

The ICU pharmacist's contribution to antimicrobial optimization through routine pharmacist interventions

La contribución del farmacéutico de la UCI a la optimización del tratamiento antimicrobiano mediante intervenciones farmacéuticas rutinarias

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Abstract

Background: Antimicrobials are among the medication groups most frequently involved in medication errors and adverse drug events in the Intensive Care Unit (ICU). Despite growing evidence supporting the role of Critical Care Pharmacists (CCPs) in antimicrobial stewardship, their integration into ICU teams remains inconsistent across European healthcare systems.

Methods: A prospective observational study was conducted over five months in an 18-bed medical-surgical ICU at a tertiary-level hospital in Spain. All admitted patients were included. A specialist pharmacist reviewed daily antimicrobial prescriptions through the electronic prescribing system. Pharmaceutical interventions (PIs) were classified as proactive or reactive and categorised by intervention type according to a predefined taxonomy. A descriptive analysis was performed.

Results: A total of 331 PIs were recorded, of which 150 (45.31%) corresponded to antimicrobial therapy, representing the most frequently involved medication group. This figure corresponds to a mean of 1.50 antimicrobial-related PIs per working day. Of these, 115 (76.67%) were proactive. The most frequent intervention type was dose adjustment for overdosing or excessive duration (47.33%), followed by dose adjustment for underdosing or insufficient duration (18.00%), therapeutic drug monitoring recommendations (10.67%), and drug information to clinical staff (6.66%).

Conclusions: CCPs identify a substantial number of antimicrobial-related drug problems in the ICU through routine prospective review. The coexistence of overdosing and underdosing interventions reflects the pharmacokinetic complexity of this population. These findings support the formal integration of CCPs into ICU antimicrobial stewardship activities.

Keywords: Critical care pharmacist. Antimicrobial stewardship. Pharmaceutical interventions. Intensive care unit. Antimicrobial optimisation. Therapeutic drug monitoring.

Resumen

Introducción: Los antimicrobianos se encuentran entre los grupos de fármacos más frecuentemente implicados en errores de medicación y eventos adversos en la Unidad de Cuidados Intensivos (UCI). A pesar de la creciente evidencia que respalda el papel del Farmacéutico de Cuidados Críticos (FCC) en la optimización del uso de antimicrobianos, su integración en los equipos de UCI sigue siendo heterogénea en los sistemas sanitarios europeos.

Métodos: Se realizó un estudio observacional prospectivo durante cinco meses en una UCI médico-quirúrgica de 18 camas de un hospital de nivel terciario en España. Se incluyeron todos los pacientes ingresados durante el período. Un farmacéutico especialista revisó diariamente las prescripciones de antimicrobianos a través del sistema de prescripción electrónica. Las intervenciones farmacéuticas (IF) se clasificaron como proactivas o reactivas y se categorizaron por tipo según una taxonomía predefinida. Se realizó un análisis descriptivo.

Resultados: Se registraron 331 IF en total, de las cuales 150 (45,31%) correspondieron a terapia antibiótica, representando el grupo de medicamentos más frecuentemente involucrado. Esta cifra corresponde a una media de 1,50 IF relacionadas con antibióticos por día laborable. De estas, 115 (76,67%) fueron proactivas. El tipo de intervención más frecuente fue el ajuste de dosis por sobredosificación o duración excesiva (47,33%), seguido del ajuste por infradosificación o duración insuficiente (18,00%), las recomendaciones de monitorización farmacocinética (10,67%) y la información sobre medicamentos al personal clínico (6,66%).

Conclusiones: Los FCC identifican un número sustancial de problemas relacionados con antimicrobianos en la UCI mediante la revisión prospectiva rutinaria. La coexistencia de intervenciones por sobredosificación e infradosificación refleja la complejidad farmacocinética de esta población. Estos hallazgos respaldan la integración formal de los FCC en las actividades de *stewardship* antimicrobiano en UCI de nivel terciario.

