

Antonio Ramos¹
Laura Benitez-Gutierrez¹
Angel Asensio²
Belén Ruiz-Antorán³
Carlos Folguera⁴
Isabel Sanchez-Romero⁵
Elena Muñoz¹

Antimicrobial stewardship in patients recently transferred to a ward from the ICU

¹Department of Internal Medicine (Infectious Disease Unit). Hospital Universitario Puerta de Hierro. Majadahonda. Madrid. Spain

²Department of Preventive Medicine. Hospital Universitario Puerta de Hierro. Majadahonda. Madrid. Spain

³Department of Pharmacology. Hospital Universitario Puerta de Hierro. Majadahonda. Madrid. Spain

⁴Department of Pharmacy. Hospital Universitario Puerta de Hierro. Majadahonda. Madrid. Spain.

⁵Department of Microbiology. Hospital Universitario Puerta de Hierro. Majadahonda. Madrid. Spain

ABSTRACT

Purpose. Inappropriate use of antibiotics is an important health problem that is related to increasing bacterial resistance. Despite its relevance, many health institutions assign very limited resources to improving prescribing practices. An antimicrobial stewardship programme (APS) centred on patients discharged from the ICU could efficiently undertake this task.

Methods. During this six month study the main activity was performing a programmed review of antimicrobial prescriptions in patients transferred to the ward from the ICU. In the case of inadequate antimicrobial treatment, a recommendation was included in the medical record.

Results. A total of 437 antimicrobial prescriptions for 286 patients were revised during a six month period. In all, 271 prescriptions (62%) were considered inappropriate in 183 patients. The most common reasons for inappropriateness were treating unconfirmed infection (43%), inadequate antimicrobial coverage (34%) and intravenous administration when the oral route was feasible (11%). Proposed recommendations were addressed in 212 cases (78%). There was no significant difference in adherence with respect to the type of recommendation ($p=0.417$). There was a 5% lower use of antibiotics during the year the study was conducted compared to the previous one.

Conclusions. ASPs centred on patients discharged from the ICU may be an efficient strategy to ameliorate antimicrobial use in hospitals.

Key words: Intensive Care Unit; Anti-Bacterial Agents; Anti-Fungal agents; Inappropriate prescription; Drug costs

Asesoramiento antibiótico en pacientes tras estancia en cuidados intensivos

RESUMEN

Objetivos. El uso inapropiado de antimicrobianos es un problema de salud relevante que se relaciona con aumento de la resistencia bacteriana y con el gasto farmacéutico innecesario. A pesar de su relevancia, un número elevado de instituciones sanitarias destinan escasos recursos para mejorar la prescripción antimicrobiana. Un programa de asesoramiento sobre el uso de antimicrobianos centrado en los pacientes dados de alta una unidad de cuidados intensivos (UCI) podría constituir una herramienta eficiente para mejorar este problema.

Métodos. Durante este estudio de seis meses de duración se realizó una intervención consistente en una revisión programada, por expertos en enfermedades infecciosas, de las prescripciones antimicrobiana en pacientes trasladados a una sala de hospitalización desde UCI. En el caso de prescripción inadecuada se realizaba una recomendación en la historia electrónica.

Resultados. Se revisaron de 437 prescripciones de antimicrobianos en 286 pacientes. En total, 271 prescripciones (62%) en 183 pacientes se consideran inapropiadas. Las razones más comunes identificadas fueron el tratamiento de infecciones no confirmadas clínicamente (43%), espectro antibacteriano inadecuado (34%) y el empleo de la vía intravenosa en casos que podían ser tratados por vía oral (11%). Las recomendaciones propuestas fueron aceptadas en 212 casos (78 %). No hubo diferencia significativa en la adherencia a la recomendación por parte del clínico responsable ni con el tipo de recomendación ($p = 0,417$). Durante el año en que realizó el estudio se redujo la prescripción antibiótica en un 5% en comparación con el año anterior.

Conclusiones. La revisión del tratamiento antimicrobiano en pacientes dados de alta de UCI puede ser una estrategia eficiente para mejorar el uso de estos fármacos.

