Advanced Illness Care

Palliative Care Intervention for Choice and Use of Opioids in the Last Hours of Life

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Background. The purpose of this study was to evaluate the effects of a multicomponent palliative care intervention on choice and use of opioid pain medications for symptom control for patients dying in an acute care inpatient setting.

Methods. A preintervention/postintervention trial was conducted between 2001 and 2003. Participants were physician, nursing, and ancillary staff of inpatient services of an urban, tertiary care Veterans Affairs (VA) Medical Center. The intervention included staff education to better identify actively dying patients and a Comfort Care Order Set to guide care in the last hours of life. Data abstracted from computerized medical records of 191 veterans who died during a 6-month period before (N = 98) and after (N = 93) the intervention were used to examine changes in choice and amount of medication administered in the last 3 days of life.

Results. Findings show a significant increase in orders specifically for morphine from 47.4% to 81.7% (p < .001). Orders for hydromorphone or oxycodone did not increase significantly, and no patients had orders for meperidine or codeine. There was an increase in the administration of opioids from 16.7% to 73.0% of patients (p < .001). The amount of opioid administered (in oral morphine equivalents) increased from 31.9 mg/72 hours preintervention to 52.9 mg/72 hours postintervention (p = .12).

Conclusions. The results indicate that the availability of morphine as a preferred opioid and the number of patients who received opioid medication during the last 3 days of life increased after introduction of the inpatient palliative care program.

Key Words: End-of-life care—Palliative care—Comfort care—Inpatient—Physician practice—Veterans.

PAIN and dyspnea are among the most common symptoms experienced by patients at the end of life (1–5). Opioid medications are known to be effective for relieving pain not responding to nonopioid analgesics and for managing dyspnea that is not responding to other measures, such as oxygen (6). According to the World Health Organization, opioids are the medication of choice for pain management and can be safely administered in increasing amounts until the right dose is achieved for pain relief (7).

Opioids are widely used in home hospice programs in which providers have expertise in managing the symptoms of actively dying patients (8–10). However, most people in the United States do not die at home, but in medicalized settings such as hospitals and nursing homes (11–13). In these settings, patients may not be recognized as being near the end of life, and their suffering may not be properly appreciated or managed (14,15). In addition, the life-saving orientation of care in the medical setting often interferes with access to opioid pain medications and their use, resulting in poor symptom control. Multiple studies, in this country and others, have demonstrated that opioids are often underutilized in these settings, and many patients in hospitals and nursing homes receive inadequate or no treatment for pain (1,3,16–18).

To address the need for better symptom control at the end of life, a physician-led Inpatient Comfort Care Program was developed to improve the quality of end-of-life care in Veterans Affairs (VA) Medical Centers. Previous research on this program has shown that the intervention increased documentation and care plans for pain, dyspnea, and a number of other symptoms, and increased the proportion of patients who had orders for opioid medication available at the time of death (19). However, the presence of an order for opioid medication does not necessarily ensure that the most appropriate medication will be ordered or that the medication will be administered to the patient.

The purpose of the present study was to examine the effectiveness of this program to change outcomes related to the choice, availability, and administration of opioid medication in general for treating end-of-life pain and dyspnea in the acute care setting of a VA hospital.
OPIOIDS IN THE LAST HOURS OF LIFE

METHODS

Samples and Settings
The sample for this study consisted of the staff and patients at the Birmingham VA Medical Center (Birmingham, AL), a 135-bed urban medical center with tertiary medical and surgical inpatient services. In 2001, a broad-based Palliative Medicine Program was established to improve the quality of end-of-life care for patients in all settings served by the Medical Center. Under the broad umbrella of the Palliative Medicine Program, the Inpatient Comfort Care Program was established to improve the care of patients who would most likely die in the inpatient setting. This study assessed the impact of this Comfort Care Program on care provided to patients who died in the acute care inpatient settings of the hospital. The study was approved by the Institutional Review Board, which waived the requirement for informed consent.

