

ORIGINAL RESEARCH

USE OF ALTERNATIVE TREATMENTS BY CHRONIC FATIGUE SYNDROME DISCORDANT TWINS

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Background: Patients with chronic fatigue syndrome (CFS) have been faced with difficulties in diagnosis and lack of effective treatments. Anecdotal evidence suggests that use of alternative treatments may be common in these patients. Our primary objective was to compare the prevalence and patterns of alternative medicine use among twins who met the Centers for Disease Control and Prevention (CDC) CFS criteria to that of their non-CFS co-twins. Secondary goals were to assess how often alternative medicine use was discussed with physicians and the perceived benefit of these therapies. *Methods:* Sixty-three twin pairs discordant for CFS completed a survey about their use of 22 alternative therapies. Matched pair odds ratios and 95% confidence intervals were used to examine differences in the use between CFS twins and their non-CFS co-twins.

Results: 91% of twins with CFS and 71% of non-CFS twins had used at least 1 alternative treatment in their lifetime. Twins with CFS were more likely to use homeopathy, mega-vitamins, herbal therapies, biofeedback, relaxation/meditation, guided imagery, massage therapy, energy healing, religious healing by others, and self-help groups than their non-CFS counterparts. A large proportion of all twins (CFS = 81%; non-CFS = 71%) found alternative therapies helpful; however, only 42% of those with CFS and 23% of those without CFS discussed their use of alternative medicine with a physician. *Conclusions:* Individuals with CFS frequently used alternative medical treatments yet rarely communicated this use to their medical doctor. Future research should ascertain the usefulness of alternative practices in the management of CFS. (Int Med 1999;2:97–103) © 2000 Elsevier Science Inc.

Key Words: chronic fatigue syndrome; alternative therapies; twins.

Chronic fatigue syndrome (CFS) is a condition of unknown etiology characterized by disabling fatigue of at least 6 months duration, and other symptoms such as muscle pain, pharyngitis, and changes in mood, sleep, and neurocognition [1]. In clinical settings, CFS is most commonly diagnosed in relatively young, educated, and previously healthy women [2]. There are no consistent laboratory findings or diagnostic tests for CFS [2,3]. As defined by the Centers for Disease Control and Prevention (CDC), CFS is a diagnosis of exclusion [1]. The

treatment of CFS has focused on symptoms [4]. While these treatments may work for some patients and some symptoms, there are no specific and definitive treatments for CFS. In addition, family, friends, and physicians often dismiss CFS patients' complaints as psychosomatic and therefore "not real" [5].

A growing trend in health care is the use of alternative medical practices in the general population [6,7], among family practice patients [8], and those with chronic illnesses [9–11]. These practices are defined broadly as self- or other-assisted health care strategies that are unconventional or historically have not been a component of western medical practice. Yet, in a 1994 survey, 10% of Americans reported receiving 1 of 4 alternative treatments [6]; in another study, 34% had used at least 1 of 16 unconventional treatments [7]. Likewise, a survey of family practice patients found that half previously had or currently were using some form of alternative medicine [8]. In contrast, 91% of patients with fibromyalgia, a syndrome of chronic mus-

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Supported by grant U19 AI38429 from the National Institutes of Health (Buchwald).

culoskeletal pain, reported using alternative treatments in a recent study [12].

Individuals with CFS also report the use of alternative medicine. For example, between 19% and 35% of 208 patients with CFS from a clinic sample visited an acupuncturist, chiropractor, or naturopath [13]. In a smaller study, all CFS patients ($n = 30$) had seen an acupuncturist, massage therapist, or another allied health professional in the previous year [14]. Individuals with CFS have indicated that the failure of conventional medicine in treating their illness and the lack of satisfaction with the support received from medical professionals, are the primary reasons for seeking alternative care [15]. Treatment by alternative practitioners, however, has not been predictive of improvement in symptoms of CFS [16].

The purpose of the present study was to compare the prevalence and patterns of alternative medicine use among a sample of twins who met the CDC CFS criteria with that of a matched control group, their non-CFS co-twins. Another goal was to assess the extent to which those who used alternative therapies had related this information to their physicians or found these therapies useful.

