

Integrating Palliative Medicine into the Care of Persons with Advanced Dementia: Identifying Appropriate Medication Use

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OBJECTIVES: To evaluate the feasibility of developing consensus recommendations for appropriate prescribing for patients with advanced dementia using a new conceptual framework and to determine the frequency of inappropriate medication use based on these recommendations in a small sample of patients with advanced dementia.

DESIGN: Medication data were obtained using chart review. Recommendations for appropriate prescribing were achieved using a modified Delphi consensus panel.

SETTING: Three long-term care facilities.

PARTICIPANTS: Thirty-four patients with advanced dementia enrolled in the Palliative Excellence in Alzheimer Care Efforts Program were selected to evaluate medication use. Twelve geriatricians at the University of Chicago participated in the modified Delphi consensus panel.

MEASUREMENTS: Prescription and over-the-counter medications were recorded for the 34 patients. Following the modified Delphi process, medications were characterized into one of four categories for use in palliative care patients with advanced dementia: never appropriate, rarely appropriate, sometimes appropriate, or always appropriate.

RESULTS: Patients were taking an average of 6.5 medications at enrollment. Six patients were taking 10 or more medications daily. Consensus was reached ranking the ap-

propriateness of 69 of 81 medication classes for patients with advanced dementia. Overall, 5% of the 221 medications prescribed at enrollment were considered to be never appropriate, and 10 of 34 patients (29%) had been taking a medication considered to be never appropriate.

CONCLUSION: Based on these preliminary findings, consensus criteria for prescribing in advanced dementia are needed to decrease polypharmacy and reduce the use of medications that are of minimal benefit or high risk. *J Am Geriatr Soc* 2008.

Key words: polypharmacy; palliative care; Delphi technique

Advancing age is associated with an increasing number of morbidities, including coronary artery disease, diabetes mellitus, chronic lung disease, and dementia, which may ultimately become life-defining illnesses.¹ As such diseases progress, the goals of care often shift from curative or disease modifying to primarily management of symptoms.² Reconsidering and adjusting a medication regimen to fit changing goals is essential to provide better care. To improve the quality of prescribing, many medications previously indicated for the treatment of chronic diseases may need to be discontinued in patients with advanced disease near the end of life in order to promote quality of life and substantially reduce the burden on the patient, including costs and adverse effects.

Few studies have addressed whether current medication use in patients with advanced disease adheres to existing criteria of prescribing appropriateness. A retrospective review of insurance claims for medications used in the last year of life showed that 44% of Medicare + Choice beneficiaries received at least one medication considered inappropriate according to the Beers criteria,³ although the appropriateness of a medication may vary depending on the life-limiting condition for which it is prescribed. It seems intuitive that strict blood pressure control may provide

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symptomatic benefit in persons dying of congestive heart failure but may provide little short-term benefit or even worsen symptoms for persons dying of advanced dementia.⁴

Persons with advanced dementia are at greater risk of receiving overly aggressive care that may not align with the intended goals of therapy.⁵ At the same time, these patients often have a prolonged terminal phase of advanced illness and may experience many physical and psychological symptoms, including agitation, depression, constipation, and pain.^{6,7} Such patients could greatly benefit from improved use of medications near the end of life. Yet, to the authors' knowledge, no characterization has been made of previously indicated and appropriate medications that are no longer useful or have an unfavorable risk-benefit profile in patients with advanced dementia nearing the end of life.^{8,9}

A model of prescribing for patients late in life that takes into account important factors that can better individualize prescribing practices was previously described.¹⁰ It included considering whether a patient is likely to benefit from a particular medication by comparing the patient's estimated remaining life expectancy with the time until the medication benefit is achieved. In addition, the medication must fit into a logical treatment plan as determined by the concordance between the patient's goals of care and the treatment targets of the medication. For reasons described above, certain populations, such as patients with advanced dementia, may particularly benefit from this approach.

The purpose of this pilot study was to identify medications prescribed to a group of patients with advanced dementia and to develop consensus recommendations for appropriate prescribing for such patients in whom palliation of symptoms was the primary goal. A second purpose was to determine the frequency of appropriate and inappropriate medication use in patients with advanced dementia on the basis of the consensus criteria.

