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Original article

Antifungal stewardship in a tertiary hospital



Antonio Ramos^{a,*}, Claudia Pérez-Velilla^b, Angel Asensio^c, Belén Ruiz-Antorán^d, Carlos Folguera^e, Mireia Cantero^c, Beatriz Orden^f, Elena Muñez^a

- ^a Department of Internal Medicine (Infectious Disease Unit), Hospital Universitario Puerta de Hierro, Majadahonda, Madrid, Spain
- ^b Department of Internal Medicine, Hospital Universitario Puerta de Hierro, Majadahonda, Madrid, Spain
- ^c Department of Preventive Medicine, Hospital Universitario Puerta de Hierro, Majadahonda, Madrid, Spain
- ^d Department of Pharmacology, Hospital Universitario Puerta de Hierro, Majadahonda, Madrid, Spain
- e Department of Pharmacy, Hospital Universitario Puerta de Hierro, Majadahonda, Madrid, Spain
- f Department of Microbiology, Hospital Universitario Puerta de Hierro, Majadahonda, Madrid, Spain

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ABSTRACT

Background: The inappropriate use of antifungals is an important health problem related to increasing adverse effects, unnecessary cost and promotion of resistant and emerging fungal infections. Despite its relevance, many health institutions assign few resources to improve prescribing practices.

Aims: To evaluate the efficiency of an antifungal stewardship programme (ASP) centered on restricted antifungal agents.

Methods: The main activity during the eight-month study was to perform a programmed review of restricted antifungals (lipid formulations of amphotericin B, echinocandins and voriconazole) prescribed in hospitalized patients. In the case of amendable antifungal treatment, a recommendation was included in the electronic medical record.

Results: A total of 280 antifungal prescriptions for 262 patients were revised during the study period. The indications were prophylactic in 85 cases (30.4%), pre-emptive in 10 cases (3.5%), empiric in 122 cases (43.6%), and directed in 63 cases (22.5%). A total of 70 prescriptions (25%) in 61 patients were considered to be amendable. In most of these cases, treatment could have been reduced considering the patient's clinical improvement and microbiological results. The most common advice was antifungals change (70%), antifungal withdrawal (21%), removal of one antifungal drug in cases of combined therapy (7%), and switching to oral route (1%). Proposed recommendations were addressed in 28 cases (40%). There was no significant difference in adherence with respect to the type of recommendation (p = 0.554). There was a 42% lower use of antifungals during the period of the study compared to that observed during a similar previous period. Mortality among patients who were treated according to the recommendations of the ASP was 17% and in whom treatment was not modified it was 30% (p = 0.393).

Conclusions: ASPs centered on hospitalized patients may be an efficient strategy to ameliorate antifungal use in hospitals.

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Asesoramiento en la prescripción de antifúngicos en un hospital terciario

RESUMEN

Antecedentes: El uso inadecuado de los antifúngicos es un problema de salud relevante que puede incrementar los efectos adversos y generar costes innecesarios, además de favorecer la aparición de resistencias y de infecciones micóticas emergentes. A pesar de su importancia, muchas instituciones sanitarias destinan escasos recursos para mejorar las prácticas de prescripción.

Objetivos: Evaluar la eficiencia de un programa de asesoramiento sobre antifúngicos basado en la prescripción de agentes antifúngicos restringidos.

Palabras clave:
Agentes antifúngicos
Equinocandinas
Anfotericina B liposomal
Fluconazol
Prescripción inadecuada
Coste farmacológico

E-mail address: aramos220@gmail.com (A. Ramos).

^{*} Corresponding author.

Métodos: La principal actividad durante el estudio de ocho meses de duración fue la realización de una revisión programada de antifúngicos restringidos, prescritos en los pacientes hospitalizados (formulaciones lipídicas de anfotericina B, equinocandinas y voriconazol). En el caso del tratamiento antifúngico modificable, se procedió a anotar una recomendación en la historia clínica electrónica.

