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Complementary and Alternative Medicine Use Was Associated with Higher Perceived Physical and Mental Functioning in Early Systemic Sclerosis

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Abstract

Objective—This study assessed the use of complementary and alternative medicine (CAM) therapies in patients with early systemic sclerosis (scleroderma, SSc).

Methods—At the annual visit, SSc patients enrolled in the Genetics versus Environment in Scleroderma Outcomes Study (GENISOS) were queried about their use of CAM therapies and intended symptom target, including herbal or nutraceutical therapy, acupuncture, transcutaneous electrical neural stimulation (TENS) and mind-body therapy (relaxation, meditative, imagery). The CAM user SSc patients were compared to matched non-CAM users over two years for database results of demographic, clinical and health-related quality of life SF-36 questionnaires by analysis of covariance.

Results—25% of the university GENISOS group were CAM users: age: 54 years; female: 89%; diffuse cutaneous involvement: 47%; total skin score: 13.5; Medsger severity index: 5.8. Over 70% used ≥ 1 CAM therapies for over 1 year, independent of health insurance. Symptoms targeted included arthritis/arthralgia, pain, GI dysmotility and fatigue. CAM users had significantly higher mean mental component summary (MCS) scores on SF-36 at Baseline and Year 2, (49 and 49.9), compared to non-CAM users (42 and 40.2, respectively, $p < 0.01$). At Year 2, the CAM user group had significantly higher scores of SF-36 domains physical component score, role-physical, bodily pain and vitality, whereas scores declined in the non-CAM user group.

Conclusion—In SSc, 70% of those in the CAM user group reported a long-term commitment to CAM therapies. Higher perceived mental functioning in CAM users might reflect more self-motivation to manage symptoms and subsequently, promote practices that result in higher perceived physical functioning.

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Keywords

CAM; SF-36; Integrative Medicine; Pain; Arthritis; GI Hypomotility; Scleroderma; GENISOS

Introduction

Systemic Sclerosis or Scleroderma (SSc) is an autoimmune connective tissue disease in which fibrosis of the skin and internal organs occurs in association with a small vessel vasculopathy and autoantibody production. These produce a wide spectrum of constitutional and/or organ specific impairments. Constitutional complaints include Raynaud's syndrome, generalized fatigue, arthralgias or arthritis, myalgias or myositis and depression. Organ specific impairments associated with SSc include pulmonary fibrosis, pulmonary hypertension, gastroesophageal reflux disease, gastrointestinal dysmotility disorders, such as diarrhea or constipation, varying degrees of heart block and scleroderma renal crisis. Any of these can progress to organ failure. These impairments when present may lead to severe limitations in physical, work and social activities (Reviewed in 1). There is no cure for SSc, treatment is prescribed to manage symptoms and organ pathologies on an individual basis.

Forty to sixty percent of adults with autoimmune or arthritic diseases have reported using some form of CAM, or using modalities for non-approved use for the management of symptoms (reviewed in 2, 3, 4). Recently, most CAM related studies have addressed their evidence-based proof of efficacy. Few studies have protocols to assess over time the functioning of those patients who try these modalities for symptom reduction. This study assessed perceived functioning in patients with early systemic sclerosis enrolled in the Genetics versus Environment in Scleroderma Outcomes Study (GENISOS) project, who self-reported the use of CAM therapies for symptom management.

Materials and Methods

Patient Selection

The research protocol was approved by the UTMB Institutional Review Board and written informed consent was obtained from all subjects before study entry. Patients who fulfilled the ACR criteria for SSc (5) and had disease duration for less than 5 years were enrolled in Genetics versus Environment in Scleroderma Outcomes Study (GENISOS) between 1997 and 2004. The GENISOS cohort and database is reviewed elsewhere (6). Patients (n=76) were interviewed at their yearly GENISOS visit and self-reported or brought in their medications with dosage schedules. Additionally, patients were specifically queried regarding their use of complementary or alternative modalities. Patients were also asked for any treatments they engaged in for symptom reduction (regardless of recommended indication) that were recommended/prescribed by their physicians, or other source. Patients were assigned to the CAM User group (n=19) based on their self-report of: specific CAM modalities, use of non-prescribed medical treatments, or a non approved use of treatment for symptom reduction. The non-CAM user control group (n=17) included patients from the same site matched to the CAM user group for age, race/ethnicity and gender enrolled in GENISOS in the same time period, who did not report the use of any CAM or non-prescribed treatments in the medication list at the annual visit and denied such use when specifically queried. During the time of the study, two patients from each group were on immunosuppressive agents (methotrexate, azathioprine or low dose corticosteroids) but none were taking cyclophosphamide.

