



The Use of Antibiotics in Hospice and Palliative Care Settings

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Antibiotics are commonly prescribed medications in the hospice and palliative care setting, as well as in many other healthcare settings. The overuse or negligent use of antibiotics is associated with the harmful consequence of fostering the development of antibiotic-resistant pathogens. Thus, there is an urgent need to critically examine and audit antibiotic use in all aspects of healthcare. In the status quo, there is a lack of consistent standards and guidelines surrounding the use of antibiotics in hospice and palliative care settings, leading to significant variations in how antibiotics are prescribed and administered in end-of-life care. It is apparent that greater thought needs to go into antibiotic decisions for patients receiving hospice or palliative care, especially considering the harmful consequences of the overprescription of antibiotics. The literature suggests that many clinicians prescribe antibiotics inappropriately for patients who would not benefit from their use or prescribe them without adequate documentation. Clinicians should be deliberate about when they prescribe antibiotics and adhere to the appropriate documentation standards and procedures within their institution or community. Future research should seek to generate generalizable knowledge about which patients will benefit most from antibiotic therapy during end-of-life care.

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BACKGROUND

The discovery and widespread adoption of antibiotic therapies—beginning with Alexander Fleming’s discovery of penicillin in 1928—have changed the course of medicine [1,2]. Given their proven effectiveness in treating bacterial infections, antibiotics are widely prescribed. Globally, antibiotics have been estimated to make up roughly 5% of the world’s pharmaceutical market [3]. In hospice and palliative care settings, reports suggest that rates of antibiotic use vary from 4 to 84% [4].

In addition to being a blessing, the popularity of antibiotics

has also been a burden, as pathogens with antibiotic resistance are becoming a growing concern [5,6]. Some have even called antibiotic-resistant bacteria “the greatest risk to human health” [7]. Each year, an estimated 2.8 million individuals are infected with antibiotic-resistant pathogens and 35,000 die from these infections in the United States alone [8]. Reducing the clinical overuse of antibiotics is one method to reduce the burden of antibiotic-resistant pathogens. Given the need to reduce nonessential antibiotic use, there is an urgent need to critically examine and audit antibiotic use in all aspects of healthcare [9]. The status quo is particularly troubling since estimates suggest that a majority of antibiotic use lacks definitive therapeutic

value [5,6]. Currently, there is a lack of consistent standards and guidelines surrounding the use of antibiotics in hospice and palliative care settings [10,11]. This has led to significant variations in how antibiotics are prescribed and administered in end-of-life care [12].

OVERUSE OF ANTIBIOTICS IN HOSPICE AND PALLIATIVE CARE

There is ample evidence suggesting antibiotics are currently overused in hospice and palliative care settings. One study published in 2013 examined 3,884 patients from the 2007 National Home and Hospice Care Survey and found that approximately 27% of patients received antibiotic medications, most of whom did not have a documented infection [13]. The finding that antibiotics may be unnecessarily prescribed to recipients of palliative or hospice care has been replicated by other studies. A similar study examined patients discharged from inpatient care to hospice care and found that 21.1% were prescribed antibiotics and 28.2% of the patients prescribed with antibiotics lacked a documented infection [14]. A study examining the clinical intentions of antibiotic therapies in patients discharged to hospice care found that the explicit rationale for antibiotics was documented in just 45.3% of cases [15]. A recent study of 230 hospice patients treated with antibiotics between April 2019 and September 2020 found that just 42% of antibiotics were appropriately prescribed; appropriateness was defined as meeting Loeb's Minimum Criteria for Antibiotic Initiation [11]. Even still, among patients appropriately prescribed antibiotics, only 60% experienced symptom relief [11]. Formal medication reconciliation for end-of-life patients is one way to reduce the unnecessary use of antibiotics in hospice and palliative care settings [16].

GOALS OF ANTIBIOTIC THERAPY AT THE END OF LIFE

The goals of antibiotic therapy for recipients of hospice and palliative care are different than the goals of antibiotic therapy in a non-hospice patient population. One of the main goals of hospice and palliative care overall is quality of life preservation during patients' final stages of life and letting patients "die

with dignity" [17–19]. Because of this, many have argued that the primary goal of antibiotic therapy in hospice and palliative care settings should be symptom relief [20].

Antibiotics are not universally effective at achieving this goal. For instance, many studies have reported variations in symptom relief based on infection type, and there is a consensus in the literature that symptom relief following antibiotic administration is not guaranteed during end-of-life care [4,19,20–22]. For instance, one study examining advanced cancer patients receiving outpatient hospice care found complete or partial symptom relief was achieved in 79% of patients with urinary tract infections, 46% of patients with oral cavity infections, 43% of patients with respiratory tract infections, 41% of patients with integumentary infections, and 0% of patients with bacteremia [19]. A systematic review of 11 studies conducted by Rosenberg et al. also showed that patients with urinary tract infections were the most likely to achieve symptom relief [4]. A more recent study from Sweden found the overall rate of symptom relief in end-of-life patients prescribed with antibiotic therapy was around 37% [22]. When antibiotics were used to prevent or treat sepsis in these patients, however, the rates of symptom relief climbed to 50% [22]. This could suggest that more severely infected patients benefit the most from antibiotic therapy. It is worth noting that symptom relief is a subjective metric, and some percentage of patients studied by retrospective analyses might have been affected by the placebo effect.

