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Utilization of herbal and nutritional compounds among older adults with bipolar disorder and with major depression

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SUMMARY

Objectives Herbal and nutritional compounds (HNC) are widely used among geriatric populations with depression, however little data exists on HNC use in older populations with bipolar disorder. The goal of this study was to evaluate orally-ingested HNC use in individuals with bipolar disorder and with major depression.

Methods This was a cross-sectional analysis of self-reported factual knowledge of HNC, individual perspective on efficacy and safety of HNC, patterns of HNC use, and discussion of HNC with health care providers in 50 older adults with bipolar disorder and 50 older adults with major depression.

Results In this sample, approximately 30% of older individuals with depression or bipolar disorder used orally- ingested HNC. Over 40% of older adults believed that HNC is FDA-regulated and 14-20% preferred to take HNC compared to physician-prescribed psychotropic medications. Use of HNC was more common among older adults with bipolar disorder (44%) compared to older adults with major depression (16%, $p = 0.003$). The majority of older adults with mood disorders (64%) had not discussed use of HNC with their treating physicians.

Conclusion Orally ingested HNC was used by nearly one in three older adults with mood disorders, and was more common among those with bipolar disorder compared to those with major depression. Most individuals did not discuss HNC use with their physicians. Clinicians need to assess for HNC use, particularly with respect to potential drug-drug interactions.

KEY WORDS — complementary medicine; alternative medicine; herbal compounds; nutritional supplements; mood disorders; geriatrics; depression; bipolar disorder

INTRODUCTION

Kennedy (2005) demonstrated that an estimated 38.2 million adults in the United States used complementary or alternative treatments in 2002, and use of herbal or nutritional compounds (HNC) in geriatric populations can be extensive (Cohen *et al*., 2002). Grzywaczs and colleagues (2006) demonstrated that 81.7% of older adults with depression or anxiety self-reported using complementary/alternative therapies in the past year, compared to 64.6% of elders without mental conditions. Kales and colleagues (2004) demonstrated that the prevalence of herbal and 'natural' product use among older adults may correlate with psychiatric symptoms and higher education levels; 75% of individuals were also taking potentially interacting medications. Older adults have also been identified as a group increasingly using HNC—however; these individuals may not discuss HNC use with their mainstream medical clinicians (Cohen *et al*., 2002).

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As with FDA-approved medications, there are potential benefits and adverse effects with HNC, (Pittler and Ernst, 2000; Plushner, 2000; Ernst, 2002; Matthews *et al*., 2002; Izzo, 2004; Shibayama *et al*., 2004; Edie and Dewan, 2005; Linde *et al*., 2005; Fuller and Sajatovic, 2007; Meeks *et al*., 2007; Tachil *et al*., 2007; Andeescu *et al*., 2008). Orally ingested HNC may interact with conventional prescribed medications. For example, St John's Wort, has demonstrated efficacy in treating depression (Linde *et al*., 2005). However, serotonin syndrome has been reported with concomitantly prescribed antidepressant (Izzo *et al*., 2004; Shibayama *et al*., 2004). Ginkgo biloba may slow cognitive decline in dementia, however, bleeding complications, amplified by use of anticoagulant medication, are a concern (Ernst, 2002).

A better understanding of HNC use among older adults with mental disorders is needed in order to optimize care for this vulnerable population. This cross-sectional analysis of HNC use in older adults with bipolar and depressive disorders evaluated factual knowledge of HNC, individual perspective of efficacy and safety of HNC, patterns of HNC use, and discussion of HNC with health care providers.

METHODS

This was a cross-sectional survey of 100 older adults with mood disorders (bipolar disorder $n = 50$ and major depression $n = 50$) on use of orally ingested HNC. The assessment period for which HNC use was evaluated was the last 3 months prior to the date of interview using a one-time, self-report survey. Demographic information was collected via participant self-report, and by medical record review. Self-reported use of HNC was evaluated on three primary domains including: (1) factual knowledge (HNC use in the US, FDA regulatory status, and potential medication interactions); (2) attitudes towards HNC (effectiveness in comparison to physician-prescribed medications, patient preference and perceived relative safety in comparison to physician-prescribed treatments); and (3) HNC practice (patterns of use and discussion with physician health providers). Questions asked about HNC were an exploratory effort to determine general attitudes and patterns of HNC use by older patients with bipolar and depressive disorders, and specific content was based upon the investigator's clinical experience in geriatric mood-disordered populations. The series of questions were intended to identify areas of potential clinical concern and inform future systematized analyses of HNC. HNC use was described to participants as 'Types of treatments that are also known as herbal medications, natural treatments or supplements,' and individuals were provided with an example list of HNCs (Ernst, 2002; Fuller and Sajatovic, 2007) (Table 1). Once-daily multivitamins were not included as HNC.

