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Complementary and Alternative Medicine Use in Chronic Liver Disease Patients

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Abstract

Goals—To examine a wide range of sociodemographic and clinical characteristics as potential predictors of complementary and alternative medicine (CAM) use among chronic liver disease (CLD) patients, with a focus on CAM therapies with the greatest potential for hepatotoxicity and interactions with conventional treatments.

Background—There is some evidence that patients with CLD commonly use CAM to address general and CLD-specific health concerns.

Study—Patients enrolled in a population-based surveillance study of persons newly diagnosed with CLD between 1999 and 2001 were asked about current use of CAM specifically for CLD. Socio-demographic and clinical information was obtained from interviews and medical records. Predictors of CAM use were examined using univariate and multivariate logistic regression analysis.

Results—Of the 1040 participants, 284 (27.3%) reported current use of at least 1 of 3 CAM therapies of interest. Vitamins or other dietary supplements were the most commonly used therapy, reported by 188 (18.1%) patients. This was followed by herbal medicine (175 patients, 16.8%) and homeopathy (16 patients, 1.5%). Several characteristics were found to be independent correlates of CAM use: higher education and family income, certain CLD etiologies (alcohol, hepatitis C, hepatitis C and alcohol, and hepatitis B), and prior hospitalization for CLD.

Conclusions—Use of CAM therapies that have the potential to interact with conventional treatments for CLD was quite common among this population-based sample of patients with CLD.

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There is a need for patient and practitioner education and communication regarding CAM use in the context of CLD.

Keywords

complementary and alternative medicine; chronic liver disease; epidemiology

In 2004, the National Institutes of Health estimated there were 5.5 million Americans living with chronic liver disease (CLD)[1] or cirrhosis, and CLD was the twelfth leading cause of death in the United States in 2005, with an age-adjusted mortality rate of 9/100,000 population.[2] CLD disproportionately affects men, the economically disadvantaged, and minorities, especially African Americans, American Indians and Alaskan Natives, and Hispanics.[1,3,4] Risk factors for CLD include alcohol use, chronic hepatitis B and C, drug use, exposure to environmental and industrial toxins, as well as genetic predisposition.[3]

Conventional treatments for the underlying etiologies of CLD, such as antiviral therapies, are often difficult for patients to tolerate.[5] In addition, the limited efficacy of conventional therapy in certain cases has prompted some individuals with CLD to seek complementary and alternative medicine (CAM) therapies,[5] which include: acupuncture, biofeedback, chiropractic therapy, herbal medicine, homeopathy, hypnosis, meditation, prayer, and vitamins.[6] CAM is growing in popularity as an option not only for the treatment of illness, but also as a way to promote overall health and well-being both in parallel and in lieu of Western medicine.[7,8] Data from 2 national telephone surveys indicated that CAM use among the general American public increased from 34% in 1990 to 42% in 1997.[9] Research also indicates that many Americans use CAM therapies without the advice or knowledge of their physicians.[5,9]

Use of CAM among patients with CLD has not been well characterized, but is estimated to be higher than in other patient populations and increasing.[10,11] There is a special need for physicians to be aware of CAM use among patients with CLD because of the increased risk of hepatotoxicity in patients with existing liver damage and possible interaction with conventional CLD treatments.[9,12–20] Herbal medicine, dietary supplements, and vitamins pose the greatest potential danger, as some of these substances are metabolized by the liver.

Previously, a study examined a sample of patients with CLD from 6 liver disease clinics across the United States and found that 39% of patients reported use of CAM in the previous month.[21] Analyzing a limited number of potential demographic correlates, CAM use was significantly associated with female sex, younger age, and higher education and income levels.[21] High rates of CAM use have been found in other populations of patients with liver diseases,[22–25] but these studies have generally been limited by small sample sizes, including only patients with hepatitis C, or drawing patients from a single institution.

