JOURNAL OF PALLIATIVE MEDICINE
Volume 13, Number 6, 2010

DOI: 10.1089/jpm.2009.0378

Soliciting an Herbal Medicine and Supplement Use History at Hospice Admission

Holly M. Holmes, M.D.,[1] Karen Kaiser, Ph.D., R.N.,[2] Steve Jackson, PharmD,[3] and Mary Lynn McPherson, PharmD[4]

Abstract

Background: Reconciling medication use and performing drug utilization review on admission of a patient into hospice care are essential in order to safely prescribe medications and to prevent possible adverse drug events and drug–drug interactions. As part of this process, fully assessing herbal medicine and supplement use in hospice patients is crucial, as patients in hospice may be likely to use these medications and may be more vulnerable to their potential adverse effects.

Objective: Our purpose was to identify herbals, vitamins, and supplements that should be routinely assessed on every hospice admission because of their higher likelihood of use or higher risk of adverse effects or drug interactions.

Methods: Experts in the fields of palliative medicine, pharmacy, and alternative medicine were asked to complete a Web-based survey on 37 herbals, vitamins, supplements, and natural products, rating likelihood of use, potential for harm, and recommendation to include it on the final list on a scale of 1 to 5 (least to most likely to agree).

Results: Twenty experts participated in the survey. Using a cutoff of 3.75 for inclusion of a medication on the final list, 12 herbal medicines were identified that should be routinely and specifically assessed on hospice admission.

Conclusions: Although assessing all herbal medicine use is ideal, thorough detection of herbals may be challenging. The list of herbals and supplements identified by this survey could be a useful tool for medication reconciliation in hospice and could aid in identifying potentially harmful medication use at the end of life.

Introduction

The goal of medication reconciliation is to resolve discrepancies in medication use, which is especially important during transitions of care.[1] At the time of discharge from one institution or level of care, medication reconciliation is essential to communicate important changes in a medication regimen. Medication reconciliation is necessary to prevent medical error and adverse events during transitions.[2] An estimated 20% of patients experience an adverse event after hospital discharge, approximately two thirds of which are related to medications.[3] All medications, including prescription drugs, over-the-counter medications, vitamins, minerals, dietary supplements, and herbal medicines must be assessed to fully address the benefits and risks of a patient's medication profile.[4] Errors of omission are frequent barriers to accurately reconciling medications.[5] The use of an explicit tool to assist nurses in listing nonprescription medications by therapeutic indication or pharmacologic class resulted in detecting over-the-counter medication use of 67% as opposed to 9% prior to implementation of the tool in a home health care population.[6] A similar tool has not been reported for use during transitions to hospice.

Medication reconciliation and detecting all medication use are important in all patients, but knowing about a patient's medications on admission to hospice care is particularly essential to prevent harm at the end of life. Hospice patients are vulnerable to the negative effects of progression of terminal disease, changes in pharmacokinetics, high rates of medication use, and high exposure to medical errors.[7] In addition, patients in hospice may have multiple transitions in care from different sources and are more likely to have medications

[1]Department of General Internal Medicine, UT MD Anderson Cancer Center, Houston, Texas.
[2]University of Maryland Medical Center, Baltimore, Maryland.
[3]University of Maryland School of Pharmacy, Baltimore, Maryland.
[4]Department of Pharmacy Practice and Science, University of Maryland School of Pharmacy, Baltimore, Maryland.
Accepted January 6, 2010.

added to their regimen during their terminal care.[8] Finally, the goals of palliation of symptoms and promotion of quality of life in hospice care necessitate a careful review of medications to minimize any potential deleterious effects of medication use.[9] The use of undetected herbal medications and supplements is a concern, because herbals cause many side effects, adverse effects, drug-drug interactions, and drug–disease interactions.[10] Vulnerable populations, such as those advanced in age or those with terminal illness, may be more susceptible to adverse reactions caused by herbal medicines due to altered physiology, pharmacokinetics, and high symptom burden at the end of life.[7,11] In addition, definitive evidence for the efficacy of many herbals is lacking.[12] Thus, assessing herbal use at the end of life may also be important to avoid exposure to therapies that are not beneficial.

A further concern is the potential for higher use of herbal medicines and dietary supplements in hospice populations. Herbal medication use is prevalent and under-reported in the United States, with approximately 12% of the U.S. population taking an herbal product, and only one third reporting this use to their health care providers.[13,14] One common reason for which people report potential interest in taking herbal medicines is the diagnosis of a terminal illness.[15] Of patients with common cancers, 60% report regular herbal medicine use.[16,17] Thus, as patients focus on palliative measures rather than curative treatments, they may increasingly use alternative therapies that are not supervised by health care providers.

