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Original article

Antibiotic resistance in adult female patients hospitalized for acute pyelonephritis: Rates and predicting factors

Pyélonéphrites aiguës des femmes adultes hospitalisées : état de l'antibiorésistance et analyse de ses facteurs prédictifs

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Abstract

Introduction. – The empiric treatment of acute pyelonephritis (APN) with third generation cephalosporins (3GC) or fluoroquinolones (FQ) has been challenged by *Escherichia coli* resistance reported by community surveillance networks. But these could overestimate resistance because they do not discriminate between uncomplicated and complicated, or between community and care-related infections.

Objectives. – We had for aim to: quantify resistance rates in hospitalized patients presenting with APN; identify subgroups with resistance < 10% that could still be treated empirically with FQ or 3GC.

Patients and methods. – We retrospectively analyzed files of patients presenting with documented APN, hospitalized in an Infectious Diseases Department from October 2010 to December 2012.

Results. – Hundred and fifty-six female patients (median age: 66, interquartile range: 37), were admitted for uncomplicated APN (36%) or APN (64%) at risk of complications by 1 (46%), 2 (40%), or 3 or more (14%) risk factors. Bacteremia was associated in 44% of uncomplicated and 8% of APN at risk of complications. *E. coli* was predominant (82%), resistant to 3GC in 6% of patients (including 4% ESBL) and to FQ in 15% of patients. The rate of resistance to FQ increased with the number of risk factors for complication, from 6% in uncomplicated APN, to 25% in patients with ≥ 3 risk factors. No enterobacteria was resistant to either 3GC or aminoglycosides.

Conclusion. – The resistance rates of 3GC and aminoglycosides were < 10% in patients hospitalized for APN. FQ resistance rates reached 15% but only 6% in uncomplicated APN. Hence, FQ empiric regimen should now be restricted to the treatment of uncomplicated APN without severe sepsis.

Keywords: Pyelonephritis; Antibiotic resistance; Fluoroquinolones; Third generation cephalosporins; Extended spectrum beta-lactamase producing enterobacteria

Résumé

Introduction. – Le traitement probabiliste des pyélonéphrites aiguës (PNA) par céphalosporines de troisième génération (C3G) ou fluoroquinolones (FQ) est remis en cause par la hausse des taux de résistance (R) d'*Escherichia coli* rapportée par des observatoires de ville. Mais ceux-ci pourraient surestimer la R, mêlant PNA simples/à risque de complication, et communautaires/liées aux soins.

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Objectifs. – Déterminer pour les PNA hospitalisées, les taux de R et identifier des sous-groupes à risque de R < 10 % pouvant relever en probabiliste de FQ ou C3G.

Patients et méthodes. – Analyse rétrospective des PNA documentées admises en infectiologie entre 01/2010 et 12/2012.

Résultats. – Cent cinquante-six patientes (âge médian 66 ans, écart interquartile : 37) ont été admises pour PNA simple (36 %) ou à risque de complication (64 %) par 1 (46 %), 2 (40 %), 3 ou plus (14 %) facteurs de risque (FDR). Une bactériémie était associée à 44 % des PNA simples et 8 % des PNA à risque de complication. *E. coli* prédominait (82 %) et les taux de R étaient de 6 % pour les C3G (dont 4 % de BLSE), et 15 % pour les FQ. Le taux de R aux FQ était corrélé au nombre de FDR de complication : 6 % pour les PNA simples, 25 % pour les PNA avec ≥ 3 FDR. Aucune souche d'entérobactérie n'était R aux C3G et aux aminoglycosides.

Conclusion. – Les taux de R observés au cours des PNA hospitalisées sont < 10 % pour C3G et aminoglycosides, permettant leur utilisation probabiliste. La R aux FQ est de 15 %, mais 6 % seulement pour les PNA simples, imposant de limiter les FQ au traitement probabiliste des formes simples non graves.

