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Complementary and Alternative Medicine among Persons living with HIV in the Era of Combined Antiretroviral Treatment

Sean N. Halpin*,

Emory Prevention Research Center, Rollins School of Public Health, Emory University, 1518 Clifton Road, Atlanta, Georgia 30322

Edwin Clayton Carruth,

Veterans Affairs Medical Center, Decatur, GA

Ramona P. Rai,

Veterans Affairs Medical Center, Decatur, GA

E. Jennifer Edleman,

Yale University School of Medicine

David A. Fiellin,

Yale University School of Medicine

Cynthia Gibert,

Veterans Affairs Medical Center, West Haven, CT

Kirsha S. Gordon,

Veterans Affairs Medical Center, West Haven, CT

Wei Huang,

Veterans Affairs Medical Center, Decatur, GA

Amy Justice,

Yale University School of Medicine, Veterans Affairs Medical Center, West Haven, CT

Vincent C. Marconi,

Veterans Affairs Medical Center, Decatur, GA, Emory University School of Medicine

David Rimland, and

Veterans Affairs Medical Center, Decatur, GA, Emory University School of Medicine

Molly M. Perkins

Veterans Affairs Medical Center, Decatur, GA, Emory University School of Medicine

Abstract

Complementary and alternative medicine (CAM), often pursued independent of prescribing clinicians, may interact with traditional treatments, yet CAM use has not been well characterized

corresponding author: Phone- 404-728-7253, sean.nathaniel.halpin@emory.edu.

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among people living with HIV (PLWH) in the combined antiretroviral therapy (ART) era. We analyzed data from the Veterans Aging Cohort Study (October-2012 to April-2015) to characterize CAM use in PLWH on ART. CAM users were more likely to have lived longer with HIV, report more bothersome symptoms, be prescribed more benzodiazepines and opioids, and consume less nicotine and alcohol. Given its high prevalence, clinicians should routinely assess for CAM use and its impact among PLWH.

Keywords

HIV/AIDS; complementary and alternative medicine; polypharmacy; veteran; acupuncture

INTRODUCTION

Combined antiretroviral therapy (cART) has dramatically extended the lifespan of people living with HIV (PLWH). Concurrently, medical and psychiatric comorbidities such as chronic pain, hypertension, cardiovascular disease, stroke, diabetes, and depression have become more common for PLWH, leading to greater pharmacological burden and the possibility for polypharmacy and drug interactions. In addition to traditional medications, many patients also utilize complementary and alternative medicines (CAM), products and treatments which are not considered to be part of traditional medicine. While CAM use in PLWH was well-characterized prior to cART less is known about CAM use in the current HIV treatment era.

PLWH often turn to CAM in an effort to improve or “normalize health” [1]. A variety of CAM modalities exist, ranging from physical and psychological treatments to ingestible substances, and in previous eras have been used by as many as 70% of PLWH [2]. Some evidence indicates that use of CAM is related to a longer length of time since infection and greater number of bothersome side effects related to cART, such as pain [1]. While CAM is frequently thought of by patients as a “safe” treatment, there have been reports of adverse drug interactions with HIV and other medications. One study demonstrated that ingestible CAM may alter prescribed medication concentrations, distribution, and half-life [3]. Yet CAM are oftentimes pursued independently of a patient’s healthcare provider [4], raising concerns of medication adherence and that adverse interactions might go unnoticed and impact health. Studies assessing HIV medication adherence and CAM use have generated mixed results [1] and show that observed differences in adherence might be related to whether a patient views CAM as a complimentary (i.e. aiding in managing) or alternative (i.e. replacement) therapy.

This study sought to characterize CAM use among PLWH who use CAM in the era of cART utilizing a sample of U.S. Military Veterans from the Veterans Aging Cohort Study (VACS). VACS is an observational, prospective longitudinal study of HIV-positive and age, race/ethnicity, sex, and site-matched under HIV negative patients receiving care at US Department of Veterans Affairs (VA) medical centers across the United States [5].