METHODS

Medication Use in Patients with Advanced Dementia

This study was part of the Palliative Excellence in Alzheimer Care Efforts (PEACE) Program, which sought to integrate palliative care into the ongoing care of persons with dementia incrementally from the time of diagnosis to the end of life.¹¹ Between July 1999 and June 2000, the PEACE investigators enrolled community-dwelling and long-term care residents with dementia. This analysis focused on patients with advanced dementia who were residing in one of three long-term care facilities. Eligible patients for this portion of the study had to have advanced dementia, defined as having a Functional Assessment Stages (FAST) score of 6E, 7A, 7B, or 7C. These scores correspond to patients who need assistance with bathing, dressing, and toileting; have fecal or urinary incontinence (FAST 6E), and may have minimal verbal ability and inability to ambulate (FAST 7C).^{12,13} For patients to be included, their primary physician had to determine that primarily palliative care was appropriate. Patients with less-severe dementia, defined as those having a FAST score below 6E, were excluded. Informed consent was obtained from the patients' proxy de-

cision-makers, along with verbal assent of the patient when feasible.

At a patient's enrollment in the program, demographic data and medical information were collected using a review of nursing home records and proxy interviews. Trained study personnel collected data using chart review using a standardized data extraction form, which included data on comorbidities based on the Charlson Comorbidity Index.¹⁴ All prescription and over-the-counter medication orders at enrollment, including as-needed medications, were recorded.

Consensus Panel Survey

Between January and April 2005, attending geriatricians on the faculty at the University of Chicago were invited to participate in a consensus panel survey that sought to rate medication appropriateness in persons with advanced dementia in whom palliation of symptoms was the primary goal of therapy. Survey participants did not provide or supervise any care for the subset of PEACE patients in this study.

Before the survey, participants received a packet of current literature regarding medication use in palliative care, as well as the previously developed conceptual model on which to base their decisions.¹⁰ In a questionnaire administered in a three-round modified Delphi process, the participants were asked to rate the appropriateness of a comprehensive list of individual medications or medication classes ($n = 81$ medications/classes).¹⁵ After Rounds 1 and 2 of the survey, participants were reminded of their responses and given feedback containing an anonymous summary of responses of all participants, which provided the opportunity to revise the medication appropriateness categorization on the basis of the group's responses. The aim of feedback in a modified Delphi process is to increase consensus with each successive round. Consistent with other modified Delphi methods, consensus for a medication or medication class was defined according to agreement on categorization by at least seven of the 12 respondents.¹⁶

The inclusion of 81 medications and medication classes was based upon the classification system of the British National Formulary,¹⁷ the United States Pharmacopeia and National Formulary,¹⁸ and the Lexi-Comp alphabetical drug index.¹⁹ The use of all three sources ensured a logical organization of medications into classes and minimized important exclusions. In some cases, individual drugs were the sole representatives of a class (e.g., finasteride, digoxin, clonidine) or were separated from other drugs in the same class because of clinically relevant differences (e.g., tamsulosin vs other alpha-blockers for use in benign prostatic hyperplasia, tricyclic antidepressants vs other antidepressants). Respondents were asked to place medications into one of four categories (see below) on the basis of their appropriateness for use in patients with advanced dementia. Respondents had the opportunity to add any medications not included that they thought were important in this context during Rounds 1 and 2, resulting in the addition of 16 medications or medication classes.

Participants were instructed to consider medication appropriateness based on the conceptual model provided and in the context of treating patients with moderate to severe dementia approximating FAST Stages 6E, 7A, 7B,

and 7C. Participants were asked to place medications into one of four appropriateness categories: never appropriate, rarely appropriate, sometimes appropriate, or always appropriate. Detailed descriptions were provided to help differentiate the categories along the spectrum ranging from never appropriate to always appropriate. Examples given included the following statements: medications with no use in palliative care that should be stopped or should not be started (never appropriate); medications seldom used in palliative care, likely to be stopped and unlikely to be started (rarely appropriate); medications with uses depending on their indications in palliative care that might be started and would be less likely to be stopped unless burdens or risks to the patient were present (sometimes appropriate); and medications that are useful in palliative care and could be continued or started without reservations (always appropriate).

