

Adherencia a las recomendaciones terapéuticas respecto al uso de antibióticos en un Servicio de Urgencias tras una intervención de baja intensidad

Adherence to therapeutic recommendations regarding the use of antibiotics in an Emergency Department after a low-intensity intervention

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ABSTRACT

Introduction: The discovery of antimicrobials significantly reduced mortality from severe infections. However, antibiotic resistance has become a major issue, necessitating new strategies for antibiotic use. The aim of this study is to assess the impact of the Antimicrobial Stewardship Program (ASP) in a tertiary hospital's Emergency Department (ED), focusing on adherence to antibiotic guidelines before and after its implementation.

Methods: A retrospective descriptive study was conducted from May 2022 to February 2023, including patients admitted to the ED with respiratory infections (RI), skin and soft tissue infections (SSTI), or intra-abdominal infections (IAI). Antibiotic adherence was compared between pre-ASP (May-September 2022) and post-ASP (October 2022-February 2023) periods. The intervention involved training sessions and providing accessible documentation for ED staff.

Results: A total of 494 patients were included, with 50% in each period. Adherence to ASP guidelines improved significantly from 45.45% to 56.80% post-intervention ($p < 0.01$). RI adherence increased notably, while SSTI and IAI adherence did not change significantly. Mortality was also evaluated. At 72 hours, mortality was 1.22% (4/328) in the adherent group and 4.82% (8/166) in the non-adherent group ($p < 0.05$). At 30 days, mortality was 4.57% (15/328) and 12.05% (20/166), respectively ($p < 0.005$). Carbapenem use decreased from 21.12% to 13.08% post-intervention, though this reduction was not significant.

Conclusions: Low-intensity interventions can improve antibiotic adherence in EDs, potentially enhancing clinical outcomes and reducing resistance. Future studies should investigate reasons for non-adherence and examine the effects on patient outcomes and costs.

Keywords: Antibiotics, antibiotic resistance, adherence, emergency.

RESUMEN

Introducción: El descubrimiento de los antimicrobianos redujo significativamente la mortalidad por infecciones graves. Sin embargo, la resistencia a los antibióticos se ha convertido en un problema grave, lo que exige nuevas estrategias para el uso de los antibióticos. El objetivo de este estudio es evaluar el impacto del Programa de Gestión de Antimicrobianos (PGA) en el Servicio de Urgencias (SU) de un hospital terciario, centrándose en el cumplimiento de las directrices sobre antibióticos antes y después de su implantación.

Métodos: Se llevó a cabo un estudio descriptivo retrospectivo entre mayo de 2022 y febrero de 2023, en el que se incluyó a pacientes ingresados en el SU con infecciones respiratorias (IR), infecciones de la piel y de los tejidos blandos (IPTB) o infecciones intraabdominales (IIA). Se comparó la adherencia al tratamiento antibiótico entre los periodos anterior al PGA (mayo-septiembre de 2022) y posterior al PGA (octubre de 2022-febrero de 2023). La intervención consistió en sesiones de formación y en proporcionar documentación accesible al personal del SU.

Resultados: Se incluyó a un total de 494 pacientes, con un 50 % en cada periodo. El cumplimiento de las directrices de la PGA mejoró significativamente, pasando del 45,45 % al 56,80 % tras la intervención ($p < 0,01$). El cumplimiento de las directrices sobre infecciones respiratorias (IR) aumentó notablemente, mientras que el de las infecciones cutáneas y de tejidos blandos (IPTB) y las infecciones intravasculares (IIA) no varió de forma significativa. También se evaluó la mortalidad. A las 72 horas, la mortalidad fue del 1,22 % (4/328) en el grupo adherente y del 4,82 % (8/166) en el grupo no adherente ($p < 0,05$). A los 30 días, la mortalidad fue del 4,57 % (15/328) y del 12,05 % (20/166), respectivamente ($p < 0,005$). El uso de carbapenémicos disminuyó del 21,12 % al 13,08 % tras la intervención, aunque esta reducción no fue significativa.