The objective of the present analysis was to describe the prevalence of CAM use and examine sociodemographic and clinical characteristics associated with CAM use among CLD patients in a large, multisite population-based referral sample. This analysis focused on the 3 CAM therapies, herbal medicine, vitamins or supplements, and homeopathy, which have the greatest potential for hepatotoxicity and adverse drug-drug interactions, in a setting of increasing popularity among the general public.[9,26]

MATERIALS AND METHODS

Study Population

The data for this study came from a population-based outpatient study of patients newly diagnosed with CLD by gastroenterologists in 3 US counties between 1999 and 2001 described elsewhere.[27] Briefly, the surveillance population included patients who (a) were seen in an outpatient setting by a participating gastroenterologist during the study period; (b) were at least 18 years old; (c) were residents of New Haven County, CT, Alameda County, CA, or Multnomah County, OR (total surveillance population of approximately 1.48 million people across the 3 study sites); (d) did not have recognized HIV infection; and (e) in the case of Alameda County residents, were enrolled in the Kaiser Permanente Medical Care Program. The study was approved by the institutional review boards at each participating institution and the Centers for Disease Control and Prevention.

CLD Case Definition

We defined CLD as evidence of any of the following in the patient's chart: (a) at least 2 of the same liver tests (ie, alanine aminotransferase, aspartate aminotransferase, or alkaline phosphatase with confirmatory 5′ nucleotidase or γ-glutamyl transpeptidase) documented as abnormal at least 6 months apart; (b) an imaging study indicating portal hypertension, varices or collateral circulation, a mass lesion, or other findings indicative of CLD; (c) a liver biopsy indicating cirrhosis, fibrosis, chronic hepatitis, or granulomata; or (d) a diagnostic clinical event (variceal bleed, hepatic encephalopathy, spontaneous bacterial peritonitis, ascites).

Data Collection

Each participant was interviewed using a standardized instrument that contained questions pertaining to demographic and clinical information, as well as a behavioral history to elicit other relevant exposures. A lifetime drinking history was established using the Lifetime Drinking History measure.[28] Data pertaining to age, race, ethnicity, sex, country of origin, highest level of education, family income, current employment status, and insurance status were obtained from the interview. Family income incorporated wages, salaries, pensions, and insurance payments as reported by the patient. During the interview, patients were also asked if they had been hospitalized for their liver disease.

CAM therapy use was based on responses to the following question from the in-person interview: "Are you currently using any of the following therapies or changes in lifestyle specifically for your liver disease?" Respondents could choose 1 or more items from a list of 14 CAM modalities. For our analysis, current CAM use for CLD was defined as a positive response to use of at least one of the following 3 CAM modalities: herbal medicine, vitamins or other dietary supplements, or homeopathy.

We reviewed patient medical charts or extracted electronic data using a standard chart abstraction form to obtain clinical information pertaining to etiology, cirrhosis status, conventional CLD medication related to underlying etiology (eg, interferon, ribavirin, lamivudine, methotrexate), and non-CLD related comorbidities. One study clinician at each site (ANS, NT, AZ) used all available clinical data to assign 1 or more diagnoses to each participating patient, using standard criteria. Cirrhosis was defined as any pathologic, clinical (varices, ascites, portosystemic encephalopathy, spontaneous bacterial peritonitis), or radiographic (liver nodularity, varices, ascites) evidence of cirrhosis.

Data Analytic Strategy

Simple descriptive statistics were used to characterize the study population and CAM usage by study site. The χ^2 test was used to assess the unadjusted associations between sociodemographic and clinical characteristics of the patients and CAM usage. Multivariate logistic regression was then performed to identify independent correlates of CAM use (including study site), using a backward elimination strategy to derive the most parsimonious model. To ensure that there was no negative confounding and that potentially important variables were not being missed, the excluded variables were then tested in the resulting model in a stepwise fashion. All variables significant at the 0.05 level were retained in the final model. Analyses were performed using SAS, Version 9.1.3 (SAS, Cary, NC).

RESULTS

Description of the Sample

Between 1999 and 2001, 2109 eligible patients with CLD were identified and 1040 (49%) were enrolled across the 3 study sites. The sociodemographic and clinical characteristics of study population have been described in full elsewhere[27] and are presented in Table 1 by study site.

