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Antimicrobials at the End of Life:

An Opportunity to Improve Palliative Care and Infection Management

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Patients in the final stage of an advanced illness often face challenging decisions about the direction of their overall medical care and treatment of specific complications that occur as the end of life approaches. Infections and febrile episodes are among the most common acute complications experienced by terminally ill patients.

Close to 90% of hospitalized patients with advanced cancer receive antimicrobials during the week prior to death,[1] and 42% of nursing home residents with advanced dementia are prescribed antimicrobials during the last 2 weeks of life.[2] Approximately one-quarter of hospice recipients, for whom the intended goal of care is comfort, receive antimicrobials during the final weeks of life.[3,4] Research suggests that antimicrobials are commonly prescribed to dying patients in the absence of adequate clinical symptoms to support a bacterial infection.[4,5] How decisions for suspected infections are made in these patients warrants increased scrutiny by clinicians, patients, and family members.

Risks and Benefits

Although antimicrobial use may be viewed as relatively less burdensome than other potentially life-prolonging interventions (eg, intubation, dialysis), risks of this therapy are not trivial, especially among frail patients with advanced disease. Adverse outcomes of antimicrobial administration include drug reactions, drug-drug interactions, and *Clostridium difficile* infection. Moreover, the evaluation (bladder catheterization, chest radiographs, blood draws) and treatment (intravenous lines) of suspected infections can contribute considerable burden in terminally ill patients, particularly when hospitalizationisinvolved.[6]

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Antimicrobialexposureisthe most important factor associated with the acquisition of multidrug-resistant organisms among patients at the end of life and is an increasing public health concern across care settings.[5,7]

Two potential benefits of antimicrobials, prolonged survival and symptom relief, may motivate physicians to prescribe these drugs when treating terminally ill patients. No randomized trials have been conducted examining these outcomes in this population. A systematic review[8] included 8 observational studies that had measured symptoms following antimicrobial therapy among patients receiving hospice and palliative care. None of these studies, which were published between 2002 and 2008, had comparison groups of untreated patients, and their methodological heterogeneity and contrasting findings further limited any conclusions about whether antimicrobials provide symptom relief for patients at the end of life.

A subsequent prospective study[9] reported greater comfort, albeit shorter survival, among patients with advanced dementia and suspected pneumonia who were not treated with antimicrobials compared with those who were treated. Another notable finding in this study was that the survival benefit associated with antimicrobial use (vs no treatment) was similar regardless of the route of administration, whereas the most aggressive treatment approaches (intravenous therapy or hospitalization) were associated with the greatest discomfort. To date, no rigorously conducted study has reported the survival outcomes of patients in the final stages of other terminal diseases who did and did not receive antimicrobials for suspected infections.

Approach to Decision Making

The decision of whether to prescribe antimicrobials can be challenging to address with terminally ill patients and their family members. Patients and families may incorrectly perceive antimicrobials as relatively benign and decisions about their use primarily under the purview of physicians. However, this issue should be approached using a framework of shared decision making similar to other end-of-life treatment choices.

To the extent possible, decision making about antimicrobial use should be done as part of advance care planning rather than in the moment at the time of a crisis, with treatment preferences documented in advance directives (eg, Physician/Provider Orders for Life Sustaining Treatment form). The first step is to inform patients and families that infections are expected near the end of life, and are commonly a terminal event. Individuals should understand that even if the infection were cured, the underlying illness (eg, metastatic cancer, advanced dementia) would remain.

Families and patients should also recognize what the evaluation of a suspected infection entails, and be advised about common scenarios that lead to unnecessary antimicrobial use (eg, asymptomatic bacteriuria). The risks and burdens of evaluating and treating an infection should be presented, as well as the possible benefits, while acknowledging the lack of high-quality outcome data. In addition, the option of a purely palliative approach should be described (eg, oxygen, morphine, antipyretics).

The ultimate goal of high-quality end-of-life care is to deliver treatment concordant with the patient's goals and preferences. After providing basic information, the next step is to help patients and families decide which approach best aligns with the stated goals of care. If the preference is only for treatments that optimize comfort, it is reasonable to recommend that no evaluation be initiated for a suspected infection and palliative care provided.

If the patient's goal is to live as long as possible, and the potential benefits of antimicrobials are believed to outweigh its burdens, then it is reasonable to proceed with a clinical assessment for suspected infection. Provided there is adequate evidence to support a bacterial infection, antimicrobials by the least invasive route should be initiated and may offer the same survival benefit as parenteral therapy or hospitalization, but with less patient discomfort and health care expenditures.[9]

Next Steps

Improving infection management and optimizing the delivery of preference-based, safe, and cost-effective care to dying patients are currently 2 of the most pressing public health issues. Improving the care of terminally ill patients with suspected infections would require merging best practices and research initiatives from both infectious diseases and palliative care, and the collaboration of experts from both fields. Several opportunities exist.

First, evidence-based and goal-directed counseling about infection management at the end of life must be a routine part of advance care planning and treatment discussions between clinicians and patients with advanced illness. Second, clinical algorithms aimed at improving antimicrobial stewardship from an infectious disease standpoint must also integrate treatment preferences when applied to patients near the end of life. Multifaceted clinical interventions that encompass patient and family counseling, clinician training, and appropriate antimicrobial prescribing should be designed and evaluated specifically for the palliative care setting. Third, to the extent that inadequate outcome data hinder decision making, researchers should consider whether there is adequate clinical equipoise and need to justify a carefully designed randomized trial comparing symptom control and survival among patients with advanced illness who receive antimicrobials vs high-quality palliative care for suspected infections.

Antimicrobials are commonly prescribed at the end of life. Just as many other aspects of end-of-life care are being reconsidered, improving palliative care requires reassessment of the best use of antimicrobials in the final weeks of life.

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