Design and Measures
The study was a preintervention/postintervention trial, designed to evaluate the impact of the Inpatient Comfort Care Program on the processes of care provided during the last 72 hours of life, a period representative of the care of actively dying patients. Patient cases were identified postmortem, and outcomes were evaluated from the institutional perspective. Data on all inpatients whose deaths occurred during the 6 months prior to initiation of the program in 2001 (1/1/01–6/30/01) were compared to data on inpatients whose deaths occurred after the program was fully established (1/1/03–6/30/03). Data were derived from the Computerized Patient Record System (CPRS). Records were reviewed using a structured medical record abstraction tool designed to quantify processes of care at the end of life.

Orders for opioid medications were investigated in detail to determine the type and amount of opioid prescribed, and medication administration records were examined to ascertain whether patients actually received the medication in the last 72 hours of life. Amount of pain medication administered was determined by reviewing the doses of all opioids given in this time frame and converting the doses to oral morphine equivalents using a standard equianalgesic conversion table (20).

The Inpatient Comfort Care Program
Details of the Inpatient Comfort Care Program have been described previously (19). The program included three primary components: staff education, case identification, and implementation of a Comfort Care Order Set (CCOS). Hospital staff palliative care education was provided through the American Medical Association’s Education for Physicians on End-Of-Life Care (EPEC) training course and regular teaching rounds on the inpatient services conducted by the first author. Physicians, nurses, and other staff received comprehensive training in how to identify patients who were near the end of life (21–26) and in how to implement nursing care plans appropriate for this population, including management of pain and nonpain symptoms. So that staff on all shifts and floors of the acute care units could receive training, the training program was conducted in 1-hour sessions at 12:00 PM or 3:00 PM, in three cycles of 16 weeks each.

In-service training was also provided to pharmacists and administrative personnel to ensure that the inpatient staff had the resources and environment necessary to implement the care plans. The intervention included issuing new nursing and pharmacy policies and offering training in novel delivery systems, such as subcutaneous lines, so that nurses would have the tools and flexibility to deliver adequate pain and symptom management.

A major focus of the training was on learning to identify patients who were entering the actively dying process. Indicators included: preexisting Do Not Resuscitate (DNR) order; length of stay exceeding 7 days; bed confinement; semicomatose state; minimal fluid intake; inability to take oral medications; decline in function with no identifiable reversible precipitant; optimum disease-modifying therapy already received; declining renal function; failure to improve within 2–3 days of admission; diagnosis of cancer (hospital admission is a poor prognostic sign because most cancer treatment is now provided in the outpatient setting) (24,25). To promote case identification, a tool was designed to remind and assist staff to identify patients who were near the end of life. “Consider Palliative Care” included a list of simple screening criteria and was developed into a laminated pocket card that was widely distributed to physicians and other staff. The tool was adapted from guidelines published by the National Hospice Organization (26).

A set of comfort care plans was developed based on the best practices for care in the last days or hours of life as practiced in the home hospice setting and modified for use in the acute care inpatient setting (6,27–31). The CCOS was condensed into a laminated pocket card that was widely distributed to staff for easy reference (32,33). Among the Comfort Care interventions were management of pain and nonpain symptoms. The section of the CCOS that related to opioids encouraged the use of morphine and provided the physician with suggested orders for sublingual or parenteral opioids on a scheduled “offer—patient may refuse” basis instead of as an “as needed” (prn) order. This method was suggested to increase the availability of opioids in various formulations, and at scheduled intervals instead of prn, to increase access to opioids for pain or dyspnea. The “offer—patient may refuse” approach required nurses both to assess patient pain and dyspnea and to make available needed medication at every dosing interval.

Data Analysis
Because of the preintervention/postintervention design of this study nested within one hospital, deaths in the different intervention periods cannot be considered statistically independent. Because almost all statistical tests, including the chi-square test of proportions, assume independence, the nonindependence between observations and time periods preclude the use of common statistical methods.