Current CAM Use for CLD

Of the 1040 patients interviewed, 284 (27.3%) reported current use of at least one of the following CAM therapies for their CLD: herbal medicine, homeopathy, or vitamins or other dietary supplements. Vitamins or other dietary supplements were used most frequently, with 188 (18.1%) patients reporting use, followed by herbal medicine with use reported by 175 (16.8%) patients. Only 16 (1.5%) patients reporting usage of homeopathy for CLD. Eighty-six (8.3%) patients used more than one of the CAM therapies of interest. CAM use was significantly higher among participants in California (32.9%) than among those in Connecticut (24.0%) and Oregon (27.5%) (P=0.029).

In separate analyses of data limited to the patients in Connecticut (data not shown), the most commonly used herbal medicines among the entire population (n=476) were milk thistle (12.7%), echinacea (5.5%), St. John's wort (4.6%), valerian (1.9%), and gingko biloba (0.6%). When we looked at only those patients who reported using 1 of 3 CAM modalities of interest specifically for their CLD (n=112), there was a similar pattern of use with the most common herbal medicine being milk thistle (43.8%), followed by St. John's wort (10.7%), echinacea (8.9%), and valerian (4.5%).

In univariate analyses, sociodemographic characteristics significantly associated with CAM use were male sex, younger age, higher education, higher family income, and current employment status (Table 2). Use of CAM varied widely by CLD etiology, ranging from 14.7% among patients with nonalcoholic steatohepatitis (NASH) and fatty liver disease to 33.3% among those with CLD attributed to hepatitis B. CAM use was significantly associated with hospitalization for liver disease (P<0.001). Among those who had been hospitalized for liver disease (n=117), the most common CAM therapy was vitamins (39.3%), followed by herbal medicine (16.2%) and then homeopathy (1.7%). CAM use also appeared to be inversely associated with number of comorbid conditions (P=0.050) (Table 2).

Multivariate Predictors of CAM Use

In the multivariate analysis, education, family income, CLD etiology, and history of hospitalization from CLD were significantly associated with CAM use (Table 3). Patients

who reported being hospitalized for their CLD were twice as likely as those who had not been hospitalized to report current CAM use for their CLD [odds ratio (OR)=2.08, 95% confidence interval (CI)=1.36–3.17]. Compared with patients with NASH and fatty liver disease, those with etiologies of hepatitis C and alcohol (OR=2.58, 95% CI=1.33–4.98), hepatitis C (OR=2.85, 95% CI= 1.54–5.26), hepatitis B (OR=2.75, 95% CI=1.10–6.87), and alcohol alone (OR=2.81, 95% CI=1.31–6.03) were significantly more likely to use CAM.

Patients with a family income of $50 000 or more were 1.66 (95% CI=1.19–2.33) times more likely than those with an income of $0 to $29,999 to use CAM for their CLD. Those with at least some college education were 1.46 (95% CI=1.08–1.98) times more likely to use CAM for their CLD than patients with a high school education or less.

DISCUSSION

In this multisite study, we found that CAM use was quite common, with more than one-quarter (27.3%) of patients with newly diagnosed CLD reporting current use of herbal medicine, vitamins or other dietary supplements, or homeopathy specifically for their CLD. In addition, we found patient education level, family income, CLD etiology, and hospitalization for liver disease to be significant, independent correlates of CAM use.

Consistent with previous studies in the general population,[9,26] as well as among patients with liver disease specifically, higher income[21,23] and education[21,23,25] were strongly associated with use of CAM. Both higher income and education may be indicative of one's ability to pay for care outside of conventional medicine, as well as one's knowledge of and access to CAM.[9] In contrast to previous research, which suggests that women are more likely than men to use CAM,[9,21,26,29,30] we found no association between sex and CAM use after adjusting for education and income. Consistent with previous studies,[9,25,26] we found that non-Hispanic blacks were less likely than whites to report use of CAM, although this association failed to reach statistical significance.