Compounding the issue is that herbal medications may be underreported due to a misperception that herbals are natural and therefore not medications that need to be disclosed.[15] Physicians frequently fail to detect or document herbal medication use known to have adverse effects.[18] An urgent concern is the possibility that physicians adopt a benign approach to herbal medicine use despite their lack of knowledge about the harms of herbals.[19] Even more challenging are the plethora of herbal products available with variable content and the difficulty identifying the herbal medicines that should be specifically addressed due to high prevalence of use or safety concerns.[20,21]

As part of comprehensive care at the end of life, hospice providers must identify all medication use and provide drug utilization review to identify important adverse drug reactions and interactions.[9] However, because of the overwhelming number of herbal medicines, vitamins, natural products, and dietary supplements available, multiple confusing terms used to identify them, and uncertainty about their safety and efficacy, hospice providers may have significant difficulty addressing herbal medication use. Currently, there are no tools or guidelines to help in identifying herbal medicine and supplement use, particularly those that are likely to produce harm in the hospice patient.

The purpose of this study was to identify a specific list of herbal medicines and supplements that should routinely be assessed by hospice providers when admitting any patient into hospice care. Creation of this list of important herbals was accomplished using a Web-based survey of experts in relevant fields, including hospice physicians and nurses, pharmacists, and herbalists. Participants in the survey identified herbal medicines and supplements the use of which should always be queried on hospice admission, based on prevalence of use, potential for adverse reactions, and drug interactions.

Methods

To create a list of herbal medicines and supplements important to assess in hospice patients, an Internet-based survey was conducted of experts in palliative medicine, pharmacy, and alternative medicine. The snowball sampling technique was used to identify survey participants. Experts were identified through specialty organizations and author searches, focusing on leaders in hospice and palliative care professional organizations, complementary and alternative medicine, or pharmacology. Potential respondents were recruited using an individual introductory e-mail inviting them to participate in an Internet-based survey to identify herbal medicines important for hospice nurses to identify in patients' medication lists. Survey participants were asked to provide demographic data including their level of expertise and duration of practice in hospice/palliative medicine as well as herbal medicines. They were also asked to provide their degrees, affiliations, and relevant board certifications.

Participants were sent an e-mail containing instructions and a brief description of the survey and its purpose. They were sent additional information reminding them of the criteria for hospice admission and hospice demographic data as published by the National Hospice and Palliative Care Organization.[22] In addition, participants were given two tables for reference information on herbal medicines and natural products. The following literature search strategy was used to develop the list of herbals and supplements and to provide the reference information: MEDLINE was searched using the search words "hospice," "palliative," "dying," "cancer," "terminal," "end-of-life," combined with "herbals," "supplements," "alternative," "CAM," "complementary," or "dietary," combining two terms per search. Current medical and palliative care journals were also reviewed for pertinent titles containing the above terms. Table 1 shows the summary table provided to participants containing prevalence data for herbal medicine and dietary supplement use in populations frequently treated in hospice care. The second reference table provided the common indication or purpose for each herbal included in the survey, as well as evidence regarding effectiveness, adverse effects, and drug interactions for each herbal. See Table 2 for a full list of all herbal medicines and supplements included in the survey. The full table that was provided to participants is not included here.

The survey was created using a web-based application (www.surveymonkey.com). Based on the initial literature search identifying the most commonly used herbal medicines as well as available data regarding commonly used herbals in patients with medical conditions frequently seen in hospice, 37 herbal medicines and supplements were included in the survey (Table 2).[16,23–31] Participants were asked to rate their agreement on a scale of 1 to 5 (with a score of 1 equivalent to strongly disagree to 5 meaning strongly agree) for each medicine regarding four areas: high potential for use in hospice patients, high potential for serious adverse effects, high potential for serious drug interactions, and recommendation to include the medication on a list that hospice nurses ask about on every admission. In addition, participants were given the opportunity to list other herbals or supplements not included in the 37 medications that should be considered, as well as to state other general concerns regarding herbal use in hospice patients.

Table 1. Prevalence of Herbal and Supplement Use in Specific Populations

	General Population[23]	*Cancer*[a,24]	*Fibromyalgia*[25]	*Cancer*[26]	*Ovarian Cancer*[27]
Overall prevalence[b]	*18.9%*	*42.9%*	*51%*	*62.6%*	*51%*
Population size[b]	n = *31,044*	n = *3100*	n = *289*	n = *453*	n = *41*
1	Echinacea (40%)	Agaricus (60.6%)	Green tea (24%)	Melatonin (20.3%)	Soy products (52%)
2	Ginseng (24.1%)	Propolis (28.8%)	Glucosamine (18%)	Shark/bovine cartilage (25.3%)	Ginseng (52%)
3	Ginkgo biloba (21.1%)	Active hexose-correlated compounds (8.4%)	Echinacea (14%)	Misc. herbs (38%)	Echinacea (43%)
4	Garlic (19.9%)	Chinese herbs (7.1%)	Chondroitin (13%)		Garlic (43%)
5	Glucosamine (14.9%)	Chitosan (7.1%)	Flaxseed (13%)		Ginger (43%)
6	St. John's wort (12.0%)	Shark cartilage (6.7%)	Acidophilus (13%)		Ginkgo (29%)
7	Peppermint (11.8%)		Coenzyme Q-10 (12%)		Flaxseed (29%)
8	Fish oil/Omega-fatty acids (11.7%)		Fish oil (11%)		Mushrooms (24%)
9	Ginger (10.5%)		Garlic (9%)		Licorice (24%)
10	Soy products (9.4%)		Ginseng (8%)		Black cohosh (24%)