Mots clés : Pyélonéphrites ; Antibiorésistance ; Fluoroquinolones ; Céphalosporines de troisième génération ; Entérobactérie productrice de bêta-lactamase à spectre étendu

1. Introduction

Acute pyelonephritis (APN) is both frequent (estimated at 50,000 cases per year in France, with 90% of female patients) and potentially severe (50 to 90% of cases requiring hospitalization) [1]. It exposes to a double risk: complication to severe urosepsis (sometimes fatal) and to nephronic reduction when the infectious focus is not rapidly controlled. Any delay before effective treatment, typically in case of empirical antibiotic treatment finally inappropriate for the causative bacterium, will potentially worsen the prognosis. The French recommendations issued in 2008 by the French Agency for the Safety of Health Products (French acronym Afssaps, since then renamed National Agency for the Safety of Drugs, French acronym ANSM) allowed choosing between a third generation cephalosporin (C3G) or a fluoroquinolone (FQ) for the initial antibiotic treatment of community-acquired APN, to which an aminoglycoside should be added in case of severe sepsis or for some presentations of complicated APN (for example due to obstruction) ; it was specified that exposure to a fluoroquinolone in the previous 6 months increased the risk of infection by a strain with decreased susceptibility, thus limiting the use of this antibiotic family [2]. These recommendations were made according to data from the National Epidemiology Observatory on Bacterial Resistance to Antibiotics (French acronym ONERBA) published in 2007, and mentioning for *Escherichia coli* (bacterial species involved in 80 to 90% of cases according to studies) a 2% resistance rate to injectable C3G and a 10% resistance rate to fluoroquinolones (but only 5% in women 15 to 65 years of age) [3].

Since then, the increasing *E. coli* resistance to FQ and in a lesser manner to C3G [4–8] has put to question the pertinence of these recommendations, and led to their reviewing by the French Infectious Diseases Society (French acronym SPILF).

It was important for this review to obtain recent epidemiological data on the antibiotic resistance of strains causing APN. Unfortunately, in France as in other countries, the data provided by various observatories corresponds to global results, from all the strains isolated in positive urinalysis, which includes very different clinical presentations considering the mode of acquisition (community-acquired or care-related infection), the clinical presentation (colonization or infection, type of cystitis, of APN, or of prostatitis), and the context (non-complicated infection, infection at risk of complication or recurrent) [9]. The results do not allow determining the microbial epidemiology of APN even when the authors tried to stratify the data according to the very limited clinical and biological information available at the laboratory such as gender, age range, or positive blood cultures [10].

Thus, we had for aim to build a recent series of APN cases, all microbiologically documented, so as to analyze FQ and C3G resistance, especially of *E. coli*, so as to identify sub-populations of female patients for whom these rates remained inferior to 10%, level under which the empirical use of an antibiotic class seems to be allowed. The study was focused on APN requiring hospitalization for any reason, a clinical presentation for which it is especially important that empirical antibiotic therapy covers the causative germ.

2. Patients and methods

We conducted a retrospective analysis, including all patients hospitalized for a microbiologically documented APN in a Teaching Hospital's Infectious Diseases Department (IDD) between January 1st, 2010 and December 31st, 2012.

We included only adult female patients, younger patients being hospitalized elsewhere, and male patients were excluded so as to obtain homogeneous clinical and microbiological series. A prostatic focus is always possible in male patients, even when the clinical presentation suggests APN, and the microbial epidemiology may be different in terms of species and antibiotic resistance.

The inclusion criteria for APN were those of the Afssaps 2008 guidelines, as well for clinical parameters (urinary symptoms, fever and/or lumbar pain) or for biological parameters (leukocyturia $>10^4$/ml and bacteriuria normally $\geq 10^4$/UFC/ml, but allowing inclusion of cases with lower bacterial inoculum in case of certain clinical presentation) [2].

A contrario we excluded cases with sterile urinalysis (except if concomitant hemoculture was positive for a bacterium known