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Short Communication

Misuse of antibiotics reserved for hospital settings in outpatients: a prospective clinical audit in a university hospital in Southern France ☆

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ABSTRACT

Some antibiotics are reserved essentially for hospital settings owing to cost effectiveness and in order to fight the emerging antibiotic resistance crisis. In some cases, antibiotics reserved exclusively for use in hospitals may be prescribed in outpatients for serious infections or in the absence of a therapeutic alternative. A 30-day prospective audit of outpatient prescriptions of antibiotics reserved exclusively for use in hospitals was performed. The objective of this study was to evaluate the relevance of outpatient antibiotic prescriptions by measuring appropriateness according to guidelines. During the study period, 53 prescriptions were included, only 40% of which were appropriate. Among the 32 inappropriate prescriptions, 4 cases lacked microbial arguments, 1 case was not adequate for the infection type, 1 case involved an incorrect antibiotic dosage, 1 case involved an incorrect interval of dose administration, 3 cases had a therapeutic alternative and 22 cases were not recommended. Of the 53 prescriptions, 66% were started in hospital and 34% in outpatients. Only 25% of cases were prescribed with infectious diseases specialist (IDS) advice, 64% were based on microbiological documentation and 13% had a negative bacterial culture. Inappropriate prescriptions were usually observed in antibiotic lock therapy, skin infections, *Clostridium difficile* colitis, intra-abdominal infections and intravascular catheter-related infections. Outpatient prescriptions of antimicrobial drugs reserved exclusively for use in hospitals are frequently inappropriate. We recommend a real-time analysis algorithm with the involvement of an IDS for monitoring prescriptions to improve the quality of these prescriptions and possibly to prevent antibiotic resistance.

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1. Introduction

Some infections can be rapidly managed in ambulatory care, including bone and joint infections, soft tissue infections, central nervous system infections, infective endocarditis, infected intravascular catheter bloodstream infections, intra-abdominal infections, urinary tract infections and febrile neutropenia [1–3]. In addition, administration of antibiotics or other anti-infective therapies at home or in the outpatient setting is possible as long as the clinical situation allows it [1–3]. In this case, antibiotics usually reserved for exclusive use in hospitals for severe infections may be delivered to the outpatient.

Measuring the quality of antimicrobial therapy in outpatient settings is usually focused on economic benefits, clinical outcomes and the adverse events of this managed care [4–6]. In previous studies, authors have usually provided details of the antibiotic drugs used and the infection types [4–6]. None has provided a real-time evaluation of an outpatient's prescription of antibiotics reserved for exclusive use in hospitals for severe infections. According to the French regulatory requirements, some antibiotic drugs must be dispensed in hospital pharmacies (http://legifrance.gouv.fr/

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affichTexte.do?cidTexte=JORFTEXT000000251171). The list of these antibiotic drugs is detailed in Supplementary Table S1. The University Hospital of Marseille, France, provides these antibiotic drugs in the pharmacy department for outpatients. In our opinion, this managed care could be considered a risk factor for antibiotic misuse. In fact, antibiotics usually used in hospitals have been administered at home to patients in a generally complicated infectious context: this type of dispensing concerns patients with periodic care and a complex clinical and drug history. According to all these elements, a study of the quality of antibiotic use in the case of this managed care was relevant and necessary.

Here we report a prospective audit of outpatient antibiotic prescriptions in a university hospital centre in Southern France. The relevance of outpatient antibiotic prescriptions was evaluated by measuring the appropriateness of the national antibiotic prescription guidelines and based on the relevance of antibiotic prescriptions in relation to antibiotic sensitivity. The objective of this study was to evaluate the relevance of outpatient antibiotic prescriptions by measuring the appropriateness of the national antibiotic prescription guidelines with respect to antibiotic resistance.

2. Materials and methods

A 30-day prospective audit of outpatient antibiotic prescriptions was performed in the 4000-bed university hospital centre in Marseille, France. During September 2014, a real-time analysis of all prescriptions of antibiotics in an outpatient setting was performed. According to the French regulatory requirements, some antibiotics must be dispensed only in hospital pharmacies (Supplementary Table S1) and some can be delivered to outpatients and do not need approval from an expert, e.g. an infectious disease specialist (IDS) or a pharmacist, to be dispensed.