	Advanced breast Cancer[16]	*Prostate Cancer*[c,28]	*General mental Illness*[c,d,29]	*Elderly Veterans with Depression and Dementia*[30]	*Elderly General Use*[31]
Overall Prevalence[b]	—	*26.5%*	—	*18%*	*49%*
Population Size[b]	n = *115*	n = *534*	—	n = *82*	n = *186*
1	Herbal medicine (40%)	Vitamin E (14.9%)	St. John's wort	Ginkgo biloba (47%)	Spearmint (40%)
2	Vitamin/shark cartilage (25%)	Saw palmetto (11.8%)	Evening primrose	St. John's Wort (27%)	Chamomile (32%)
3		Lycopene (10.5%)	Ephedra	Ginseng (20%)	Aloe (32%)
4		Selenium (9.9%)	Ginseng	Echinacea (6%)	Garlic (26%)
5		Vitamin C (9.0%)	Kava-Kava	Ginger (6%)	Brook-mint (22%)
6		Green tea (8.2%)	Valerian	Saw Palmetto (6%)	Osha (13%)
7		Soy (8.2%)	Ginkgo		Lavender (12%)
8		Garlic (7.6%)	Yohimbine		Ginger (11%)
9		Zinc (6.9%)			Ginseng (11%)
10		Vitamin D (6.7%)			Camphor (11%)

[a]Study in Japanese population.
[b]If applicable and if data were reported.
[c]Study in Canadian population.
[d]Not listed according to prevalence.
All other studies were conducted in U.S. populations.

Herbals were ranked according to their mean score for the recommendation to include on the final list. In addition, an aggregate score was generated for each medication combining the results from the other three questions—high potential for use, adverse effects, and drug interactions. These aggregate scores were correlated with the recommendation of whether to include the herbal medicine on the final list using Pearson's test of comparisons, with $\alpha = 0.05$. This correlation was to evaluate whether the medications on the final list were also considered important by these other indicators. Finally, internal consistency for the scores was tested using Cronbach's α.

Results

Twenty-five experts were recruited for the survey, and 20 respondents participated (Table 3). The mean number of years of hospice and palliative medicine experience was 8.03 years ($\pm$6.31), and 80% of the respondents reported having intermediate or expert experience in hospice and palliative medicine. In addition, 80% had intermediate or expert experience in herbal medicines. All respondents completed the survey, with less than 1% of individual items unanswered. There were no significant correlations detected in respondents' answers with their level of hospice and palliative medicine experience or with their level of herbal medicine experience.

Using the question item recommending inclusion of the medicine on the final list, 12 herbal medicines and supplements were identified with a score of 3.75 or greater. These single-item scores were compared to the aggregate scores for prevalence, adverse effects, and drug interactions. Comparisons correlated significantly ($p < 0.05$) between $r = 0.941$ and 0.486 for all herbal medicines in the final list except fish oil ($r = 0.36$, $p = 0.12$) and ginger ($r = 0.31$, $p = 0.2$). In addition to these 12 medicines, 4 others had a relatively high

Table 2. Herbal Medications and Supplements Included in the Survey

Aloe	Black cohosh	Camphor
Chamomile	Chondroitin	Coenzyme Q-10
Echinacea	Evening primrose oil	Fish oils
Flaxseed oil	Garlic	Ginger
Ginkgo	Ginseng	Glucosamine
Green tea	Kava	Lactobacillus
Lavender	Licorice	Lycopene
Melatonin	Milk thistle	Osha
Peppermint	St. John's wort	Saw Palmetto
Selenium	Shark cartilage	Soy
Spearmint	Valerian	Vitamin C
Vitamin D	Vitamin E	Yohimbine
Zinc		

Table 3. Participant Characteristics

Characteristic	*Number (%)*
Profession[a]	
Nurse	3 (15)
Pharmacist	8 (40)
Physician	7 (35)
Basic science/research	1 (5)
Other (included acupuncturist, herbalist, naturopath)	3 (15)
Hospice/palliative care experience	
No experience	3 (15)
Novice	1 (5)
Intermediate	9 (45)
Expert	7 (35)
Herbal experience	
No experience	2 (10)
Novice	2 (10)
Intermediate	14 (70)
Expert	2 (10)

[a]Total equals 22 because one recipient was a nurse and naturopath and another was a pharmacist and accupuncturist/herbalist.

aggregate score despite a lower score to include on the final list. These were green tea, saw palmetto, yohimbine, and milk thistle. The scores to include on the list and the aggregate scores for each of these 4 medicines were correlated significantly, except for milk thistle. Cronbach's α, using all four of the questions, was 0.97, and each individual scale also had an alpha >0.91. The final list of 12 herbals recommended for routine inquiry on all hospice admissions is shown in Table 4. Detailed information on the indication, efficacy, adverse effects and drug interactions for the final list is included in Table 5.