To overcome this issue, randomization tests were used to test the research hypotheses (34). Specifically, the statistic of interest, typically the difference of proportions in the two time periods, was first calculated. Then, through a process of 1000 simulations, the distribution of this statistic was...
estimated assuming that the null hypothesis was true. Assuming that the null hypothesis is true implies that there is no association between outcome and time period, which allows the permutation or shuffling of observations between the two time periods. Keeping the number of observations in each time period constant, the data were randomly permuted 1000 times, and the observed value of the statistic of interest was recorded for each permutation. After the 1000 permutations, the true observed test statistic was compared against the simulated null distribution of the randomly permuted observations, and a $p$ value was estimated by counting the number of simulations that produced a statistic more extreme than the one observed in our data. All analyses were conducted using SAS 9.0 (SAS Institute, Cary, NC).

RESULTS

Characteristics of Participants

A total of 191 veterans who died in the hospital were identified (187 men and 4 women). Patients ranged in age from 37 to 93 years (mean = 67.8 years). Average length of stay was 11.2 days (range = 1–141 days). Characteristics of patients are presented in Table 1. The pre- and postintervention groups were not significantly different on any of these variables.

There were 98 deaths in the 2001 sample and 93 deaths in the 2003 sample. The sample used for this study differs slightly from that used in our previous report (19) due to stricter criteria for defining in-hospital deaths.

Pain Medication

Similar to our previous report, the availability of opioid pain medication at the time of death increased significantly from 55.7% to 82.8% ($p < .0001$). This increase in opioid orders was attributable primarily to an increase in orders for morphine sulfate, either as a parenteral or sublingual form, which would be appropriate for patients who are very near the end of life and may not be able to take other formulations of medications (Table 2). Morphine orders at the time of death increased from 47.4% to 81.7% ($p < .001$). There was a modest, nonsignificant increase in orders for oxycodone from 8.3% to 11.8%, but all of these patients also had morphine available as an order, such that they could have received breakthrough medication if needed. There were no orders for meperidine, methadone, or codeine in either group. Only 17.2% of patients did not have an opioid order active at the time of death, and almost all of them experienced sudden death precluding the use of the CCOS.

In the preintervention group, although 55.7% of patients had an opioid order at the time of death, only 16.7% of patients had actually received any opioid medication. In the postintervention group, this was increased to 73.0% of all patients receiving some opioid medications in the last 72 hours of life ($p < .001$). The mean amount of pain medication (in oral morphine equivalents) was 31.9 mg/72 hours (standard deviation [SD] = 37.7) in the preintervention group and increased to 52.9 mg/72 hours (SD = 55.9) in the postintervention group ($p = .12$). This result indicates a trend to a higher total dose of opioids, but it did not reach statistical significance, due in part to the large variability in doses received by individual patients.

DISCUSSION

Previous research on this Comfort Care Program has demonstrated an increase in physician orders for opioid medication following this intervention (19). The results of the present study extend these findings by showing an increase in the number of patients actually receiving opioids. Prior to intervention, only 16.7% of patients received any opioid medication at all, which is much lower than reported rates of pain and dyspnea at end of life. After the intervention, 73.0% of all patients received some opioid medications in the last 72 hours, which is much closer to the reported rates of pain and dyspnea for which the medication would be indicated. The postintervention figures are within the range of common practice for home hospice and consistent with rates of opioid use reported in other studies of patients at end of life (35,36).

We had anticipated that physicians might be uncomfortable with ordering morphine and would choose instead to use nonrecommended medications, such as meperidine (37) or oral medications such as codeine and oxycodone, which, in tablet form, can be difficult for patients to swallow (32).

<table>
<thead>
<tr>
<th>Table 1. Characteristics of Patients and Length of Hospital Stay</th>
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<tbody>
<tr>
<td>Characteristics</td>
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<tr>
<td>Age, y, mean (SD)</td>
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<tr>
<td>Gender, % male</td>
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<tr>
<td>Race, %</td>
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<tr>
<td>African American</td>
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<tr>
<td>White</td>
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<tr>
<td>Primary diagnosis</td>
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<tr>
<td>Cancer</td>
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<td>Progressive neurological disease</td>
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<td>Heart disease</td>
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<td>Lung disease</td>
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<tr>
<td>Liver disease</td>
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<tr>
<td>Other</td>
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<tr>
<td>Length of stay in days (mean [SD])</td>
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</tbody>
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Note: SD = standard deviation.