Identification of Appropriate Medications in Patients with Advanced Dementia

After completion of the consensus panel survey, the consensus recommendations were used to classify the PEACE patients' medications at enrollment into one of the four appropriateness categories. The final consensus medication list was used to calculate the frequency of medication use in each category and of individual patient exposure to medications in each category.

RESULTS

Medication Use in Patients with Advanced Dementia

Patient characteristics at enrollment in the PEACE program are shown in Table 1. Thirty-four patients had been taking a total of 222 medications, with a mean \pm standard deviation of 6.5 ± 2.7 medications per person. Six people had each been taking at least 10 medications daily. The most commonly used medications were cardiovascular drugs, non-

narcotic analgesics, laxatives, vitamins, and antipsychotic agents. Eleven of 34 patients (32%) had been taking two or more cardiovascular drugs, the most common of which was a daily aspirin.

Consensus Panel Survey

All 12 geriatricians at the University of Chicago participated in the consensus survey. All were certified by the American Board of Internal Medicine with additional qualification in geriatric medicine, and three of the 12 geriatricians were also board certified in palliative medicine by the American Board of Hospice and Palliative Medicine. On average, respondents reported spending approximately 10% of their clinical activity providing palliative care, and all but three reported having received formal or informal training in palliative care.

All respondents completed the three rounds of the survey. As expected, increasing consensus was achieved over subsequent survey rounds. After Round 2, consensus still had not been achieved for 27 medications. After Round 3, consensus was achieved for 69 (85%) of the 81 medications and medication classes that were included. Consensus was not achieved for the following: aspirin, sedative-hypnotics, central nervous system stimulants, muscle relaxants, anti-vertigo agents (e.g., meclizine), calcitonin, iron supplements, red blood cell colony-stimulating factors (e.g., epoetin alpha), vitamins, mineral supplements, finasteride, and bladder stimulants. The full final list of medications and their appropriateness ratings are shown in Table 2.

Identification of Appropriate Medications in Patients with Advanced Dementia

The numbers of medications that had been prescribed in each appropriateness category are summarized in Table 3. Of 222 total medications, one was excluded from analysis because of an inadequate medication description (eye-drops). Of the 221 remaining medications, 51 (23% of the total) were drugs or drug classes for which there was insufficient agreement between consensus panel participants to rate appropriateness. Medications without consensus were vitamins ($n = 29$, 57% of those without consensus), aspirin ($n = 13$, 25% of those without consensus), iron, minerals, meclizine, finasteride, calcitonin, and bladder stimulants. Of the 221 medications, 68% were considered sometimes or always appropriate, whereas 11 of the 221 medications (5%) were considered never appropriate.

The numbers of patients taking medications in each category are summarized in Table 3. Although few of the medications taken by the PEACE patients were considered never appropriate, 10 of 34 patients (29%) were prescribed at least one medication the panel classified as never appropriate for patients with advanced dementia. This included acetylcholinesterase inhibitors, clopidogrel, estrogen, and 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase inhibitors (statins).

DISCUSSION

Long-term care patients with advanced dementia who were enrolled in a palliative care program had been prescribed many medications, with a mean of 6.5 medications per person and with 6 of 34 patients (18%) prescribed 10 or

Table 1. Characteristics of Patients (N = 34) Enrolled in the Palliative Excellence in Alzheimer Care Efforts Program

Patient Characteristic	Value
Age, mean (range)	83.8 (57–100)
White, n (%)	27 (79)
Female, n (%)	25 (74)
Primary dementia diagnosis, n (%)	
Alzheimer's disease	20 (59)
Vascular dementia	6 (18)
Alzheimer's and vascular disease	4 (12)
Parkinson's disease	3 (9)
Lewy body disease	1 (3)
Charlson Comorbidity Index, mean \pm SD	2.1 \pm 1.4
Functional Assessment Stage, n (%)	
6E	1 (3)
7A	18 (53)
7B	14 (41)
7C	1 (3)
Number of medications prescribed, mean \pm SD	6.5 \pm 2.7

SD = standard deviation.