When asked about any additional herbal medicines that should have been included in the survey, respondents offered the following additional suggestions: essiac, psyllium seed, niacin, DHEA, dong quai, feverfew, pycnogenol, vitex, SAM-e, grape seed extract, L-carnitine, folic acid, B_{12}, hawthorne berry, mushroom extracts, and Chinese/ayurvedic blends. These were not included on the final list due to only 8 respondents answering this question. Warfarin was also considered an important drug to trigger a thorough assessment of all medication, herbal, supplement, and food use, but was not included on the list of herbals and supplements because it is a prescription medication. In addition, wafarin was included in the drug interaction information provided to the participants, if there was an interaction with a specific herbal or supplement.

Discussion

In this study, experts in palliative medicine, pharmacy, and herbal medicine use were surveyed in order to create a list of herbal medicines that should be explicitly queried routinely on every admission into hospice care. Participants designated herbals that should be included on the final list and identified the herbals most likely to be used by hospice patients, to cause serious adverse effects, or to cause serious drug interactions.

No tools currently exist to guide hospice providers in the assessment and management of herbal medicines, which are widely used and potentially harmful. The list generated by this research could therefore be a useful aid in medication reconciliation in hospice care. Although detection of all herbal medicine use is important, providing this explicit list

Table 4. Herbal Medicines and Supplements Recommended for Routine Assessment at Hospice Admission

Ranking (based on recommending to include on list)	*Mean (SD)*				
	1. Include on list	*2. High potential for use*	*3. Adverse effects*	*4. Drug interactions*	*Aggregate of 2, 3, and 4*
1. St. John's wort	4.35 (0.75)	4.05 (0.83)	3.40 (1.14)	4.20 (1.01)	11.65 (2.18)
2. Melatonin	4.15 (0.93)	4.10 (0.79)	2.85 (1.14)	3.20 (1.36)	10.15 (2.56)
3. Ginkgo	4.05 (1.23)	3.80 (1.15)	3.15 (1.18)	3.75 (1.02)	10.70 (2.67)
4. Fish oil	4.05 (0.76)	4.10 (0.97)	2.25 (1.12)	2.75 (1.07)	9.10 (1.92)
5. Kava	4.00 (0.92)	3.20 (1.15)	3.90 (0.97)	3.90 (0.91)	11.00 (2.29)
6. Vitamin E	3.95 (1.15)	3.85 (1.14)	2.70 (1.08)	3.20 (1.15)	9.75 (2.63)
7. Valerian	3.94 (0.80)	3.84 (0.83)	3.11 (0.99)	3.32 (1.11)	10.26 (1.97)
8. Licorice	3.90 (0.91)	3.20 (1.01)	3.50 (1.05)	3.75 (0.85)	10.45 (1.85)
9. Ginseng	3.85 (1.14)	3.70 (0.80)	3.10 (1.17)	3.25 (1.16)	10.05(2.80)
10. Ginger	3.80 (0.95)	3.75 (0.72)	2.42 (1.12)	3.15 (1.18)	9.20 (2.02)
11. Garlic	3.80 (1.24)	3.55 (0.95)	2.95 (1.19)	3.35 (1.14)	9.85 (2.85)
12. Echinacea	3.75 (1.12)	3.80 (1.20)	2.65 (1.09)	2.75 (1.16)	9.20 (2.31)

Table 5. Information for the Final List of Twelve Herbal Medications and Dietary Supplements

Effectiveness	*Adverse effects*	*Interactions*
Echinacea		
Possibly effective for reducing symptom severity and duration of the common cold. Possibly effective when taken orally with topical antifungal cream to prevent recurrent vaginal yeast infection. **Possibly ineffective** at preventing or treating recurrent genital herpes infection. **Insufficient evidence** to rate effectiveness at reducing influenza symptoms or reducing leukopenia caused by chemotherapy.	Safe for most people when used short-term. Reported adverse effects include fever, nausea, vomiting, unpleasant taste, stomach pain, diarrhea, constipation, sore throat, dry mouth, headache, allergic reactions, numbness of the tongue, dizziness, insomnia, disorientation, and joint and muscle aches. May cause allergic reaction in some patients. Topical echinacea may cause redness, itchiness or rash.	Increases caffeine plasma concentrations. Inhibits 1A2 and 3A4 enzymes. May interfere with immunosuppressant therapy. May increase effects of midazolam.
Fish oils		
Effective at reducing triglyceride level (20%–50%) **Likely effective** at reducing risk of cardiovascular disease **Possibly effective** in improving the outcomes of a wide variety of disorders, including hypertension, rheumatoid conditions, hypercholesterolemia, prevention of CVA, renal disease, and multiple others. Orlistat may decrease absorption of fish oils.	Safe for most people at less than 3 grams a day. Adverse effects include belching, "fishy" aftertaste, halitosis, heartburn, nausea, loose stools, and rash. Doses in excess of 3 grams per day can inhibit platelet aggregation and increase bleeding risk (e.g., hemorrhagic stroke). Supratherapeutic doses may also impair immune function.	High doses of fish oils have antiplatelet effects and may increase risk of bleeding with anticoagulant or antiplatelet drugs. May exaggerate blood pressure lowering effects of antihypertensives. Contraceptive drugs may interfere with TG-lowering effects of fish oils.
Garlic		
Possibly effective for hypercholesterolemia, hypertension, atherosclerosis, cancer prevention (colon, rectal, stomach), preventing tick bites, fungal skin infections. **Possibly ineffective** for diabetes, eradication of *H. pylori*, hypercholesterolemia in children, treatment of breast or lung cancer, treatment of peripheral arterial occlusive disease. **Insufficient evidence** to rate for BPH, common cold, corns, preeclampsia, prostate cancer and warts.	Breath and body odor Mouth and GI burning or irritation, heartburn, flatulence, nausea, vomiting, diarrhea, gastrointestinal upset Platelet dysfunction, prolonged bleeding time, increased risk of bleeding Asthma/allergic reactions Dermal reactions with topical application	**May enhance** antithrombotic effects with fish oil, anticoagulants, and antiplatelets. **May decrease** effectiveness of contraceptive agents and cyclosporine. Inhibits 2E1 enzyme activity by 39%, possibly induces 3A4 enzymes May reduce INH levels by 65%, may reduce saquinavir levels by 50%
Ginger		
Possibly effective for morning sickness, postoperative nausea and vomiting, and vertigo. **Possibly ineffective** for motion sickness. **Insufficient evidence** for chemotherapy-induced nausea and vomiting, migraine headache, osteoarthritis and rheumatoid arthritis.	Higher doses (over 5 grams per day) may cause abdominal discomfort, heartburn, diarrhea, irritant effect in mouth/throat.	May increase bleeding risk when taken with anticoagulants and antiplatelets. May increase insulin levels, and have additive effects with antidiabetes drugs. May have additive effects with calcium channel blockers (hypotensive and calcium blocking effects).