METHODS

We used data on HIV-positive VACS participants who completed a survey during October 2012 to April 2015 and were currently receiving antiretroviral therapy (N=1763) [5]. Since only a minority of CAM and nonCAM users were not receiving ART (6% in each group) we excluded these individuals from analysis. Socio-demographic variables included sex, race/ethnicity (Black, White, other), age, educational level, income, and marital status.

Respondents' use of 12 common CAM types over the past year was assessed through a yes/no list. Respondents were first divided into categories based on dichotomous response format. CAM use (CAM users and non-CAM users) and CAM modality. These 12 modalities were then collapsed into ingestible (i.e. herbs/herbal medicine, homeopathy, special diet, St. John's Wort, vitamins/minerals), physical CAM (i.e. acupuncture/acupressure, chiropractic, massage), and psychological CAM (i.e. imagery, meditation/prayer/spiritual healing, relaxation/breathing exercises, self-help/support groups). Respondents were first divided into CAM users and non-CAM users, and categorized based on CAM modality (ingestible, physical, and psychological).

Symptoms were assessed using the HIV Symptom Index [6], a validated instrument of 20 bothersome symptoms common among patients with HIV, such as fatigue or loss of energy, nervousness or anxiety, and difficulty falling or staying asleep. Possible responses include "I do not have the symptom," "I have it but it doesn't bother me," "It bothers me a little," "It bothers me," and "It bothers me a lot." For the current analysis, a symptom was considered to be present if it was reported as "bothers me a little," "it bothers me," or "it bothers me a lot." A symptom was considered to be absent if it was reported as "I don't have this symptom," or "I have this symptom and it doesn't bother me." Symptoms were summed for a total number of bothersome symptoms. After completing the HIV Symptom Index, participants were also asked to complete a single (yes/no) item related to whether they believed their symptoms were attributable to antiretroviral medications.

Laboratory values for CD4 lymphocyte count, HIV viral load, and other chronic conditions were abstracted from medical records from the time point closest to the survey completion. Prescription opioid and benzodiazepine receipt was determined using outpatient pharmacy data [7]. Prescription opioids included both oral and transdermal formulations; medications used to treat opioid use disorder (i.e. methadone and buprenorphine) were excluded. Benzodiazepines included alprazolam, chlordiazepoxide, clonazepam, clorazepam, diazepam, estazolam, flurazepam, lorazepam, midazolam, oxazepam, temazepam, and triazolam.

Past year alcohol use was recorded using the Alcohol Use Disorders Identification Test-Consumption (AUDIT-C) [8]. Illicit drug use over the past year was collected by self-report. Current smoking behavior was assessed using a self-report item, "How many cigarettes do you smoke per day NOW?"

All data were entered and analyzed in SAS version 9.4 (SAS Institute Inc., Cary, North Carolina). Descriptive statistics were performed first for the full sample of individuals and then stratified based on CAM use (yes/no). Two-sided Wilcoxon rank sum, χ^2 , and t-tests

were used to compare covariates across the two groups. Logistic regression was used to compare binary outcomes between the two groups based on the likelihood of viral load suppression, and an ordinal logistic model was applied for likelihood of having CD4 counts equal or greater than 500. Both models were assessed for interaction using backwards elimination and adjusted for the same covariates: age (continuous), income level, race/ethnicity, and duration of HIV infection.

RESULTS

Our sample consisted of 1763 patients with a median age of 57 years. Most respondents identified as black (71%) and male (96%). Although most had at least some college education (62%), over half (64%) reported that their annual income was \$24,999 or less. CAM users were more likely to be white [CAM: 27% vs. No CAM: 20%, $p=0.005$], college educated [23% vs. 14%, $p<0.0001$], and have an income over \$50,000 [14% vs. 8%, $p=0.002$] compared to respondents who did not use CAM (Table I). In addition to having lived longer with HIV [median: 17 yrs. vs. 15 yrs, $p=0.0003$], CAM users also had higher median CD4 counts [522 cells/mm³ vs. 505 cells/mm³, $p=0.01$] when compared to respondents who did not use CAM. CAM users also experienced more bothersome symptoms [median: 7 vs. 5, $p<0.0001$], reported smoking fewer cigarettes each day [median: 2 vs. 5, $p=0.03$], and consumed less alcohol as measured using AUDIT-C scores [median: 1 vs. 2, $p=0.02$]. Pharmacy data confirmed that CAM users were more likely to receive prescription opioids [44% vs. 35%, $p=0.0005$] and benzodiazepines [29% vs. 23%, $p=0.01$].