METHODS

Construction and Content of the CFS Twin Registry

The twin pairs assessed as part of this study were drawn from the Chronic Fatigue Twin Registry at University of Washington that was established in 1995. Twin pairs in which at least one member was chronically fatigued (a specified fatigue duration or diagnosis of CFS was not required) were solicited through advertisements placed in twin organization and patient support group newsletters, electronic bulletin boards for CFS, from existing twin registries, and by contacting clinicians and researchers familiar with CFS. Written informed consent was obtained from each Registry member in accordance with the regulations of our institutional Human Subjects Review Board.

A detailed description of the construction of the Registry has been presented elsewhere [17]. Briefly, the Registry questionnaires included information on demographics, zygosity, habits, lifestyle, social support, distress, and a checklist of the revised 1994 CDC criteria for CFS [1]. For non-fatigued participants, a control version of questions was used that did not reference fatigue. Physical health was determined by self-report using a checklist of medical disorders. To ascertain psychiatric conditions, the Diagnostic Interview Schedule Version III-A (DIS) [19], a highly structured interview that assigns current and lifetime diagnoses based on DSM-III-R criteria [20], was administered by telephone.

Case Definition

Chronically fatigued twins were classified according to the 1994 CDC CFS research definition using data obtained from the Registry questionnaire and telephone interview. A

criteria-based algorithm was developed that made a diagnosis of presumptive CFS using both the inclusionary and exclusionary components of the CDC case definition. Identical exclusionary criteria were applied to both the chronically fatigued and non-fatigued twins. To be classified as presumptive CFS, twins were required to report fatigue for at least 6 months that was not life-long and that resulted in a substantial reduction of their occupational, educational, social, or personal activities. Furthermore, participants had to endorse the presence of at least 4 of the following 8 complaints which comprise the CDC CFS symptom criteria: impaired memory or concentration, sore throat, tender glands, aching or stiff muscles, multi-joint pain, new headaches, unrefreshing sleep, and post-exertional fatigue.

Twins were not included in the presumptive CFS sample for obesity (body mass index ≥ 45), and the presence of specific physical and psychiatric disorders. Consistent with the CDC case definition, the exclusionary psychiatric disorders included the DIS generated diagnoses of lifetime mania, hypomania, bipolar disorder, schizophrenia, major depression with psychotic or melancholic features, anorexia nervosa or bulimia, or current alcohol or substance abuse/dependence. The CDC defined exclusionary medical conditions were assessed via a comprehensive checklist of self-reported medical problems; twins indicated whether a condition was currently active and whether a physician had evaluated it. Examples from the comprehensive list of exclusionary disorders included (but were not limited to) steroid-dependent asthma, diabetes, cancer (other than skin), congestive heart failure, multiple sclerosis, Lyme disease, rheumatoid arthritis, and systemic lupus erythematosus. For the purposes of this report, individuals meeting the inclusionary and exclusionary criteria for presumptive CFS are hereafter referred to as having CFS.

Survey of Alternative Medicine Use

In 1997, twins were mailed an annual follow-up packet of questionnaires that augmented their baseline Registry information. As part of this survey, twins were asked an extensive battery of questions about their lifetime use of alternative medicine. Since there are diverse practices within alternative medicine, the goal of the survey was to broadly assess the use of any practice that historically had not been taught widely in US medical schools, was not routinely available in US hospitals, or was not considered to be a standard part of medical care. For example, energy healing typically is viewed as unconventional while biofeedback, hypnosis, and other mind/body strategies are part of standard care for some, but not all, indications. Thus, 22 alternative therapies were categorized into: Systems of Medicine, Diet and Nutrition, Mind/Body Control, Manual Healing, Uses of Substances, Biomagnetic Therapy, Religious Practices, and Other. These categories of alternative therapies were informed by those in the national survey by Eisenberg and colleagues [7].