(*continued*)

Table 5. Continued

Effectiveness	*Adverse effects*	*Interactions*
Ginkgo **Possibly effective** for improving age-related memory impairment, cognitive functioning, and improving symptoms of dementia. May improve color vision in diabetic retinopathy, improving visual fields in glaucoma. May improve symptoms associated with PMS, PAD, Raynaud's symptoms, and vertigo. **Possibly ineffective** for altitude sickness, antidepressant-induced sexual dysfunction, seasonal affective disorder and tinnitus. **Insufficient evidence** for age-related macular degeneration, ADHD, colorectal cancer, hearing loss, and stroke recovery.	Minor adverse effects include stomach upset, headache, dizziness, constipation, palpitations and allergic skin reactions. May increase risk of bleeding and bruising.	May decrease effectiveness of alprazolam. May increase risk of bleeding when taken with anticoagulant or antiplatelet agents. **In large quantities** may increase risk of seizures, and decrease effectiveness of anticonvulsant agents. **May** alter insulin section and metabolism, increasing blood glucose levels and lessening effectiveness of diabetes medications. Mildly inhibits 1A2, modestly inhibits 2D6, and significantly inhibits 2C9. Induces 2C19 enzymes. Reduces omeprazole serum levels. Use with trazodone may cause coma.
Ginseng **Possibly effective** for diabetes mellitus (reducing blood glucose) and decreasing risk of develop URI symptoms. **Insufficient evidence** for improvement in athletic performance, ADHD and breast cancer.	May cause diarrhea, itching, insomnia, headache, and nervousness. May cause tachycardia, hypertension, breast tenderness, vaginal bleeding. Uncommonly may cause Stevens-Johnson syndrome, liver damage, and severe allergic reaction.	May enhance blood-glucose lowering effects of diabetes medications. May increase adverse effects associated with antidepressants such as anxiousness, headache, restlessness, and insomnia. May reduce effectiveness of warfarin.
Kava **Possibly effective** for anxiety, benzodiazepine withdrawal, and menopausal anxiety **Insufficient evidence** for cancer, insomnia, and social anxiety	Kava may cause serious liver damage, even with short-term use. Kava may also cause GI upset, headache, dizziness, drowsiness, enlarged pupils and disturbances of oculomotor equilibrium and accommodation, dry mouth and allergic skin reactions. May also cause extrapyramidal side effects.	May exaggerate drowsiness and motor reflex depression when given with CNS depressants May decrease levodopa action **Inhibits** 1A2, 2C19, 2C9, 2D6, 2E1, 3A4 enzymes, potentially reducing the metabolism of a wide variety of drugs. **May potentiate** hepatotoxic effect of numerous medications
Licorice **Possibly effective** for dyspepsia. **Insufficient evidence** for atopic dermatitis, hepatitis, muscle cramps, peptic ulcers, and weight loss.	Orally, licorice may cause hypertension, sodium and water retention, edema, lethargy, amenorrhea, and headache. High levels of consumption may cause hypokalemia, hypokalemic myopathy, rhabdomyolysis, myoglobinuria, severe CHF, pulmonary edema, lower extremity weakness, hypertensive encephalopathy and quadriplegia. May decrease libido and cause sexual dysfunction in men. .	**May reduce** effect of antihypertensive agents May potentiate effect of corticosteroids. May inhibit 2B6 enzymes. **May** inhibit or induce 2C9 or 3A4 enzymes. **May** increase cardiac glycoside toxicity due to potassium loss, may exaggerate potassium loss from diuretics, and interfere with hormone therapy due to estrogenic effects. Loop diuretics may enhance mineralocorticoid effects of licorice. **May** increase metabolism or warfarin.