The most common types of CAM reported were Vitamins/Minerals (60%) followed by meditation/prayer/spiritual healing (37%), relaxation/breathing exercises (35%), self-help/support groups (27%), massage (22%), special diet (18%), herbs/herbal medicine (13%), chiropractic (10%), acupuncture/acupressure (8%), Imagery (6%), homeopathy (4%), and St. John's Wort (1%). The majority of persons using CAM reported using two or more modalities (88%).

Respondents using CAM were significantly more likely to believe that their comorbidity symptoms were caused by their HIV medications [37% vs. 26%, <0.0001]. CAM users were also more likely to have ICD-9 codes in their medical charts for any psychiatric illness [43% vs. 36%, $p=0.02$], and particularly major depression [15% vs. 10%, $p=0.02$], and PTSD [12% vs. 7%, $p=0.002$]. While non-CAM users were more likely to have alcohol listed as a substance abuse in their charts [15% vs. 19%, $p=0.03$] (Supplemental Table II).

CAM use by modality was reported as follows: ingestible (60%), physical (4%), and psychological (19%). There were no significant differences in use of physical or psychological CAM modalities across demographic or clinical groups. As such physical and psychological CAM modalities were combined into an 'other-CAM' category and compared with ingestible CAM. The majority of participants (64%) reported using at least one ingestible CAM modality. Across all age groups (<40, 40–49, 50–64, and >64), the reported median number of ingestible CAM modalities remained constant (median= 1.3) while the number of physical (median= 0.7, 0.8, 0.5, and 0.4) and psychological (median= 1.6, 1.6, 1.4, and 1.0) CAM modalities declined with increasing age. Ingestible CAM users were

significantly more likely to be male [98% vs. 95%, $p=0.05$] compared with other-CAM users, and more likely to report muscle aches or joint pain [88% vs. 81%, $p=0.04$]. Ingestible and other-CAM groups did not differ based on any other clinical characteristics.

The odds of being virally unsuppressed were higher among CAM users [OR=1.06 (95% CI: 0.83, 1.37)]. Similarly, for CAM users, the odds of having a CD4 count of less than 500 versus 500 or greater is 0.9 times the odds of non-CAM users [OR=0.9 (95% CI: 0.73, 1.12)] (Supplemental Table III).

DISCUSSION

In the current study, older PLWH used less physical and psychological CAM modalities than younger PLWH, but ingestible CAM remained constant and prevalent across age groups, and were used by over half of our sample. CAM users had a longer length of time since HIV diagnosis; while at the same time they complained of more bothersome symptoms such as feeling nervous or anxious and having sleep difficulties. In order to avoid possible CAM-medication adverse interactions, it is important to recognize the full spectrum of treatments patients are ingesting to treat their symptoms, particularly among persons with multiple interrelated chronic conditions.

PLWH who used CAM reported less nicotine and alcohol use, counter to higher rates of use in the previous studies [9]. Our finding of lower nicotine and alcohol use may be explained by these individuals taking a greater interest in their own health, and possibly feeling empowered by the use of CAM as a complementary treatment [1].

CAM use was also associated with greater receipt of prescription opioids and benzodiazepines; both of which are associated with bothersome symptoms in up to two thirds of PLWH, and are implicated in the risk of polypharmacy and adverse drug interactions [10]. Similar to nicotine and alcohol use, long-term use of prescription opioids and benzodiazepines medications has been implicated in worse health outcomes among PLWH as well as increased mortality risk among PLWH [7]. Although pain is one of the most common reasons for CAM use, CAM is not effective for all pain symptoms [11]. Rather, using CAM as an adjunctive therapy may help to make pain and other bothersome symptoms, many of which can be attributed to HIV medications, more tolerable.