Individuals who reported using any alternative treatment

were asked to rate the usefulness of individual therapies on a 1 to 4 scale (1 = very helpful, 4 = not at all helpful), and to report whether they had discussed the use of such therapies with their medical doctor in the previous year. These individuals also responded to (true/false) a list of reasons for using alternative therapies and for not discussing this use with their medical doctor.

Statistical Analysis

Initial analysis compared the prevalence (in percent) of use of alternative medical practices in twins with CFS and their non-CFS co-twins. The magnitude of the association between CFS and alternative medical practices was estimated using matched pair odds ratios (OR) and exact 95% confidence intervals (CI) for each of the 22 individual alternative medical practices. A matched pair *t*-test was used to compare the mean number of alternative medical practices between the CFS and non-CFS twins.

Twins who did not report a lifetime use of alternative therapies were not asked about the usefulness of alternative therapies or whether they had discussed their therapy use with their physician. For these variables, the participants were treated as an unmatched sample and the frequencies in the 2 groups were compared using a 2-tailed Fisher's exact test.

RESULTS

Of the 177 twin pairs who had Registry data available for both members of the pair, 63 pairs were classified as discordant for CFS (i.e., one member of the pair had CFS while the other did not) and responded to the alternative medicine questionnaire. Over one half of the twin pairs were monozygotic; nearly 73% were female-female twin pairs, and 100% were white. On average, the twins were in their early to mid 40's at the time of their alternative medicine survey; 62% were married; and they had almost 15 years of education. Twins with CFS had experienced fatigue for an average of 9.4 years with a mean severity of 7.5 on a 1 to 10 scale (1 = none; 10 = a great deal).

In general, twins with CFS had a higher prevalence of alternative medicine use than their non-CFS co-twins; 91% of twins with CFS and 71% of their co-twins had used at least one alternative practice in their lifetime (prayer excluded). In addition, twins with CFS used a significantly larger number of therapies overall compared to their non-CFS co-twins (mean CFS = 5.7 vs. mean non-CFS = 2.9, $p = 0.000$). Six out of 63 (10%) individual twins with CFS and 16 out of 63 (25%) non-CFS individual twins reported never using any of the therapies cited in the survey; thus they did not answer the remainder of the questionnaire.

Comparisons of twin pairs on their lifetime use for each alternative treatment are shown in Table 1. There was a great deal of variability in the types of alternative medical practices used. For 10 therapies, the likelihood that a twin with CFS used these therapies was significantly greater

than the likelihood of use by the non-CFS co-twin. These included: homeopathy (OR = 11.0; 95% CI 1.5–228.1), mega-vitamins (OR = 3.4; 95% CI 1.2–10.5), herbal therapies (OR = 10.0; 95% CI 2.3–61.9), biofeedback (OR = 9.0; 95% CI 1.2–189.8), relaxation/meditation (OR = 5.7; 95% CI 1.6–24.3), guided imagery (OR = 5.5; 95% CI 1.2–35.9), massage therapy (OR = 2.6; 95% CI 1.2–5.8), energy healing (OR = 5.5; 95% CI 1.2–35.9), religious healing by others (OR = 5.5; 95% CI 1.2–35.9), and self-help groups (OR = 5.3; 95% CI 1.5–23.0).

Table 2 presents the proportion of individuals with and without CFS who spoke with their physicians about their use of various alternative treatments by therapeutic category. Across all treatment modalities, 42% of those with CFS who reported alternative therapy use also informed their physician about their use of such treatments. In contrast, reporting the use of any alternative therapies was observed among 23% of those without CFS. As would be expected, significantly more participants with CFS spoke with their physicians about their use of self-help groups than those without CFS (CFS = 39% vs. non-CFS = 0%, $p = 0.02$).

In investigating the reasons why participants did not discuss their use of alternative medicine with their medical doctor, almost 57% of those with CFS and 68% of those without CFS indicated that their physician had not asked them about these therapies. Interestingly, compared to individuals with CFS, a significantly larger proportion of those without CFS believed that it was not important for their physicians to know about their alternative medicine use (CFS = 32% vs. non-CFS = 54%, $p = 0.03$), or thought that their alternative medicine use was "none of their doctor's business" (CFS = 9% vs. non-CFS = 33%, $p = 0.005$).

