Treating Infections near the End of Life

- *Betty R. Ferrell, PhD, RN , February 03, 2020*

How many times in your nursing career has a parent or family member turned to you and said, "What would *you* do?"

Most likely, many times, if nurses kept count, and it's rarely an easy question to answer. Nurses are at the bedside and in contact with the patient and family much more frequently than any other healthcare provider. This means that nurses often witness family members wrestling with decisions about the care of their loved ones. One of these decisions is whether to start or continue antibiotic treatment for an infection in a patient with a poor prognosis who is nearing the end of life.

The goal of palliative care is to promote comfort and quality of life for patients with serious illnesses. Palliative care clinicians and others who care for seriously ill patients nearing the end of life seek to balance providing enough care to ensure comfort while avoiding care that could diminish quality of life. Thus, a decision about a treatment such as antibiotics, which is relatively simple in any other patient, becomes complicated and difficult in the final weeks or months of life.

Antibiotic treatment near the end of life is actually quite common, especially in patients with cancer. Antibiotics are often continued up until the day before death, even in patients whose death is expected and are otherwise receiving only comfort care. But when the overriding concern is the patient's comfort, does treating an infection with antibiotics lessen or worsen the symptom burden?

In a review of eight studies that measured symptom response following antimicrobial therapy in hospice or palliative care patients, symptom improvement varied by the type of infection driving the need for antibiotic treatment. Patients with urinary tract infections (which are known to cause the uncomfortable symptoms of urgency and burning with urination) experienced the greatest improvement from antimicrobial therapy.

Other research has pointed to additional factors to consider when making decisions about antibiotic therapy, some of which are not well recognized. These include drug-drug interactions, adverse effects such as nausea or diarrhea, development of secondary infections, cost, the need for follow-up cultures and blood work, and delays in transitioning patients to hospice or palliative care settings (for example, if an intravenous line is required for antibiotic administration).

Vaughan and colleagues created an antibiotic decision tree that nurses and others can use to guide patients and families in clinical and ethical decision-making surrounding the medical treatment of infections near the end of life. In most cases, when the overarching goal is to keep the patient comfortable but not to prolong life, antibiotics aren't used. However, in patients who are expected to survive to benefit from the administration of antibiotics that carry a low likelihood of burdensome symptoms, a trial of antibiotics may offered. Even in patients who still desire aggressive care and prolongation of life, antibiotics would not be indicated if they are deemed to be ineffective or harmful, according to the decision algorithm. The final decision to treat, or not treat, an infection is highly individual and must always be guided by the key question: Is treatment consistent with the individual goals of this patient?

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Ethical and Clinical Considerations in Treating Infections at the End of Life

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Patients often affirm the goal to pursue comfort at the end of life, although clinicians may struggle with how best to provide comfort and face the ethical dilemma of treating or allowing a suspected infection to unfold. Treating an infection at the end of life does not allow for uniform improvement in symptoms and more time with family and friends. Additionally, there is potential for burden to the patient or health care system and treatment may occur to the exclusion of other comfort measures. Currently, the practice of providing or forgoing antibiotics at the end of life is variable, and literature supporting best practices can be contradictory. Data to support the use or withholding of treatment have been scant and vary across settings and patient populations. We review common obstacles providers face, prognostication tools that may assist in clinical decision making, the ethical support for withholding therapy, and how to factor in potential burdens of treatment. We propose that nurses, whether at the bedside in an acute care or nursing facility or in the home setting as a member of the interdisciplinary home hospice team, are uniquely qualified to help patients and families navigate this challenging clinical decision.