In our study, CAM use was associated with a history of hospitalization for CLD, an indicator of disease severity. As a group, patients who have been hospitalized for their CLD may be more likely to have end-stage disease with more severe symptoms, for which conventional therapies may not be very successful. This finding is consistent with previous research indicating that CAM users are more likely than nonusers to report poorer health status[31] and have a greater number and intensity of somatic symptoms, as well as more progressive disease.[32,33]

The lowest usage of CAM was reported by patients with NASH and fatty liver disease. These patients had significantly more non-CLD related comorbidities than all other etiologies combined (data not shown), a clinical characteristic with a suggestive inverse association with CAM use in univariate analysis in this population. Current treatment options for NASH and fatty liver mainly entail lifestyle changes (eg, nutrition, exercise) for weight loss, in contrast to treatment options for other etiologies, such as hepatitis C and hepatitis B, that have many side effects for which patients may be more likely to seek CAM. In this population, almost 42% (15/36) of the hepatitis B cases were Asian. Although not statistically significant, we did observe that CAM use was more common among Asians in the univariate analysis (OR=1.28, 95% CI=0.66–2.47) and we noted that among the hepatitis B patients, Asians were more likely than non-Asians to use CAM (47% vs. 24%, P=0.175). No such differences were suggested among other CLD etiologies. The small numbers of Asians and cases with an etiology of hepatitis B precluded the confirmation of this association in the full multivariate model. An additional reason for high use of CAM among patients with hepatitis B may have been the limited number of conventional therapies

available for this etiology at the time of the study. Further studies are needed to investigate how underlying CLD etiologies and race/ethnicity affect CAM use.

Some of the specific herbal products being taken by participants in Connecticut, such as valerian that may be taken as a sedative, sleep aid, or pain reliever, have been implicated in cases of liver injury.[10,16,21,34] Additionally, new cases of herbal-related hepatotoxicity are constantly emerging, pointing toward the complex interaction between herbal medicines and the liver.[10,11,17,20,35] Certain vitamins may also pose risks for liver damage. In the Connecticut sample, 7 patients reported used of vitamin A (data not shown); a vitamin which has been linked to hepatotoxicity, with patients taking no more than typical over-the-counter (OTC) preparations.[36,37] Data from 41 case studies found that vitamin A doses even in the low "therapeutic" range can result in life-threatening liver damage.[38] In addition to herbal medicines and vitamins, there is evidence that certain OTC medicines, such as acetaminophen,[39] may be hepatotoxic, and we noted high use of OTC medicines in this population (data not shown).

This study had several limitations. Information was not collected on the duration or intensity of use of the CAM therapies of interest. Our estimate of utilization of CAM is lower than those previously reported in general (42%)[9] and CLD patient (39%)[21] populations, but these studies included a wide range of CAM therapies. This dataset offered a unique opportunity to identify patient-reported CAM use specific to CLD and we had the ability to identify CAM therapies that were most biologically relevant to those with CLD. Due to the cross-sectional nature of the data collection, it is difficult to assess the temporality of relationships between some of the correlates and CAM use. As was seen in the multivariate model, those patients who reported hospitalization for CLD were more likely to use CAM, but this analysis was not able to disentangle whether hospitalization preceded or postdated the use of CAM. However, 2 of the other significant correlates, education and income, can be seen as more stable characteristics and less likely to suffer from temporal bias. Patients in this referral-based sample tended to have generally high levels of income, education, and insurance coverage and were predominantly non-Hispanic whites. Thus, future studies should seek to examine CAM use among CLD patients in other treatment settings. In addition, our strict case definition may have limited our sensitivity to ascertain particular CLD cases. Also, it is unknown how our participation rate might have affected the estimates of CAM use and the observed relationships. Nevertheless, this study provides important information on CAM use in a referral-based population. Finally, it is not known whether these patients discussed their use of CAM therapies with their healthcare providers, but previous studies suggest that patients often do not inform their physicians of CAM use.[5,9]

CONCLUSIONS

Using data from a population-based study of patients with newly diagnosed CLD, this analysis was able to broaden the scope of potential correlates of CAM use. In addition, focusing the analysis on herbal medicine, vitamins or other dietary supplements, and homeopathy highlighted the CAM therapies that are most important in a conventional clinical setting. Given the high prevalence of use of these therapies and the potential for interactions and hepatotoxicity, there is a special need for patient and practitioner education and communication regarding herbal and vitamin preparations in relation to CLD.

