

Overuse of antimicrobials in the end-of-life care: Factors influencing physicians' prescribing behaviors in treating patients with an advanced stage of illnesses in the robust era of antimicrobial stewardship

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REVISED ABSTRACT

Objective: Antimicrobials are frequently administered to patients with an advanced-stage illness. Understanding the current practice of antimicrobial use at the end of life and the factors influencing physicians' prescribing behavior is necessary to develop an effective antimicrobial stewardship program and to provide optimal end-of-life care for terminally ill patients.

Design: A 1-year retrospective cohort study.

Setting: A public tertiary-care center.

Patients: The study included 260 adult patients who were hospitalized and later died at the study institution with an advanced-stage illness.

Results: Of 260 patients in our study cohort, 192 (73.8%) had an advanced-stage malignancy and 136 (52.3%) received antimicrobial therapy in the last 14 days of their life; of the latter, 60 (44.1%) received antimicrobials for symptom relief. Overall antimicrobial use in the last 14 days of life was 421.9 days of therapy per 1,000 patient days. Factors associated with antimicrobial use in this period included a history of antimicrobial use prior to the last 14 days of life during index hospitalization (adjusted odds ratio [aOR], 4.86; 95% confidence interval [CI], 2.67–8.84) and antipyretic use in the last 14 days of life (aOR, 4.19; 95% CI, 2.01–8.71).

Conclusion: Approximately half of the patients hospitalized with an advanced-stage illness received antimicrobials in the last 14 days of life. The factors associated with antimicrobial use at the end of life in this study are likely to explain physicians' prescribing behaviors. In the current era of antimicrobial stewardship, reconsidering antimicrobial use in terminally ill patients is necessary.

INTRODUCTION

- Whether we use the antimicrobials for end-of-life patients is still controversial.
- Approximately 30% of antimicrobial use in the inpatient setting is unnecessary and has contributed to the development of various adverse events such as antimicrobial resistance and CDI.
- The purpose of this study was to examine current antimicrobial use during the last 14 days of the life of terminally ill patients and to assess the factors influencing physicians' prescribing behavior.

METHODS

Study design and Setting:

We performed a retrospective cohort study of antimicrobial use at end of life patients at a Japanese tertiary care hospital (a 790-bed hospital with 29 subspecialties) from January 2016 to December 2016.

Identification of patients

We initially enrolled all patients who died during index hospitalization within the study period at the study institution. We excluded those who died within the first 48 hours of hospitalization. We then screened potentially eligible patients reviewing their electronic medical records and subsequently identified patients with advanced stage of illnesses, who fulfilled the pre-specified criteria of advanced stage of illnesses. Two investigators (K.K. and Y.T.) manually performed the screening of eligible patients using these criteria.

Definition

Advanced stage of illnesses was defined as either active malignancies with advanced stages (e.g., stage III or IV malignancies), conditions or non-malignancy illnesses with the mostly progressed stages, or end-organ damages due to wide spectrum of non-malignancy illnesses, based on current guidelines or definitions used in previous literatures. We then categorized advanced stage illnesses as active malignancies, advanced stage of cardiovascular diseases (i.e., congestive heart failure), advanced stage of pulmonary diseases, end-stage of renal diseases, advanced stage of liver diseases, and advanced dementia.

METHODS (cont.)

Variables of interest and data collection

The variable of interest was defined as at least 1 day of either oral or intravenous antimicrobial therapy in the last 14 days of life in patients with an advanced-stage illness. The demographic characteristics, microbiological data, and clinical data were retrospectively obtained from the electronic medical records.

Statistical analysis

We performed multivariate logistic regression to predict the administration of antimicrobial agents in our study population. The factors associated in previous studies with antimicrobial use during advanced-stage illness and factors with $P < .10$ in univariate analysis were included in the final model. We assessed multicollinearity by examining the tolerance value and the Pearson correlation to ensure the independence of the explanatory variables. Variables were retained in the final model if $P < .05$.

RESULTS

Characteristics of study population

- In total, 742 patients who died at the study institution during the study period were screened for eligibility. Among them, 482 patients (65.0%) were excluded either because they died within 48 hours of admission ($n=290$; 39.1%) or did not have an advanced-stage illness ($n=192$; 25.9%).
- Of the 260 patients included in the study, 136 patients (52.3%) received antimicrobial therapy in the last 14 days of life and 124 patients (47.7%) did not.

Characteristics of patients who received antimicrobial therapy in the last 14 days of life

- Symptom relief was a primary indication for antimicrobial use in 60 patients (44.1%).
- Seventy patients (51.5%) received antimicrobial therapy until death, and 95 patients (69.9%) failed to achieve symptom relief via antimicrobial therapy.
- The total amount of antimicrobial use (DOT per 1,000 patient-days) in the last 14 days of life was 421.9 DOT per 1,000 patient days.