Individuals were also evaluated with respect to global psychopathology [Clinical Global Impression scale (CGI; Guy, 1976)], functional status [Global Assessment Scale (GAS; Endicott *et al*., 1976)], cognitive status [Mini Mental State Examination (MMSE; Folstein *et al*., 1975)], and self-reported adherence with prescribed psychotropic medications (percentage closest to 0%, 25%, 50%, 75% or 100%) during the past 3 months. Standardized scales were administered by a trained rater.

All study participants met the following inclusion criteria: (1) Age 55 or older with DSM-IV-TR diagnosis of major depression or bipolar disorder; (2) without substantial cognitive impairment as evidenced by MMSE score of 22 or higher; (3) received treatment with prescribed psychotropic medications within the past 6 months; and (4) inpatients on a geropsychiatry unit, outpatients at a general outpatient clinic at an academic medical center, or outpatients at a Community Mental Health Clinic (CMHC). Inpatients were all stabilized patients in the discharge-planning phase who were asked to provide information on their HNC use prior to their hospitalization (average length of stay on the inpatient unit was approximately 1 week–10 days). Participants were referred by their clinicians/treatment team. The study was conducted at the academic medical center and the CMHC. All participants provided written, informed consent. This study was approved for use of human subjects by the local Institutional Review Board (IRB).

Table 1. Examples of commonly utilized herbal and nutritional compounds

Aloe	Ginseng
Bilberry	Glucosamine/Chondroitin
Black Cohosh	Golden Seal
Cartilage (bovine and shark)	Growth Hormone
Cayenne	Hawthorn
Chamomile	Kava Kava
Colloidal Silver Products	LaPacho
Dong Quai	Licorice
Echinacea	Melatonin
Ephedra	Milk Thistle
Feverfew	Peppermint
Garlic	St. John's Wort
Ginger	Saw Palmetto
Ginkgo	Valerian
	Zinc Supplements

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Data analysis

Descriptive statistics were obtained on demographic and clinical characteristics, HNC knowledge, attitudes and practice, as well as scores on the CGI, GAS, and MMSE. Bipolar disorder and major depression groups were compared via *t*-test and chi-square analysis as appropriate. Statistical significance were adjusted for multiple comparisons using the Bonferroni method at $\alpha = 0.10$ and adjusted level of significance of 0.004.

RESULTS

Clinical characteristics of older adults with serious mood disorders

Table 2 identifies group demographic and clinical characteristics of all individuals, individuals with major depression ($n = 50$) and bipolar disorder ($n = 50$). Mean age was 68.7 ± 9.74 years. Over one-third of the sample were minorities (34%), primarily African-American. Clinical characteristics of bipolar *vs* depressed individuals were similar. Most individuals had mood disorder for 3–5 decades and were mildly-moderately ill as demonstrated by a global psychopathology (CGI) mean score of 3.2. Forty-seven percent ($n = 47$) were inpatients. Clinical characteristics of inpatients vs. outpatients were similar. Most of the patients were well-educated with a mean of 13.4 ± 3.0 years of education and were relatively cognitively intact with a mean MMSE of 28/30. Approximately one quarter of patients noted that they were at least partially non-adherent with prescribed psychotropic medications. While bipolar patients were numerically slightly less adherent to prescribed psychotropic than unipolar patients (28% *vs* 14%) this was not statistically significant. Most individuals had between 2–3 medical conditions, with the most common being hypertension (52%, $n = 52$), diabetes/endocrine abnormalities (41%, $n = 41$), dyslipidemia

Table 2. Demographic and clinical characteristics of older adults with major depression ($n = 50$) and bipolar disorder ($n = 50$)