Palabras clave: Farmacéutico de cuidados críticos. *Stewardship* antimicrobiano. Intervenciones farmacéuticas. Unidad de cuidados intensivos. Optimización antibiótica. Monitorización farmacocinética.

Introduction

Patients admitted to the Intensive Care Unit (ICU) are at particularly high risk of medication-related problems. The complexity of their clinical condition, combined with the frequent use of broad-spectrum antimicrobials, creates an environment prone to prescribing errors, dosing errors, and sub-optimal therapeutic decisions [1]. Antimicrobials consistently rank among the drug groups most frequently involved in medication errors and adverse drug events (ADEs) in the ICU [2,3], a finding with direct implications for patient outcomes, length of stay, and the emergence of antimicrobial resistance.

The pharmacokinetic profile of critically ill patients amplifies this risk considerably. Altered volume of distribution, augmented renal clearance, and hepatic impairment make standard dosing unreliable, creating a narrow and shifting window between therapeutic and toxic concentrations [4]. In this context, both overdosing and underdosing carry serious consequences: the former increases the risk of toxicity, whereas the latter may compromise microbiological efficacy and contribute to selective pressure for resistance.

Over the past two decades, a growing body of evidence has demonstrated that the integration of a Critical Care Pharmacist (CCP) into the multidisciplinary ICU team reduces medication errors, improves antimicrobial prescribing, and contributes to better patient outcomes [2,5]. A recent systematic review including

24 studies across multiple countries and healthcare settings confirmed that pharmacist-led interventions within Antimicrobial Stewardship Programs (ASPs) significantly improve antimicrobial prescribing practices, reduce unnecessary antimicrobial use, shorten therapy duration, and generate cost savings, with high rates of physician acceptance of pharmacist recommendations [6]. These benefits have been demonstrated even in hospitals without infectious disease specialists [6], underscoring the added value of clinical pharmacists regardless of institutional resources.

Despite this evidence, the presence of CCPs in ICUs remains neither systematic, nor continuous and is not formally mandated in most European healthcare systems, with studies reporting that as few as 35% of ICUs in some countries have access to a dedicated pharmacy service [7]. In addition, CCPs may not officially be integrated into many ASPs, even though they routinely perform *stewardship*-like activities—medication review, therapeutic drug monitoring (TDM), microbiological culture follow-up, and direct consultation with medical and nursing staff. As a result, the specific contribution of CCPs to antimicrobial optimisation is rarely quantified in prospective studies, particularly in tertiary-level hospitals. Most published data aggregate pharmaceutical interventions (PIs) across all drug groups, without isolating the antimicrobial component or characterising its qualitative profile.

The aim of this study was to evaluate the contribution of the CCP to antimicrobial optimisation in a

tertiary-level ICU through the prospective analysis of all PIs related to anti-infective therapy performed over a five-month period.

Material and methods

A prospective observational study was conducted over five months (January–May 2025) in the ICU of a tertiary-level hospital in Spain, with a capacity of 400 beds serving a reference population of approximately 270,000 inhabitants. The unit comprises 18 medical-surgical beds. All patients admitted to the ICU during the study period were included.

A specialist pharmacist, accompanied by a pharmacy resident on clinical rotation, worked in both the ICU and the pharmacy service from Monday to Friday, between 08:00 and 15:00. This dual presence was structured to allow the pharmacist's participation in daily multidisciplinary clinical rounds within the ICU, facilitating the direct communication of proactive interventions to the clinical team. This clinical activity was balanced with periods in the pharmacy service dedicated to the systematic review of medications through the electronic prescribing system.

Daily activities consisted of reviewing patients' medical records and evaluating prescribed medications through the electronic prescribing system. This review covered indication, dosage and dosing regimen, appropriateness of the administration route, pharmaceutical form, contraindications, drug interactions, allergies, and potential adverse effects. Pharmaceutical interventions were classified as proactive when identified and communicated by the pharmacist during routine medication review without a prior request from the clinical team, or as reactive when initiated by a member of the medical or nursing team through a direct consultation.

