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Brief Communication

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Ethical and Practical Issues with the Use of Antimicrobial Agents during the End of Life

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The use of antimicrobials in patients receiving end-of-life (EOL) care, which is generally defined as supportive care provided to patients anticipated to live less than 1 year, has been actively debated in the realm of palliative care medicine due to the nebulous nature of the topic. In this article, we explore the use of antimicrobial use near EOL as it relates to both the ethical and practical issues that face physicians. We also discuss the reasons underlying the scarcity of prospective studies on this topic.

Key Words: Anti-bacterial agents, Antimicrobial stewardship, Palliative care, Bioethics, Terminal care

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BACKGROUND

It has been consistently shown that over 50% of hospitalized patients, at the time they are deemed to be at the end of life (EOL) (defined as patients who are anticipated to live less than 1 year and receive supportive care [1]), receive antimicrobials [2]. Chun et al. reviewed 131 patients requiring palliative care consultation during their hospital stay, finding that 70 of these patients were deemed to have an infection. Piperacillin/tazobactam was the most frequently used antimicrobial, followed by vancomycin [3]. The study highlighted a high prevalence of empiric antimicrobial use in EOL care, with nearly 59% of suspected infections in the study being treated with these drugs [3]. Other studies have reported that up to 84% of patients received antimicrobials near the EOL [4]. The most rigorous study identified was conducted by Tagashira and colleagues, who found an average of 421 days of antimicrobial therapy per 1,000 patient-days in the last 14 days of patients' lives [5].

Despite the widespread use of antimicrobials at the end of life, several unanswered questions remain concerning this practice. These questions can be divided into ethical considerations and practical issues. The practical issues include identifying which types of infections are suitable for palliative antimicrobial treatment, determining the most appropriate route and duration of antimicrobial therapy to meet palliative needs, and understanding the impact of antimicrobials on the survival curve of patients receiving EOL care. A recent literature review has been published focusing on antibiotic stewardship in the context of EOL care [6]. However, this paper has a more expanded scope, as outlined below.

ETHICAL CONCERNS REGARDING THE USE OF ANTIMICROBIALS DURING END-OF-LIFE CARE

Ethical questions arise from concerns that the use of antimicrobials may lead to an unintended protraction of the dying process and a creation of a false hope for recovery, as well as ultimately delaying the transition to hospice care. Other concerns include the burden of maintaining venous access for

parenteral antimicrobials and the possibility of direct antimicrobial toxicity. Ethical questions also relate to the overall cost to the healthcare system both from a monetary standpoint [7] and from the perspective of increasing the reservoir of resistant pathogens [8]. Prescribing physicians should be cognizant of the aforementioned ethical problems and should weigh them against the benefits of the palliative effects of antimicrobials as a part of the shared decision-making process [9].

CHALLENGES TO STANDARDIZING THE USE OF ANTIMICROBIALS DURING END-OF-LIFE CARE

The lack of evidence-based standardization in antimicrobial use among EOL patients stems from a shortage of prospective studies on this subject. This absence of clear guidance from the literature may be partly due to the numerous variables that are challenging to control, complicating the design and implementation of such studies. For instance, distinguishing symptoms caused by an infection from those arising from the natural progression of an end-stage disease or its complications can be difficult. This challenge is exacerbated by the difficulty in assessing symptoms in patients who suffer from cognitive impairments, such as dementia or delirium, which unfortunately affect a significant number of patients at or near EOL [10]. Additionally, medications like opioids, commonly used for symptom management in EOL care, may obscure the independent palliative effects of antimicrobials.

WHICH INFECTIONS SHOULD WE PRIORITIZE FOR TREATMENT FROM THE STANDPOINT OF SYMPTOM CONTROL?

A central topic is the identification of the types of infections that are amenable to symptomatic management with antimicrobials. Reinbolt and colleagues performed a prospective study of 1,598 cancer patients enrolled in outpatient hospice, of whom 623 had one or more infections [11]. Overall, they found the highest benefit of antimicrobials in patients with urinary tract infections (UTIs), with symptomatic response in 79% of patients, followed by oropharyngeal infections, respiratory tract infections and skin and soft tissue infections. These findings regarding the types of infections in EOL patients and their response to antimicrobials have been corroborated by other retrospective studies [12-15]. Additionally, a review of 11 studies found that the treatment of UTIs with antibiotics provided the highest symptomatic relief, with improvements ranging from 67% to 92% [4].

WHAT ARE THE CHALLENGES TO FINDING THE OPTIMAL ROUTE FOR ADMINISTERING ANTIMICROBIALS AT THE END OF LIFE?

In terms of assessing the optimal route of administration of antimicrobials, we found no studies that directly compared the efficacy of parenteral (intravenous and intramuscular) versus oral antimicrobials for palliative care. Parenteral antibiotics at the EOL are typically used when patients cannot tolerate oral medications or when they exhibit severe symptoms, as determined by a physician. One study examined the use of parenteral antibiotics and discovered that single doses of intravenous or intramuscular antibacterials were as effective as longer courses of parenteral treatment [16]. Additionally, the study found that patients who received oral antibiotics following parenteral doses experienced better symptomatic relief than those who did not receive oral antibiotics after the initial parenteral treatment [16].

DO ANTIMICROBIALS AFFECT SURVIVAL AT THE END OF LIFE?

One important question is whether there is an unwanted increase in overall survival for EOL patients receiving antimicrobials. Reinbolt et al. observed no differences in overall survival (median days) between patients considered to have an infection and those not considered to have an infection. Similarly, no difference in overall survival was noted between patients who received antimicrobials and those who did not [11]. These findings are supported by other studies [5,17,18]. Conversely, a separate body of research indicates that antimicrobial therapy may lead to longer survival in patients receiving EOL care [12,19,20].

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THE EFFECT OF PALLIATIVE CARE CONSULTATION ON THE USE OF ANTIMICROBIALS

It is important to discuss the role of palliative care consultation and the impact of code status on the decision to administer antimicrobials in EOL care. Marra et al. [2] noted three studies [21–23] that identified a significant correlation between palliative care consultations and increased use of antimicrobials. This surprising correlation likely stems from the fact that patients who require palliative care consultations often have high morbidity and are therefore more susceptible to infections that necessitate antimicrobial treatment. In contrast, Tan and colleagues demonstrated that palliative care consultations were associated with a reduction in antibiotic use by as much as 40% in EOL patients [24], a finding that another study has supported [25].

Another study examined the impact of code status changes on antimicrobial use in the ICU during palliative care consultations. It found no statistically significant difference in the duration of inpatient antimicrobial use between patients who changed their code status from full code to do-not-resuscitate (DNR) or do-not-intubate (DNI) and those who did not [26]. However, at discharge, a significantly higher percentage of patients who remained full code were prescribed antibiotics compared to those who changed their code status to DNR/DNI. Another study highlighted that up to 17.6% of patients discharged to hospice were still receiving antibiotics, indicating substantial antimicrobial use even after a change in code status and transition to hospice care [27].

CONCLUSION

The use of antimicrobials during EOL care is debated for numerous reasons. This is likely due to a lack of standardization of treatment resulting from an absence of prospective studies that provide guidance. Furthermore, the few retrospective studies that tried to shed light on the topic presented discordant findings, posing further unanswered questions in relation to the use of antimicrobials in EOL care. We underscore the importance of conducting further investigations regarding this topic.

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CONFLICT OF INTEREST

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

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