Melatonin **Likely effective** for circadian rhythm sleep disorders, sleep-wake cycle disturbances. **Possibly effective** in treating benzodiazepine withdrawal, cluster headache, delayed sleep phase syndrome, insomnia, jet lag, nicotine withdrawal, preoperative anxiety and sedation, prostate cancer, solid tumors, sunburn, tardive dyskinesia and thrombocytopenia. **Possibly ineffective** for shift work disorder **Likely ineffective** for depression **Insufficient evidence** for ADHD, β-blocker induced insomnia, chronic fatigue syndrome, fibromyalgia, irritable bowel syndrome, menopausal symptoms, migraine headache, seizures, or stabbing headache.	Adverse effects include daytime drowsiness, headache, dizziness, transient depressive symptoms, mild tremor, mild anxiety, abdominal cramps, irritability, reduced alertness, confusion N, V, and hypotension. May cause resumption of spotting or menstrual flow in perimenopausal women.	May increase effects of anticoagulant and antiplatelet medications May impair glucose utilization and increase insulin resistance, decreasing the effectiveness of antidiabetes drugs. Chronic benzodiazepine therapy and caffeine consumption may decrease endogenous melatonin levels. **May** increase effects of other sedating medications such as alcohol, benzodiazepines, sedative/hypnotics. Contraceptives and fluvoxamine may increase the levels of melatonin. Flumazenil may inhibit the effect of melatonin. **Can** stimulate immune function and might interfere with immunosuppressive therapy. **May** decrease the effectiveness of nifedipine GIT. Verapamil may increase melatonin excretion.
St. John's Wort **Likely effective** for depression **Possibly effective** for menopausal symptoms and somatization disorder	May cause insomnia, vivid dreams, restlessness, anxiety, irritability, GI upset, fatigue, dry mouth, dizziness, headache, skin rash, diarrhea, and tingling. May cause photodermatitis.	Concurrent use with triptans, antidepressants, fenfluramine, meperidine, MAO inhibitors, nefazodone, pentazocine, tramadol, and dextromethorphan may increase serotonergic effects, and possibly serotonin syndrome. May decrease effect of alprazolam. May increase aminolevulinic acid potential to cause phototoxicty. May reduce amitritpyline, nortriptyline, and digoxin serum concentrations. May decrease opioid- and barbiturate-induced sleep time. May increase activity of clopidogrel. May decrease contraceptive drug levels causing breakthrough and irregular. bleeding, or unwanted pregnancy May decrease plasma cyclosporine levels by up to 70% and NNRTI's by 35%. Induces 1A2, 3A4, 2C93A4 enzymes. Induces P-glycoprotein. Increases metabolism of phenobarbital and phenytoin. Reduces serum concentration of protease inhibitors, tacrolimus, and digoxin. May decrease therapeutic effects of warfarin and methylphenidate.
Possibly ineffective for hepatitis C, HIV/AIDS, and polyneuropathy **Insufficient evidence** for OCD, PMS, seasonal affective disorder, and smoking cessation.	May cause intermenstrual or abnormal menstrual bleeding, reduced fertility, and neuropathy May cause withdrawal effects with discontinuation	

(*continued*)

Table 5. Continued

Effectiveness	*Adverse effects*	*Interactions*
Valerian **Possibly effective** for insomnia **Insufficient evidence** for anxiety and dyssomnia	Headache, excitability, uneasiness, cardiac disturbances, insomnia Gastric discomfort, dry mouth, vivid dreams, morning drowsiness	May have additive sedative effects when taken with alcohol or benzodiazepines and CNS depressants. Increases alprazolam levels by 19%. May inhibit 3A4 enzymes.
Vitamin E **Effective** for vitamin E deficiency and ataxia associated with vitamin E deficiency.	Uncommonly, may cause N, diarrhea, intestinal cramps, fatigue, weakness, headache, blurred vision, rash, gonadal dysfunction, and creatinuria. Unclear if vitamin E contributes to increased risk of hemorrhage stroke, bleeding, and bruising. High doses may increase all-cause mortality	**May** increase bleeding risk from anticoagulants and antiplatelets. May reduce activity of some chemotherapeutic agents. May increase absorption of cyclosporine. May increase activity of 3A4 enzymes. Along with other antioxidants, may attenuate therapeutic effectiveness of statin/niacin therapy. More than 400 IU of vitamin E per day with warfarin may prolong PT/INR and increase risk of bleeding.
Possibly effective for age-related macular degeneration, Alzheimer's disease, anemia, beta-thalassemia, bladder cancer, chemotherapy extravasation, cisplatin-induced neurotoxicity, dementia, dysmenorrhea, dyspraxia, glomerulosclerosis, G6PD deficiency, granuloma annulare, Huntington's disease, infertility, intracranial hemorrhage, intraventricular hemorrhage, nitrate tolerance, Parkinson's disease, photoreactive keratectomy, preeclampsia, PMS, physical performance, radiation-induced fibrosis, retrolental fibroplasia, rheumatoid arthritis, sunburn, tardive dyskinesia, and uveitis. **Possibly ineffective** for angina, atherosclerosis, breast cancer-related hot flashes, bronchopulmonary dysplasia, cancer, colorectal cancer, congestive heart failure, Duchenne muscular dystrophy, head and check cancer, hemolytic anemia, hypertension, intermittent claudication, myotonic dystrophy, oral mucosal lesions, osteoarthritis, pancreatic cancer, pharyngeal cancer, prostate cancer, respiratory tract infections, retinitis pigmentosa, scarring, **Likely ineffective for** benign breast disease, breast cancer, cardiovascular disease, and lung cancer. **Insufficient evidence** for asthma, cataracts, chemotherapy-related infection, diabetes, gastric cancer, hyperlipidemia, ischemic reperfusion injury, ischemic stroke, liver transplant, melanoma, nocturnal leg cramps, nonalcoholic steatohepatitis, overall mortality, sickle cell disease, and steatohepatitis.		