KEY WORDS

antibiotics, antimicrobials, comfort care, end of life, ethical, hospice, nursing, palliative, prognostication, withhold

CASE PRESENTATION

An 84-year-old man with progressive Alzheimer dementia, diagnosed 8 years prior, with hypertension and diabetes is brought to the emergency department from home when his wife notes increased somnolence, cough, and fever for 2 days. On evaluation, he meets criteria for sepsis with leukocytosis, fever, and hemodynamic stability. He is diagnosed with aspiration pneumonia, fluid resuscitated, and started on broad-spectrum parenteral antibiotics. At baseline, he is hand-fed by his wife, bedbound, and nonverbal. He is incontinent to bladder and bowel but will gesture or attempt to verbalize at baseline. In addition to his wife, the patient has a home health aide who comes in 3 times per week and home health nursing once per week to assist in caregiving. He also has 3 children in the area who rotate staying overnight to assist with his care. The patient and the wife have support through their church as members visit weekly.

On day 2 of hospitalization, the family meets with the primary team and reviews his previously stated wishes. There are no advanced directives, but he previously indicated to his wife and children that he did not want to be kept alive on machines. The family has already agreed upon an Allow Natural Death in light of these wishes. His wife and children now concede that his quality of life has deteriorated, and they do not want him to suffer. He was formerly a fisherman and hunter and was active in his church and community. His wife mentions that over the past few months she has increasingly felt guilty as she believes "he would never have wanted to live this way." He appears comfortable on examination. Plans are made to transition fully to comfort care and go home with hospice the following day. He cannot swallow, and all medications are being provided parenterally. What should be done with his antibiotics? If they are continued, for how long should the treatment course be and by what route?

INTRODUCTION

When discussing end-of-life care, patients often affirm the goal to "be as well as I can, for as long as I can." The challenge for the clinician is to choose a treatment plan that is individualized and aligned with a patient's and family's goals while balancing the burden versus benefit of treatment in the context of prognosis. Treatment with antibiotics does not allow for uniform improvement in symptoms or guarantee more time with

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family and friends.[1] Additionally, there is burden associated with treatment, which may negatively affect the patient or health care system or can result in the exclusions of other comfort measures.[2] However, data to support the use or withholding of treatment have been scant and vary across settings and patient populations. This makes the decision of whether to treat an infection at the end of life very complicated, both medically and emotionally. Common questions that providers face are whether treatment will improve survival, compounded by the uncertainty of prognostication; whether it is ethical to withhold therapy; and how to factor in potential burdens of treatment. We attempt to address these concerns and present data and an algorithm to help clinicians navigate the decision-making process for antibiotic treatment of an infection at the end of life. We propose that nurses, whether at the bedside in an acute care or nursing facility or in the home setting as a member of the interdisciplinary home hospice team, are uniquely qualified to help patients and families navigate this challenging clinical decision.

The use of antibiotics at the end of life is highly variable. In a study of hospitalized patients with advanced cancer, the authors found 87% of patients received antibiotics in the terminal hospitalization, and fewer than 50% of those met standard criteria for documenting an infection.[3] A national survey of more than 3000 home hospice patients identified that 27% of patients receive antibiotics in the last 7 days of life, and of those, only 15% had documented infection; the authors concluded that their results were irrespective of region, diagnosis, or socioeconomic status.[4]

Cancer patients seemingly have among the highest use of antibiotics at the end of life, even those in whom death is expected and the clinical decision is to "transition to comfort care." In one study, after patients were "transitioned" to a more comfort-based care plan, antibiotics were continued in up to one-third of patients, and the eventual discontinuation was at approximately 1 day prior to death.[5] Although treatment with antibiotics for a suspected infection can be part of a plan to provide comfort care, one questions whether that benefit was still present in the patients 1 day prior to death. In advanced dementia, when there is a fairly predictable decline allowing families more time to plan, patients still receive antibiotics at the end of life. In one study, 42% of patients with advanced dementia in a nursing home received antibiotics within the last 2 weeks of life.[6] Authors in this study do not address if treatment was initiated because it was consistent with those patients' goals; nor do they define intended benefit of treatment (symptom relief, increase in survival); rather, the study surveys antibiotic use and characterizes the targeted infections.