Table 2. Appropriateness Rating of Medications from Consensus Panel

Always appropriate		
Antidiarrheals	Antiepileptic drugs	Expectorants
Laxatives	Anxiolytics	Lubricating eye drops
Antiemetics	Narcotic analgesics	Pressure ulcer products
Inhaled bronchodilators	Nonnarcotic analgesics	Lidoderm
Sometimes appropriate		
Proton pump inhibitors	Antidepressants	Insulin
Histamine-2 receptor blockers	Tricyclic antidepressants	Antihistamines
Beta-blockers	Antibacterials	Decongestants
Calcium channel blockers	Antivirals	Electrolytes
Diuretics	Antiparasitic agents	Nutritional supplements
Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers	Antifungal creams	Antiglaucoma drops
Nitroglycerin	Oral hypoglycemics	Antiinflammatory eye drops
Mucolytics	Thyroid hormones	Capsaicin
Inhaled corticosteroids	Antithyroid medications	Allopurinol
Antipsychotics	Corticosteroids	Colchicine
Rarely appropriate		
Alpha blockers	Antiandrogens	Appetite stimulants
Digoxin	Bisphosphonates	Bladder relaxants
Clonidine	Mineralocorticoids	Tamsulosin
Antiarrhythmics	Heparin and low molecular-weight heparins	Antispasmodics
Hydralazine	Warfarin	
Never appropriate		
Lipid-lowering medications	N-methyl-D-aspartate receptor antagonists (memantine)	Cytotoxic chemotherapy
Antiplatelet agents, excluding aspirin	Antiestrogens	Hormone antagonists
Leukotriene receptor antagonists	Sex hormones	Immunomodulators
Acetylcholinesterase inhibitors		
No consensus		
Aspirin	Antivertigo agents (meclizine)	Bladder stimulants
Sedatives and hypnotics	Vitamins	Iron
Central nervous system stimulants	Mineral supplements	Finasteride
Muscle relaxants	Calcitonin	Red blood cell colony stimulating factors

more medications per day. Broad consensus was achieved among surveyed geriatricians, demonstrating the feasibility of rating the appropriateness of a comprehensive list of medications for use in patients with advanced dementia based on a new model of prescribing for patients late in life. Applying these recommendations to this pilot study population, it was possible to categorize the appropriateness of most of the medications used in these patients, although consensus was not achieved for several commonly used

Table 3. Proportion of Medications in Each Appropriateness Category and Proportion of Patients Taking Medications in Each Appropriateness Category

Appropriateness Category	Medications Prescribed (N = 221 Medications)	Patients Taking Medications in Each Category (N = 34 Patients)
	n (%)	
Never	11 (5)	10 (29)
Rarely	8 (4)	7 (21)
Sometimes	82 (37)	31 (91)
Always	69 (31)	27 (79)
No consensus	51 (23)	24 (71)

therapies, including vitamins, aspirin, mineral supplements, and iron supplements.

The high rate of medication use in this population was similar to that in other studies of medication use in long-term care settings,²⁰ although to the authors' knowledge, this is the first study that attempted to comprehensively identify medications prescribed to patients with advanced disease near the end of life and to classify these medications as appropriate or not appropriate for continued use in palliative care. In 57 palliative care units in Germany, the most commonly used medications were opioids and nonopioid analgesics, steroids, laxatives, antiemetics, gastric protection drugs, antipsychotics, and anxiolytics.²¹ It was reassuring that the consensus panel considered these drugs to be sometimes or always appropriate. In addition, older patients were more likely than younger patients to take antihypertensives and antiarrhythmics,²¹ similar to the high use of cardiovascular drugs in this study.

