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Original article

Antifungal agents use in a French administrative region☆

Le bon usage des antifongiques à l'échelle d'une région française

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Abstract

Background. – The increased use of new costly antifungal agents has led to a considerable increase in pharmaceutical expenditure. In December 2011, the Lorraine Regional Health Agency commissioned the Antibiolor network to evaluate costly antifungal agent stewardship using as reference regional, French, and international recommendations.

Methods. – We performed a regional retrospective multicenter study. The criteria for evaluation were the appropriateness of the indication for treatment, the choice of the agent or of a combination, compliance with dose and treatment duration, and the absence of any alternative.

Results. – One hundred and fourteen prescriptions were analyzed, in 7 intensive care units, 4 hematology units, and 1 infectious diseases unit. The indication for costly antifungal treatment was appropriate in 110 cases (96.5%), the choice of the antifungal agent in 102 cases (93%), the dose in 98 cases (89%), treatment duration in 102 cases (93%), and an alternative antifungal treatment was possible in 10 cases (9%). Eighty-two prescriptions (74.5%) complied with the marketing authorization, 19 (17%) were related to a protocol for temporary use, and 9 (8%) were considered as inappropriate.

Conclusion. – Our results show a high rate of appropriate prescriptions. The easily accessible and regularly updated local recommendations probably resulted in the standardization and optimization of costly antifungal agent prescriptions.

Keywords: Antifungal treatment; Antifungal stewardship; Evaluation of professional practices

Résumé

Contexte. – Les nouveaux antifongiques sont des molécules onéreuses et l'augmentation de leur consommation est à l'origine d'une forte augmentation des dépenses pharmaceutiques. En décembre 2011, l'Agence régionale de santé de Lorraine a mandaté le réseau Antibiolor pour la réalisation d'un audit sur le bon usage des antifongiques dans les établissements de santé prescripteurs de la région, en prenant comme références le référentiel local et les recommandations françaises et internationales.

Méthode. – Étude rétrospective multicentrique régionale. Les critères d'évaluation étaient la pertinence de l'indication du traitement, du choix de la molécule ou de l'association, le respect de la posologie et de la durée de traitement, et l'absence d'alternative.

Résultats. – Cent quatorze prescriptions ont été analysées, dans 7 services de réanimation, 4 d'hématologie et 1 de maladies infectieuses. Le traitement antifongique était indiqué dans 110 cas sur 114 (96,5 %). Sur les 110 prescriptions indiquées, le choix de la molécule antifongique était pertinent dans 102 cas (93 %), la posologie dans 98 cas (89 %), la durée du traitement dans 102 cas (93 %) et un traitement antifongique alternatif était possible dans 10 cas (9 %). Quatre-vingt-deux prescriptions (74,5 %) étaient conformes au libellé de l'autorisation de mise sur le marché, 19 (17 %) étaient en lien avec un protocole temporaire d'utilisation et 9 (8 %) étaient considérées comme situations non acceptables.

☆ The results of this study were presented in an oral communication at the RICAI, in November 2013, in Paris.

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Discussion. – Notre évaluation montre une proportion élevée de prescriptions conformes. L'existence d'un référentiel régional actualisé et accessible a probablement permis d'uniformiser et d'optimiser les prescriptions d'antifongiques coûteux.

Mots clés : Antifongique ; Bon usage ; Évaluation des pratiques professionnelles

1. Introduction

Over the past 2 decades, the epidemiology and management of invasive fungal infections (IFIs) have changed considerably. The incidence of severe infections has been increasing, due to the development of immunosuppressive therapies and advances in medical technology, especially in intensive care [1–3]. These changes have made the pharmaceutical industry develop and market new antifungal agents in the last 10 years (voriconazole, posaconazole, echinocandins). These systemic antifungal agents have broader spectra of action and better safety, but are also very expensive.

The management of IFIs is complex for the clinician, firstly because the diagnostic tools are not sensitive and specific enough, not always allowing a definitive diagnosis [4,5], and secondly because of a high death rate in case of delayed treatment initiation. Thus, antifungals are used according to the definitions of the "Invasive Fungal Infection Cooperative Group" (IFICG) as curative treatment for documented IFIs, but also as prophylactic treatment (based on risk factors), as preemptive treatment in case of possible IFI (suggestive radiological signs, colonization, or positive biomarkers in patients at risk for IFI), or probabilistic treatment in case of a persistent fever despite antibiotic therapy in patients at high risk of IFI without radiological or clinical markers (signs of sepsis without fungal documentation) [6]. Systemic antifungal agents have therefore been increasingly prescribed, resulting in a very significant increase of hospital drug expenditures (+11.3% in French hospitals between 2009 and 2010), higher than those related to antibiotics, and raising the risk of developing resistance to these new antifungal agents. Most new antifungal injectable agents are listed as reimbursable drugs in addition to the drug-related group cost (DRGc, French acronym T2A); the reimbursement is ensured by the health insurance under the condition that these agents are used in compliance with indications or with the temporary protocol of use. French, European, and international expert societies have published recommendations guiding the definition of cases for which prescribing these antifungals should be reimbursed in addition to the DRGc [7,8].

In December 2011, the general director of the Lorraine Regional Health Agency (French acronym ARS) commissioned the Antibiolor (Lorraine Antibiology network) and the Observatory of Drugs, Medical Devices, and Therapeutic Innovations (French acronym OMEDIT) to perform an audit on the appropriate use of costly antifungal agent stewardship reimbursed in addition to the DRGc, in regional healthcare institutions prescribing these agents.

The objective of our study was to assess the compliance of expensive antifungal prescriptions reimbursed in addition to the DRGc with French and the latest international recommendations, in Lorraine healthcare institutions prescribing these agents.

2. Patients and method

We conducted a regional multicenter, retrospective study. The included hospitals and units were targeted by the ARS according to their consumption of antifungals reimbursed in addition to the DRGc: liposomal amphotericin B, caspofungin, micafungin, and voriconazole (injectable form). We included the records of the first 10 patients having received antifungal reimbursed in addition to the DRGc, from October 1, 2011 to September 30, 2012 in each participating unit.

The data was collected with a standardized data collection form that included the identification of the institution and the prescribing unit, the patient's characteristics, the risk factors for fungal infection at treatment initiation, the clinical status, antifungal treatment data (agent(s) prescribed, dose, date of initiation and end of treatment, type of infection (nosocomial or community), treatment type (prophylactic, probabilistic, preemptive, documented)), the main indication for prescribing, the microbiological results, and the outcome of the patient under treatment. The duration of treatment was considered as appropriate, in case of empirical prescription, when the clinical outcome was favorable under treatment, and when the usual duration of treatment for the suspected indication was applied, or when treatment was continued at best during the usually recommended time or stopped 48 hours after resolution of aplasia for neutropenic patients.

An evaluating physician, external to the unit, collected data for each form directly on the site by consulting the patient's medical record.

A group of experts including at least 1 infectious disease specialist, a pharmacist, a mycologist, and unit prescribing physicians assessed the relevance and compliance of prescriptions on anonymized data, according to a model of professional practice evaluation, as part of a continuing professional development approach.

Physicians of the region could consult the Antibioguide when they prescribed agents, and the guide is available on the Internet at http://www.antibiolor.org. If the clinical presentation was not mentioned in the Antibioguide, the prescribing physician could justify his prescription according to international recommendations available at the time of the study [7,8], or on more recent scientific data published or presented in meetings.