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TABLE 1

Sociodemographic and Clinical Characteristics of the Sample (N = 1040)

Characteristic	Overall N* (%)	Connecticut (N=476)*	California (N=280)*	Oregon (N=284)*	P†
Age (y, mean ± SD)	47.9 ± 10.6	47.3 ± 11.1	50.0 ± 10.4	46.6 ± 9.6	0.748
Sex					0.022
Male	627 (60.3)	305 (64.1)	168 (60.0)	154 (54.2)	
Female	411 (39.5)	169 (35.5)	112 (40.0)	130 (45.8)	
Country of origin					<0.001
United States	917 (88.2)	427 (89.7)	227 (81.1)	263 (92.6)	
Other	123 (11.8)	49 (10.3)	53 (18.9)	21 (7.4)	
Race/Ethnicity					<0.001
Non-Hispanic White	726 (69.8)	365 (76.7)	127 (45.4)	234 (82.4)	
Non-Hispanic Black	102 (9.8)	44 (9.2)	40 (14.3)	18 (6.3)	
Hispanic	115 (11.1)	46 (9.7)	58 (20.7)	11 (3.9)	
Asian	43 (4.1)	6 (1.3)	31 (11.1)	6 (2.1)	
Other	42 (4.0)	11 (2.3)	21 (7.5)	10 (3.5)	
Education					<0.001
≤High school graduate	448 (43.1)	234 (49.2)	91 (32.5)	123 (43.3)	
At least some college	592 (56.9)	242 (50.8)	189 (67.5)	161 (56.7)	
Family income					<0.001
$0 to $29,999	363 (34.9)	182 (38.2)	54 (19.3)	127 (44.7)	
$30,000 to $49,999	224 (21.5)	113 (23.7)	60 (21.4)	51 (18.0)	
$50,000 or more	418 (40.2)	168 (35.3)	160 (57.1)	90 (31.7)	
Current employment status					<0.001
Employed at least part-time	656 (63.1)	282 (59.2)	205 (73.2)	169 (59.5)	
Other	383 (36.8)	194 (40.8)	75 (26.8)	114 (40.1)	
Insurance	988 (95.0)	449 (94.3)	276 (98.6)	263 (92.6)	0.003
Etiology					<0.001
Hepatitis C	442 (42.5)	181 (38.0)	132 (47.1)	129 (45.4)	
Hepatitis C and alcohol	228 (21.9)	114 (23.9)	39 (13.9)	75 (26.4)	
NASH and fatty liver	95 (9.1)	36 (7.6)	35 (12.5)	24 (8.5)	

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Characteristic	Overall N* (%)	Connecticut (N=476)*	California (N=280)*	Oregon (N=284)*	P†
Alcohol	82 (7.9)	51 (10.7)	18 (6.4)	13 (4.6)	
Hepatitis B	36 (3.5)	12 (2.5)	18 (6.4)	6 (2.1)	
Other	68 (6.5)	32 (6.7)	22 (7.9)	14 (4.9)	
Insufficient data to determine etiology	89 (8.6)	50 (10.5)	16 (5.7)	23 (8.1)	
Cirrhosis	184 (17.7)	111 (23.3)	39 (13.9)	34 (12.0)	<0.001
Hospitalized for CLD	117 (11.3)	54 (11.3)	37 (13.2)	26 (9.2)	0.355
CLD medication prescribed by physician	287 (27.6)	153 (32.1)	67 (23.9)	67 (23.6)	0.011
Non-CLD related comorbidities					<0.001
0	159 (15.3)	98 (20.6)	54 (19.3)	7 (2.5)	
1	497 (47.8)	230 (48.3)	88 (31.4)	179 (63.0)	
2	178 (17.1)	77 (16.2)	51 (18.2)	50 (17.6)	
≥3	206 (19.8)	71 (14.9)	87 (31.1)	48 (16.9)	

*Numbers may not sum to total due to missing data.

†*P* value is for χ^2 or analysis of variance (*F* test) for difference across study sites.