Adapted from the Natural Medicines Comprehensive Database.[33]

CVA, cerebrovascular accident; GI, gastrointestinal; TG, triglyceride; BPH, benign prostatic hyperplasia; INH, isoniazid; PMS, premenstrual syndrome; PAD, peripheral artery disease; ADHD, attention-deficit hyperactivity disorder; URI, upper respiratory infection; CHF, congestive heart failure; OCD, obsessive-compulsive disorder; MAO, monoamine oxidase; PT/INR, prothrombin time/international normalized ratio.

at the time of admission may help providers to detect the herbals that are more likely to be used or more likely to be harmful. In addition, prompting patients to discuss herbal use by using this list may help educate them as to the nature of herbals, which are drugs of natural origin with pharmacologic properties similar to conventional drugs.[32] The final list of herbals generated by this survey could also be useful in other vulnerable populations, such as home care patients and elderly persons. Table 5, which shows the final list of 12 herbals and evidence for their indication, efficacy, adverse effects, and interactions,[33] is meant to serve as a useful tool for hospice practitioners needing quick information on these medications at the point of care.

A potential limitation of this study is that the analysis is based on the opinions of our participants. However, participants were chosen for their experience and competence in hospice and palliative medicine or herbal medicines. Although our respondents had high self-reported levels of experience, to minimize the concern of lack of knowledge in the area of herbals, participants were provided with information about the 37 herbal medicines included in the survey based on a review of the literature regarding effectiveness, adverse effects, drug interactions as well as nationally recognized hospice and palliative care criteria.

Currently, there have been no studies of the prevalence of herbal medicine use in hospice settings and no examination of the efficacy or safety of herbals in hospice patients. However, high use of herbals in populations frequently seen in hospice, such as those with cancer, suggests hospice patients' herbal and supplement use should be assessed. The large number of herbal products on the market precludes asking a patient about use of each herbal or supplement by name. Therefore, a list of high use herbals associated with potentially severe adverse effects or interactions would increase efficiency for the hospice professional. The recommendations from this survey are preliminary and should prompt further study to specifically address herbal use in hospice patients and the potential outcomes associated with herbals.

Accurately identifying all medications used at hospice admission is essential to provide safe, effective, and complete care at the end of life. Promotion of patient safety is crucial in all patient care settings, and is especially important at the end of life, when the priority is to promote quality of life and comfort and minimize any deleterious consequences of medical care. Further study is needed to determine whether hospice populations are more likely to use herbal medicines and to investigate the evidence for safety and efficacy in these vulnerable populations.

Acknowledgments

The authors acknowledge Dr. Ruili Luo, who provided assistance with statistical analysis. Dr. Holly Holmes is supported by a Hartford Geriatrics Health Outcomes Research Scholars Award.

This work was presented at a poster session of the Annual Assembly of the American Academy of Hospice and Palliative Medicine, Salt Lake City, Utah, in February 2007.

Author Disclosure Statement

No competing financial interests exist.

