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Widespread use of complementary and alternative medicine among non-Hodgkin lymphoma survivors

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Abstract

There are few studies examining complementary and alternative medicine (CAM) use and beliefs among non-Hodgkin lymphoma (NHL) survivors. Seven hundred and nineteen patients with NHL from the University of Iowa/Mayo Clinic Molecular Epidemiology Resource who completed the 3-year post-diagnosis questionnaire were included in this study. Altogether 636 (89%) reported ever using CAM, with 78% utilizing vitamins, 54% alternative therapies and 45% herbals. Female gender was associated with increased overall CAM use ($p = 0.0001$) as well as use of vitamins ($p = 0.0001$), herbals ($p = 0.006$) and alternative therapy ($p = 0.0002$) for cancer. Older age (>60) was associated with increased vitamin use ($p = 0.005$) and decreased herbal use ($p = 0.008$). Among users, 143 (20%) believed CAM assists healing, 123 (17%) believed CAM relieves symptoms, 122 (17%) believed CAM gives a feeling of control, 110 (15%) believed CAM assists other treatments, 108 (15%) believed CAM boosts immunity, 26 (4%) believed CAM cures cancer and 36 (5%) believed CAM prevents the spread of cancer.

Keywords: Complementary therapies, neoplasms, lymphoma, survivors, vitamins

Introduction

There are an estimated 630 000 people living with or in remission from lymphoma in the United States [1]. From 1960 to 2006, the 5-year relative survival rate increased from 31% to 69%, leading to many more long-term survivors [1]. However, advances in medical treatment have far outpaced knowledge of complementary and alternative medicine (CAM) use in this population, resulting in a significant knowledge gap and unclear clinical guidelines regarding the safety and effectiveness of CAM use for this population.

CAM is defined by the National Center for Complementary and Alternative Medicine as the array of health care approaches with a history of use or origins outside of mainstream medicine [2]. The prevalence of CAM use among patients with cancer has grown significantly in the past decade. Recent studies report that the frequency of CAM use in patients with cancer is typically 50–80% [3–7], while rates of CAM use in the general US population are approximately 40% [8]. However, frequency reports specific to patients with or surviving a hematologic malignancy are limited. A pilot study of long-term lymphoma survivors reported that 68% of those surveyed had used CAM [9].

CAM modalities have been investigated in patients with solid tumors. Initial evidence has suggested some benefits for symptom management (e.g. nausea, pain, fatigue) and survival [10–17]. Patients with cancer commonly report turning to CAM therapies to better treat both physical and emotional symptoms [3]. CAM interventions have been found to be effective in randomized clinical trials for treatment of cancer-related pain [11,12], fatigue [16,17], nausea [11,12], anxiety [15,16], depression [14–16] and improved quality of life [10–17]. Mind–body techniques such as structured relaxation interventions for hematologic cancer populations may have beneficial outcomes, with recent studies reporting improvement in pain, nausea and quality of life [11–17]. However, several CAM modalities are contraindicated for the patient with cancer [18–20], and many are not well understood. The potential benefits, risks and mechanisms of CAM modalities for this population are currently

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unknown. In addition, the use of CAM modalities often continues long after completion of conventional oncology care and is not always well documented [21–24].

We sought to examine the prevalence of CAM use among a cohort of NHL survivors and further define the beliefs of this subset of cancer survivors with regard to CAM.

Methods

Study population

This study was reviewed and approved by the human subjects Institutional Review Board at Mayo Clinic and the University of Iowa, and written informed consent was obtained from all participants. All subjects in this analysis were from the Molecular Epidemiology Resource (MER) of the University of Iowa/Mayo Clinic Lymphoma Specialized Program of Research Excellence (SPORE), which has been previously reported [25]. Briefly, since September 2002, we have offered enrollment to consecutive, newly diagnosed patients with lymphoma (within 9 months) who were evaluated at Mayo Clinic in Rochester and the University of Iowa, were age 18 years and older, a resident of the USA and had no history of human immunodeficiency syndrome (HIV) infection. All diagnoses were confirmed by a hematopathologist and coded according to the World Health Organization (WHO) classification [26]. Baseline clinical, laboratory and treatment data were abstracted from medical records using a standard protocol. All patients were then systematically contacted every 6 months for the first 3 years and then annually thereafter. Disease progression, retreatment and death were validated against medical records.