A Microsoft Excel® database was designed to document all PIs and process the study variables. PIs were classified into specific subcategories, defined as follows:

A) Treatment efficacy

- Pharmaceutical form: Optimisation of the dosage form or route of administration (e.g., switching from intravenous to oral therapy).
- Dose/interval adjustment (underdosing or insufficient duration): Interventions aimed at increasing the dose, shortening the dosing interval, or extending the treatment duration to ensure microbiological efficacy, based on the Summary of Product Characteristics, EUCAST dose recommendations, and current clinical guidelines.

- Prescription suggestion: Initiation of an antimicrobial agent based on clinical or microbiological findings.
- Deprescribing suggestion: Discontinuation of an antimicrobial that is no longer clinically indicated.
- Switch to a better alternative: Replacement with a more effective or narrower-spectrum antimicrobial agent.
- Interaction reducing efficacy: Discontinuation of an antimicrobial due to a drug–drug interaction that could compromise the effectiveness of antimicrobial therapy.

B) Treatment toxicity

- Adverse effects: Discontinuation of an antimicrobial to prevent or manage drug-related toxicity.
- Contraindication: Discontinuation of an antimicrobial prescribed despite patient-specific contraindications.
- Interaction increasing toxicity: Discontinuation of an antimicrobial due to a drug–drug interaction that may increase the risk of adverse events.
- Dose/interval adjustment (overdosing or excessive duration): Interventions aimed at decreasing the dose, lengthening the dosing interval, or limiting the duration of therapy to avoid toxicity.

C) Support activities

- TDM recommendation: Monitoring of serum drug concentrations and subsequent dose optimisation based on pharmacokinetic parameters.
- Drug information to physician/nurse: Provision of pharmacological information, intravenous compatibility data, or administration instructions.

For each PI, the following variables were recorded: the active ingredient and its classification according to the Anatomical Therapeutic Chemical (ATC) classification system [8], whether the intervention was proactive or reactive, and the type of intervention performed. To prevent overestimation of the results, each PI was assigned to a single subcategory based on its primary clinical objective. In cases where an intervention could potentially fulfil multiple criteria, the most significant reason for the pharmacist's

clinical contribution was prioritised, ensuring that no incident was double-counted.

A descriptive analysis was conducted. Absolute frequencies and percentages were calculated for all categorical and discrete variables.

Ethics. This study was conducted in accordance with the Declaration of Helsinki and applicable national and institutional regulations. Approval was obtained from the hospital Ethics Committee (CEAS; reference number 25-011). Patient anonymity was preserved throughout the study.

Results

A total of 338 patients were admitted to the ICU, and 331 PIs were recorded during the study period. Of these, 150 (45.31%) corresponded to antimicrobial therapy, representing the medication group most frequently involved in PIs. This figure corresponds to a mean of 1.50 antimicrobial-related PIs per working day. Of the 150 PIs, 115 (76.67%) were proactive. The distribution of intervention types is shown in **Table 1**.

The majority of interventions were related to potential treatment toxicity concerns (53.32%), with overdosing due to inappropriate dosing or excessive duration being the most frequent single intervention type (47.33%). Interventions for underdosing

or insufficient duration represented 18.00% of the total. TDM recommendations accounted for 10.67% of PIs. Support activities comprising drug information provided to physicians and nurses represented 6.66% of the total.

Discussion

Antimicrobials represented the medication group most frequently involved in PIs, accounting for 45.31% of all interventions recorded during the study period. This finding is consistent with previously reported data describing anti-infective agents as a recurrent focus of clinical pharmacy activity in the ICU [2,3], and supports the relevance of CCP involvement in antimicrobial optimisation as a distinct and quantifiable contribution within the multidisciplinary team.

The predominance of proactive interventions (76.67%) reflects the active integration of the CCP into daily clinical practice, beyond a purely consultative role. This proportion is consistent with findings from other studies evaluating pharmacist activity in critical care settings, where proactive interventions have been shown to be associated with greater clinical impact and earlier identification of drug-related problems [5,6].