Resultados: Se revisó un total de 280 prescripciones de antifúngicos en 262 pacientes durante el período de estudio. Las indicaciones fueron de tipo profiláctico en 85 casos (30,4%), anticipado en 10 (3,5%), empírico en 122 (43,6%) y dirigido en 63 (22,5%). Se consideraron modificables un total de 70 prescripciones (25%) en 61 pacientes. En la mayoría de estos casos, el tratamiento podía reducirse teniendo en cuenta la mejoría clínica y los resultados microbiológicos del paciente. La indicación más frecuentemente realizada fue el cambio de antifúngico (70%), seguido por la retirada de dicho fármaco (21%), la eliminación de uno de los fármacos antifúngicos en casos de tratamiento combinado (7%) y, finalmente, la sustitución del tratamiento por la administración oral (1%). Las recomendaciones propuestas se aceptaron en 28 casos (40%). No se produjo una diferencia significativa en la adherencia con respecto al tipo de recomendación (p=0,554). Durante el período de estudio se evidenció un descenso en el uso de antifúngicos del 42%, en comparación con el uso observado en un período previo similar. La mortalidad de los pacientes que fueron tratados de acuerdo con las recomendaciones fue del 17%, y del 30% en aquellos en los que no se modificó el tratamiento (p=0,393).

Conclusiones: El programa de asesoramiento sobre los antifúngicos prescritos en pacientes hospitalizados puede resultar una estrategia eficaz para mejorar el uso de estos fármacos.

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Invasive fungal infections (IFI) are a major cause of morbidity and mortality in hospitalized patients in many countries worldwide.^{4,9} The prompt initiation of effective antifungal therapy reduces patient mortality.² The poor prognosis associated with IFI combined with suboptimal diagnostic tools has driven the overuse of antifungal drugs which account for an important and increasing part of the cost of drugs for inpatients.^{2,20,24} Inappropriate use of antifungals also contributes to the global increase in antifungal resistance and the incidence of IFI due to emerging fungi.^{3,10,16}

According to previous studies, most inappropriate antifungal prescriptions are due to difficulties in distinguishing between colonization and infection, little knowledge of the local rate of fluconazole resistance, limited awareness of the first line of treatment for IFI, low switching from intravenous to oral antifungal administration, no adjustment after microbiological results, and excessive length of therapy.^{27,30,34,35} Among the strategies to improve this situation the use of new technology for a rapid identification of fungal species must be highlighted.¹

The important role of antifungal agents in the management of IFIs along with the high costs and their recognized toxicities has been addressed as the principal justification for antifungal stewardship.^{3,10,16} However, antifungal stewardship has received very little attention in comparison with antibiotic stewardship.³⁵ It should be noted that the antifungal stewardship programmes (ASP) conducted to date have promoted a reduction in spending on antifungal drugs but not in mortality.^{20,27}

The aim of this study was to determine the usefulness of an ASP programme in a tertiary hospital with a high number of hematological and solid organ transplantation patients.

Methods

Between 1st October 2012 and 31st May 2013, 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; they contain computerized prescriptions and progress notes made by physicians. The Local Hospital Infections Committee created a team responsible for implementing the 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 attending physicians with the primary objective of assessing their adherence to ID recommendations entered 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 eight-month study the main activity was to perform a programmed review of antifungals prescriptions in hospitalized patients. This review was carried out by two ID specialists together with an internal medicine resident. A list of patients who were prescribed an antifungal considered restricted was provided by the hospital pharmacy department. Lipid formulations of amphotericin B, echinocandins and voriconazole were considered restricted antifungals. Posaconazole was not included in the study because its use was specifically restricted to prophylactic indications in hematologic patients. In the case of patients who were prescribed inadequate systemic antifungal 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. Patients could be included more than once if they received any antifungal several times during the study period. Fungal infections in study patients were classified as possible, probable or proven according to recent European Organization for Research and Treatment of Cancer criteria.⁷ Antifungal prescriptions were regarded as amendable if they were not considered clinically justified and/or did not follow local, national or international guidelines. 12,15,24,32 The identification of fungal species was performed by conventional cultures, implementing special techniques when necessary. 6 Antifungal susceptibility testing was performed on the isolates according to the microdilution broth procedures CLSI M27-A3 and EUCAST.²⁶

Special care was taken to neither criticize nor discredit current antifungal prescriptions due to the fact that several suitable options to treat the infections may exist, and also because the judgement of the investigators could not take into account certain patient characteristics only known by the treating clinicians.

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

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