Palabras clave: Unidad de Cuidados Intensivos, Agentes Antibacterianos , Antifúngicos, Prescripción Inadecuada, Coste Farmacológico

Correspondence:
Antonio Ramos
Department of Internal Medicine (Infectious Diseases Unit). Hospital Universitario Puerta de Hierro. Universidad Autónoma de Madrid.
Maestro Rodrigo nº 2. 28220 Majadahonda. Madrid. Spain.
Telephone +34 911916342. - Fax +34 911916807.
E-mail: aramos220@gmail.com

INTRODUCTION

The increasing bacterial resistance and expected shortage of antimicrobials in the next few years constitutes a difficult situation that may compromise the prognosis of infected patients¹⁻³. Inappropriate use of antibiotics has been identified as an important factor directly related to increasing bacterial resistance⁴. It has been observed that, in most clinical settings, more than half of all antimicrobial prescriptions could be considered inappropriate⁵. The development of antimicrobial stewardship programmes (ASPs) in hospitals are being promoted by scientific societies throughout the world and have proved to be effective in controlling bacterial resistance and antibiotic expenditure^{2,5-8}. Several national scientific societies recently published a consensus document aimed at implementing ASPs in Spanish medical centres⁷.

Despite worldwide concern with respect to improving antimicrobial use, many health institutions devote very limited resources to this objective⁹. Therefore, many hospitals would apply programmes designed to improve antimicrobial prescribing which only require limited human resources. The expression "low-hanging fruit" has recently been employed in this field when referring to interventions oriented towards the most obtainable targets rather than confronting the problems that are most difficult to solve^{10,11}.

ASPs could be focused on ICU patients, however patient instability and severity, among many other reasons, may significantly hinder their implementation¹¹⁻¹². Taking these facts into consideration, we decided to develop an ASP centred on reviewing antimicrobial treatment when patients are transferred to the ward from the ICU.

METHODS

Between 1st January 2012 and 30th June 2012, a prospective study was carried out in the Hospital Puerta de Hierro, Madrid, a tertiary university hospital with 600 beds that includes a surgical ICU (20 beds), medical ICU (20 beds) and an active solid-organ and hematopoietic stem-cell transplantation programme. Electronic medical records are available with computerized physician order entries and electronic progress notes. The Local Hospital Infections Committee created a team responsible for implementing the antimicrobial stewardship programme. The team was coordinated by two infectious diseases (ID) specialists, and included a pharmacist, a pharmacologist, a preventive medicine specialist and a microbiologist.

The study protocol was approved by the Local Ethics Committee. Requirements for patients' informed consent were waived because the study was directed at treating physicians with the primary objective of assessing their adherence to ID recommendations written in the patients' electronic record. The aim of the programme was presented and discussed in the hospital's main departments during clinical meetings between staff and internal medicine residents.

During this six month study the main activity was per-

forming a programmed review of antimicrobial prescriptions in patients transferred to the ward from the ICU. This review was carried out by two ID specialists together with an internal medicine resident. A list of patients transferred from the ICU was provided by the clinical documentation department. In the case of patients who were being prescribed inadequate systemic antimicrobial treatments, a recommendation was included in the electronic medical record during the first working day. In most cases, there were neither direct interviews with the prescribing doctor nor patient examinations. On average, the physicians responsible for reviewing the patients (two ID specialists) devoted approximately one hour per day to this activity.

Antimicrobial prescriptions were considered inadequate if they were not clinically justified and/or did not follow local, national or international guidelines¹³⁻¹⁶. Special care was taken to neither criticize nor discredit the current antimicrobial prescription, nor to put in writing that the current prescription was incorrect.

The record was reviewed again one week later in order to establish whether or not the prescribing physician had adhered to each recommendation. The physician was considered to have followed the recommendation if the appropriate modification had been made within 24 hours of the advice being given. The clinical records were reviewed six weeks later to assess complications and mortality. Data concerning nosocomial infections due to multiresistant bacteria and *C. difficile* colitis observed during 2011 and 2012 were also collected. The quantities of antimicrobials administered were recorded using defined daily doses (DDD).