Variable	All patients ($n = 100$)	Bipolar Disorder ($n = 50$)	Major Depression ($n = 50$)	Test Statistics
Age in years (mean ± SD)	68.7 ± 9.74	66.2 ± 8.90	71.2 ± 9.99	$t = 2.62$, df = 98, $p = 0.01$*
Ethnicity (*n*, %)				
African American	29 (29%)	17 (34%)	12 (24%)	
Caucasian	66 (66%)	31 (62%)	35 (70%)	ns[1]
Asian	3 (3%)	1 (2%)	2 (4%)	
Other	2 (2%)	1 (2%)	1 (2%)	
Gender (*n*, %)				
Women	70 (70.0%)	32 (64%)	38 (76%)	ns
Marital Status (*n*, %)				
Married	37 (37%)	13 (26%)	24 (48%)	ns
Single	17 (17%)	10 (20%)	7 (14%)	
Widowed	22 (22%)	11 (22%)	11 (22%)	
Divorced	24 (24%)	16 (32%)	8 (16%)	
Education in years (mean ± SD)	13.4 ± 3.03	13.4 ± 3.11	13.5 ± 2.97	ns
Age of Mood Disorder Onset in years (mean ± SD)	41.2 ± 22.13	36.6 ± 19.87	45.9 ± 23.52	ns
Duration of Mood Disorder in years (mean ± SD)	26.8 ± 21.86	28.8 ± 21.13	24.6 ± 22.63	ns
Family history of psychiatric illness (*n*, %)	50 (53%)	28 (61%)	22 (46%)	ns
Lifetime substance abuse (*n*, %)	15 (15%)	7 (15%)	8 (16%)	ns
Number of prescribed psychiatric medications (mean ± SD)	2.74 ± 1.52	2.61 ± 1.59	2.88 ± 1.44	ns
Number of co-morbid medical illnesses (mean ± SD)	2.89 ± 2.00	2.75 ± 2.14	3.02 ± 1.87	ns
Number of prescribed medications for comorbid medical problems (mean ± SD)	5.80 ± 4.40	5.39 ± 4.82	6.20 ± 3.94	ns
Global Assessment Scale (GAS) (mean ± SD)	57.9 ± 16.54	59.7 ± 17.62	56.0 ± 15.33	ns
Mini Mental State Examination (mean ± SD)	27.6 ± 2.24	27.7 ± 1.98	27.5 ± 2.49	ns
Clinical Global Impression (CGI) (mean ± SD)	3.2 ± 1.15	3.1 ± 1.20	3.3 ± 1.10	ns
Partial/poor adherence with prescribed psychotropic medications[2]	$n = 97$ 20 (21%)	$n = 47$ 13 (28%)	$n = 50$ 7 (14%)	ns

[1]Comparing ethnicity Caucasian *vs* Others.
[2]Based upon self-reported adherence with prescribed psychotropic medications in the previous 3 months. Partial or poor adherence defined as taking 75% or less of prescribed psychotropic medication.
ns = not significant.
*Not statistically significant after adjusting for multiple comparisons.

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(32%, $n = 32$), arthritis / rheumatic conditions (26%, $n = 26$), gastrointestinal conditions (25%, $n = 25$), and cardiovascular/coronary artery disease (20%, $n = 20$).

HNC factual knowledge, attitudes and practice

Table 3 demonstrates HNC knowledge, attitudes and practice among older adults with mood disorders. Individuals were defined as knowledgable if they knew how common complementary/alternative medicine use in the U.S. is, and were aware of FDA-regulatory status, and potential for HNC to interact with prescribed medications. Approximately 36–50% incorrectly believed that the FDA regulates HNC to ensure safety for the American Public. However, most individuals (56–66%) correctly believed that HNC

Table 3. Knowledge, attitudes and practice of orally ingested herbal and nutritional compounds (HNC) among 100 older adults with mood disorders