The use of antibiotics is considerable even in those who have indicated a preference for less aggressive treatment at the end of life. In one study, 15% of patients who were placed on "comfort care" orders were still on antibiotics 24 hours later.[7] Again, the author does not specify if this decision to continue antibiotic therapy was based on an individual goal or what was the intended benefit of treatment; rather, the study intent was to survey prevalence.

THE CHOICE TO TREAT WITH ANTIBIOTICS

Of all factors that go into decision making, the goal of reducing symptom burden may be the most compelling argument leading to treatment. But does antibiotic treatment actually reduce symptoms? The data supporting relief of symptoms are variable, and relief is inconsistently measured. In a systematic review of 11 studies from 2001 to 2011, there was wide variability in antibiotic use in hospice or palliative care settings and considerable inconsistencies in the definition of improvement, ranging from resolution of fever, to improvement in score on a standardized symptom assessment scale. Only 1 study reported quantitative data, utilizing the Edmonton Symptom Assessment Scale to measure symptomatic benefit.[7] In studies that do show benefit in treatment, the improvement varied by site of primary infection. The literature appears to support that, although survival was unaffected, patients at the end of life with symptomatic urinary tract infection likely derive the most relief of symptoms when treated with antibiotics. There are few data that show treating infections in the respiratory tract, oral cavity, or skin with antibiotics leads to symptomatic improvement.[8] However, in a 2016 retrospective study with palliative care cancer patients, the authors identified a trend toward benefit in symptom relief among those cancer patients who presented with sepsis or presumed sepsis, although notably they did not find similar benefit in those with urinary tract infections, an infection positively linked in prior studies with treatment.[9]

Another factor that may lead to use of antibiotics at the end of life is the desire to prolong survival. However, no rigorously conducted study to date has reported the survival outcomes of patients with a suspected infection at the end of life who were treated versus those where treatment was not provided.[1]

Clinicians often perceive that antibiotics are less burdensome than other life-prolonging therapies, such as mechanical ventilation, hemodialysis, transfusions, or artificial feeds. These interventions are often characterized as "aggressive care," whereas antibiotics are more likely to fall under "usual care," thus receiving less scrutiny.[10] In discussions with patients and families about transitioning toward comfort care, there is a potential for the clinician to use antibiotics as a "bargaining chip" to negotiate for the withdrawal of other perceived more burdensome therapies such as hemodialysis or ventilator support.[11]

BURDENS OF ANTIBIOTIC TREATMENT

The burdens of antibiotic use often go unappreciated. Antimicrobial adverse effects including diarrhea, allergic reactions, nausea, and anorexia are not negligible. There is the potential that antimicrobial use may necessitate the use of a peripheral intravenous line, leading to increased discomfort, cost, and burden to both patient and provider. There are also significant drug-drug interactions with antimicrobials and medications utilized at the end of life. One problematic drug-drug interaction for patients is antimicrobials and methadone. Methadone, often preferred in hospice for its long half-life, affordability, and ease of oral administration, inhibits the CYP3A4 enzyme and thus makes it dangerous, even potentially deadly, when combined with fluoroquinolones or macrolides.

Additionally, there is potential for the development of secondary infection from antimicrobial use, such as *Clostridium difficile*. Even if a secondary infection is avoided, questions of antibiotic stewardship cannot be ignored as antibiotic resistance remains of principal concern in patients who reside in a nursing home or acute care facility.[2]

Finally, the continuation of parenteral antibiotics can often result in a delay to the transition to more comfort-based environment prolonging a patient's hospital course, resulting in additional invasive and costly testing. Because of the concerns over costly antimicrobial treatment often not covered in a hospice model, patients who receive antibiotics often will be required to complete the course in an acute care facility. This delay in the transition to a more comfort-based environment can result in a delay in receiving the expertise of palliative symptom management.

ETHICAL CONSIDERATIONS

As with all medical decision making at end of life, the perspective of the patient and family should be the lens through which decisions are made. The principle of respect for autonomy gives the patient and family the right to request or reject medical treatment based on their values and beliefs. At the same time, clinicians are tasked with balancing benefit versus harm and action versus inaction. The absence of supportive data concerning the use or nonuse of antibiotics at the end of life makes this balance more difficult to achieve.