Despite the harms of polypharmacy, many patients receiving palliative care will have medications added to their regimens to alleviate symptoms.^{22,23} A possible reason for the inability of palliative care interventions to decrease medication use is the lack of a systematic recommendation for reducing unnecessary medications, especially those for chronic diseases unlikely to manifest symptoms toward the end of life. Existing medication appropriateness criteria are not adequate to improve medication use for such patients, because previously indicated and appropriate medications may have diminishing benefits or rising risks for patients at the end of life.

The homogeneity of the respondents limits the validity of this consensus process; the participant geriatricians practiced in the same university setting and may have been influenced by their colleagues' clinical practices. A larger, representative consensus panel of experts from various backgrounds and settings is needed to extend the scope of these findings. However, despite this limitation, medications identified as always appropriate by the consensus panel show substantial overlap with medications identified in other studies as essential in palliative care.²⁴⁻²⁶

The different implications of using the term "appropriate," which this study employed, versus "essential," a term often used in palliative medicine recommendations, might explain differences in the rankings of some medications from those in other studies.²⁶ Labeling medications as

never appropriate implies the need to more aggressively limit or withdraw such therapy, and the survey participants might therefore have been more cautious about applying such an absolute term to medication use. The difficulty encountered in reaching agreement among survey participants with some medications such as aspirin, vitamins, and minerals may reflect the complex decision to label as “inappropriate” those medications that, although posing little risk or burden, also offer little benefit. Given that most of the patients took a vitamin or mineral supplement, and one-third took aspirin, this is an important area for further investigation.

Many medications have different (or multiple) indications that may make them more useful in palliative care, and some medications may be more appropriate if used only as needed rather than on a scheduled basis. Because medication indication and pattern of actual use were not captured in the study sample and were not distinguished in the survey, inappropriate prescribing may be overemphasized in this study. For example, aspirin may have been considered appropriate for periodic analgesic use but inappropriate for daily use for cardiovascular protective effects. Using an angiotensin-converting enzyme inhibitor for the indication of preventing diabetic nephropathy in a patient with advanced dementia might be considered inappropriate, whereas using one to relieve symptomatic congestive heart failure might be appropriate and worth the risk of drug interactions, safety concerns, and monitoring requirements.

Inappropriate prescribing may also be difficult to estimate because of changes in prescribing patterns over time, especially as new therapies are introduced and new indications are discovered or approved for existing medications. An example specific to this patient population is the use of acetylcholinesterase inhibitors, which were approved for the treatment of severe dementia after this consensus panel survey was concluded. Therefore, a consensus process should ideally be as concurrent as possible with the evaluation of medication use, and given the potential for controversy regarding medications such as acetylcholinesterase inhibitors, a panel should consist of a diverse group of representative experts in relevant fields.

This was a pilot study to evaluate medication use in patients with advanced dementia. The applicability of the survey results to a broader population with advanced disease is not clear. Given the small sample size, medication use in advanced dementia warrants further examination in larger samples and should aim to detect any correlation between comorbidities and medication use, as well as particular medication classes that may be overused. Further work should also aim at detecting actual burden or harm as a result of inappropriate prescribing at the end of life.

This study is one of the first to provide information quantifying medication use in patients with advanced dementia and to recommend specific medications as potentially inappropriate for use in such patients. This study is preliminary in nature and, as such, is not intended to serve as a clinical guideline for the treatment of advanced dementia. Rather, it demonstrates the need for and feasibility of such recommendations. Few studies have comprehensively evaluated medication use in palliative care, and most recommendations focus on optimizing quality of life by improving pain and symptom management,^{24–26} although

withdrawing and withholding any form of medical treatment, including medications, is also an important component of care in advanced disease.²⁷ Medications no longer appropriate for patients with advanced disease receiving palliative care should be identified to facilitate discontinuation of those that no longer conform with the goals of care.^{10,23} Discontinuing such medications at the end of life could improve quality of life and significantly reduce burdens on the patient. Future work based on this pilot study should extend the findings to a larger group of patients with advanced disease, using consensus recommendations from a larger, representative sample of experts. Further research is needed to better identify which medications are useful in patients with advanced disease and to provide a systematic way of approaching medication discontinuation.

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