

## Correction

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

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#### ABSTRACT

This paper is a corrigendum to the previously published paper: "Antimicrobial stewardship in patients recently transferred to a ward from the ICU" [Rev Esp Quimioter. 2014 Mar;27(1):46-50.] This corrigendum was prepared in order to correct some erroneous comments included in the discussion section. First, it should be pointed out that there could have been several suitable options for treating many infections and that, therefore, the word "inadequate" was not the most appropriate in this situation. In addition, some comments about the interpretation of microbiological results made by ICU physicians have been removed from the first article because this variable was not included in the study. Finally, another change made to the discussion was to clarify the ICU physicians' alleged low level of compliance with advice given by infectious disease specialists. This has been suggested in previous studies it cannot be substantiated when analyzing the results of the study.

**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 amendable 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 and a total of 271 prescriptions (62%) in 183 patients were considered to be amendable. In most of these cases, treatment could have been

reduced taking into consideration each patient's clinical improvement and their location in a hospital area with a lower risk of infection due to resistant bacteria. The most common advice was antimicrobial withdrawal (64%), antimicrobial change (20%) and switching to oral route (12%). 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

Este artículo es una corrección del artículo previamente publicado: "Antimicrobial stewardship in patients recently transferred to a ward from the ICU" [Rev Esp Quimioter. 2014 Mar;27(1):46-50.] Esta corrección ha sido elaborada para subsanar algunos comentarios erróneos incluidos en la discusión. Primero, hay que señalar que podría haber habido varias opciones adecuadas para el tratamiento de muchas infecciones y que, por tanto, la palabra "inadecuada" no era el más apropiada en esta situación. Además, algunos comentarios sobre la interpretación de los resultados microbiológicos realizados por médicos de la UCI se han eliminado del primer artículo porque esta variable no se incluyó en el estudio. Por último, otro cambio realizado en la discusión fue aclarar que los médicos de la UCI alegaron bajo nivel de cumplimiento con las recomendaciones dadas por los especialistas en enfermedades infecciosas. Esto ha sido sugerido en estudios previos y no puede ser demostrado en el análisis de los resultados de este estudio.

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**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 modificable 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 consideraban modificables. En la mayoría de estos casos, el tratamiento podría ser ajustado a la baja teniendo en cuenta la mejoría clínica del paciente y su actual ubicación en un área hospitalaria con menos riesgo de infección por bacterias resistentes. El consejo más común fue retirada a los antimicrobianos (64%), el cambio a los antimicrobianos (20%) y la administración por vía oral (12%). 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 50% 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

## 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 patients<sup>1-3</sup>. Inappropriate use of antibiotics has been identified as an important factor directly related to increasing bacterial resistance<sup>4</sup>. It has been observed that, in most clinical settings, more than half of all antimicrobial prescriptions could be considered inappropriate<sup>5</sup>. 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<sup>2,5-8</sup>. Several national scientific societies recently published a consensus document aimed at implementing ASPs in Spanish medical centres<sup>7</sup>.

Despite worldwide concern with respect to improving antimicrobial use, many health institutions devote very limited resources to this objective<sup>9</sup>. 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<sup>10,11</sup>.

ASPs could be focused on ICU patients, however patient instability and severity, among many other reasons, may significantly hinder their implementation<sup>11-12</sup>. 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 1<sup>st</sup> January 2012 and 30<sup>th</sup> 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 performing 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 regarded as amendable if they were not considered clinically justified and/or did not follow local, national or international guidelines<sup>13-16</sup>. Special care was taken to neither criticize nor discredit the current antimicrobial prescription due to the fact that there may have been several suitable options to treat infections, and also because the judgment of the investigators could not take into account

| Table 1                           |  | Origin of inappropriate antimicrobial treatment according to its indication |
|-----------------------------------|--|---|
|                                   |  | N (%)   |
| Perioperative Prophylaxis         |  |   |
| Treatment duration                |  | 24 (9)  |
| Empirical treatment               |  |   |
| No confirmed infection            |  | 116 (43)  |
| Broad antimicrobial coverage      |  | 92 (34)   |
| Oral route indicated <sup>a</sup> |  | 29 (11)   |
| Targeted treatment                |  |   |
| Treatment duration                |  | 8 (3)   |
| Bacterial resistance to agent     |  | 2 (1)   |

<sup>a</sup>Intravenous 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)                                   |  |

certain patient characteristics which were only known to the clinicians responsible.

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 amendable 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 ( $p=0.019$ ).

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 consultations<sup>17-19</sup>. Although many studies have analyzed the role of ID consultation in relation to improve antimicrobial prescribing<sup>9,10,12,17-20</sup>, to the best of our knowledge, none have focused on inpatients shortly after discharge from the ICU.

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

| Antimicrobial drug        | Year 2011 | Year 2012 |
|---------------------------|-----------|-----------|
| Quinolone IV <sup>a</sup> | 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      |

<sup>a</sup>Intravenous quinolone was prescribed in 16 cases (55%)

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, a patient's clinical severity and the frequent need for empirical broad antibiotic coverage, as well as an environment with a higher bacterial resistance than in conventional wards, constituted relevant additional difficulties to perform antimicrobial advice<sup>21-25</sup>.

Antimicrobial treatment checking when patients are discharged from the ICU may be effective and rewarding because most patients have adequate intestinal transit and the majority of microbiological results are already available<sup>26</sup>. This may enable a reduction in the antibacterial spectrum, switching to oral route (removing the IV line) or the withdrawal of antimicrobial drugs<sup>10,23</sup>. This was particularly striking in the case of intravenous quinolones, which was the group most frequently implicated in "switch to oral route" recommendations<sup>28</sup>. Stressing the importance of switching to the oral route may promote removal of intravenous lines and prevent the development of bacteremia<sup>29</sup>. Unlike other studies, lower adherence was not found when the advice related to changes or removal of antimicrobial treatment<sup>12,19</sup>. These kinds of programmes are compatible with other antimicrobial stewardship actions established in each institution taking into consideration the 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 strategy<sup>24</sup>.

Significant differences regarding antibiotic use and bacterial resistance have been described between ICUs, sometimes within a single hospital<sup>30</sup>. Some authors have found that antibiotic misuse was higher in the surgical than in the medical ICU<sup>31</sup>. In our study, one of the areas of antibiotic overuse was surgical prophylaxis (frequently due to the surgeon's preference)<sup>32</sup>. However, there was no difference between surgical and medical departments with respect to adherence to advice<sup>17,19</sup>, whereas previously published results observed less compliance in surgical wards<sup>18,23</sup>.

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 prescriptions<sup>27</sup>. 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 secretions<sup>27</sup>.

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 addition, it should be noted that options other than those suggested by the researchers could have resulted in a favourable clinical outcome. The need to maintain a broad antibiotic coverage or an intravenous route may be justified due to different medical opinions. The main objective of this study was to emphasize that the moment of transfer from the ICU to conventional wards may be an ideal opportunity to review patients' antimicrobial treatment according to their current clinical status.

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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