PSYCHIATRIC MEDICINE IN PRIMARY CARE

The essential guide to developments in psychiatry and behavioral health

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Medical Care for Patients with Dementia

ABSTRACT & COMMENTARY

Source: Morrison RS, et al. Survival in end-stage dementia following acute illness. *JAMA* 2000;284:47-52.

An estimated 1.8 million people are in the final stages of dementia and are unable to recognize family, dependent in activities of daily living, unable to communicate, and experience repeated infections and other complications. Data from nursing homes and hospice care suggest that survival for patients with end-stage dementia following an acute illness is limited. Therefore, if prognosis is poor, palliation of symptoms and enhancement of comfort may be more important to the patient than the application of burdensome interventions directed at life prolongation or cure.

This study by Morrison and colleagues was a six-month prospective cohort study that examined survival for patients with advanced dementia who were hospitalized with either pneumonia or hip fracture. The study compared the care these patients received with that of cognitively intact adults with the same diagnoses.

Patients older than 70 years who were admitted to a large hospital in New York with diagnoses of hip fracture or pneumonia over an 18-month period were eligible for the study. Patients were excluded if they had multiple internal injuries, a previous fracture in the affected hip, or a known diagnosis of cancer that was not considered cured or in remission, were non-English speaking, or were identified more than 48 hours after admission.

Patients with hip fractures or pneumonia were eligible for inclusion if they were cognitively intact or had end-stage dementia. Patients who scored 18 of 24 on the telephone version of the Mini-Mental State Exam were eligible for enrollment in the cognitively intact group. Patients who scored less than 18 and whose functional/cognitive status was classified as stage 6 or 7 (severe to very severe dementia) on the Global Deterioration Scale were

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enrolled in the end-sage dementia group. Patients who score 6 or 7 on the Global Deterioration Scale are dependent in all activities of daily living, display sleep-wake cycle disturbances, and cannot remember the names of close relatives.

Of the 235 eligible patients, 216 agreed to participate (119 with pneumonia, 39 cognitively intact/80 end-stage dementia, and 109 with hip fracture, 59 cognitively intact/38 end-stage dementia). Median age was 84 years for hip fracture patients and 86 years for pneumonia patients. Most patients were women (81% of hip fracture patients, 61% of pneumonia patients). End-stage dementia patients with pneumonia or hip fractures were significantly older (four and six years older, respectively) than cognitively intact patients. Dementia patients were also more likely to reside in nursing homes (82% vs 5% with hip fracture and 63% vs 55% with pneumonia).

At six months, 42 of 80 (53%) pneumonia patients with end-stage dementia had died compared to five of 39 (13%) cognitively intact patients. Twenty-one of 38 hip fracture patients (55%) with end-stage dementia had died within six months compared to seven of 59 cognitively intact hip fracture patients (12%). Fifty-four percent of the end-stage dementia patients who died were readmitted to the study hospital within six months of their index hospitalization compared with 58% of the cognitively intact patients who died.

Additional factors associated with decreased survival among hip fracture patients included a high Charlson comorbidity index score, and being unable to walk or transfer without total assistance. Pneumonia patients with high pneumonia severity scores were also at increased risk of death. End-stage dementia patients were significantly more likely to receive a third-generation cephalosporin or antipseudomonal penicillin (43% vs 13%).

There was no significant difference in the number of burdensome procedures received by end-stage dementia and cognitively intact patients. However, end-stage dementia patients were significantly more likely to be restrained. In addition, hip fracture patients with end-stage dementia received a mean of 1.7 mg/d of morphine sulfate equivalents compared with 4.1 mg/d for cognitively intact patients ($P < 0.001$) and no end-stage patient received premedication prior to being turned, transferred, or repositioned. Only nine of the 38 hip fractured patients with end-stage dementia received a standing order for analgesics.

Finally, no documentation was found regarding discussions about goals of care, or decision to withhold or withdraw life-sustaining treatment for 106 of the 118 end-stage dementia. Only two patients with end-stage dementia were discharged to a nursing home with hospice care. Decisions were made to forego life-prolonging therapies for eight end-stage dementia patients (7%) compared to one cognitively intact patient (1%). These decisions were made only after patients were comatose or hypotensive in the setting of multisystem organ failure and death appeared imminent.