References

1. Thompson Coon J, Pittler M, Ernst E: Herb-drug interactions: Survey of leading pharmaceutical/herbal companies. Arch Intern Med 2003;163:1371.
2. Delate T, Chester EA, Stubbings TW, Barnes CA: Clinical outcomes of a home-based medication reconciliation program after discharge from a skilled nursing facility. Pharmacotherapy 2008;28:444–452.
3. Cua YM, Kripalani S: Medication use in the transition from hospital to home. Ann Acad Med Singapore 2008;37: 136–136.
4. Persell SD, Osborn CY, Richard R, Skripkauskas S, Wolf MS: Limited health literacy is a barrier to medication reconciliation in ambulatory care. J Gen Intern Med 2007;22:1523–1526.
5. Gordon W, Perrott J, Dahri K: Accuracy of medication histories: The first step of medication reconciliation. Ann Pharmacother. 2008;42:144.
6. McPherson ML: Nonprescription drug documentation and nursing knowledge in a home health care population. Consult Pharm 1989;4:32–36.
7. Myers SS, Lynn J: Patients with eventually fatal chronic illness: Their importance within a national research agenda on improving patient safety and reducing medical errors. J Palliat Med 2001;4:325–332.
8. Currow D, Shelby-James T, Plummer J, Stevenson J, Abernethy A: Polypharmacy worsens as death approaches. J Palliat Care 2006;22:214–214.
9. Lee J, McPherson ML: Outcomes of recommendations by hospice pharmacists. Am J Health Syst Pharm 2006;63:2235–2239.
10. Lewis JD, Strom BL: Balancing safety of dietary supplements with the free market. Ann Intern Med 2002;136:616–618.
11. Hoblyn JC, Brooks JO: Herbal supplements in older adults—Consider interactions and adverse events that may result from supplement use. Geriatrics 2005;60:18–23.
12. Marcus DM, Grollman AP: Botanical medicines—The need for new regulations. N Engl J Med 2002;347:2073–2076.
13. Eisenberg DM, Davis RB, Ettner SL, Appel S, Wilkey S, Van Rompay M, Kessler RC: Trends in alternative medicine use in the United States, 1990–1997: Results of a follow-up national survey. JAMA 1998;280:1569–1575.
14. Gardiner P, Graham RE, Legedza ATR, Eisenberg DM, Phillips RS: Factors associated with dietary supplement use among prescription medication users. Arch Intern Med 2006;166:1968–1974.
15. Blendon RJ, DesRoches CM, Benson JM, Brodie M, Altman DE: Americans' views on the use and regulation of dietary supplements. Arch Intern Med 2001;161:805–810.
16. Shen J, Andersen R, Albert PS, et al: Use of complementary/alternative therapies by women with advanced-stage breast cancer. BMC Complement Altern Med 2002;2:1–7.
17. Lawsin C, DuHamel K, Itzkowitz SH, Brown K, Lim H, Thelemaque L, Jandorf L: Demographic, medical, and psychosocial correlates to CAM use among survivors of colorectal cancer. Support Care Cancer 2007;15:557–564.
18. Cohen RJ, Ek K, Pan CX: Complementary and alternative medicine (CAM) use by older adults: A comparison of self-report and physician chart documentation. J Gerontol A Biol Sci Med Sci 2002;57:M223–227.
19. Clement YN, Williams AF, Khan K, Bernard T, Bhola S, Fortuné M, Medupe O, Nagee K, Seaforth CE: A gap between acceptance and knowledge of herbal remedies by physicians: The need for educational intervention. BMC Complement Altern Med 2005;5:20.

20. Fontanarosa PB, Rennie D, DeAngelis CD: The need for regulation of dietary supplements—Lessons from ephedra. JAMA 2003;289:1568–1570.
21. Garrard J, Harms S, Eberly LE, Matiak A: Variations in product choices of frequently purchased herbs: Caveat emptor. Arch Intern Med 2003;163:2290–2295.
22. National Hospice and Palliative Care Organization: NHPCO's 2005 Facts and Figures. www.nhpco.org (Last accessed November 16, 2007).
23. Natural Center for Complementary and Alternative Medicine: The use of complementary and alternative medicine in the United States. http://nccam.nih.gov/news/camsurvey_fs1.htm (Last accessed November 16, 2007).
24. Hyodo I, Amano N, Eguchi K, Imanishi J, Hirai M, Nakano T, Takashima S: Nationwide survey on complementary and alternative medicine in cancer patients in Japan. J Clin Oncol 2005;23:2645–2654.
25. Wahner-Roedler DL, Elkin PL, Vincent A, Thompson JM, Oh TH, Loehrer LL, Mandrekar JN, Bauer BA: Use of complementary and alternative medical therapies by patients referred to a Fibromyalgia Treatment Program at a Tertiary Care Center. Mayo Clin Proc 2005;80:55–60.
26. Richardson MA, Sanders T, Palmer JL, Greisinger A, Singletary SE: Complementary/alternative medicine use in a comprehensive cancer center and the implications for oncology. J Clin Oncol 2000;18:2505–2514.
27. Powell CB, Dibble SL, Dall'Era JE, Cohen I: Use of herbs in women diagnosed with ovarian cancer. Int J Gynecol Cancer 2002;12:214–217.
28. Boon H, Westlake K, Stewart M, Gray R, Fleshner N, Gavin A, Brown JB, Goel V: Use of complementary/alternative medicine by men diagnosed with prostate cancer: Prevalence and characteristics. Urology 2003;62:849–853.
29. Vermani M, Milosevic I, Smith F, Katzman MA: Herbs for mental illness: Effectiveness and interaction with conventional medicines. J Family Pract 2005;54:789–800.
30. Kales HC, Blow FC, Welsh DE, Mellow AM: Herbal products and other supplements: Use by elderly veterans with depression and dementia and their caregivers. J Geriatr Psychiatry Neurol 2004;17:25–31.
31. Zeilmann CA, Dole EJ, Skipper BJ, McCabe M, Dog TL, Rhyne RL: Use of herbal medicine by elderly Hispanic and non-Hispanic white patients. Pharmacotherapy 2003;23:526–532.
32. De Smet PA: Herbal remedies. N Engl J Med 2002;347:2046–2056.
33. Natural Medicines Comprehensive Database. www.naturaldatabase.com (Last accessed October 2009).

Address correspondence to:
Holly M. Holmes, M.D.
Department of General Internal Medicine
UT MD Anderson Cancer Center
1515 Holcombe Boulevard
Unit 1465
Houston, TX 77030

E-mail: hholmes@mdanderson.org