Conclusiones: Las intervenciones de baja intensidad pueden mejorar el cumplimiento del tratamiento antibiótico en los SU, lo que podría mejorar los resultados clínicos y reducir la resistencia. Los estudios futuros deberían investigar las causas del incumplimiento y analizar los efectos sobre los resultados de los pacientes y los costes.

Palabras clave: Antibióticos, resistencia a los antibióticos, cumplimiento terapéutico, urgencias.

INTRODUCTION

One of the most important advances in the history of medicine has been the discovery of antimicrobials. Its application in clinical practice has reported numerous benefits, not only directly by curing infections, but also indirectly by promoting the use and development of other procedures, such as transplants¹. In fact, it has been demonstrated in the literature and in daily clinical practice that the early use of an appropriate antibiotic is the most effective in severe infections (septic shock and severe sepsis) in terms of mortality reduction.²

However, since the introduction of antibiotics, it has been proven how microorganisms lose their natural sensitivity to these agents over time through the selection and transmission of various resistance mechanisms³. The causes of this phenomenon are multiple, highlighting the horizontal transmission of resistant microorganisms or resistance mechanisms, as well as the influence of exposure to antimicrobials⁴. To date, this problem has been solved with the development of new antimicrobials. However, given the speed of emergence of resistance in relation to the discovery of new antimicrobials today, it indicates that this model is not sustainable over time.⁵

As a consequence, in clinical practice, it is increasingly difficult to empirically select an active antimicrobial in patients with severe infections, leading to worse clinical outcomes⁶. This is especially relevant in emergency services, where Approximately 15% of patients undergoing treatment are administered antimicrobial therapy, with the majority of these treatments being empirical⁷. In this scenario, in addition to the importance of a correct choice of antibiotic for the patient's prognosis at the critical moment, it is important to take into account that, in many cases, this treatment will be maintained during admission for an indeterminate period of time, which greatly influences the prognosis. In the literature, taking into account the appropriate empirical prescription, series of data are observed that indicate that even in 40% of cases, the choice of antimicrobial may be incorrect.⁸

To prevent this increase in antimicrobial resistance, the National Plan against Antimicrobial Resistance (PRAN) has been developed. In its strategic line "Control of antibiotic resistance", it proposes that prescribers use empirical antimicrobial treatment guidelines adapted to the local ecology of each center⁹. In our environment, an Antimicrobial Stewardship Program (ASP) has been developed to develop the PRAN.

The purpose of this work is to know the impact of these recommendations on the daily clinical practice in our Emergency Department (ED). To achieve this goal, we will evaluate the effectiveness of the implementation method by comparing 2 time periods (pre-implementation of the ASP and post-implementation of the ASP).

MATERIAL AND METHODS

A retrospective descriptive study was proposed in patients treated in the ED who require hospital admission for the treatment of a respiratory infection (RI), skin and soft tissue infection (SSTI) or intra-abdominal infection (IAI) from May 2022 to February 2023. A low-intensity intervention was carried out in September 2022 with the implementation of the ASP, making a comparison of period 1 (May 2022-September 2022) and period 2 (October 2022-February 2023) in relation to adherence to the recommendations of prescription. The interven-

tion was based on two training sessions in the ED and the availability of documentation for each professional to use during the prescription of treatment for a patient. Our hospital is a tertiary center, with a rate of around 100,000 medical visits per year.

The term RI encompassed exacerbations of chronic obstructive pulmonary disease (COPD), infectious exacerbations in patients with bronchiectasis, and community-acquired pneumonia. For its part, SSTI encompassed cellulitis (regardless of location) and necrotizing fasciitis. Finally, the IAI group included those patients treated in the ED with acute appendicitis, acute cholecystitis, digestive perforations, acute diverticulitis, intra-abdominal abscesses, peritonitis and acute necrotic pancreatitis.