Ethical concerns may compel a provider to either offer or forgo antimicrobial treatment. At the end of life, clinicians want to provide the best comfort care possible but do not necessarily want to shorten what little time a patient has. Clinicians might struggle with the decision of forgoing antibiotics even when the family's goals of care are clear that the priority is comfort, as there is a perception that not offering antimicrobials for a suspected infection will shorten the prognosis.

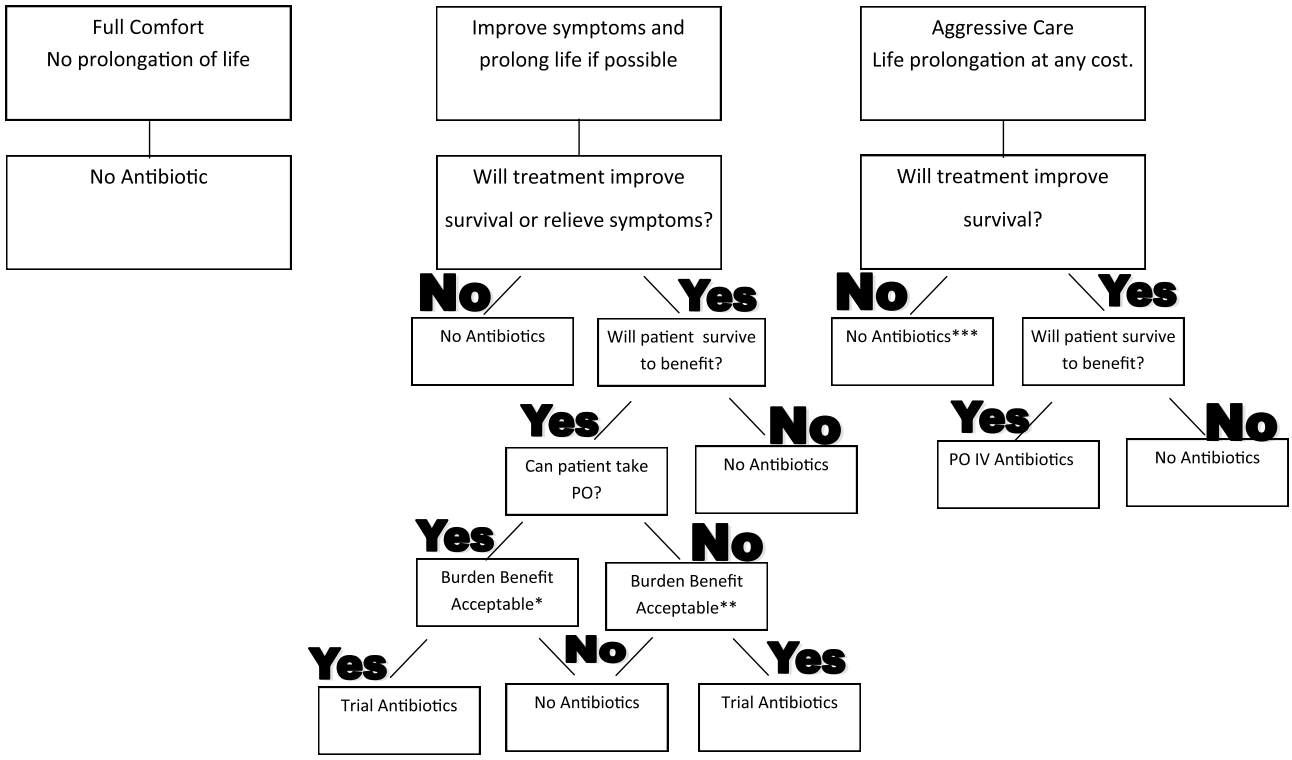
Conversely, a clinician may be concerned about crossing the ethical principle of "treatment futility" in offering antibiotics to a patient who is at the end of life where little benefit is expected from antimicrobials; however, discussing futility with families is often avoided. Families may still cling to hope or even insist that the clinician in such a scenario do "everything possible" to save their loved one; broaching the topic of treatment futility can come across as a clinician's attempt to cut costs, rather than a desire to avoid harm by offering burdensome therapy. Families whose goals have been for more aggressive care can perceive the discontinuation of antimicrobial treatment as the clinician "giving up." Clinicians might choose to avoid a heavy emotional conversation, and therefore providing or continuing antimicrobial treatment can be considered the path of least resistance.