Our study has some limitations. Although these data on U.S. veterans who receive care in the VA may not be generalizable to non-veterans or veterans who do not receive care in the VA, many of our results mirror findings found within the larger non-veteran populations [12]. Within the current study, PLWH who are white, have a higher educational attainment, and a higher income were more likely to use CAM. These results are consistent with previous literature [2, 12]. Self-reported use of socially undesirable behaviors such as smoking and excessive alcohol consumption may cause some participants to omit answers to appear more favorably. If this were true, our results would be biased toward the null, giving greater credence to our findings. Finally, there were some limitations to our data. Namely, no questions were asked for reason for CAM use, and we were unable to investigate CAM use in relation to polypharmacy, drug interactions, adherence, or engagement in care. Our results

demonstrate that in the combined antiretroviral era the use of CAM modalities among PLWH is common. As PLWH age and receive more medications, it is increasingly important to understand potential adverse interactions between ingestible CAM and prescribed medications.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table I**Participant Characteristics**

Participant Characteristics	CAM (n=1332)	No CAM (n=431)	P value
Education			
<i>High School or less</i>	466 (32.76)	212 (46.29)	
<i>Some college</i>	635 (44.66%)	180 (39.3%)	
<i>College</i>	224 (15.75%)	38 (8.3%)	
<i>Graduate degree</i>	97 (6.82%)	28 (6.11%)	
Income			
<i><\$25,000</i>	878 (63%)	313 (70%)	
<i>\$25,000 to \$49,999</i>	312 (22.54%)	91 (20.54%)	
<i>Over \$50,000</i>	194 (14.02%)	39 (8.8%)	
White	376 (26%)	89 (19%)	
Duration of HIV infection, Years, median	17	15	0.0003
CD4 count, median	522	504.5	0.02
CD4 Count, copies/mL, n (%)			0.2
500	704 (54%)	216 (51%)	
350–499	270 (21%)	78 (18%)	
200–349	224 (17%)	95 (22%)	
100–199	75 (6%)	21 (5%)	
50–99	20 (2%)	6 (1%)	
<50	19 (2%)	8 (2%)	
Viral Load, median (IQR)	40 (55)	40 (55)	0.6
Viral Load, n (%)			0.3
<i>Undetectable (<500 copies/mL)</i>	932 (70%)	297 (70%)	
<i>Detectable</i>	392 (30%)	130 (30%)	
Hep B coinfection, n (%)	47 (3%)	15 (3%)	0.96
Hep C coinfection, n (%)	405 (30%)	136 (32%)	0.7
Median number of Bothersome symptoms in past four weeks	7	5	<0.0001
Cigarettes smoked per day, median	2	5	0.03
AUDIT-C, median	1	2	0.02
Illicit Drug Use			
<i>Marijuana or Hashish</i>	920 (69%)	287 (67%)	0.3
<i>Cocaine or Crack</i>	661 (50%)	211 (49%)	0.8
<i>Stimulants (amphetamines, uppers, speed, crank, crystal meth, bam)</i>	395 (30%)	116 (27%)	0.3
<i>Heroin</i>	325 (24%)	111 (26%)	0.6
<i>Prescription Painkillers (such as Oxycontin, Vicodin, Percocet)</i>	588 (44%)	149 (35%)	0.0005

Participant Characteristics	CAM (n=1332)	No CAM (n=431)	P value
<i>Prescription, benzodiazepines (Valium, Deastat, Ativan)^a</i>	381 (29%)	97 (23%)	0.01
<i>Other</i>	199 (15%)	66 (15%)	0.9

Notes:

^aPrescription painkillers were prescribed to the patient

Continuous variables are indicated as medians.