COMMENT BY CLAUDIA A. ORENGO, MD, PhD

Morrison et al have presented a well-designed and controlled study finding that end-stage dementia patients who received routine hospital care for pneumonia or hip fracture have a 4-fold increase in six-month mortality compared with elderly cognitively intact adults with the same diagnoses. Despite this high mortality, they find almost no differences in the care end-stage dementia patients received compared with cognitively intact adults, and no evidence that palliative care was undertaken, either in conjunction with or instead of, life-prolonging measures for dementia patients. These findings suggest that advanced dementia is not viewed as a terminal

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Questions & Comments

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diagnosis by physicians or families, and perhaps there is a lack of awareness of the poor short-term prognosis for these patients.

Patients with end-stage dementia are unable to communicate their preference for care, the presence of pain or discomfort, or the need for analgesia. Two of the most alarming findings of this study were that end-stage dementia patients with hip fractures received significantly less pain medication than cognitively intact patients, and end-stage dementia patients did not receive premedications prior to being turned, repositioned, or transferred. Only nine of 38 hip fracture patients with end-stage dementia received a standing order for analgesia. Also of concern was that there did not appear to be consideration of limiting burdensome interventions (e.g., phlebotomy, catheter insertion) in patients with end-stage dementia and that no palliative care plans or discussions to forgo life-sustaining therapy were documented.

A few limitations exist that deserve discussion. First, this study was conducted in only one New York Hospital and may not be generalizable to other institutions or states. Morrison et al relied on medical records to determine whether conversations about goals of care occurred between families of end-stage dementia patients and the physician(s). It is possible that these discussions occurred and that families opted for standard medical care. It also is possible that upon readmission, families of end-stage dementia patients opted for palliative care, and hence the higher mortality rate. However, 54% of the end-stage dementia patients who died were readmitted compared to 58% of the cognitively intact patients who died, suggesting no difference in whether cognitively intact or end stage dementia patients were to be re-hospitalized when acutely ill.

Individuals with end-stage dementia are dependent in all activities of daily living, cannot communicate, and cannot remember the names of their closest relatives or their spouse. They are unable to express their wishes for medical interventions, their pain or discomfort, or the need for analgesics. It would be fair to say that they have a compromised quality of life. Given the burdens of treatment associated with the two common conditions in elderly individuals—pneumonia and hip fractures, and the high mortality observed following these illnesses—we should all be more attentive to decreasing pain and suffering and minimizing burdensome interventions in individuals with end-stage dementia. We should not forego quality of life for quantity of life in patients with end-stage dementia anymore than we should in patients with terminal cancer. ❖

Herb-Drug Interactions: An Evidence-Based Table

By Mary L. Hardy, MD

As patients' use of herbal products increases, so do physicians' concerns regarding the possibility of herb-drug interactions. Uncertainty in this area is rife (e.g., active constituents, mechanisms of action, consistency of products) and complicates the assessment of available data. Current literature consists mainly of case reports that often are not adequately investigated. There are few clinical trials and the pharmacologic data available have not been assessed for clinical relevance.

Further, patients have been reluctant to fully disclose their use of natural products to their physicians, so interactions generally only come to light when a serious problem occurs. Most doctors, without adequate training in this area, feel uncomfortable commenting on or even reporting cases that involve the use of herbal medications. Too much of our experience is theoretical or anecdotal.

For commonly used herbs and commonly prescribed drugs, I have assembled a detailed compendium of herb-drug interactions. This table is designed to provide clinicians with guidance in assessing the potential for interaction. It cites a mechanism for interaction where one is known or postulated. It reports the level of evidence for that interaction. It also offers a clinically useful scale for the evidence, outlined in Table 1.