Another ethical consideration is clinician's fear that in treating an infection at the end of life they are prolonging the dying process; we propose this concern is an even more challenging conversation as families often only wish for more time. Prolongation of the dying process, while a fear of the clinician, may be seen as the opposite to a family—the hope for prolonging life. Yet in the patient in whom death is imminent, continuation of antibiotics may in fact prolong the dying process. Similarly, the concern of prolonging the dying process is one that must be evaluated through the perspective of the family. In the case presented, the patient's wife conceded that she was fearful that her husband would suffer further in a condition of which he would have never chosen for himself. This case gives rise to the difficult ethical dilemma: Is this life or death prolongation?

It is essential to provide clinicians with the data for the ethical support of not providing those at the end of life with antibiotics, even in the presence of a known pathogen with known antimicrobial sensitivities if consistent with the patient's wishes. Evidence supports that antibiotics are not helpful, and even harmful, when death is imminent and patients cannot take oral medications or there is multisystem failure.[11]

We offer up a "thought algorithm," rather than an evidence-based guideline, which can assist clinicians in precisely this quandary and remind providers how individualized the treatment scheme is when considering the question for which the evidence is scant and patients' goals are prioritized (Figure).

Providing clinicians with supportive data on the benefits of comfort care at the end of life can assist in navigating the decision to forgo antimicrobial treatment. For example, in a patient with pneumonia, pursuing symptom management with opiates for the relief of cough or dyspnea, rather than using antimicrobial therapy to target the suspected pathogen, is a viable treatment if in line with a patient's wishes. In Blinderman and Billings'[12] article in the *New England Journal*



*Symptom/Survival Benefit Vs. Risks: Allergy, Diarrhea, Nausea, Anorexia, Drive/Drug Secondary Infection

**No Empiric Transfer Cultures Required. IV access needed. Potential loss of Hospice benefit

***Harmful or ineffective treatment should not be offered

FIGURE. Antibiotic decision tree based on goals of care.

of Medicine in 2016, the authors present the evidence-based approach for providing "comfort care" in the hospital. They recommend treating fever with antipyretics or steroids and only offering that antibiotics be considered when clinicians are targeting a specific infection and it is consistent with the family's or patient's goals. Others have proposed an algorithm for management decisions that begins with a goals-of-care discussion, incorporates prognosis, proposes clinicians consider a differential for other causes of fever, and offers the option to treat a targeted infection or refrain from treatment if consistent with the patient's or family's wishes.[13] Such studies have helped normalize the strategy for withholding potentially burdensome care at the end of life when the default for the acute care facility is otherwise aggressive.

GOALS OF CARE

In order to help guide a patient or family through the decision-making process, it is important to know both the patient's goals and the current state of his/her disease. Advanced directives and the increasingly accepted Physician Order for Life-Sustaining Treatment (POLST) form help inform clinicians of a patient's end-of-life preferences.[14] Physician Order for Life-Sustaining Treatment is distinguished from the traditional advanced directives, because it is completed in consultation with a health care provider and is usually reserved for those with a serious illness. Patients are afforded the opportunity to discuss the benefits or harms of therapy as it relates to their own goals of care. This allows patients to be more specific in their preference not only for life-sustaining measures such as cardiopulmonary resuscitation or ventilatory support but also for using or withholding antibiotics. An additional advantage is POLST document's transferability among health settings (ie, from an acute care facility to nursing facility). In nursing home patients with advanced dementia, health care proxies are often not contacted about suspected infections, so addressing this issue upfront with a POLST may lead to care that is more aligned to patient's stated goals.[15]

PROGNOSTICATION AND EDUCATIONAL TOOLS

The challenges of disease prognostication often belie the clinician's challenges in assessing whether a patient will

die of advanced disease prior to seeing a potential reduction in symptom burden with antimicrobials. It is essential that clinicians are aware of prognostication tools that can provide additional support for transitioning to comfort and result in reduced antibiotic use at the end of life.