Follow-up 3-year survey

In April 2006, we initiated the 3-year follow-up survey, which was a self-administered, 20-page survey that included a variety of topics on health and lifestyle behaviors and lymphoma survivorship, many of them from a survey used in a previous study of lymphoma survivors at Mayo Clinic (see Supplementary Appendix [to be found online at http://informahealthcare.com/doi/abs/10.3109/10428194.2014.916803] for questionnaire materials analyzed in this study) [9]. At 3 years after their diagnosis (± 3 months), surviving patients in the MER were mailed a survey, and had 3 months to return it. There were no follow-up attempts for non-respondents. For this analysis, we excluded patients with Hodgkin lymphoma, chronic lymphocytic leukemia (CLL) and primary central nervous system (CNS) lymphoma, leaving 1597 eligible patients with non-Hodgkin lymphoma (NHL). Prior to the 3-year follow-up, 288 patients died, 78 withdrew from the study, 62 had not yet reached the time point and 39 were lost to follow-up. Of the remaining 1130 patients eligible for the 3-year follow-up, 719 (63.6%) returned the survey. Patient characteristics were similar between respondents and non-respondents.

Vitamin use

We asked about multivitamin use ("Have you ever taken multiple vitamins in the last year?") and individual vitamin use ("Not counting multiple vitamins, did you take any of the following vitamins or minerals in the last year?"). For multivitamins, we asked participants to list the brand name, and then report how often they used them (1–3, 4–6, 7, >7 times/week) and whether they had changed their use since diagnosis (less, same, more). For individual vitamins, we asked frequency of use, change in use since diagnosis, and usual dose for vitamin A (not beta carotene), beta carotene, vitamin C, vitamin E, folic acid, vitamin B6, vitamin B12, vitamin D, calcium (including Tums), zinc, selenium, niacin, iron and magnesium. We also provided space for participants to specify other vitamins or minerals and provide the same information on use patterns. For previous and current use, they also indicated whether it was used for cancer or for other health issues.

Herbal supplements

We asked about the use of 44 herbal supplements ("Have you ever tried any of the following herbal supplements?"). Participants indicated whether they never used the herbal supplement or they previously used it or currently used it. For previous and current use, they also indicated whether the herbal supplement use was used for cancer or for other health issues.

CAM treatment and therapies

We asked "Have you ever tried any of the following alternative therapies: bioelectromagnetics, meditation, relaxation, yoga, acupuncture, chiropractic, massages or therapeutic touch?" We also asked respondents to specify up to four other CAM medical therapies, traditional Chinese medicine, religious/spiritual, naturopathy and homeopathy. For each treatment or therapy, participants indicated whether they never used it, previously used it or currently used it. For previous and current use, they also indicated whether the therapy was used for cancer or for other health issues.

Beliefs

We used a previously published [27] 15-item instrument regarding beliefs about CAM. Participants were asked (regardless of their use of CAM): "In your opinion, how true are the following statements about complementary/alternative products or therapies for cancer care?" The possible responses were "not true at all," "not very true," "don't know," "fairly true" and "very true." The 15 statements are listed in Table I.

Data analysis

χ^2 tests and Wilcoxon rank-sum tests were used to assess the association of CAM use with demographic and clinical characteristics. p-Values < 0.05 were considered statistically significant.

Results

Seven hundred and nineteen patients completed the 3-year follow-up questionnaire and were included in this study. A description of patient demographics is provided in Table II.

Among our population of NHL survivors, 89% reported having ever used any CAM modality (Table III). The most commonly used CAM modality was vitamins and minerals,

Table I. Complementary and alternative medicine (CAM) beliefs among NHL survivors ($n = 719$), Molecular Epidemiology Resource.

	n	%
CAM can assist the body's natural forces to heal	143	20%
CAM can relieve cancer symptoms	123	17%
CAM gives a feeling of control over cancer	122	17%
CAM can assist other treatments to work	110	15%
CAM can boost the immune system	108	15%
CAM has side effects	100	14%
CAM can increase quality of life	87	12%
CAM is perfectly safe	62	9%
CAM can prevent the spread of cancer	36	5%
CAM can reduce the chance that conventional medicine will work	34	5%
It is easy to understand how CAM works	34	5%
CAM can cure cancer	26	4%
CAM can prevent cancer recurrence	14	2%
CAM can weaken the body's natural reserves	11	2%
It is the patient's fault if CAM does not work	11	2%

NHL, non-Hodgkin lymphoma.

Table II. Patient demographics.