The drug-herb interaction table is not exhaustive and should be considered a work in progress. New data will become available, and as we learn more about which herbs interact with which drugs, we will report significant findings in future newsletters. A limited bibliography is available on request. (*Dr. Hardy is Medical Director at Cedars-Sinai Integrative Medicine Medical Group in Los Angeles.*) ❖

Table 1

Level of Evidence to Support Use

CT = Controlled trial	CS = Case series
CR = Case report	AS = Animal study
TU = Traditional use	P = Pharmacology
TH = Theoretical	

Table 2

Herb-Drug Interactions

Drug Category	Herbs	Herb Effect	Mechanism (Evidence Type)
Alkaloids	High tannin-containing (e.g., caffeine-containing herbs, cat's claw, tea, uva ursi)	Decreased plasma levels	Precipitation of alkaloids by tannins (TU)
Anesthetics	Kava, valerian	Prolongation of sedation time	Additive effect (CR)
Antihypertensives	a. Licorice b. Sympathomimetic herbs (e.g., ephedra)	Decreased therapeutic effect	a. Increased salt and water retention (CR) b. Opposition of therapeutic action (P)
Antiarrhythmics	Cathartic laxatives (e.g., aloe, cascara, senna, yellow dock), diuretics (e.g., celery seed, corn silk, horsetail, juniper), licorice	Increased side effects (arrhythmia)	Increased potassium loss (P)
Antiarrhythmics	Anticholinergic herbs (not generally used clinically, e.g., belladonna)	Decreased therapeutic effect	Decreased absorption (P, TH)
Anticoagulants	Antiplatelet-aggregating (e.g., *Panax ginseng*, feverfew, garlic, ginkgo)	Increased side effect (bleeding)	Inhibition of platelet aggregation through inhibition of thromboxane synthetase (ginger) (P); arachadonic acid production (feverfew) (P); inhibition of epinephrine induced in vitro (garlic) (P); platelet thromboxane synthetase aggregation (garlic) (P, CR); inhibition of platelet activating factor (ginkgo) (CR)
Anticoagulants: Warfarin	*Panax ginseng*, St. John's wort	Opposition of therapeutic effect; decreased enzyme bioavailability	Unknown (CR); hepatic induction (CS)
Anticoagulants: Warfarin	Coumarin-rich herbs, (e.g., sweet clover, danshen), white clover	Increased therapeutic effect	Only danshen has been observed to do this clinically. Increased maximum concentration and decreased volume of distribution (CR, P)
Anticoagulants: Warfarin	Vitamin K-rich herbs (e.g., collard, kale, spinach)	Decreased therapeutic effect	Opposes activity (CR, P)
Anticonvulsants	a. GLA-rich herbs b. Thujone-containing herbs (e.g., cedar, tansy, sage)	Decreased therapeutic effect	GLA (CR) and thujone may decrease seizure threshold; mechanism unknown

Drug Category	Herbs	Herb Effect	Mechanism (Evidence Type)
Anticonvulsants	Salicylate-rich herbs (e.g., cramp bark, willow, wintergreen)	Increased therapeutic effect	Transient; unknown mechanism (CR)
Anticonvulsants: Phenytoin	Shankapulshpi (Ayurvedic preparation with multiple herbs)	Opposition of therapeutic action	Decreased effectiveness of drug; decreased drug levels (CR)
Antiplatelet-aggregating	Antiplatelet-aggregating (e.g., *Panax ginseng*, feverfew, garlic, ginkgo)	Increased side effect (bleeding)	Similar therapeutic action (P, CR)
Barbiturates	Valerian	Increased therapeutic effect; increased side effects	Shown to prolong barbiturate-induced sleep (AS)
Benzodiazepines	St. John's wort, kava	Decreased therapeutic efficacy; may increase side effects; increased sedation	Herb binds to GABA receptor site (AS, P)
Cardiac glycosides	Cardiac glycoside-containing herbs (e.g., foxglove, lily of the valley)	a. Enhanced therapeutic effect b. Increased side effects (arrhythmia)	Same active constituents (TH)
Cardiac glycosides	Cathartic laxative herbs (e.g., aloe, cascara, senna, yellow dock), licorice, diuretic herbs (e.g., celery seed, corn silk, horsetail, juniper)	Increased side effects (arrhythmia)	Increased potassium loss (TH)
Cardiac glycosides	Quinine-containing herb (e.g., cinchona bark)	Increased plasma levels	(TH)
Cholesterol-lowering drugs	Garlic, artichoke, ginger, fenugreek	Increased therapeutic effect	Similar clinical effect via different mechanism (TH)
Corticosteroids	Cathartic laxative herbs (e.g., aloe, cascara, senna, yellow dock), diuretic herbs (e.g., celery seed, corn silk, horsetail, juniper)	Increased side effects	Both cause increased potassium loss (TH)
Corticosteroids	Licorice	Increased plasma levels	Increased half-life (increased bioavailability) (CR); inhibition of ll-ß-dehydrogenase (P)
Corticosteroids	*Panax ginseng*	Increased side effects	Similar side effects of CNS stimulation and insomnia (CR)
Digoxin	Siberian ginseng	Increased plasma level	Mechanism unknown; validated by rechallenge (CR)