To carry out the work, all those patients from the analyzed period who met the inclusion and exclusion criteria were consecutively collected.

Inclusion criteria:

- Patients admitted in the ED in the study time period who require hospital admission for the treatment of a RI, SSTI or IAI.
- Administration of antibiotic the day of hospital admission.

Exclusion criteria:

- Patients under 18 years of age.
- Patients admitted in the ED with a biological culture related to the current illness that influences the antibiotic prescription given that the ASP recommendations are for empirical prescription in the Emergency Department.
- Patients with more than 1 infection that requires the use of antibiotic therapy at the time of hospital admission.

In addition to the antibiotic prescription provided to each patient, the following variables were analyzed: Sex, age, culture collection or not (including urine, blood, sputum or another one related with the infection focus) prior to the antibiotic administration, mortality after 72 hours of admission and 30 days after admission, and use of carbapenem if the antibiotic were not agree to the guidelines.

This study received the approval of our hospital Ethics Committee.

Statistical analysis

Firstly, a descriptive analysis of all the variables was carried out. Quantitative measurements were described with mean and standard deviation (SD) or median and 25th and 75th percentiles, according to normality criteria. Categorical variables were presented with absolute frequencies and percentages. The 95% confidence interval (95% CI) was calculated for the variables of interest.

To analyze the associations between clinical actions and sociodemographic factors, in the case of qualitative variables, the Chi Square test or Fisher's exact test was used if the conditions required it. For quantitative variables, depending on whether or not they fit a normal distribution, the Student T or the Mann-Whitney U will be used. The level of statistical significance was $p \leq 0.05$.

Data analysis will be carried out with the Statistical Package for the Social Sciences for Windows (SPSS Version 20.0 for Windows) program.

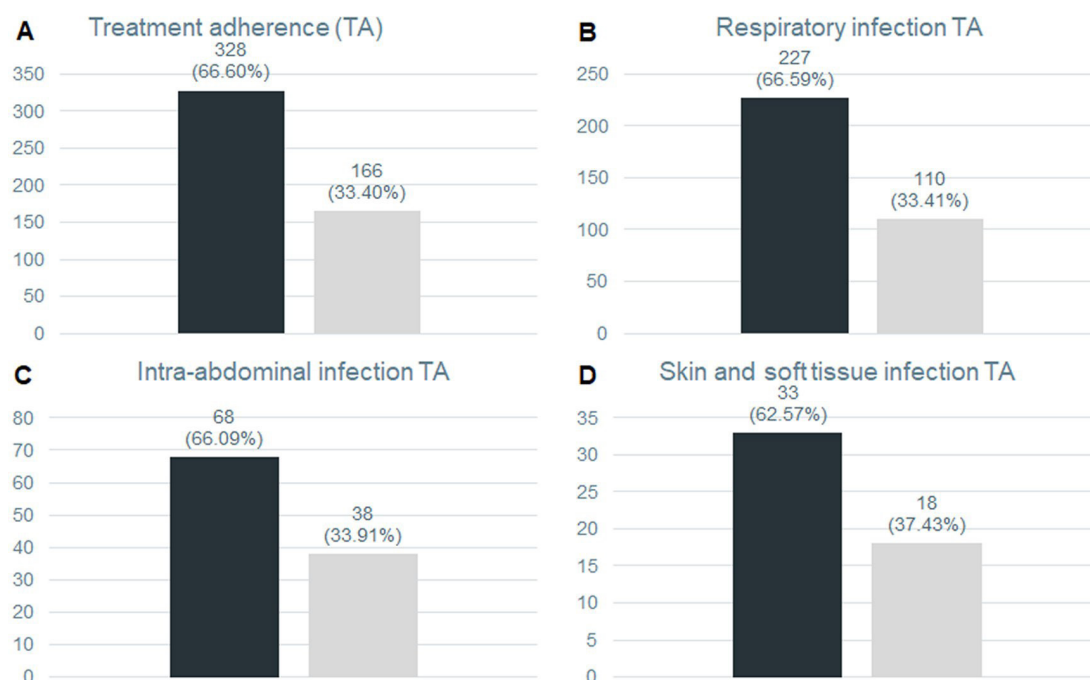


Figure 1. Treatment adherence (TA) (A), respiratory infection TA (B), intra-abdominal infection TA (C), and skin and soft tissue infection TA (D) attending the recommendations. Globally, all the patients were treated agree with the guidelines.