	Total ($n = 719$)	%
Age, years		
Median	63	
Range	22–92	
≤ 60	314	44%
> 60	405	56%
Sex		
Female	335	47%
Male	384	53%
NHL type		
Diffuse large B-cell lymphoma	207	29%
Follicular lymphoma	245	34%
Mantle cell lymphoma	48	7%
Marginal zone lymphoma	97	13%
T-cell lymphoma	45	6%
Other NHL	77	11%
Ann Arbor stage at diagnosis		
Missing	8	1%
I–II	275	38%
III–IV	436	61%
Performance status at diagnosis		
Missing	1	$< 1\%$
< 2	660	92%
≥ 2	58	8%

NHL, non-Hodgkin lymphoma.

with an overall use of 78%. The most commonly used vitamins were multivitamins (63%), calcium (41%), vitamin D (30%), vitamin C (26%) and other (20%). The second most commonly utilized CAM modality was alternative therapy (54%), including chiropractic (36%), massage (24%), relaxation techniques (16%), meditation (13%) and religious/spiritual practices (11%). Herbal supplements were used by 45% of patients. The most commonly used herbals were green tea (26%), flaxseed (17%), herbal tea (14%), garlic (14%) and *Echinacea* (11%).

Older age (> 60 years) was associated with slightly higher vitamin use (80% vs. 75%; $p = 0.005$) and decreased herbal supplement use (40% vs. 50%; $p = 0.008$). Female gender was associated with a higher prevalence of overall CAM use (94% vs. 84%; $p \leq 0.0001$), use of vitamins (86% vs. 70%; $p \leq 0.0001$), herbal supplements (50% vs. 39%; $p = 0.006$) and alternative therapy (62% vs. 47%; $p = 0.0002$). To test the hypothesis that individuals with more aggressive hematological malignancies may have different patterns of CAM use than those with an indolent/chronic malignancy, we compared patients with follicular lymphoma (FL) grades 1–2 (i.e. indolent/chronic) and those with non-relapsed diffuse large B-cell lymphoma (DLBCL) (i.e. aggressive malignancy) and found no significant differences in overall CAM use, although massage therapy was utilized more often by FL survivors (29% vs. 18%; $p = 0.005$). There were no significant differences in overall CAM use among NHL subtypes (Table IV), disease stage or prognostic indices or performance status at diagnosis (data not shown). However, those with mantle cell lymphoma and T-cell lymphoma were more likely to report use of CAM therapies and techniques specifically for cancer compared to patients with other NHL subtypes ($p = 0.04$).

Table III. Overall complementary and alternative medicine (CAM) use as reported 3 years after NHL diagnosis, Molecular Epidemiology Resource ($n = 719$).

Vitamins	*n* (%)	Herbal supplements*	*n* (%)	Therapies and techniques†	*n* (%)
Multivitamins	452 (63%)	Green tea	188 (26%)	Chiropractic	256 (36%)
Calcium	293 (41%)	Flaxseed	122 (17%)	Massage	175 (24%)
Vitamin D	212 (30%)	Herbal tea	103 (14%)	Relaxation	118 (16%)
Vitamin C	188 (26%)	Garlic	101 (14%)	Meditation	91 (13%)
Other vitamins	145 (20%)	*Echinacea*	81 (11%)	Religious/spiritual	78 (11%)
Vitamin E	132 (18%)	*Ginkgo*	53 (7%)	Yoga	65 (9%)
Vitamin B12	125 (17%)	Ginseng	43 (6%)	Acupuncture	61 (9%)
Folic acid	117 (16%)	Saw palmetto	37 (5%)	Therapeutic touch	38 (5%)
Magnesium	107 (15%)	*Aloe*	36 (5%)		
Vitamin B6	90 (13%)	Parsley	34 (5%)		
Zinc	89 (12%)	St. John's wort	32 (5%)		
Iron	84 (12%)				
Niacin	75 (10%)				
Selenium	73 (10%)				
Vitamin A	63 (9%)				
Beta carotene	56 (8%)				

NHL, non-Hodgkin lymphoma.
*Herbal supplements used $< 5\%$: Chinese herbs, dandelion, dehydroepiandrosterone (DHEA), essiac tea, primrose oil, grape seed extract, Hawaiian herbs, Hawaiian salt, herb mixtures, horse tail, licorice root, marijuana, milk thistle, mushroom tea, noni, orange zest, pau darco, peppermint, red clover, royal jelly, shark cartilage, wheat grass, white fish supplement and yam.
†Alternative therapy used $< 5\%$: bioelectromagnetics, alternative medicine, traditional Chinese medicine, naturopathy and homeopathy.

Table IV. Complementary and alternative medicine (CAM) use by NHL type, Molecular Epidemiology Resource.