<table>
<thead>
<tr>
<th>Table 2. Types of Opioids Ordered at the Time of Death</th>
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<tbody>
<tr>
<td>Type of Opioid</td>
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<tr>
<td>All opioid orders</td>
</tr>
<tr>
<td>Morphine</td>
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<tr>
<td>Hydromorphone</td>
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<tr>
<td>Oxycodone</td>
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<tr>
<td>Meperidine</td>
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<tr>
<td>Methadone</td>
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<tr>
<td>Codeine</td>
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<td>Fentanyl</td>
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Note: NA = not applicable.
However, in the postintervention group, there was indeed an increase in orders for morphine as the preferred opioid and increases in orders for opioids in forms and routes recommended by the Palliative Care and Hospice Opioid Dosing Guidelines and the American Pain Society (38–40).

The results of this study also indicate that the Comfort Care intervention enabled nurses to administer opioid medication to the dying patients significantly more often and at a rate that would be more consistent with the reported rates of pain and dyspnea in this patient population. The absence of clear ethical guidelines concerning the professional obligations of nurses who administer opioids may contribute to the undertreatment of pain and suffering (41). Education on the nature and purpose of end-of-life pain management is essential to overcoming misconceptions surrounding opioid use in general and fears of addiction in particular.

In addition to the education that nurses received, the specific “offer—patient may refuse” opioid order may have enabled them to use the opioid more effectively. Assessing the patient’s need for medication at regular dosing intervals is potentially more effective than prn orders for getting pain medication to patients. Regular assessments may increase patients’ awareness that medications are available to help pain and dyspnea and allow family members to provide assessments for patients unable to speak for themselves.

In this study, we found that the difference in amount of pain medication between the pre- and postintervention groups was not statistically significant. The amounts of opioid administered were lower, even in the postintervention group, than those reported in some studies of patients in home hospice (36). However, this could be due to earlier recognition of the dying process in most home hospice patients, allowing weeks to months for upward dose titration. Our sample was composed of hospitalized patients who frequently are not recognized as being in the dying process until very near the time of death, and therefore would not have had the time or need to escalate the dose of opioid. Consistent with findings in several other studies (10,36,39,42,43), our analysis confirmed a wide variability in amount of pain medication a patient received. This variability reflects considerable individual differences in the amount of opioid needed due to symptom severity and relative effectiveness of the opioid due to variable sources of pain and differences in metabolism (44).

It is a limitation of this study that the intervention was evaluated in a single site using a preintervention/post-intervention design without a control group for the potential effects of secular trends. Thus, it is possible that the changes in opioid use could be due in part to factors other than the intervention—for example, broader changes in medical education or acceptability of opioid use. However, no other programmatic changes were implemented during the time frame of the intervention that reasonably could account for the changes we observed. Furthermore, data on location of death from five other VA hospitals in the geographic region indicate increases in the proportion of deaths occurring in the intensive care unit (ICU) during the timeframe when, as previously reported, ICU deaths were decreased in the present study (19). To overcome this limitation, research is ongoing to replicate these findings in other inpatient settings using an appropriate time series control design.

**Conclusion**

The results of this study indicate that the availability of morphine as a preferred opioid and the number of patients who received opioid medication during the last 3 days of life increased after introduction of the inpatient palliative care program. Good control of pain and dyspnea can translate into improved quality of care and provide more patients and families with the opportunity for a “good death.”

**Acknowledgments**

This work was supported in part by a grant from the Project on Death in America (Faculty Scholars Program), Open Society Institute, to Dr. Bailey.

We thank Deborah M. Saunders and Joe Lindsey programming; Janice Taylor, Kevin Harris, and Martha June for medical record abstraction; and Kate Clark Wright for data management.

This work was presented at the 2006 Annual Assembly of the American Academy of Hospice and Palliative Medicine (Nashville, TN).

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**References**


Received August 9, 2007
Accepted March 28, 2008

Decision Editor: Darryl Wieland, PhD, MPH