Overall, both those with and without CFS found alternative therapies helpful. The proportion of participants with and without CFS who found the various alternative therapy categories somewhat to very useful is shown in Table 3. A greater proportion of those with CFS than non-CFS participants found biomagnetic therapy (CFS = 80% vs. non-CFS = 0%, $p = 0.03$) and self-help groups (CFS = 100% vs. non-CFS = 50%, $p = 0.002$) helpful. The most common reason given by all participants (CFS = 71%, non-CFS = 81%, $p = 0.26$) for using alternative therapies was the belief that using both conventional and alternative therapies is better than using either one alone. Other frequent reasons were illness control, disease prevention, and to increase energy. A sizable proportion of those with CFS reported using alternative therapies to prevent their medical conditions from worsening (CFS = 53% vs. non-CFS = 30%, $p = 0.005$). In contrast, those without CFS used these therapies to prevent diseases (CFS = 19% vs. non-CFS = 43%, $p = 0.003$).

DISCUSSION

The results of the present study indicate that many non-CFS twins and those with CFS have used at least one alter-

Table 1. Lifetime use of alternative treatments in CFS discordant twin pairs: prevalence, odds ratios, and 95% confidence intervals

Treatment	Twins discordant for CFS		Odds ratio	95% CI
	With CFS (n = 63)	Without CFS (n = 63)		
Systems of medicine (%)				
Acupuncture	27	16	2.8	0.8–10.2
Naturopathy	11	5	3.0	0.5–21.5
Homeopathy	25	10	11.0	1.5–228.1
Osteopathy	11	5	5.0	0.6–113.1
Diet and nutrition (%)				
Megavitamins	49	30	3.4	1.2–10.5
Special diet	27	18	2.2	0.7–7.3
Lifestyle diet	18	14	1.3	0.4–4.3
Herbal therapies	46	18	10.0	2.3–61.9
Mind/body control (%)				
Biofeedback	14	2	9.0	1.2–189.8
Hypnosis	13	6	2.3	0.5–11.4
Relaxation/meditation	41	19	5.7	1.6–24.3
Guided imagery	24	10	5.5	1.2–35.9
Yoga	14	6	6.0	0.7–132.3
Manual healing (%)				
Massage	54	29	2.6	1.2–5.8
Chiropractic	60	46	2.5	0.9–7.2
Use of substances (%)				
Chelation therapy	3	3	1.0	0.1–10.0
Aromatherapy	10	3	3.0	0.5–21.5
Biomagnetic therapy (%)				
Energy healing	18	3	5.5	1.2–35.9
Religious practices (%)				
Prayer	48	32	2.4	0.9–6.4
Religious healing by others	18	3	5.5	1.2–35.9
Other (%)				
Folk remedy	5	2	3.0	0.3–74.8
Self-help group	68	11	5.3	1.5–23.0

Table 2. Proportion of individuals with and without CFS who discussed alternative treatment use with a physician

Treatment ^a	With CFS % (ratio)	Without CFS % (ratio)
Systems of medicine	50 (9/18)	30 (3/10)
Diet and nutrition	70 (19/27)	46 (7/15)
Mind/body control	58 (11/19)	30 (3/10)
Manual healing	48 (12/25)	26 (5/19)
Use of substances	18 (2/11)	0 (0/7)
Biomagnetic therapy	29 (5/17)	0 (0/7)
Religious practices	42 (11/26)	23 (3/13)
Other		
Folk remedy	0 (0/13)	10 (1/10)
Self-help group	39 (9/23)	0 (0/10) ^b
Median % across all modalities	42	23

^a *Systems of medicine* include acupuncture, naturopathy, homeopathy, and osteopathy; *Diet and nutrition* includes mega-vitamins, special diet, lifestyle diet, and herbal therapies; *Mind/body control* includes biofeedback, hypnosis, relaxation/meditation, guided imagery, and yoga; *Manual healing* includes massage and chiropractic care; *Use of substances* includes chelation therapy and aromatherapy; *Biomagnetic therapy* includes energy healing; *Religious practices* includes prayer and religious healing by others; *Other* includes folk remedy and self-help groups.