	Total ($n = 719$)	DLBCL ($n = 207$)	FL ($n = 245$)	MCL ($n = 48$)	MZL ($n = 97$)	Other NHL ($n = 77$)	T-cell ($n = 45$)	p-Value
Vitamins								
Any vitamin use	557 (78%)	157 (76%)	190 (78%)	40 (83%)	76 (78%)	59 (77%)	35 (78%)	0.93
Herbal supplements								
Any herbal supplement use	320 (45%)	84 (41%)	118 (48%)	18 (38%)	49 (51%)	33 (43%)	18 (40%)	0.36
Any herbal supplement use for cancer	116 (16%)	28 (14%)	42 (17%)	9 (19%)	17 (18%)	14 (18%)	6 (13%)	0.83
Any herbal supplement use for other health issues	284 (40%)	76 (37%)	105 (43%)	15 (31%)	45 (46%)	28 (36%)	15 (33%)	0.29
Therapies and techniques								
Any use	389 (54%)	112 (54%)	132 (54%)	28 (58%)	54 (56%)	37 (48%)	26 (58%)	0.87
Any use for cancer	132 (18%)	40 (19%)	42 (17%)	15 (31%)	11 (11%)	12 (16%)	12 (27%)	0.04
Any use for other health issues	367 (51%)	104 (50%)	127 (52%)	24 (50%)	53 (55%)	36 (47%)	23 (51%)	0.94
Any CAM use	636 (89%)	178 (86%)	223 (91%)	44 (92%)	84 (87%)	67 (87%)	40 (89%)	0.83

NHL, non-Hodgkin lymphoma; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; T-cell, T-cell lymphoma.

Survivors were surveyed about their beliefs and motivations for CAM use (Table I). Among all 719 survivors, the most commonly held beliefs were that CAM can assist the body's natural forces to heal (20%), can relieve cancer symptoms (17%), gives a feeling of control over cancer (17%), can boost the immune system (15%) and can assist other treatments to work (15%). However, only 14% believed that CAM has side effects and only 5% believed that CAM can reduce the chance that conventional medicine will work. Although of relatively lower prevalence, but of clinical significance, 4% of patients in our study believed that CAM can cure their cancer. In addition, 5% believed that CAM can prevent the spread of cancer and 2% believed that CAM can prevent a cancer recurrence. CAM users were significantly more likely than non-users to believe that CAM can cure cancer, prevent the spread of cancer, assist other therapies, relieve symptoms, assist the body to heal, boost the immune system, is perfectly safe and increases quality of life; and less likely to believe that CAM weakens natural reserves (data not shown).

Among those who utilized CAM, many reported use specifically to treat either their cancer or other health issues (Table V). The most commonly utilized modality specifically for either cancer or other health issues was alternative therapy, with 18% of patients reporting its use for cancer and 51% for other health issues. Similarly, 16% of patients reported use of herbal supplements for cancer and 40% for other health issues.

Discussion

Among our cohort of over 700 NHL survivors surveyed 3 years after diagnosis, approximately 90% reported ever use of any type of CAM modality. This is higher than previously reported, possibly due to inclusion of different patient populations or broader exposure assessment. Among a sample of 68 patients on active treatment for varied hematological cancers in Europe, 18 (27%) reported CAM use following their cancer diagnosis [28]. Homeopathy (39%), herbal medicine (22%) and use of psychic therapies (22%) were among the most commonly utilized CAM modalities among this population of patients. Hensel *et al.* [24] conducted a study consisting of 87 patients with CLL (treated and untreated), among whom 44% had ever used CAM. Similar to our patient population, vitamin supplements were most utilized (26%); however, other frequently used modalities differed somewhat, with minerals (18%), homeopathy (14%) and mistletoe (9%) among other most used CAM. Conversely, D'Arena *et al.* [29] reported only 16.5% CAM use among their cohort of 442 patients with CLL (treatment status not reported), with green tea (41%), *Aloe* (19%) and high dose vitamins (8%) most utilized.

We found that female gender was associated with increased utilization of all CAM modalities when compared to males. These findings are similar to previous studies in patients with cancer, which suggest a higher prevalence of CAM use among females [30]. D'Arena *et al.* [29] reported that female gender was among the strongest predictors for CAM use ($p < 0.01$) in their cohort. Older age (>60) was directly associated with vitamin use and inversely associated with herbal supplement use among our population of lymphoma survivors. In contrast, much of the data

Table V. Use of complementary and alternative medicine (CAM) for cancer and other health issues (OHI) among NHL survivors ($n = 719$), Molecular Epidemiology Resource.