Cam Modalities

CAM Modalities included the use of nutritional supplements, such as phytoestrogens, or L-carnitine, large doses (sometimes called or “mega” doses) of vitamins or minerals, in addition to usual daily supplements, herbal therapies, glucosamine or chondroitin sulfate. Other modalities included mind-body, (such as yoga, meditation or biofeedback), acupuncture-related procedures or electrostimulation, (such as electroacupuncture) or transcutaneous electrical nerve stimulation (TENS).

GENISOS Clinical Data

Patients were assessed for clinical activity and filled out questionnaires annually after enrollment in GENISOS (6). Variables collected were sociodemographic information, (such as age, gender, formal education level completed, insurance status and Texas counties of origin), limited or diffuse cutaneous involvement, and total skin scores (TSS) by modified Rodnan skin scores, (7, 8). Perceived functioning by eight domains were measured by SF-36 version 1.0 (9, 10), completed every year at the patient study visit. Raw SF-36 version 1.0 scores were normalized to version 2.0 and scores of mental component summary (MCS) and physical component summary (PCS) were calculated using a 2.0 conversion kit (SF Health Outcomes Scoring Software, QualityMetric Incorporated, Lincoln, RI). The modified Medsger severity scores (11) were also obtained. Yearly diffusing capacity of carbon monoxide (DLco) was also obtained.

Data Presentation and Statistics

Data presented as a percentage of the total for that variable, or as the mean $\pm$ SE scores. “Baseline” in this study refers to the annual study visit before the initiation of CAM therapy for the CAM user group. “Year 2” refers to the annual study visit two years after the Baseline visit. Analysis of covariance using baseline values as a covariate was performed between CAM user and non-CAM user groups. A $p < 0.05$ was considered significant.

Results

Table 1 demonstrates no significant differences in sociodemographic features between CAM user and non-CAM user groups. The sociodemographic comparisons were: % female: (89% vs 86%); diffuse cutaneous involvement: (47 vs 33%); TSS: (13.5 ± 8.8 vs 10.5 ± 8.2), the modified Medsger severity score: (5.8 ± 3.4 vs 7.2 ± 2.1) and percent predicted DLco (76.4 ± 4.8 vs 76.2 ± 5.7), respectively. CAM users included Caucasian (N=13), African Americans (N=2) and Hispanics (N=4). About 79% of the CAM user group had health insurance, compared to 73% of the non-CAM user group. In comparison of CAM users vs non-CAM user controls, the percentage of employed were 53 vs 40% respectively and the average highest formal educational grades completed were 12.6 and 11.3, respectively. The average number of years between the patient’s diagnosis of SSc and the patient’s initiation of CAM therapy was 3.9 years.

About 70% reported use of the CAM modality for over a year (avg 1.7 ± 2.1 years). Five CAM Users reported discontinuation of a CAM modality within one month, for lack of efficacy. The subjects resided in 10 Southeastern Texas counties and most were within 200 miles of the university.

Table 2 demonstrates the primary symptoms or condition and the CAM modalities initiated for symptom reduction. The most frequent CAM modalities were mineral supplementation (44%), large doses of vitamins or B-complex (39.9%), or herbal therapies (39.9%). Less frequently, glucosamine sulfate or chondroitin sulfate, phytoestrogens, acupuncture or electrostimulation were used. Multiple CAM modalities were noted in 10 SSc patients (55%)

who were CAM users usually treating more than one symptom. The major symptoms for which CAM therapy was used to treat in order of more to less frequency were constitutional/fatigue/pain (N=12), arthritis/arthralgias (N=11), GI symptoms of gastroesophageal reflux disease (GERD) or hypomotility (ie bloating, constipation, N=9) and peri-menopausal “hot flashes” (N=1).

Figure 1 demonstrates the SF-36 domain scores for both non-CAM user (A) and CAM user (B) groups at baseline (BsL) and year 2 (Yr 2) evaluations. As previously reported, SSc patients demonstrated lower SF-36 scores relative to normative values (scored at 50 in version 2.0, 12–14), including the use of SF-36 scores to assess treatment efficacy, (15–16). At our study baseline, physical component summary (PCS), role-physical (RP), bodily pain (BP) and vitality (VT) scores were very similar between CAM user and non-CAM user groups. However, the baseline mental health (MH) and mental component summary (MCS) scores of the CAM user group were significantly higher than the non-CAM user controls (47.2 ± 2.4 vs 40.1 ± 2.3 , $p=0.04$ and 49 ± 2.7 vs 42.2 ± 2.7 , $p<0.01$, respectively).