Tools that assist clinicians in prognostication are widely available. Although imperfect, there are multiple disease-specific prognostic tools to assess risk in an individual patient. Finally, there are multiple assessments of functional status, such as Eastern Cooperative Oncology Group, Karnofsky, or Palliative Performance Scale, which when used in conjunction to disease-specific prognostic scales add to accuracy in prognostication.

The nursing profession has made an effort to provide nurses with formal palliative care training through the End-of-Life Nursing Education Consortium. This education has been an essential component of providing nurses with prognostic data, communication tools, and evidence-based medicine on symptom management, all of which have served as the foundation to help nurses advocate for patients whose wish is to pursue comfort care at the end of life.[16]

NURSING IMPACT

As identified in the Institute of Medicine's report "Dying in America," even when patients and families have opted for a symptom-based care plan at the end of life, the default mode of hospital treatment is acute care, and patient's wishes are often not prioritized.[17] Nurses are uniquely positioned to be a patient advocate in their ability to know the patient more intimately, question the default mode of aggressive care, and remind the care team to inquire about previously stated wishes.

Nurses are the first point of contact for patients and families in a wide variety of clinical settings: the ED, hospitals, home care, nursing homes, or other medical facilities. As such, they are in the best position to discuss the utility of using antibiotics at end of life. In the case study presented at the beginning of our article, a nurse with adequate training on symptom management, communication skills, and education on the ethical dilemma could have been able to ascertain the reason this patient presented to the ED, the details of the patient's decline, and the wife's wish for her husband not to suffer. The nurse has the opportunity to educate the wife with respect to how patients die of Alzheimer disease, the natural progression of the disease resulting in inability to manage oral intake leading to dehydration and urinary tract infection or aspiration and pneumonia, and how at the use of antibiotics may or may not be of benefit. The nurse may have been able to share that the decision about whether to prolong life in the end stage of Alzheimer disease with antibiotics is less a medical decision than it is a personal, family decision about end-of-life wishes. If the case presentation had involved a nurse in a hospice care setting, it would have allowed for ongoing conversations with the patient and family at different decision points along the way, as she developed a relationship founded in trust; there may have been options offered prior to ED presentation before the family felt the situation had become too urgent.

Nurses have the unique opportunity to lead these discussions at the bedside and allow the patient and families to understand the harm/benefit of antibiotics at the end of life. In a piece in ONS Voice, Dr Ferrell has advocated that for nurses "solid knowledge of pain and symptom management, excellent communication skills, and skill in spiritual and psychological care are important." But "EOL is also a sacred time and we are very, very fortunate to have the opportunity to be present with patients and families at EOL."[18]

CONCLUSIONS

Ultimately, the questions to consider prior to treating or forgoing treatment of a documented or suspected infection in an individual patient vary, as does a patient's goal in his/her care. Clinicians are likely to consider the functional status of the patient, the prognosis or stage of illness, and the degree of multisystem involvement when making treatment decisions. However, equally important are the concerns of delaying transition to a more comfort-based setting, prolonging the dying process, providing drugs that are inconsistent with a patient's goals, increasing the reservoir for resistant pathogens, and increasing health care cost.[10,11]

The factors affecting the decision to treat an infection or not are highly individual and depend on personal characteristics of the patient and family, the psychosocial circumstances, a patient's religious beliefs, and cultural context. It is important as the clinician to explore all these factors when discussing antibiotics at the end of life; most importantly, the decision should be guided by the central consideration: Is treatment consistent with the individual goals of the patient?

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