RESULTS

494 patients were obtained during the study period (279 males, 56.48%, and 215 females, 43.52%). Age expressed as mean $\pm$ SD was 74.21 $\pm$ 17.39. 247 patients (50%) were collected in each period. Attending to the different groups of illness, 337 patients (68.22%) were admitted in the ED affected by RI. 106 subjects (21.46%) were included in the IAI group, whereas 51 (10.32%) were affected by SSTI.

Treatment provided by physicians in the ED agree ASP recommendations in 328 patients (66.60%), whereas 166 (33.40%) differs with the guidelines. This tendency of accordance with the guidelines was generally adopted in the three group of diseases evaluated (Figure 1).

Comparing the two periods (May 2022-September 2022, October 2022-February 2023), a statistical difference was observed after the intervention in a global manner attending the adherence to the ASP recommendations. This results was also observed in the RI group, whereas no statistical differences were observed in the IAI group as well as in patientes affected by STTI (Figure 2).

Mortality was also evaluated globally. At 72 hours, mortality was 1.22% (4/328) in the adherent group and 4.82% (8/166) in the non-adherent group ($p < 0.05$), showing a significant difference. At 30 days, mortality was 4.57% (15/328) and 12.05% (20/166), respectively ($p < 0.005$), indicating an even stronger association between adherence and lower mortality.

Attending culture collection, globally, 302 interventions (61.13%) obtained it, whereas 192 (38.87%) not. The intervention promoted a statistical difference between the two periods, increasing the collection from 135 (45.45%) to 167 (56.80%) ($p < 0.01$).

Finally, carbapenem administrarion was observed in 22 patients (13.25%) of the 166 patients without adherence to the antibiotic

prescription guidelines in our area. Comparing both groups, 15 patients (21.12%) patients received carbapenem in the pre-intervention group, whereas 7 patients (13.08%) received it in the post-intervention group. Non statitiscal differences were observed attending to the effect of the intervention.

DISCUSSION

Our results observed that alow-intensity intervention could improve the antibiotic adherence in the Emergency Department. This data was observed in the three groups of pathology, being statistically significant manner globally as well as in patients admitted in the hospital affected by respiratory infections.

Infectious disease is one of the most prevalent diseases in hospital ED, with antimicrobials being one of the most prescribed pharmacological groups. Despite the importance of adapting the prescription to the therapeutic guidelines in EDs, there are few studies in our area that analyze this situation. A recent study performed by González-Morcillo *et al.* observed that 39.6% of prescriptions performed in the ED were inappropriate. These results are similar to our study (33.40%). Similar results were observed by Yunquera-Romero *et al.* and Ramos-Martínez *et al.* (38% and 43%, respectively)^{8,10}. Despite the high ratio of inadequate prescription due to the relevance to the patient outcomes, our results are better than other studies observed in other countries in the literature. A study conducted in France found that 59.86% of antibiotic prescriptions did not adhere to local guidelines¹¹. Similar results were observed in Lebanon (67.4%)¹², Australia (47.6%, 42%)^{13,14}, Denmark (47%)¹⁵, South Africa¹⁶, The Netherlands (42.7%)¹⁷. The literature suggests that inappropriate antibiotic prescriptions are linked to the assessment of the severity of the illness and the healthcare provider responsible for treatment.^{10,14}