Statement	All Patients ($n = 100$)	Major Depression ($n = 50$)	Bipolar Disorder ($n = 50$)	Test Statistic
1. Complementary/alternative medicine is used by at least one-third of the American Public				
Agree	43 (43%)	17 (34%)	26 (52%)	ns
Neutral/Don't Know	52 (52%)	28 (56%)	24 (48%)	
Disagree	5 (5%)	5 (10%)	0 (0%)	
2. The FDA regulates HNC to ensure their safety for the American Public				
Agree	43 (43%)	25 (50%)	18 (36%)	ns
Neutral/Don't Know	31 (31%)	17 (34%)	14 (28%)	
Disagree	26 (26%)	8 (16%)	18 (36%)	
3. HNC may in some cases interact with medications prescribed by a person's doctor				
Agree	61 (61%)	28 (56%)	33 (66%)	ns
Neutral/Don't Know	28 (28%)	16 (32%)	12 (24%)	
Disagree	11 (11%)	6 (12%)	5 (10%)	
4. HNC is generally not as effective compared to medications prescribed by a person's doctor				
Agree	33 (33%)	20 (40%)	13 (26%)	ns
Neutral/Don't Know	47 (47%)	21 (42%)	26 (52%)	
Disagree	20 (20%)	9 (18%)	11 (22%)	
5. HNC is equal /more effective compared to medications prescribed by a person's doctor				
Agree	20 (20%)	9 (18%)	11 (22%)	ns
Neutral/Don't Know	44 (44%)	21 (42%)	23 (46%)	
Disagree	36 (36%)	20 (40%)	16 (32%)	
6. I prefer to take HNC compared to medications prescribed by my doctor.				
Agree	17 (17%)	7 (14%)	10 (20%)	ns
Neutral/Don't Know	20 (20%)	7 (14%)	13 (27%)	
Disagree	62 (63%)	36 (72%)	26 (53%)	
7. HNC is safer than medications prescribed by a doctor.				
Agree	14 (14%)	8 (16%)	6 (12.2%)	ns
Neutral/Don't Know	43 (43%)	18 (36%)	25 (51.0%)	
Disagree	42 (42%)	24 (48%)	18 (36.7%)	
8. I use HNC				
Yes	30 (30%)	8 (16%)	22 (44%)	$\chi^2 = 8.973$, df = 1, $p = 0.003$
No	69 (70%)	41 (84%)	28 (56%)	
9. I use HNC daily				
Yes	18 (18%)	3 (6%)	15 (30%)	$\chi^2 = 9.485$, df = 1, $p = 0.002$
No	81 (82%)	46 (94%)	35 (60%)	
10. I use HNC at least once a week				
Yes	26 (26%)	6 (12%)	20 (40%)	$\chi^2 = 9.844$, df = 1, $p = 0.002$
No	73 (74%)	43 (88%)	30 (60%)	
11. I use HNC in addition to medications prescribed by my doctor				
Yes	29 (29%)	8 (16%)	21 (42%)	ns
No	70 (71%)	41 (84%)	29 (58%)	
12. I have used HNC in the past				
Yes	48 (57%)	15 (39%)	33 (73%)	$\chi^2 = 10.374$, df = 1, $p = 0.001$
No	36 (43%)	24 (62%)	12 (27%)	
13. I have discussed use of HNC with my doctor**				
Yes	25 (36%)	5 (16%)	20 (53%)	$\chi^2 = 9.846$, df = 1, $p = 0.002$
No	44 (64%)	26 (84%)	18 (47%)	

**Discussion of HNC with doctor independent of whether individual was using CAM or not using HNC.

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could in some cases interact with prescribed medications.

With respect to perceived efficacy and safety of HNC, most individuals were either neutral or disagreed with the notion that HNC was equal to or more effective than prescribed medication treatments, while 14–20% preferred HNC over prescribed medications, and 12–16% felt that HNC is safer than prescribed medications.

Approximately 30% of older adults with bipolar and depressive disorders reported using HNC. Of the total sample, 18% of patients reported using HNC daily, while 26% reported HNC use at least once per week. Older adults with bipolar disorder reported significantly more use of HNC than older adults diagnosed with depression ($n = 22$, 44% of the bipolar group *vs* $n = 8$, 16% of the depression group, ($p = 0.003$). There was no significant difference between those that self-reported using HNC vs. those with no HNC use with respect to adherence with prescribed psychotropic medications. There was also no significant difference in reported CAM use between inpatients and outpatients. Finally, over half ($n = 20$, 53%) of individuals with bipolar disorder reported discussing HNC use with physicians compared to only 16% ($n = 5$) of individuals with depression ($p = 0.002$).

DISCUSSION

These findings support research showing HNC use to be common among psychiatric populations, and older adults (Unutzer *et al*., 2000; Cohen *et al*., 2002; Alderman and kiepfer, 2003; Grzywacz, 2006). In the group presented here, approximately one-third of older adults with bipolar and depressive disorders used orally ingested HNC, somewhat lower than the 54% of individuals with depression using alternative treatments in a 2001 US survey (Kessler *et al*., 2001). It has been reported that depression is one of the ten most frequent indications for using HNC (Astin, 1998; Kessler *et al*., 2001).

To the best of our knowledge, there are no previous reports on HNC use specifically in older adults with bipolar disorder. In our sample, HNC use was more common among bipolar elders *vs* elders with major depression. A study of broadly defined alternative health care practices (Russinova *et al*., 2002) including 70 mixed age (mean 46.6 years) individuals with bipolar disorder and 39 individuals with depression noted herb use in 20% of bipolar and 10% of depressed individuals, and nutritional supplement use in 14% of bipolar and 10% of depressed individuals. However, in this report (Russinova *et al*., 2002) there were no statistically significant differences between populations with different diagnoses in either herb or nutritional supplement use, possibly related to small sample size.

Older adults with mood disorders in the study presented here were only moderately informed regarding HNC use and in understanding lack of FDA-regulation of HNC. There were minimal differences between diagnostic groups on HNC factual knowledge. With respect to attitudes towards HNC, a substantial minority (18–22%) of individuals felt that HNC was as effective or was more effective compared to medications prescribed by physicians, and 12–16% of individuals preferred HNC over prescribed medications. It is possible that older individuals with mood disorders may have relatively high comfort with CAM because of (incorrect) perception that CAM compounds are closely monitored for safety by the federal government. Alternately, comfort with HNC may arise from misperception that products that are 'natural' or 'non-chemical' may be somehow safer than prescription medications.