In the non-CAM user group (Fig 1A), the SF-36 domain scores at year 2 were lower compared to baseline scores in PCS (31.3 ± 2.1 vs 28.7 ± 1); RP (35 ± 2.7 vs 32.2 ± 2.6); BP (36.6 ± 2.2 vs 30.3 ± 2.2 , $p=0.06$); VT (39.1 ± 2.4 vs 38.3 ± 2.6); MH (40.1 ± 2.3 vs 38.8 ± 2.6) and MCS (42.2 ± 2.7 vs 40.2 ± 2.2), $p=NS$ for all comparisons. In contrast, the CAM user group (Fig 1B) demonstrated significantly higher year 2 domain scores compared to their baseline scores; PCS (41.6 ± 2 vs 32.8 ± 3.1 , $p=0.03$); RP (43.1 ± 2.6 vs 34.6 ± 2.6 , $p=0.02$); BP (46.4 ± 2.7 vs 36.6 ± 2.7 , $p=0.01$) and VT (47.9 ± 2.2 vs 39.7 ± 2.2 , $p=0.02$, respectively). SF-36 domains PF, SF and GH were also improved in year 2 compared to baseline scores in the CAM user group ($p=NS$). In the CAM user group, MH and MCS scores were very similar between baseline and Year 2 (47.2 ± 2.4 vs 51.6 ± 2.3 and 49 ± 2.7 vs 49.9 ± 2.3 , $p=NS$, respectively) and equivalent to normative values. As expected, the CAM user year 2 scores were also significantly higher compared to the baseline and year 2 scores of the non-CAM user groups for SF-36 domains PCS, RP, BP, VT, MH and MCS.

Figure 2 compares the mean changes in SF-36 domain scores between non-CAM user and CAM user groups in year 2, adjusted for baseline values. Significantly higher changes were noted between non-CAM users and CAM users for PCS (-2.6 ± 2.4 vs 8.5 ± 2.7 , $p<0.01$); RP (-2.8 ± 3.9 vs 9.1 ± 3 , $p=0.02$); BP (-6.3 ± 2.7 vs 10.2 ± 2.8 , $p<0.01$); VT (-0.6 ± 3 vs 9.1 ± 2.6 , $p=0.02$) and MH (-1.3 ± 1.8 vs 5.7 ± 2.1 , $p=0.02$). Mean changes in MCS (-2 ± 2 vs 2.7 ± 2.3) were not significant between groups.

To determine the extent to which race/ethnicity may confound our results, we adjusted for race/ethnicity in our statistical models. The same analysis adjusting for race/ethnicity did not change any of the results.

Discussion

Our early SSc cohort allowed an analysis of overall health related quality of life measured by SF-36, before and after initiation of CAM therapies. Perceived mental and physical functioning were higher in the CAM users at year 2 compared to matched controls, despite equivalent measurements of disease involvement or severity measured in this study by total skin score, diffuse cutaneous involvement, percentage of predicted DLco and Medsger severity scores.

Over two years, the CAM users had significantly improved scores in perceived functioning (PCS and specifically, RP, BP and VT domains), while the scores of the non-CAM user group declined. Of note, the baseline MH and MCS scores in the CAM user group were significantly higher compared to the non-CAM users. Higher perceived mental functioning at baseline in the CAM users might select for those SSc patients more motivated to personally participate in

their health care, beyond conventional medical advice. Or possibly, higher perceived mental functioning may be more predictive of better scores at two years, independent of their use of CAM therapies.

Higher SF-36 domains have been reported in SSc patients after one year of treatment with oral cyclophosphamide for treatment of pulmonary alveolitis, including role-physical, general health, vitality, role-emotional, mental health and MCS. PCS scores trended higher in those patients who showed improved pulmonary function (16). In this previous study, the baseline MCS scores (49.3 ± 10.7) for the cyclophosphamide and placebo treatment groups were equivalent to the mean baseline score of the CAM user group (49 ± 2.7) but higher than the mean score obtained from our non-CAM user control group (43.2 ± 2.7). The reason for this is unclear but the higher MCS scores might reflect a selected patient group more motivated to enroll in a treatment study or engage in additional therapies compared to those enrolled in an observational outcomes study.

These patients with early SSc started CAM modalities to treat symptoms of arthritis, pain, GI hypomotility and constitutional complaints. Usually, CAM therapies are used in combination with conventional and prescribed medical therapies. However, three of the CAM user patients reported their CAM use for symptom management allowed them to decrease or discontinue prescribed medication. This may indirectly reflect an independent investigation by a motivated patient for more efficacious treatment, due to their more attentive focus on symptom reduction.

The limitations of this study include the small study size, difficulty matching for ethnicity and use of a single study site. This analysis does not identify factors that contributed to differences in the baseline MH and MCS scores between the two groups or provide reasons why some patients were CAM users and others were not. However, the striking differences in perceived physical and mental functioning between the two groups over time places renewed interest in behavior and perceptions that are modifiable in chronic progressive diseases.