^b $p < 0.05$.

Table 3. Proportion of individuals with and without CFS who found alternative treatments helpful

Treatment ^a	With CFS % (ratio)	Without CFS % (ratio)
Systems of medicine	81 (17/21)	71 (10/14)
Diet and nutrition	74 (29/39)	90 (18/20)
Mind/body control	81 (25/31)	100 (13/13)
Manual healing	83 (35/42)	86 (24/48)
Use of substances	67 (4/6)	67 (2/3)
Biomagnetic therapy	80 (8/10)	0 (0/2) ^b
Religious practices	85 (28/33)	100 (17/17)
Other		
Folk remedy	67 (2/3)	50 (1/2)
Self-help group	100 (16/16)	50 (3/6) ^c
Median % across all modalities	81	71

^a *Systems of medicine* include acupuncture, naturopathy, homeopathy, and osteopathy; *Diet and nutrition* includes mega-vitamins, special diet, lifestyle diet, and herbal therapies; *Mind/body control* includes biofeedback, hypnosis, relaxation/meditation, guided imagery, and yoga; *Manual healing* includes massage and chiropractic care; *Use of substances* includes chelation therapy and aromatherapy; *Biomagnetic therapy* includes energy healing; *Religious practices* includes prayer and religious healing by others; *Other* includes folk remedy and self-help groups.

^b $p < 0.05$.

^c $p < 0.01$.

native treatment in their lifetime. We examined lifetime rather than current use because the prolonged illness duration of CFS (average = 9.4 years) suggested that lifetime rates would yield a more accurate picture of alternative medicine use in this study's CFS sample. While the rate of use for CFS twins was consistent with prior reports of patients with chronic medical illnesses [12] and those with CFS [13,14], use of alternative practices among non-CFS twins was substantially higher than that previously reported for the general population [6–8]. However, since the previous community-based surveys have assessed alternative therapy use in a 1-year period, the results of the present study are not directly comparable. In addition, the non-CFS twins' exposure to their siblings' use of alternative medicine may have prompted their increased use.

When comparing twin pairs on their lifetime use of these treatments, those with CFS were significantly more likely than non-CFS twins to use homeopathy, mega-vitamins, herbal therapies, biofeedback, relaxation/meditation, guided imagery, massage therapy, energy healing, religious healing by others, and self-help groups. Detecting differences in alternative medicine use among CFS and non-CFS twins was especially interesting in light of the excellent control for genetic and environmental factors offered by our study design. The co-twin methodology is a pair-matched study design that uses disease-discordant twins to examine differences in behavioral, clinical, or laboratory factors. Of relevance to CFS in general, and to this study in particular, co-twin control studies are especially helpful when appropriate comparison groups are poorly defined.

While energy healing and religious healing by others may be viewed by some as uncommon treatments, the majority of the treatments endorsed by CFS twins were among the most widely used and studied unconventional treatments. For example, biofeedback has been used in the

treatment of many illnesses [21–23], and has been shown to be effective for reducing the number and intensity of various types of headaches [23]. More recently, a case report suggests that EEG biofeedback may improve cognitive symptoms and functional status in CFS [24]. Guided imagery has been effectively used with patients to reduce anxiety and the emotional consequences of medical illnesses [25]. Herbal substances have not been studied extensively, yet they are commonly used as folk remedies for fever, arthritis, and migraine [26]. A few studies have found various herbal preparations to be useful in the treatment of non-ulcer dyspepsia [27], cognitive functioning [28], and arthritis pain [29]. In addition, results from a recent in vitro study suggest that echinacea and Panax ginseng can enhance natural killer cell activity and cellular immune function in patients with CFS [30]. Lastly, massage therapy is one of the most frequently used alternative treatments [7], and has been found to be beneficial in patients with chronic tension headaches [31], and muscle tension and fibrositis [32]. Given the increased use of alternative therapies by patients with CFS, their apparent effectiveness for other medical conditions, and the general lack of beneficial interventions for CFS, it seems appropriate to conduct randomized controlled clinical trials in order to better understand their efficacy, cost effectiveness and, if relevant, mechanism of action in CFS. Our results might be used to prioritize research involving these particular therapies and systems of medicine in general, in the management of CFS.