Drug Category	Herbs	Herb Effect	Mechanism (Evidence Type)
Digoxin	a. Kyushin (Chinese remedy containing the venom of the Chinese toad) b. *Panax ginseng*	Increased serum levels	Interferes with assay (P, CR) without toxic effects
Diuretic: Lasix	*Panax ginseng*	Decreased therapeutic effect	Diuretic resistance with ginseng; unknown mechanism (CR)
Diuretic: Potassium sparing	Licorice	Decreased therapeutic effect	Interferes with potassium-sparing effects by wasting K^+
Estrogen replacement therapy	a. Herbs high in phytoestrogens (e.g., soy, fenugreek, licorice, black cohosh) b. *Panax ginseng*	a. Increased therapeutic effect to excess b. Increased side effect (estrogen excess)	a. Never reported (TH) b. Reported in few cases to produce postmenopausal bleeding or mastalgia (CR)
General medication	High-fiber herbs (e.g., flax, psyllium, acacia, slippery elm, marshmallow)	Decreased absorption	(P)
General medication	"Hot" remedies (e.g., ginger, garlic, black pepper, red pepper)	Increased absorption	Taken internally, "hot" remedies lead to vasodilatation of gut wall and increased absorption (TU)
GI motility drugs	Anticholinergic herbs (not generally used clinically, e.g., belladonna)	Decreased activity	Opposition of therapeutic activity
Hepatotoxic drugs	Hepatotoxic herbs (e.g., borage, coltsfoot, comfrey, rue, tansy)	Increased side effect (hepatotoxicity)	Additive toxicity from similar side effects (CR)
Hypoglycemic agents: Oral and insulin	Hypoglycemic (e.g., *Panax ginseng*, garlic, fenugreek, bitter melon, aloe, gymnema)	Enhanced therapeutic effect	a. Direct hypoglycemic activity (CR, AS, P) b. Decreased glucose absorption
Hypoglycemic agents: Oral and insulin	Hyperglycemic (e.g., cocoa, rosemary, stinging nettle)	Decreased therapeutic effect	Direct opposition of therapeutic action (CS)
Immune suppressants	Echinacea, astragalus	Opposition of therapeutic action	General immune stimulation by these herbs may interfere with ability of immunosuppressive drugs to prevent tissue rejection; never reported (TH)