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Figure 1.

depicts the scores (mean±SE) in SF-36 domains at evaluations, baseline (BsL, clear bar) and at year 2 (Yr 2, dark bar). **A.** Non-CAM users. **B.** CAM users. SF-36 summaries and domains: PCS (physical component summary), RP (role-physical), BP (bodily pain), VT (vitality), MH (mental health) and MCS (mental component summary). *: p<0.05 between BsL and Yr 2 scores.

Figure 2. depicts the score changes (mean $\pm$ SE) seen in year 2 (Yr 2) in the systemic sclerosis patients, adjusted for baseline scores. White bars represent the score changes for non-CAM users and black bars represent the changes for CAM users. SF-36 summaries and domains: PCS (physical component summary), RP (role-physical), BP (bodily pain), VT (vitality), MH (mental health) and MCS (mental component summary). *: $P < 0.05$ between non-CAM user and CAM user scores.

Table 1

Demographics of SSc Patients Using CAM Compared to Non-CAM Users

	CAM Users (N=19)	Non-CAM Users (N=17)
Average Age, yrs (range)	54.2 ± 8.9 (41–67)	48.7 ± 12.2 (31–69)
Females, % (number)	89% (17)	86% (13)
dSSc, % (number)	47% (9)	33% (5)
Avg TSS, (range)	13.5 ± 8.8 (5–32)	10.5 ± 8.2 (2–27)
Avg Medsger severity score (range)	5.8 ± 3.4 (1–14)	7.2 ± 2.2 (3–11)
Predicted DLco, %	76.5±4.8	76.2±5.7
Race/Ethnicity		
% Caucasian	68%	47%
% African American	11%	33%
% Hispanic	22%	20%
% Health insured	79%	73%
Currently employed, %	53%	40%
Education completed, yrs	12.6±0.7	11.3±0.6
History of ethanol use, %	63%	67%
Never smoked, %	42%	33%
Avg # years starting CAM after SSc diagnosis	3.9±2.4	NA

Values derived from baseline visit. Average values ± standard error, with range of responses or percentages of patients with self-reported responses or clinical values. Avg TSS: average total skin score; Avg Medsger severity score: average modified Medsger severity score; Predicted DLco, %: The percentage of the average predicted diffusion capacity of CO at baseline visit; % Health insured: The percentage of those with health insurance, including private health insurance, Medicare and Medicaid; Employed, %: The percentage of SSc patients who were employed at the baseline visit; Education completed, yrs: The last year of formal educational grade completed; History of ethanol use: The history of reported past or current ethanol use; Never smoked, %: The percentage of patients self-reported to have never smoked; Avg # years starting CAM after SSc diagnosis: The average number of years between the diagnosis of SSc and patient initiation of CAM therapy.

Table 2

CAM and Integrative Modalities Used by SSC Patients

Treatment For	Vitamins/B	Minerals	Glucosamine Chondroitin	Herbs	Enzymes/Hormones	Mind-Body	Acupuncture/TENS
Constitutional/Fatigue/Pain	4	3		2	1	1	
Arthritis/artralgias	2	3	5	1	1		
GE reflux/GI hypomotility	1	3		2			3
Hot Flashes					1		

Vitamins/B: Vitamin and/or B complex individually supplemental dosages in addition to regularly ingested vitamins: Vitamins C, E, or B complex, folic acid, choline

Minerals: potassium, calcium, iron, magnesium, selenium, zinc, copper citrate, chromium, manganese, sulfur, molybdenum, phosphorous,

Enzymes/Hormones: Enzymes, hormones and nutritional supplements: acidophilus, aloe vera juice, chlorophyll, cod liver oil, fiber, digestive enzymes, with amylase, lipase, cellulose, fish oil, L-carnitine, phytoestrogens, kelp, L-tyrosine, thyroid and brain glandular substances, vinegar, colostrum, citrus peel

Herbs:, black cohosh root, black currant oil, borage oil, cardamon fruit, cat's claw, cayenne, coenzyme Q 10, dandelion root, evening primrose, flax seed oil, garlic, ginkgo biloba, ginger root, ginseng, milk thistle, noni, Pau D' Arco bark, LBS II (contains among other agents, cascara sangria bark, buckthorn bark licorice root, capsicum fruit, red clover tops, stinging nettle, Chinese herbs, panax, astragalus root, atracylodes rhizome, hoelen plant, dioscorea root, lotus seed, chaenomeles fruit, dang gui root, dolichos seed

Mind-Body: meditation, relaxation,

Acupuncture/TENS: acupressure at GI acupuncture point PC6; TENS: transcutaneous electrical nerve stimulation at GI acupuncture points PC6 and ST36.