Writing in the journal *Bioethics*, Ford and colleagues outlined five ethical concerns associated with the use of anti-infective medications during end-of-life care [10]. For instance, do these medications prolong the dying process, are they "incongruent with a short life expectancy and goals of care," do they contribute to resistance among pathogens, and how might their use in hospice and palliative care burden the healthcare system? Ultimately, they concluded that further research is needed.

MOVING TO A CULTURE OF ANTIBIOTIC STEWARDSHIP IN PALLIATIVE CARE

Antibiotic stewardship is a term used to describe an approach

focused on optimizing the use of antibiotics in a given clinical setting [23]. Core tenets of antibiotic stewardship include: 1) measuring antibiotic prescribing; 2) improving antibiotic prescribing and use by patients and clinicians with the goal of minimizing inappropriate prescriptions; 3) minimizing incorrect or delayed diagnoses; and 4) ensuring the appropriate antibiotic medication and dose are chosen [24]. Two suggested methods to improve antibiotic accountability in healthcare settings include training for clinicians and strengthening the documentation standards surrounding antibiotic use [24]. Charani et al. [23] advocated making optimum antibiotic use the “path of least resistance” for clinicians. Preliminary evidence suggests this may be an uphill battle [25].

Having said that, conventional antibiotic stewardship can be tricky in the hospice and palliative care setting because the goals of care are different. There are conflicting reports regarding whether antibiotic use directly decreases mortality in end-of-life care [26]. This is likely due to immense between-patient variability and differing studies recruiting different numbers of patients who either showed improvement or did not show improvement in response to antibiotic therapy. Moreover, as discussed earlier, symptom relief can also vary immensely. Thus, there will not always be a right or wrong answer when it comes to determining whether antibiotic therapy should be initiated during end-of-life care.

The question of discontinuing antibiotic therapy in end-of-life care is also worth discussing. Stiel et al. [27] examined 88 cases where antibiotic therapy was discontinued. They found that the most common causes of antibiotic withdrawal were patient deterioration (41.4%), therapeutic insufficiency (25.7%), and patient wishes (14.3%). Since frequent evaluation of symptom relief is crucial to ensuring antibiotics are optimally distributed, providers will have to consider withdrawing or discontinuing antibiotic therapy for some patients. These may include patients who are not experiencing sufficient symptom relief to justify antibiotic therapy or patients who are experiencing significant side effects from the antibiotic medication.

AREAS FOR FURTHER RESEARCH

There are a number of areas where future research could

prove beneficial. First, the lack of a documented infection in many antibiotic patients has generally been assumed to be due to providers over-prescribing antibiotics. However, it could also mean there simply is a lack of adequate documentation of infections in recipients of hospice or palliative care, which has been reported before [28,29]. Thus, research examining the motivations and practices of clinicians who prescribe antibiotics would be crucial in precisely understanding how much over-prescribing is actually taking place. Related to this, it would be interesting to understand public perceptions surrounding the use of antibiotics in end-of-life care. One study reported that a significant share of antibiotic end-of-life decisions were based on familial wishes [15]. It is possible that families have incorrect perceptions about antibiotic therapy or that many clinicians do not fully disclose the harms associated with the inappropriate use of antibiotic medications, leading to their overuse.

Given that antibiotics have varying levels of effectiveness in relieving symptoms—based partially on the type of infection—further research aimed at better determining which patients would be good candidates for antibiotic therapy would be invaluable. Ideally, this research would lead to guidelines that take into account a patient’s medical history and current situation, as well as the likelihood they would suffer from a given infectious disease during end-of-life care.

Despite having the potential to offer insight, a randomized and blinded clinical trial where patients in one arm are given a placebo or withheld antibiotics may present ethical challenges [30]. However, non-blinded/non-randomized trials or observational studies do present limitations in this particular context. For instance, an observational study comparing patients who choose antibiotic therapy with patients who decline antibiotic therapy would suffer from selection bias. Namely, do patients who decline antibiotic therapy suffer from fewer or less intense symptoms than patients who elect to undergo antibiotic therapy? What other differences might be present between end-of-life patients who accept or decline antibiotic therapy? In any study examining end-of-life care, poignant questions remain as to what inclusion/exclusion criteria and endpoints should be used.

CONCLUSIONS

It is apparent that greater thought needs to go into antibiotic decisions for patients receiving hospice or palliative care, especially considering the harmful consequences of the over-prescription of antibiotics. The literature suggests that many clinicians prescribe antibiotics inappropriately in patients who would not benefit from their use or prescribe them without adequate documentation. Related to this, there might be a lack of knowledge or concern among patients, their families, and some providers about antibiotic resistance. Providers should be open about effectiveness concerns and antibiotic resistance with patients and families and closely monitor patients for symptom relief. They should be deliberate about when they

prescribe antibiotics and adhere to the appropriate documentation standards and procedures within their institution or community. Future research should seek to generate generalizable knowledge about which patients will benefit most from antibiotic therapy during end-of-life care.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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