Drug Category	Herbs	Herb Effect	Mechanism (Evidence Type)
Iron	Tannin-rich herbs (e.g., caffeine-containing herbs, cat's claw, tea, uva ursi)	Decreased therapeutic effect	Tannin binds with iron, decreasing absorption (TH, P)
Lithium	Diuretic herbs (e.g., celery seed, corn silk, horsetail, juniper)	Increased side effects	Decreased sodium leads to increased lithium toxicity
Lower seizure threshold (drugs that)	GLA-rich herbs (e.g., evening primrose, borage, black currant)	Increased side effect to additive side effect	Decreased seizure threshold (CR)
Methotrexate and similar cytotoxic drugs	Salicylate herbs (e.g., cramp bark, willow, wintergreen)	Increased plasma levels (toxicity)	Decreased excretion (TH)
Minerals	Fiber-containing herbs (e.g., flax, psyllium, acacia, slippery elm, marshmallow)	Decreased bioavailability	Psyllium has been reported to decrease the absorption of Ca, Mg, Cu, Zn (CR)
Monoamine oxidase inhibitors (MAOIs)	*Panax ginseng*, bioactive amines, licorice	Increased side effects	Additive side effects may lead to toxicity; glycyrrhizin is reported to be a very potent MAOI (TH, CR)
Monoamine oxidase inhibitors (MAOIs)	Ginkgo	Increased therapeutic effect; increased side effects	Inhibition of monoamine oxidase (P)
Nonsteroidal anti-inflammatory drugs (NSAIDs)	Gastric irritant herbs (e.g., caffeine, rue, uva ursi)	Increased side effects	Similar side effects may increase risk of gastric erosion and bleeding (TH)
Nonsteroidal anti-inflammatory drugs (NSAIDs)	Nettles	Increased therapeutic effect	Potentiation of the anti-inflammatory activity of NSAIDs (CT)
Opioids	*Panax ginseng*	Decreased therapeutic effects	Animal model demonstrated the blunting of the analgesic effects of morphine via a non-opioid receptor-mediated mechanism (AS)
Photosensitizing drugs	Photosensitizing herbs (e.g., St. John's wort, angelica, rue, fennel)	Increased side effects	Furanocoumarins found often in umbelliferae resemble psoralens (P, AS, CR)
Salicylates	Herbs that alkalinize urine (e.g., uva ursi)	Decreased plasma levels	Increased urinary excretion (P)
Sedative hypnotics	Opioid herbs (e.g., opium poppy, California poppy)	Increased side effects (CNS depression)	Additive side effects

Drug Category	Herbs	Herb Effect	Mechanism (Evidence Type)
Sedative hypnotics including alcohol	Sedative herbs (e.g., hops, kava, valerian)	Increased therapeutic action; increased side effects (CNS depression)	Additive effects lead to CNS depression *except* valerian does not potentiate the effects of alcohol (AS, P)
SSRIs	St. John's wort	Increased therapeutic activity; increased side effects	May contribute to serotonin syndrome—similar action (TH)
Statin drugs	Red yeast (Cholestin®)	Increased therapeutic effect	Similar active compounds; not known if taking both products simultaneously increases side effects of statin drugs (TH)
Thyroid hormone	a. Horseradish	a. Decreased therapeutic effect	a. Depressed thyroid function
	b. Kelp	b. Increased therapeutic effect	b. Iodine in kelp may result in hyperthyroidism (TH)

CME Questions

1. **Patients with end-stage dementia hospitalized for hip fractures or pneumonia:**
   a. have a higher mortality rate than cognitively intact patients with the same conditions.
   b. receive less distressing and painful procedures than cognitively intact adults.
   c. receive a standing order for analgesics.

2. **End-stage dementia patients with hip fractures received significantly less pain medication than cognitively intact patients.**
   a. True
   b. False

3. **End-stage dementia patients did receive premedications prior to being turned, repositioned, or transferred.**
   a. True
   b. False

4. **Which class of herbs generally is *not* used clinically?**
   a. High-tannin containing
   b. Cathartic laxatives
   c. Anticholinergic
   d. Coumarin-rich

Attention CME Subscribers

Due to an editorial error, a mistake was made in the CME numbering of the July issue of *Psychiatric Medicine in Primary Care*. Please renumber the questions so that the questions are numbered 26-30. We regret any confusion this may have caused. ❖

Readers are Invited...

Readers are invited to submit questions or comments on material seen in or relevant to *Psychiatric Medicine in Primary Care.* Send your questions to: Neill Larmore—Reader Questions, *Psychiatric Medicine in Primary Care*, c/o American Health Consultants, P.O. Box 740059, Atlanta, GA 30374. For subscription information, you can reach the editors and customer service personnel for *Psychiatric Medicine in Primary Care* via the Internet by sending e-mail to neill.larmore@ahcpub.com. We look forward to hearing from you. ❖

In Future Issues:

Long-term Treatment of Depression in the Elderly