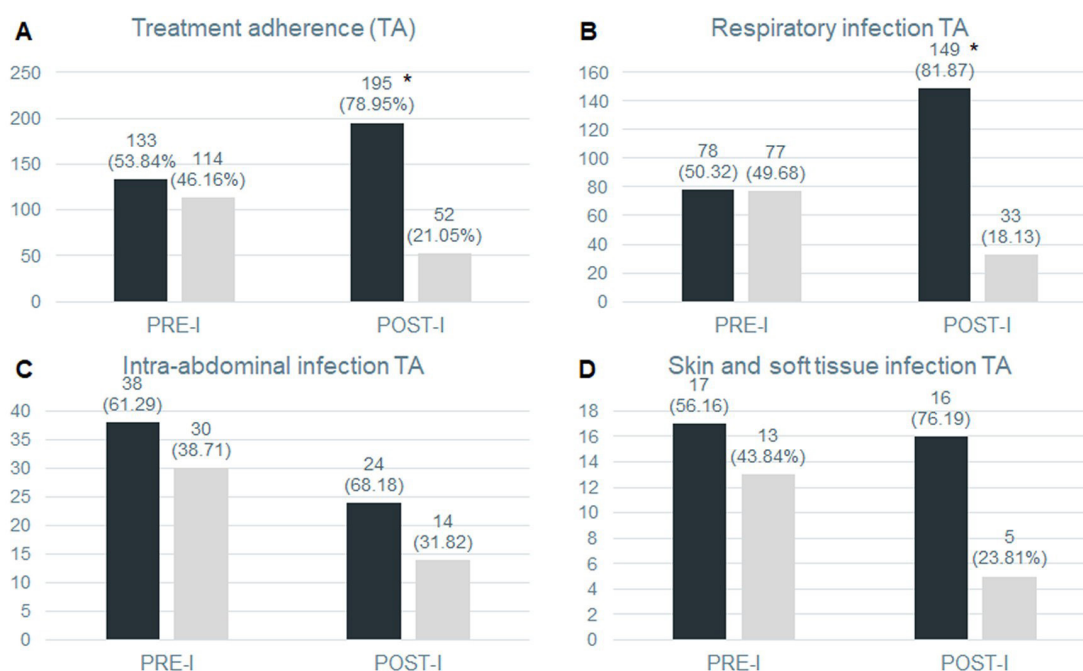


Figure 2: The intervention showed an statistical significant manner in a general manner attending treatment adherence (TA) (A) as well as respiratory infection TA (B). However, no statistical differences were observed in intra-abdominal infection TA (C), and skin and soft tissue infection TA (D). * $p < 0.001$

Since several years, different studies tried to find different manners to improve the adherence to antibiotic prescription. Pulcini *et al.* suggested that the collaboration with an infectious disease specialist reduce the number of antibiotic prescriptions¹⁸. Low-intensity interventions such as our study have been also evaluated. Galanter *et al.* observed that a one-page document focused on antibiotic treatment instead a twenty pages documents improved significantly the antibiotic prescription¹⁹. These authors also observed a significant decrease in the use of broad spectrum antibiotic.

A consequence of the lack of adherence to antibiotic prescription guidelines is the cost impact. This problem is also related with antibiotic-resistance, promoting a feedback system difficult to stop. In fact, it has been observed that the hospital economic costs could be diminished in a 12% if an appropriate antibiotic prescription will be performed.²⁰

The present study checked the antibiotic adherence agree with our local guidelines. Three main groups of diseases were evaluated: respiratory infection, skin and soft tissue infection, and intra-abdominal infection. The first one include community-acquired pneumonia (CAP), a prevalent infection in the ED. As a consequence, there are some studies that evaluate the management of this disease in the ED, especially focused on the antibiotic prescription. It has been observed that an adequate prescription is related with a decrease of 30-days mortality²¹. However, the adherence to local guidelines was inadequate, suggesting the need to establish a strategy in the ED to improve the results. A Danish study observed that 31.3% agree with the local guidelines²², similar to study performed in United States of America (31.9%)²³. These results are worst than our study. However, both results should be improved to avoid antibiotic resistance and improve the management of this pathology. Some studies observed that the use of severity scales on the management of CAP including CORB and