A complete analysis of pharmaceutical data, the medical history of each patient requested systematically from clinicians, results of microbiological testing and antibiotic resistance was performed. The prospective analysis of prescriptions of antibiotics usually reserved for exclusive use in hospitals was done by one pharmacist resident and one pharmacist (double control) in our university hospital pharmacy in Marseille, France. The systematic analysis was performed in three steps: (i) in the first step, the prescription date, antibiotic prescribed, clinical context (type of infection, previous treatment and microbiological results), modality of antibiotic treatment (dosage, route, frequency of the anti-infective treatment), specialty fields of practitioners and the eventual IDS assessment were noted; (ii) in the second step, the appropriateness of the outpatient antibiotic treatment according to the antibiotic prescription guidelines provided by the French Infectious Diseases Society (SPILF) (http://www.infectiologie.com/site/consensus_recos.php) and the French National Agency for Medicines and Health Products Safety (ANSM) (http://ansm.sante.fr) was analysed; and (iii) in the third step, these treatments were assessed according to adapted criteria previously published (Supplementary Table S2) [7,8]. All information, in particular the clinical data, was collected from the institutional patient database or collected by phone directly from the physician.

In cases of ambiguous prescriptions of antibiotics usually reserved for exclusive use in hospitals for severe infections in an outpatient setting, a practitioner from the IDS team performed a second analysis. The quality of antibiotics usually reserved for exclusive use in hospitals for severe infections in an outpatient setting was measured with the following criteria: inadequate treatment and infectious agent or locus of infection; incorrect dose; incorrect interval; more relevant therapeutic alternative exists in those cases; prescriptions outside guidelines; and appropriate antibiotherapy. A decision tree adapted from published criteria [9] is presented in Fig. 1.

Insufficient clinical or microbiological data were considered to be exclusion criteria. Patients were re-enrolled in the study if they were the subject of a new prescription. A descriptive analysis of outpatient antibiotic prescriptions was conducted using SPSS Statistics for Windows v.20.0 (IBM Corp., Armonk, NY) and data were compared using a χ^2 test. A P-value of <0.05 was considered statistically significant.

3. Results

During the study period, a real-time analysis of 63 prescriptions of antibiotics reserved for hospital settings was performed. Ten antibiotic prescriptions were excluded for insufficient clinical data. Different classes of antibiotics were included in this study: β-lactam derivatives in 4 cases [piperacillin, ertapenem and intravenous (i.v.) cefotaxime]; aminoglycosides in 9 cases (i.v. amikacin and in antibiotic lock therapy); oxazolidinones in 8 cases (linezolid); glycopeptides in 16 cases (teicoplanin, i.v. vancomycin and vancomycin in antibiotic lock therapy); nitroimidazole derivatives in 4 cases (i.v. metronidazole); polymyxins in 11 cases (i.v. colistin and local infusion); and fosfomycin in 1 case.

Among the 53 cases included, 66% of prescriptions were started in hospital care and 34% were started primarily in ambulatory care. It was observed that only 10 cases (19%) were prescribed by an IDS. In the other 81% of cases, antibiotics reserved for hospital settings were prescribed by physicians of other specialties, including 11 cases (21%) in internal medicine, 5 cases (9%) in oncology, 6 cases (11%) in pulmonology, 5 cases (9%) in gastroenterology, 11 cases (21%) in surgery, 1 case (2%) in cardiology, 1 case (2%) in intensive care medicine, 1 case (2%) in obstetrics and gynaecology, 1 case (2%) in general medicine (general practitioner) and 1 case (2%) in nephrology; among these cases, 3 were prescribed with advice from an IDS.

Prescriptions were based on microbiological documentation in 53 cases (Table 1). Seven cases (13%) presented negative bacterial cultures and 11 cases (21%) were prescribed in a prophylactic setting with no microbial data.

Besides this, antibiotics reserved for hospital settings were frequently prescribed in outpatient settings in bone and joint infections in 10 cases (19%) and lower respiratory tract infections in 6 cases (11%). Other reasons for prescribing antibiotics reserved for hospital settings in outpatients are detailed in Supplementary Table S3. The two cases of fever listed in this study concerned one case of fever after sleeve surgery for a patient with a gastrocolic fistula without the results of bacterial cultures, and a second case concerning the treatment of a chronic respiratory tract infection due to *Pseudomonas aeruginosa* in a patient with cystic fibrosis. The mean ± standard deviation duration of antibiotic treatment was 37.5 ± 50.1 days; mean durations for every medical condition have been listed in Supplementary Table S3.

Analysis of the appropriateness of prescriptions of antibiotics reserved for hospital settings in outpatients showed that only 21 cases (40%) were considered appropriate, 28 cases (52%) were considered inappropriate and 4 (8%) were considered unnecessary prescriptions according to SPILF and ANSM guidelines. Details of other reasons of antibiotic misuse are listed in Supplementary Table S4.

A high proportion of unnecessary or inappropriate prescriptions of antibiotics reserved for hospital settings in outpatients were observed in antimicrobial catheter lock solutions, skin and soft-tissue infections, *Clostridium difficile* colitis, intra-abdominal infections, burn wound infections and intravascular catheter-related bloodstream infections (Supplementary Table S4). Thirteen cases of prescriptions with advice from an IDS that were usually considered an appropriate antibiotherapy were observed (62%; $P < 0.001$).

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