Russinova *et al*. (2002) surveyed perceived benefits of complementary/alternative treatments among 157 individuals with serious mental illness (SMI). In this report (Russinova *et al*., 2002) individuals with SMI attributed improved physical, emotional and cognitive functioning with alternative health practices, and the investigators suggested that alternative practices, 'seem to promote a recovery process beyond the management of emotional and cognitive impairments, by also enhancing social, spiritual, general and self-functioning'. The report by Russinova *et al*. included spiritual practices in addition to meditation, massage, guided imagery, yoga and chiropractic interventions, in contrast to the study presented here which focused on orally ingested HNC.

In our sample, just over 36% of older adults with mood disorders reported having discussed HNC with their doctor. Similarly, Kennedy (2005), found that only 33% of the general patient population told their primary care provider about their complementary/alternative treatment use. It is possible that patients were reluctant to report the use of HNC not prescribed by their doctor, or were simply unaware that this piece of information could be medically important. In the results reported here, individuals with bipolar disorder more frequently noted discussing HNC use (53%) with their physicians compared to those with depression (16%). It is possible that depressed patients being treated by primary care

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providers may have less time to talk about alternative practices, compared to bipolar patients who may be more likely to see psychiatrists who may have longer patient visits (and presumably would discuss alternative health practices).

The number of medications an individual is typically prescribed has been demonstrated to be increased with age (Kaufman *et al*., 2002; Cannon *et al*., 2006; Hayes, 2007) and among those with mental disorders (Ananth, 2004; Kreyenbuhl, 2007; Morrato, 2007). Older adults in this sample had, on average, between 2–3 medical conditions in addition to their mood disorders, with concomitant use of, on average, 5–6 medications for medical comorbidity and 2–3 medications for psychiatric illness. There was no difference in non-adherence rates for prescribed psychotropic medications between patients that took HNC vs. those not taking HNC, although it is possible that non-adherence rates were underestimated in this study because of the self-report methodology. As the evidence mounts in the direction of doctors being mostly unaware of the prevalent use of HNC by their patients who could be on potentially interacting medications, health care providers need to be particularly diligent in their assessment of HNC use among individuals with mood symptoms.

The results of this study should be interpreted in the light of multiple limitations including relatively small sample size, clinically-based, chart-review diagnostic criteria, relative gender and ethnic homogeneity and the fact that this was a 'young-old' (mean age 68.7) geriatric population. Latino and Asian populations were not well-represented in this clinical population from Northeastern Ohio, and findings might potentially have been different had there been more ethnic/cultural diversity or if the study population had generally lower levels of education. Additional factors to consider when interpreting the results of this study are the inherent limitations of using self-report measures and the fact that the study did not evaluate use of spiritual practices or mind/body work known to be important to individuals with mental disorders (Jorm *et al*., 2002; Russinova *et al*., 2002; Grzywacz, 2006). Finally, the study did not evaluate the specific types of HNC utilized by patients in the study, why they chose to use HNC, or whether individuals used HNC in place of, or in addition to, psychotropic medications prescribed by their physicians. The HCN example list was not an all-inclusive list of all complementary or alternative treatments and some individuals may not have identified HCN that they were actually taking as it was not noted on the sample list.

KEY POINTS

- Herbal and nutritional compounds (HNC) are widely used among geriatric populations with depression, however little data exists on HNC use in older populations with bipolar disorder.
- In this study, orally ingested HNC were used by nearly one in three older adults with mood disorders, and was more common among those with bipolar disorder compared to those with major depression. Most individuals did not discuss HNC use with their physicians.
- Clinicians need to assess for HNC use, particularly with respect to potential drug-drug interactions.

CONCLUSIONS

In the sample assessed here, HNC was used by nearly one in three older adults with mood disorders, and was more common among bipolar elders compared to elders with major depression. Most individuals did not discuss HNC use with their physicians. Clinicians need to actively seek information about possible use of HNC, particularly with respect to potential drug-drug interactions. A comprehensive sample list of HNC may help patients and care providers to identify HNC that may be used in clinical settings. Finally, additional studies are needed to more fully explore HNC use in older adult populations with mood disorders.

CONFLICT OF INTEREST

Dr Sajatovic has received grants from GlaxoSmithKline, is a consultant to AstraZeneca and is on the Speakers Bureau for AstraZeneca.

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