	Cancer use	%	OHI use	%
Herbal supplements*				
Green tea	68	10%	138	19%
Flaxseed	22	3%	107	15%
Garlic	13	2%	95	13%
Herbal tea	18	3%	89	12%
Echinacea	4	1%	79	11%
Ginkgo	4	1%	51	7%
Ginseng	4	1%	40	6%
Saw palmetto	4	1%	37	5%
Parsley	3	<1%	33	5%
Therapies and techniques†				
Chiropractic	10	1%	253	35%
Massage	23	3%	164	23%
Relaxation	41	6%	98	14%
Meditation	35	5%	73	10%
Religious/spiritual	64	9%	66	9%
Yoga	23	3%	55	8%
Acupuncture	10	1%	55	8%

NHL, non-Hodgkin lymphoma.
*Herbal supplement use < 5%: algae/spirulina, *Aloe*, bee pollen, black walnut, cat's claw, Chinese herbs, dandelion, dehydroepiandrosterone (DHEA), essiac tea, grape seed extract, green barley, Hawaiian herbs, Hawaiian salt, herb mixtures, horse tail, licorice root, marijuana, milk thistle, mushroom tea, noni, orange zest, pau darco, peppermint, primrose oil, red clover, royal jelly, shark cartilage, St. John's wort, wheat grass, white fish supplement and yam.
†Therapies and technique use < 5%: alternative medicine, bioelectromagnetics, homeopathy, naturopathy, therapeutic touch and traditional Chinese medicine.

available regarding analysis of patients with cancer most likely to utilize CAM suggests a higher prevalence in younger individuals (aged 30–59) [30]. In addition, we report that patients with mantle cell lymphoma (MCL) and T-cell lymphoma used CAM therapies and techniques specifically for cancer at a higher rate than patients with other NHL subtypes, a novel finding. MCL and T-cell lymphoma generally are aggressive NHL subtypes that confer a poor prognosis, and therefore patients may be more likely to use CAM in an effort to treat their cancer or cancer-related symptoms, although we did not find significant differences in beliefs about CAM in these subtypes compared to others (data not shown).

There were varied motivations for CAM use among our cohort of survivors, with many using CAM with the belief that it would be beneficial for their immune system, relieve cancer symptoms and provide a sense of control. These findings are similar to those expressed by patients in multiple other studies [30]. D'Arena *et al*. [29] reported that 20 (27%) of their patients reported using CAM to increase physical well-being and 10 (13%) used CAM to increase the body's ability to fight cancer. Similarly, Molassiotis *et al*. [28] reported that 10 (56%) patients used CAM to increase the body's ability to fight cancer and nine (50%) used CAM to both improve physical well-being and improve emotional well-being, hope and optimism. Several studies from the Western medical tradition have reported a high percentage of patients using CAM to directly fight their cancer: among a cohort of Italian patients with CLL, 40% ($n = 30$) of patients reported using CAM to directly fight their CLL [29]. Studies from non-Western medical traditions have reported even higher numbers [31,32]. In contrast, only a very small proportion of our population reported belief that CAM could cure their cancer and/or prevent cancer spread or recurrence, although these beliefs were more common in CAM users compared to non-users. In fact, among our cohort, many utilized CAM to treat other health conditions, with use for other health conditions exceeding use for cancer.

This study is the largest, to these authors' knowledge, to investigate the prevalence and motivations behind CAM use among a cohort of lymphoma survivors. The larger sample size allowed us to investigate other correlates of use (e.g. education, gender), and a large number of specific modalities used by this patient population. In addition, we were able to identify previous and current use, as well as reasons for use (specifically for cancer or for other reasons).

There are several limitations to this study. The response rate to our survey was 65%, which could introduce bias, although responders and non-responders had similar patient characteristics on a variety of demographic and clinical characteristics. We only ascertained CAM use at the 3-year anniversary after diagnosis, and thus cannot be directly compared to patients undergoing active chemotherapy and may not reflect CAM use by patients who die within 3 years of their diagnosis. We did not query specifics of all CAM use, including specific modalities of traditional Chinese medicine and naturopathy, for example. This study consists primarily of Caucasian lymphoma survivors living in the Midwestern USA, and as such may limit the generalizability of our findings to other patient populations.

In summary, the use of CAM among lymphoma survivors is pervasive, and therefore open communication between physicians and patients about CAM use is imperative in order to provide safe, effective and comprehensive cancer care throughout the spectrum of treatment and survivorship. This is particularly important during the time of conventional chemotherapy treatment, as drug–drug interactions and side effects of CAM could be harmful. Additional research is needed to further define the beliefs and motivations of the CAM user and examine the use of CAM in patients with hematologic malignancies.

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Supplementary material available online

Questionnaire.