Paired categorical and continuous variables were compared using the chi-squared test and Mann-Whitney U-test, respectively. Significance was set at $p < 0.05$.

RESULTS

During the study period 1,100 patients were transferred to a ward from the ICU. Mean age was 62 (+/- 17) years and 660 patients (60%) were male. The mean stay was 7.6 (+/- 1.3) days in the medical ICU and 4.2 (+/- 0.6) days in the surgical ICU. A total of 437 antimicrobial prescriptions for 286 patients (26%) were revised during the study period. In all, 91 patients (31%) were receiving more than one antimicrobial. Only 21% of antimicrobials were administered orally. The most common indications for antimicrobial prescribing were for infections of the respiratory tract (37%), abdominal cavity (20%), skin (6%), urinary tract (5%) and central catheter (4%). Seventy-one drugs (19%) were prescribed to treat possible infections without clear focal location.

Overall, 271 (62%) prescriptions were considered inappropriate in 183 patients. The origins of inappropriateness are shown in table 1. A total of 182 (66%) prescriptions were considered inadequate in patients transferred from the surgical ICU and 89 (55%) in patients transferred from the medical ICU ($p=0.019$).

Table 1		Origin of inappropriate antimicrobial treatment according to its indication
		N (%)
Perioperative Prophylaxis		
Treatment duration		24 (9)
Empirical treatment		
Treating unconfirmed infection		116 (43)
Inadequate antimicrobial coverage		92 (34)
Oral route indicated ^a		29 (11)
Targeted treatment		
Treatment duration		8 (3)
Bacterial resistance to agent		2 (1)

^aIntravenous quinolone was prescribed in 16 cases (55%)

Table 2		Adherence to antimicrobial recommendations	
	Proposed recommendation	Addressed recommendation (%)	
Adding one more antibiotic	1	1 (100)	
Switch to oral route	33	29 (88)	
Dosage change	6	5 (83)	
Antimicrobial switch	56	45 (80)	
Antimicrobial withdrawal	175	132 (75)	
Total	271	212 (78)	

Proposed recommendations were addressed in 212 cases (78%). Compliance was high in both surgical (146 prescriptions, 80%) and medical departments (66 prescriptions, 74%) ($p=0.334$). There was no significant difference in adherence with respect to the type of recommendation ($p=0.417$) (table 2).

Out of the 282 patients, treatment was considered correct in 99 (35%) and some advice was given in the remaining 183 (65%), which was completely followed in 90 patients (49%) and partially in 49 (27%). However, recommendations were not followed in 44 cases. Mortality in the first and second group was 6.5% (9 patients), and 9.1% in the third (4 patients) ($p=0.556$).

Antimicrobial consumption in 2011 was 160.7 DDDs per 100 occupied bed-days, which decreased to 152.7 DDDs (5% lower) during 2012 (table 3). During 2012, a decrease was detected in the use of colistin quinolones, carbapenems, linezolid, tigecycline, glycopeptides, posaconazole, voriconazole and echinocandins. On the other hand, there was an increase in the consumption of piperacillin/tazobactam, daptomycin, cefazolin and liposomal amphotericin B (table 3).

In 2011, 31 cases of nosocomial *C. difficile* diarrhea were detected (0.15% of inpatients), whereas in 2012 there were 24

cases (0.12%, $p=0.518$). No cases of *C. difficile* diarrhea were presented in patients in whom an antimicrobial recommendation had been made.

DISCUSSION

The rate of adherence to ID advice in patients transferred to a ward from the ICU may be considered high. This result is encouraging taking into account that this study was based on unsolicited consultations¹⁷⁻¹⁹. Although many studies have analyzed the role of ID consultation in relation to improve antimicrobial prescribing^{9,10,12,17-20}, to the best of our knowledge, none have focused on inpatients shortly after discharge from the ICU.

