of physical function, impeding daily living skills and resulting in a dramatic reduction in the quality of life [1,3,4]. The standard of care for lymphedema is complete decongestive therapy (CDT) [5-8], which consists of manual lymph drainage (MLD) to mobilize movement of stagnant lymphatic fluid from the limb back to venous circulation, along with use of short-stretch bandages and various other compression garments to reduce refill after MLD [1]. The goals of therapy are to reduce swelling, restore tissue homeostasis, prevent infection, and improve function and quality of life. Successful achievement of these goals is dependent upon specially

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trained and experienced therapists and active patient participation [6]. The burdens of both the disease and the therapy are worse when the disease has progressed.

Lymphedema and its standard care, CDT, present a lifetime of stressful and physical emotional challenges [9]. CDT is time consuming and costly and often produces inconsistent limb volume reduction [10]. Patients resent and are frustrated by the daily burden of self-care, which includes therapy, appointments, exercise, bandaging, washing and rolling of bandages, and wearing compression garments [9].

Ever since CDT became the standard of care for lymphedema [5,7,8], patients have sought alternatives [11]. Complementary and alternative medicine (CAM) practices are not considered medicine because insufficient evidence exists to support their use as safe or effective [12]. Nevertheless, in 2007, it was reported that 4 out of 10 adults had used a form of CAM in the past 12 months [12]. People who use CAM are seeking ways to improve their health or to deal with symptoms of chronic disease, such as lymphedema [10,12]. In the United States about half of the population and about 70% of older adults (71 years or older) use dietary supplements [13]. In one study of the use of CAM therapies for patients with cancer, 55% took an herbal or vitamin supplement [14]. Of particular interest, Barton et al [15], authors of a literature review on alternative approaches for lymphedema management, reported the enthusiastic response of participants with breast cancer—related lymphedema to a clinical trial for coumarin, a botanical, as an alternative to CDT. The use of supplements for the treatment of lymphedema would certainly ease the burden of standard therapy.

Is There a Place for Botanicals in the Treatment of Lymphedema?

The use of plants and their derivatives as healing treatments can be traced to as early as 1500 BC [16]. A recent study [17] reported that of the 252 drugs considered by the World Health Organization as essential, 11% are derived from flowering plants. Botanicals, therefore, are worthy of exploration for management of many chronic conditions, including lymphedema.

Lymphedema is caused by an alteration in the transport capacity of the lymphatic system. It is primarily a structural problem that develops into an inflammatory problem. The etiology of lymphedema is considered within the context of 2 broad categories, primary and secondary. Primary lymphedema is the result of dysplasia of the lymph system that is often congenital or can develop later in life with or without various triggering events such as insect bites or trauma. Secondary lymphedema occurs as the result of disruption of the lymph system, most commonly after lymph node dissection or radiation therapy as a means of treating cancer or another inciting event such as trauma, infection, or orthopedic procedures. Likewise, secondary lymphedema may develop as a result of chronic venous insufficiency (CVI) in which impairment of venous valves allows backflow into the interstitial tissues. Initially a healthy lymph system increases transport of this additional fluid, but eventually chronic lymphedema develops.

CVI leads to the creation of edema, with valvular incompetence resulting in venous hypertension, endothelial vascular compromise, and inflammation [18,19]. Impaired cutaneous microcirculation triggers inflammatory cytokines, fibroblast growth factors, and proteolytic enzymes, resulting in lipodermatosclerosis and the development of ulcers [18,20]. Capillaries become dilated and their walls become thin and leak, adding fluid and proteins to the interstitial space. Because of their osmotic attraction for water molecules, proteins create an increased lymphatic load. Interstitial congestion burdens the lymph system, altering its transport capacity and triggering secondary lymphedema. A compromised lymph system cannot perform its basic function, which is returning proteins to the circulatory system, and a vicious cycle develops. A 2-fold system of management is needed: (1) a device or agent to increase venous return to decrease capillary permeability and macromolecule leakage, and (2) an agent that is capable of either increasing protein phagocytosis or protein lyses to decrease the lymphatic burden [18-20].

Compression, a standard of care for persons with CVI, benefits both the microcirculation and valvular incompetence [6,20]. Botanicals may benefit the microcirculation by inhibiting inflammatory activity, decreasing blood capillary permeability, and increasing venous tone [18,20]. Because lymph drainage is intimately involved with venous drainage, botanicals may promote both venous and lymph return [19,20]. In some types of lymphedema, no vascular compromise occurs; however, with disease progression (ie, in advanced stages of lymphedema) and in the presence of underlying clinical factors, such as diabetes, smoking, venous collateral development, and medications, a role may exist for botanical treatments [19].

There are 3 categories of venous-modifying botanicals: benzopyrones, saponins, and other plant extracts. Herbal preparations are derived from plant extracts, produced from synthetics and extracts, or produced completely from synthetics [21].

Benzopyrones

There are 2 classes of benzopyrones, the alpha and the gamma benzopyrones. Coumarin is the best known of the alpha benzopyrones. Theoretically, it acts either by binding to plasma proteins, which activate macrophage phagocytosis of the coumarin-bound protein carrier, or by stimulating macrophage proteolysis; the