The finding that the majority of all individuals who used alternative therapies did not discuss this use with their physician was consistent with reports from the general population [7]. Medical doctors were more likely to be informed of the use of diet and nutritional supplements and mind/body control strategies, and least likely to be told about use of aromatherapy or chelation, biomagnetic ther-

apy, and folk remedies. This difference may be a reflection of physicians' differing attitudes toward such therapies. For example, in a survey of 295 family physicians, 70% to 90% considered behavioral medicine, counseling, and hypnotherapy to be legitimate medical practices [33]. However, the majority did not view positively homeopathy, Native American medicine, and traditional Asian medicine. Although physicians' attitudes on the least-reported therapies surveyed in this study were not assessed directly, use of these therapies is not easily incorporated into conventional medical practice and hence may be unlikely to be accepted by, and reported to physicians. For this sample, the high proportion of all participants who were not asked about their use of alternative medicine suggests that physicians lack the necessary interest or information to discuss this topic with their patients. This may not be in the best interest of the patients, since the use of alternative therapies may have direct negative health implications or be associated with adverse effects in conjunction with conventional treatment [34]. In addition, the beneficial effects of one type of treatment may be ascribed to another ineffective treatment.

Various reasons for seeking alternative treatments have been cited including health promotion and disease prevention, preventing a medical condition from worsening, as an adjunct to conventional medicine, or when conventional therapies are not effective [34]. The majority of all individuals we surveyed held the belief that using alternative and conventional medicine together was better than either one alone. Among individuals with CFS, alternative therapies were used to prevent worsening of their condition or to treat their symptoms, while individuals without CFS relied on these treatments for health promotion and disease prevention. The differing rates of helpfulness may reflect the difference in the benefit of alternative treatments for various purposes. Future research could focus on delineating the perceived effectiveness of various alternative therapies for disease prevention and symptom relief of CFS and other chronic conditions.

The present study has several limitations. First, the reliance on a self-reported list of medical conditions to diagnose CFS was less than ideal. This methodology could result in either an overestimate of CFS if fatigued participants did not report conditions which might be exclusionary, or an underestimate if a review of medical records failed to corroborate their reports. A second limitation is related to sample size. Since not all twin pairs used alternative therapies, the analyses of subsequent questions on their helpfulness and discussions with physicians were unmatched. These analyses could be influenced by the potential confounding effects of numerous factors, including genetic effects. Thirdly, because of lifetime use estimates, results from this study cannot speak to whether the use of alternative therapies predated the development of CFS symptoms or was initiated as a response to illness. While this question is worthy of further study, the present results suggest that the lifetime use of alternative treatments is prevalent

even among those in good health. And lastly, the discipline of the twins' primary care provider may have confounded the present results since certain specialties (e.g., osteopathy) may be more likely to advocate the use of alternative treatments.

Currently, conventional medicine offers few effective treatments for CFS. The present study suggests that those with CFS are more likely to use alternative treatments in conjunction with conventional medicine than their non-CFS counterparts. They also are unlikely to discuss this use with their physician and may have unrealistic expectations regarding the benefit of such therapies for illness management. Individuals with CFS may benefit from increased communication and collaboration among those who advocate and practice traditional and alternative medicine. These treatment modalities, alternative systems of medicine, as well as patients' needs and expectations, require further scientific exploration.

The authors would like to thank the participants in the University of Washington Chronic Fatigue Twin Registry for their cooperation, patience, and goodwill, and Dr. Leigh Sawyer, Program Officer, NIAID, for her encouragement and support. We also wish to acknowledge our Advisory Panel, who with sage advice and ongoing encouragement, improved our scientific efforts.

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