SMART-COP and Pneumonia Severity Index increased the adherence to recommendations^{24,25}. In addition, the incorporation of clinical decision support tools increased the adherence to antibiotic-prescription guidelines. However, these tools did not promote a significant impact in duration of antibiotics, intubation rates, vasopressor initiation, length of stay, mortality or 30-day readmission²³. Finally, the support of emergency medicine pharmacists has been also observed as an useful option to improve the empiric treatment in the ED to manage CAP²⁶. These professionals also have an impact in IAI.²⁶

Skin and soft tissue infection are a common pathology in the ED, especially cellulitis. Our study revealed that our low-intensity intervention improved the adherence to recommendations. However, these results were non statistically significant, like IAI. It could be possible due to the few number of patients affected by these diseases in our study. In the literature, it has been observed that the application of multifaceted stewardship intervention as well as easy-to-follow treatment algorithms improve the adherence to recommendations.²⁷

We observed a decrease in the mortality rate 72 hours and 30 days after admission antibiotic recommendations were performed. These differences were statistically significant. These results agree with previous studies performed in community acquired pneumonia.^{17,21}

The limitation of this study is that is a retrospective study after a low-intensity intervention in a single ED. In addition, we did not evaluate readmission data, economic costs or causes of low adherence to antibiotic recommendations, excepting the use of carbapenem as an inadequate agreement. We focus our study to the empirical treatment due to the requirement to initiate an empirical prescription in the ED in these diseases and the effects on mortality rate. Finally, this study is single-center, with a small sample size, and that this may influence the degree of significance of the results.

Carbapenems, among the beta-lactams, are the most effective against Gram-positive and Gram-negative bacteria presenting a broad spectrum of antibacterial activity. Their unique molecular structure is due to the presence of a carbapenem together with the beta-lactam ring²⁸. Recently, it has been observed an rising incidence of carbapenem resistant isolates in the clinical practice, especially since COVID-19 pandemic²⁹. As a consequence, it is very important to preserve these drugs for strictly necessary uses. In the literature, it has been observed that the agreement to clinical guidelines decrease its use¹⁹. These results agree with our study, observing a non significant decrease of the use of carbapenems after the intervention.

In the ED, blood cultures as well as other cultures are important diagnostic tools for identifying the pathogens responsible for a patient's infection. Several times, its use in the ED is not available due to the requirement to initiate an empiric antibiotic treatment. However, they are useful in the prognosis as well as adequacy of the treatment in patient's care³⁰. Our study revealed an increase of extraction of culture samples after the intervention. However, we did not evaluate if the indication was appropriate, being necessary to perform a future study to analyze if these results improve the management of the patients in the ED.

CONCLUSIONS

The implementation of clinical guidelines in hospital emergency services improves adherence to antibiotic prescription recommendations. Therefore, it is necessary to standardize its use to reduce problems secondary to non-adherence, including the increase in antibiotic resistance.

TRANSPARENCY DECLARATION

The authors declare that the study was conducted with full transparency, ensuring the integrity of the research process. All data and findings are reported without fabrication or manipulation.

FUNDING STATEMENT

The authors confirm that no external funding was received for this study.

ETHICAL APPROVAL

This study received the approval of the Hospital Universitario San Pedro Ethics Committee on 2nd February 2022 (HUSP_020202221).

DATA AVAILABILITY STATEMENT

The authors had full access to all data related to the study throughout the entire research process, including the clinical records associated with the medical procedures described in this manuscript. Access to these data is currently available for review, as appropriate consent has been obtained. The data supporting the findings of this study are available upon request from the corresponding author.

CONFLICT OF INTEREST STATEMENT

The authors declare that there are no conflicts of interest related to this study.

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