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File: ■ Reishi Mushroom (*Ganoderma lucidum*)
■ Breast Cancer
■ Fatigue

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RE: Reishi Mushroom Spore Powder Lessens Fatigue in Breast Cancer Patients Taking Hormone Replacement Therapy

Zhao H, Zhang Q, Zhao L, Huang X, Wang J, Kang X. Spore powder of *Ganoderma lucidum* improves cancer-related fatigue in breast cancer patients undergoing endocrine therapy: a pilot clinical trial. *Evid Based Complement Alternat Med*. 2012;2012:809614. doi:10.1155/2012/809614.

Cancer-related fatigue (CRF) includes persistent physical, emotional, and cognitive tiredness and affects many breast cancer patients. It results from chemotherapy, radiotherapy, and endocrine therapy, as well as from conditions such as heart disease, anxiety, and depression. Patients with persistent CRF may have elevated concentrations of interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), inflammation-related cytokines.[1] Although exercise has been shown to be somewhat effective, not all CRF patients are able to exercise, and there are no well-established pharmaceutical interventions for CRF; thus, alternative therapies for CRF are needed. The spore powder of reishi mushroom (*Ganoderma lucidum*) is used in traditional Chinese medicine, and previous studies have found it to be an antihistamine and a modulator of the immune system. In addition, reishi mushroom triterpenoids have been shown to inhibit the expression of IL-6 and TNF-α. This randomized, placebo-controlled trial investigated the potential beneficial effects of reishi mushroom spore powder on CRF and quality of life in breast cancer patients receiving endocrine therapy.

Patients were recruited from the Third Affiliated Hospital of Harbin Medical University in Harbin, China, and had cancer that was either estrogen and progesterone receptor-positive, or estrogen receptor-positive and progesterone receptor-negative. Included in the study were patients over 18 years of age without any serious mental health problems, who were diagnosed with stage I-IIIA breast cancer, but did not have any other cancer history or other fatigue-related disease. All participants had previous surgery for breast cancer, and had completed at least 6 months of endocrine therapy or were currently using endocrine therapy. Patients were excluded if they had anemia, hemoglobin concentrations of <9 g/dL, platelets <80,000/mL, and unusual concentrations of the liver and renal markers serum alanine transaminase (ALT),

aspartic acid transaminase (AST), blood urea nitrogen (BUN), and creatinine. Also, those with thyroid disorders were excluded.

The study consisted of an experimental and control group. The experimental group took 1000 mg of reishi mushroom spore powder 3 times per day for 4 weeks; the control group took a placebo for 4 weeks. The reishi mushroom spore powder was prepared by Beijing Great Wall Pharmaceutical Factory; Beijing, China. CRF, anxiety and depression, quality of life, TNF-α and IL-6, as well as liver and kidney functions for tolerability assessment, were measured at both the baseline and endpoint of the study. The Functional Assessment of Cancer Therapy: Fatigue (FACT-F) scale was used to measure CRF and included questions about 13 aspects of fatigue with a scale ranging from 0 ("not at all") to 4 ("very much"). The Hospital Anxiety and Depression Scale (HADS) was used to assess anxiety and depression with a scale ranging from 0-21. A score between 0-7 indicates a "normal" state; scores 8-10 define a "mild disorder"; and scores ≥11 are indicative of a "moderate to severe disorder." Finally, the European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire C30 (EORTC QLQ-C30) was used for quality of life measurements. This consists of questions about physical, emotional, and cognitive aspects of quality of life ranging from 0 ("not at all") to 4 ("very much"), with some questions rated from 0 to 7 ("very much").

From 48 enrolled patients, n=25 were randomized to the experimental group and n=23 into the control group, and all randomized patients finished the study. There were no significant differences in the baseline assessments between groups. In general, the total FACT-F score of the experimental group significantly improved after 4 weeks as compared to baseline (141.09 vs. 120.31, $P<0.01$) and to the control (141.09 vs. 121.01, $P<0.01$). After 4 weeks, the FACT-F scores of the experimental group were significantly different in the physical well-being category from both baseline (24.62 ± 3.27 vs. 20.35 ± 4.07, $P<0.01$) and as compared to control after 4 weeks (24.62 ± 3.27 vs. 20.65 ± 3.97, $P<0.01$). This was also true for the fatigue category as compared to baseline (46.78 ± 5.07 vs. 39.76 ± 5.10, $P<0.01$) and the control group after 4 weeks (46.78 ± 5.07 vs. 40.92 ± 5.64, $P<0.01$). The emotional and functional aspects of the FACT-F also improved significantly in the experimental group as compared to both baseline and with the control group after 4 weeks ($P<0.05$).

The total HADS score for the experimental group significantly improved at the end of the study both as opposed to baseline (7.1 ± 3.1 vs. 10.9 ± 4.1, $P<0.01$) and in comparison to the control group (7.1 ± 3.1 vs. 9.8 ± 3.4, $P<0.01$). Both the depression and anxiety categories improved in the experimental group from baseline to endpoint and in comparison to the control group after 4 weeks ($P<0.05$). Also, the "global" quality of life EORTC QLQ-C30 score was improved significantly in the experimental group both as opposed to baseline (68.9 ± 21.4 vs. 55.8 ± 22.9, $P<0.01$) and in comparison to the control group (68.9 ± 21.4 vs. 57.7 ± 24.2, $P<0.01$). Notably, the physical and emotional functioning significantly improved in the experimental group both in comparison to baseline and the control group after 4 weeks ($P<0.01$). Cognitive functioning also improved similarly in the experimental group ($P<0.05$). Additionally, fatigue, sleep disturbance, and appetite loss scores were significantly improved in the experimental group ($P<0.05$).

At the end of the study, the concentration of TNF-α in the experimental group decreased significantly from 128.70 pg/mL to 71.89 pg/mL ($P<0.01$). This was also true for the IL-6 concentrations of the experimental group (62.43 pg/mL vs. 37.62 pg/mL, $P<0.05$). The

most frequent adverse side effects reported in the experimental group were dizziness and dry mouth, but gastrointestinal problems, epistaxes (nosebleeds), and sore throat were also reported. [Note: Adverse side effects for the control group were not included.]

The reishi mushroom spore powder significantly improved aspects of fatigue in breast cancer patients in this study. As beneficial effects were noted in both physical and psychological symptoms of fatigue, there may be multiple mechanisms of action behind the bioactivity of reishi mushroom. It is also suggested that depression may have improved due to the ability of patients to resume normal physical activities. Although the immune markers measured showed significant reductions at the end of the study, no attempt was made to more broadly monitor the immune response, or adverse side effects associated with potential fungus allergies. In addition, there is no explanation for excluding the placebo group reports of any adverse effects. Other shortcomings mentioned include a small sample size and lifestyle variables that may have impacted fatigue. Furthermore, the study was not blinded, leaving room for investigator bias. Additionally, neither the type of endocrine therapy nor the nature of the placebo was specified in this study. Lastly, the variability of the type and timing of conventional treatment (including the endocrine therapy) make the significance of the findings difficult to interpret. Future clinical studies will ideally include a more rigorous study design to further investigate the role of reishi in the management of CRF in breast cancer survivors.

—Amy C. Keller, PhD

Reference

[1]Barsevick A, Frost M, Zwinderman A, Hall P, Halyard M; GENEQOL Consortium. I'm so tired: biological and genetic mechanisms of cancer-related fatigue. *Qual Life Res*. 2010;19(10):1419-1427.

Referenced article is available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3236089/pdf/ECAM2012-809614.pdf.