Table 1. Comparison of Patients with an Advanced-stage Illness with or without Antimicrobial Use in the Last 14 days of Life (n=260)

Variables	Received antimicrobials in the last 14 days of life, No. (%)			
	Total (n=260)	Yes (n=136)	No (n=124)	P value
Baseline characteristics				
Age < 65y	54 (20.8)	28 (20.6)	26 (21.0)	Ref.
Age 65-80y	140 (53.8)	72 (52.9)	68 (54.8)	0.89
Age > 80y	66 (25.4)	36 (26.5)	30 (24.2)	0.86
Male gender	166 (63.8)	84 (61.8)	82 (66.1)	0.47
Residential status prior to admission				
Home	234 (90.0)	121 (89.0)	113 (91.1)	Ref.
Long-term care facility	17 (6.5)	10 (7.4)	7 (5.6)	0.57
Acute-care hospital	9 (3.5)	5 (3.7)	4 (3.2)	0.82
Presence of illness/past medical history				
Congestive heart failure	34 (13.1)	22 (16.2)	12 (9.7)	0.12
Chronic lung diseases	45 (17.3)	32 (23.5)	13 (10.5)	0.01
Chronic liver diseases	63 (24.2)	36 (26.5)	27 (21.8)	0.38
Dementia	11 (4.2)	7 (5.1)	4 (3.2)	0.55
Hemodialysis initiated prior to index hospitalization	15 (5.8)	11 (8.1)	4 (3.2)	0.11

Variables	Received antimicrobials in the last 14 days of life, No. (%)			
	Total (n=260)	Yes (n=136)	No (n=124)	P value
Advanced nonmalignant illness due to primary advanced-stage illness	68 (26.2)	42 (30.9)	26 (21.0)	0.07
Charlson comorbidity index score ≤ 5	68 (26.2)	44 (32.4)	24 (19.4)	0.02
DNR order prior to the last 14 days of life	64 (24.6)	30 (22.1)	34 (27.4)	0.32
History of antimicrobial use prior to the last 14 days of life during index hospitalization	101 (38.8)	76 (55.9)	25 (20.2)	<.001
Transition to comfort measure as a primary treatment status prior to the last 14 days of life	67 (25.8)	30 (22.1)	37 (29.8)	0.15
Escalation of medical care in the last 14 days of life				
Central venous catheter placement	58 (22.3)	37 (27.2)	21 (16.9)	0.05
Arterial line for blood pressure monitoring	21 (8.1)	12 (8.8)	9 (7.3)	0.64
Vasopressor	37 (14.2)	28 (20.6)	9 (7.3)	0.002
Intubation	14 (5.4)	9 (6.6)	5 (4.0)	0.36
Platelet transfusion	27 (10.4)	20 (14.7)	7 (5.6)	0.02
Red blood cell transfusion	51 (19.6)	32 (23.5)	19 (15.3)	0.11
Total parenteral nutrition	24 (9.2)	17 (12.5)	7 (5.6)	0.06
Administration of palliative care in the last 14 days of life				
Antidepressant use	19 (7.3)	13 (9.6)	6 (4.8)	0.14
Anxiolytic use	35 (13.5)	23 (16.9)	12 (9.7)	0.10
Antipyretic use	200 (76.9)	120 (88.2)	80 (64.5)	<0.001
Analgesic use including narcotic use	170 (65.4)	84 (61.8)	86 (69.4)	0.20
Psychiatric care	33 (12.7)	20 (14.7)	13 (10.5)	0.31
No formal consultation with a palliative care team	207 (79.6)	113 (83.1)	94 (75.8)	0.15

Note. Ref., reference; DNR, do not resuscitate

Table 2. Predictors of Antimicrobial Use in the Last 14 Days of Life in Patients with an Advanced-stage Illness

Variables	Adjusted OR (95% CI)	P value
History of antimicrobial use prior to 14 days of life during index hospitalization	4.86 (2.67-8.84)	<.001
Antipyretic use in the last 14 days of life	4.19 (2.01-8.71)	<.001
Vasopressor use in last 14 days of life	2.73 (1.09-5.53)	.03
Chronic lung diseases	2.33 (1.05-5.20)	.04
Charlson comorbidity index score ≤ 5	2.18 (1.06-4.53)	.04

Note. CI, confidence interval. The outcome variable was the receipt of antimicrobial therapy in the last 14 days of life. Variables considered but not retained in the final model were age, advanced illnesses due to non-malignancies as the primary advanced-stage illness, central venous catheter use in the last 14 days of life, platelet transfusion in the last 14 days of life, no formal consultation with a palliative care team, and ventilator support in the last 14 days.

CONCLUSIONS

- The current study demonstrated that approximately one-third of patients who died in an acute-care hospital had an advanced or terminal-stage illness and that half of these received antimicrobials at the end of life despite limited efficacy of antimicrobials.
- The decision to initiate antimicrobial therapy at the end of life was likely influenced by patient factors as well as the physicians' prescribing behaviors.
- From the ethical and antimicrobial stewardship perspectives, we should reconsider antimicrobial use at the end of life to provide the best end-of-life care for patients with advanced-stage illness.