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Traditional herbal medicine as adjunctive therapy for breast cancer: A systematic review

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Summary
Objectives: To assess the effectiveness of traditional herbal medicine (THM) as adjunctive therapy for breast cancer as evidenced by randomized controlled trials (RCTs).
Methods: Five electronic English and Chinese databases were systematically searched up to February, 2014. All RCTs involving THM in combination with conventional cancer therapy for breast cancer were included.
Results: Eight RCTs involving 798 breast cancer patients were systematically reviewed. Three studies reported a significant difference in the improvement of quality of life (QOL) compared to the control group. Two studies reported an increase in the white blood cell count after treatment. Data on hot flashes and sleep quality were evaluated. However, no significant differences in immediate tumor response were observed.
Conclusion: THM combined with conventional therapy in the treatment of breast cancer is efficacious in improving QOL and in decreasing the number of hot flashes per day. More research and well-designed, rigorous, large clinical trials are necessary to further address these issues.

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Introduction

Breast cancer is the most common cancer and the major cause of cancer-related deaths among women worldwide, with an expected 1,383,500 newly diagnosed cases and 458,400 deaths in 2010. In the United States, excluding skin cancer, breast cancer is the most common cancer in women.[1] The incidence of breast cancer varies by about five-fold globally.[2]

The National Cancer Institute (NCI) recognizes six types of standard treatment: surgery, sentinel lymph node biopsy followed by surgery, radiation therapy, chemotherapy, hormone therapy, and targeted therapy. Of these, radiation therapy, chemotherapy, and hormone therapy are used primarily to manage the cancer cell population after surgery or in the absence of surgery. However, these methods cause many short- and long-term adverse effects and often decrease the quality of life (QOL).[3] Short-term side effects include fatigue, alopecia, and nausea/vomiting. These generally occur during the course of treatment but usually resolve within 1 month following completion of therapy. Long-term side effects include premature ovarian failure, weight gain, and cardiac dysfunction. They generally have a much longer duration, sometimes lasting for several years. Systemic conventional therapy has been associated with significantly poorer quality of life 5—10 years after diagnosis with breast cancer.[4] Breast cancer survivors who did not undergo chemotherapy are reported to have a higher QOL than patients treated by chemotherapy.[5] New complementary methods that augment conventional treatment modalities are being used to decrease the incidence of side effects and increase the QOL of breast cancer patients.[6] Increasingly, Americans are using complementary and alternative therapies. Data from the 2002 United States National Health Interview Survey (NHIS) showed that during the preceding 12 months, 62% of adults ≥18-years-of-age had used some form of complementary and alternative medicine (CAM), including prayer, for health reasons. When prayer was excluded, 36% of adults used some form of CAM.[7]

Traditional herbal medicine (THM) has been reported to alleviate chemotherapy-induced nausea and vomiting[8] and also peripheral neuropathy.[9] THM is reported to possess immunopharmaceutical effects evident as the modulation of lymphocyte functions and immune effector cells.[10] Anti-cancer effects of some traditional herbal components have been reported to involve improved immune functions *in vitro* and *in vivo*.[11,12]

Recently, several randomized controlled trials (RCTs) of THM for the treatment of breast cancer have been published. However, no systematic review of the effectiveness of THM for breast cancer treatment has been performed. We undertook a systematic review to evaluate the efficiency of adjunctive orally administered THM in the treatment of breast cancer patients.

Materials and methods

Search strategy

Sources used for the literature review until February 2014 were The Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, Allied and Complementary Medicine Database (AMED), and the Cumulative Index to Nursing and Allied Health Literature (CINAHL). The reference lists of articles were searched for the most recent relevant publications. A manual search of relevant journals, symposia, and conference proceedings was conducted. All identified publications were cross-referenced. Personal contact was made with the authors of published studies, if necessary, to request additional data. The search terms used were Breast Neoplasms [MeSh] OR ((Breast (TIAB)) OR Mammary (TIAB) AND Neoplasms[MeSH] OR Neoplasms*[TI] OR Cancer*[TI] OR Tumor*[TI] OR Tumor*[TI] OR Carcinoma[MeSH] OR Carcinoma*[TI] OR Adenocarcinoma[MeSH] OR Adenocarcinoma*[TI] OR adenomatous[TI] OR Sarcoma[MeSH] OR Sarcoma *[TI] OR Antineoplastic agents [MeSH] OR antineoplas *[TI] OR (adenoma *[TI] OR adenopath*[TI]) AND malignant *[TI]). Since the various databases searched for this review possessed their own subject headings, each database was searched independently. No language restrictions were imposed.

Study selection

Only RCT articles were selected. Quasi-randomized or non-randomized trials were excluded. Articles involving *in vivo* and *in vitro* studies and articles with parenteral THM were also excluded. Studies of THM combined with conventional cancer therapy as the treatment group were included (Fig. 1). For the control group, the selected patients were undergoing conventional treatment with chemotherapy, hormone therapy, chemo-hormone therapy, and/or radiation therapy (Table 1).

Quality assessment

The quality of all studies was assessed following the description of these categories in the *Cochrane Handbook for Systematic Reviews of Interventions*.[13] Each included study was evaluated against the inclusion criteria by one of the reviewers. Where there was uncertainty regarding eligibility, a second reviewer also assessed the study and a decision was reached through discussion and consensus. Both reviewers independently assessed whether the studies met the inclusion criteria and discussed any disagreements. Further information was sought from the authors when papers contained insufficient information to make a decision about eligibility. The following questions were assessed and answered by the reviewers: (a) Was the allocation sequence adequately generated? (b) Was allocation adequately concealed? (c) Was knowledge of the allocated interventions adequately prevented during the study? (d) Was the blinding of the outcome assessment adequate? (e) Were incomplete outcome data adequately addressed? (f) Were the results of the study free of the suggestion of selective outcome reporting? and (g) Was the study apparently free of other problems that could put it at risk of bias? This review used 'Y, U, N' as keys for the judgments for each question assessed. An answer of 'Yes' indicated a low risk of bias (Y), 'Unclear' indicated an uncertain risk of bias (U), and 'No' indicated a high risk of bias (N).