Considering the marked use of antimicrobial treatments in patients admitted to the ICU, it could be advocated that ID consultation should be performed while patients are in this department. However, this kind of cooperation is not without potential difficulties related to recommendation adherence, such as possible interference due to a patient's clinical instability^{21,22}. It has been observed that ICU physicians do not always accept advice from ID specialists, particularly if this involves changes to diagnosis or treatment^{12,23}. In some institutions, ID specialists encounter serious problems when contacting ICU physicians or discussing clinical patient challenges^{23,24}. Sometimes ID advice can be seen as threatening a loss of autonomy²⁵. These factors may have influenced the significant differences found in ID advice acceptance¹².

Antimicrobial treatment checking when patients are discharged from the ICU may be effective and rewarding because most patients are clinically stable and most microbiological results are already available²⁶. This may enable a reduction in the antibacterial spectrum, switching to oral route (removing the IV line) or the withdrawal of antimicrobial drugs^{10,23}. In addition, this could represent an opportunity to accurately interpret culture results that could correspond to simple colonization rather than infection²⁷. These kinds of programmes are compatible with other antimicrobial stewardship actions established in each institution taking into consideration the available human resources allocated to this activity. Electronic clinical history record systems help to save time reviewing antimicrobial treatments and in optimizing the efficiency of this strategy²⁴.

Unlike other studies, lower adherence was not found when the advice related to changes or removal of antimicrobial treatment^{12,19}. Remarkably, only 20% of antimicrobials were administered orally. This was particularly striking in the case of intravenous quinolones, which was the group most frequently implicated in "switch to oral route" recommendations²⁸. Stressing the importance of switching to the oral route may promote removal of intravenous lines and prevent the development of bacteremia²⁹.

Significant differences regarding antibiotic use and bac-

Table 3 Antimicrobial use during 2011 and 2012 (DDD p per 100 occupied bed-days)

Antimicrobial drug	Year 2011	Year 2012
Quinolone IV ^a	9.98	8.81
Quinolone po	23.19	21.65
Amox/clavulanate	43.66	43.85
Cefazolin	4.53	4.74
Other cephalosporins	13.2	13.62
Piperacillin/tazobactam	6.04	6.22
Carbapenems	12.42	11.81
Daptomycin	0.62	1.03
Linezolid	2.76	2.14
Glycopeptides	4.37	4.23
Colistin	2.95	0.16
Tigecycline	1.32	1.28
Other antibiotics	35.63	33.12
Echinocandins	2.27	2.09
Liposomal amphotericin B	0.62	0.71
Voriconazole	1.37	1.18
Posaconazole	2.43	1.43
Other antifungals	4.45	4.21

^aIntravenous quinolone was prescribed in 16 cases (55%)

terial resistance have been described between ICUs, sometimes within a single hospital³⁰. The present study revealed a higher proportion of inadequate treatment in patients transferred from the surgical ICU. Other authors have also found that antibiotic misuse was higher in the surgical than in the medical ICU³¹. One of the more correctable areas of antibiotic overuse in surgical ICUs is antibiotic prophylaxis. Current recommendations for antimicrobial prophylaxis against surgical-site infection advise that an antimicrobial should be administered immediately before surgery³². Adherence to advice was no worse in surgical than in medical departments^{17,19}, however, this finding is not consistent with previously published results which observed less compliance in surgical wards^{18,23}.

Despite the study being carried out during the first half of 2012, it was decided that the consumption of antibiotics should be measured throughout the year to evaluate the possible influence of prolonged education. The impact of the programme on the overall antibiotic consumption was limited. The slight reduction detected (5%) could be as a result of including only a small part of the antimicrobial prescriptions²⁷. It should be noted that the use of most antimicrobials considered to be restricted, such as colistin, linezolid, carbapenems or tigecycline, actually declined, albeit modestly. Worthy of special mention was the decline in the consumption of antifungals, which could be related to a better understanding of the value of *Candida* species isolation in respiratory secretions²⁷.

One limitation of this study is that not all the changes in antimicrobial treatments could be attributed to the written recommendations because some of them could have been made by the attending physician on their own initiative.

In summary, unsolicited post-prescription antibiotic review in patients transferred to a ward from the ICU can be successfully implemented with a high degree of compliance. This approach may be cost effective and could be included as part of an antimicrobial stewardship programme in institutions that devote limited human resources to improve antimicrobial prescribing.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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