Table 1. Type and frequency of pharmaceutical interventions related to antimicrobial therapy

Category	Intervention type	N	%
Treatment efficacy	Pharmaceutical form	5	3.33
	Dose/interval adjustment (underdosing or insufficient duration)	27	18.00
	Prescription suggestion	4	2.67
	Deprescription suggestion	4	2.67
	Switch to better alternative	3	2.00
	Interaction reducing efficacy	1	0.67
Treatment toxicity	Adverse effects	5	3.33
	Contraindication	2	1.33
	Interaction increasing toxicity	2	1.33
	Dose/interval adjustment (overdosing or excessive duration)	71	47.33
Support activities	TDM recommendation	16	10.67
	Drug information to physician	5	3.33
	Drug information to nurse	5	3.33
Total		150	100

TDM: therapeutic drug monitoring.

The majority of PIs were related to potential treatment toxicity concerns (53.32%), with overdosing due to inappropriate dosing or excessive duration being the single most frequent intervention type (47.33%). This pattern is consistent with the pharmacokinetic complexity inherent in critically ill patients, in whom renal and hepatic impairment frequently necessitate dose adjustments that are not always reflected in initial prescriptions [4]. The high frequency of overdosing interventions likely reflects the difficulty of adapting dosing regimens in real time to a rapidly changing clinical context.

Paradoxically, underdosing or insufficient duration represented 18.00% of interventions, illustrating the bidirectional nature of dosing errors in this population. Achieving adequate antimicrobial exposure while avoiding toxicity requires continuous reassessment, particularly in patients with altered pharmacokinetic parameters such as augmented renal clearance or increased volume of distribution [4]. The coexistence of overdosing and underdosing interventions in the same cohort underscores the complexity of antimicrobial dose optimisation in the ICU and highlights the value of a pharmacist with specific expertise in critical care pharmacokinetics.

TDM-guided interventions accounted for 10.67% of PIs, a relevant proportion considering that beta-lactam TDM was not performed in this unit and vancomycin use was residual in this setting. This suggests that even with a restricted TDM programme limited to aminoglycosides and other traditional agents, the CCP identified a significant number of opportunities for concentration-guided optimisation. The growing evidence supporting extended TDM to beta-lactams and other agents in critically ill patients [4] indicates that this proportion would likely increase with broader TDM implementation.

Finally, drug information provided to physicians and nurses represented 6.66% of PIs, reflecting the role of the CCP as a resource for resolving queries related to administration methods, intravenous compatibility, and drug interactions. This function is particularly relevant in patients with limited venous access, a frequent challenge in the ICU setting.

This study has several limitations. The single-centre design and the restriction of pharmacy presence to weekday daytime hours limit the generalisability of the findings and may result in an underestimation of the total number of antimicrobial-related problems, making it difficult to accurately determine the incidence of PIs at the patient level. Although this study specifically focused on accepted pharmaceutical

interventions, the lack of data regarding rejected recommendations—along with the absence of specific clinical outcome data—precludes a comprehensive assessment of the overall impact of the CCP's activity on patient prognosis. Future studies incorporating acceptance rates, outcome measures, and extended coverage models would strengthen the evidence base for CCP integration into antimicrobial stewardship.

Conclusions

The active participation of a CCP in daily ICU rounds and the systematic review of antimicrobial prescriptions enable the identification of a substantial number of drug-related problems, with antimicrobials representing the most frequently involved medication group. The predominance of proactive interventions reflects the genuine integration of the pharmacist into the clinical team. The simultaneous occurrence of overdosing and underdosing interventions illustrates the pharmacokinetic complexity of antimicrobial management in critically ill patients and the need for continuous expert reassessment. These findings support the formal incorporation of CCPs into ICU antimicrobial stewardship activities in tertiary-level hospitals.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

AI statement

Claude.AI (Anthropic) was used to assist with translation and manuscript drafting. Following its use, all authors reviewed the complete manuscript and take full responsibility for all statements contained therein.

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