CLD indicates chronic liver disease; NASH, nonalcoholic steatohepatitis.

TABLE 2

Unadjusted Associations Between Sociodemographic and Clinical Characteristics and CAM Use

Characteristic	N	Percent Using CAM	*P**	OR (95% CI)
Sex			0.040	
Male	627	29.7		1.00
Female	411	23.8		0.74 (0.56–0.99)
Age (y)			0.029	
<55	837	28.8		1.00
55+	203	21.2		0.67 (0.46–0.96)
Country of origin			0.761	
Other	123	28.5		1.00
United States	917	27.2		0.94 (0.62–1.42)
Race/Ethnicity			0.545	
Non-Hispanic White	726	27.4		1.00
Non-Hispanic Black	102	21.6		0.73 (0.44–1.20)
Hispanic	115	27.8		1.02 (0.66–1.58)
Asian	43	32.6		1.28 (0.66–2.47)
Other	42	33.3		1.32 (0.68–2.57)
Education			0.002	
≤High school graduate	448	22.3		1.00
At least some college	592	31.1		1.57 (1.18–2.08)
Family income			0.004	
$0 to $20,999	363	24.0		1.00
$30,000 to $49,999	224	23.7		0.98 (0.67–1.45)
$50,000 or more	418	33.5		1.60 (1.17–2.19)
Current employment status			0.011	
Employed at least part-time	656	30.0		1.00
Other	383	22.7		0.69 (0.51–0.92)
Insurance			0.798	
No	52	28.9		1.00
Yes	988	27.2		0.93 (0.50–1.71)
Etiology			0.017	
NASH and fatty liver	95	14.7		1.00
Hepatitis C and alcohol	228	26.8		2.11 (1.12–4.00)
Hepatitis C	442	31.0		2.60 (1.42–4.75)
Hepatitis B	36	33.3		2.89 (1.18–7.08)
Alcohol	82	32.9		2.84 (1.37–5.90)
Other	68	22.1		1.64 (0.73–3.67)
Insufficient data to determine etiology	89	20.2		1.47 (0.68–3.16)
Cirrhosis			0.216	
No	853	26.5		1.00
Yes	184	31.0		1.25 (0.88–1.76)

Characteristic	N	Percent Using CAM	*P**	OR (95% CI)
Hospitalized for CLD			<0.001	
No	914	25.7		1.00
Yes	117	41.0		2.01 (1.35–2.99)
CLD medication prescribed by physician			0.471	
No	753	26.7		1.00
Yes	287	28.9		1.12 (0.83–1.51)
Non-CLD – related comorbidities			0.050	
0	159	28.9		1.00
1	497	30.6		1.08 (0.73–1.60)
2	178	23.6		0.76 (0.47–1.24)
≥3	206	21.4		0.67 (0.41–1.08)

*P value is for χ^2 test.

CAM indicates complementary and alternative medicine; CI, confidence interval; CLD, chronic liver disease; NASH, nonalcoholic steatohepatitis; OR, odds ratio.

TABLE 3

Multivariate Logistic Regression Model Predicting use of CAM (N = 994)

Characteristic	Adjusted OR (95% CI)	*P*
Education		
≤High school graduate	1.00	
At least some college	1.46 (1.08–1.98)	0.014
Family income		
$0 to $29,999	1.00	
$30,000 to $49,999	0.94 (0.63–1.41)	0.777
$50,000 or more	1.66 (1.19–2.33)	0.003
Etiology		
NASH and fatty liver	1.00	
Hepatitis C and alcohol	2.58 (1.33–4.98)	0.005
Hepatitis C	2.85 (1.54–5.26)	<0.001
Hepatitis B	2.75 (1.10–6.87)	0.030
Alcohol	2.81 (1.31–6.03)	0.008
Insufficient data to determine etiology	1.66 (0.76–3.62)	0.206
Other	1.57 (0.69–3.57)	0.281
Hospitalized for CLD		
No	1.00	
Yes	2.08 (1.36–3.17)	<0.001

CAM indicates complementary and alternative medicine; CLD, chronic liver disease; NASH, nonalcoholic steatohepatitis.