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Risk factors for quinolone-resistance in women presenting with *Escherichia coli* acute pyelonephritis

*Facteurs de risque de résistance aux quinolones d'*Escherichia coli *responsables de pyélonéphrites aiguës chez la femme*

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Abstract

In France, according to the National Epidemiology Observatory of Bacterial Resistance to Antibiotics, 15.3% of outpatient urinary *Escherichia coli* isolates were fluoroquinolone-resistant in 2010. This puts to question the relevance of empirical fluoroquinolone therapy for community-acquired acute pyelonephritis (APN), potentially severe infections.

Objectives. – We had for aim to identify individual risk factors for quinolone-resistant *E. coli* in community-acquired APN.

Patients and methods. – A retrospective cohort study of 344 adult female patients presenting with *E. coli* APN was conducted at the Roanne and Saint-Etienne hospital emergency departments, from January 2011 to February 2012. We studied the demographic, administrative, and clinical factors. *E. coli* strains with intermediate susceptibility on the antibiogram were considered as resistant.

Results. – There was 23% of isolates that were resistant to nalidixic acid and 17.4% to ofloxacin. Complicated APN was not a significant risk factor (univariate analysis). Three risk factors of resistance to nalidixic acid and ofloxacin were independent (multivariate analysis): fluoroquinolone use in the previous 3 months, hospitalization in the previous 6 months, and stay in a long-term care facility. The resistance to ofloxacin reached 30.6% if at least 1 of these risk factors was present; it was 9% when none of the factors were present.

Conclusions. – These results suggest that local recommendations for the empirical therapy of APN should be reviewed. The limitations of our study require backing up our results with prospective multicentric studies that could lead to drafting new national recommendations.

Keywords: *Escherichia coli*; Risk factors; Pyelonephritis; Quinolone-resistance

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Résumé

Selon l'Observatoire national de l'épidémiologie de la résistance bactérienne aux antibiotiques, 15,3 % des *Escherichia coli* urinaires de ville étaient résistants aux fluoroquinolones en 2010. Ceci interroge sur la pertinence du traitement probabiliste par fluoroquinolone des pyélonéphrites aiguës (PNA) communautaires, infections potentiellement graves.

Objectifs. – Identifier les facteurs de risque individuels de résistance aux quinolones d'*E. coli* responsables de PNA « communautaires ».

Patients et méthodes. – Une étude de cohorte rétrospective de 344 PNA à *E. coli* de femmes adultes a été menée dans les services d'accueil des urgences des hôpitaux de Roanne et Saint-Étienne, de janvier 2011 à février 2012. Étaient étudiés des facteurs démographiques, administratifs et cliniques. Les souches d'*E. coli* de sensibilité intermédiaire sur l'antibiogramme étaient considérées résistantes.

Résultats. – Les taux de résistance à l'acide nalidixique et à l'ofloxacine étaient respectivement de 23 % et 17,4 %. Le caractère compliqué de la PNA n'était pas un facteur de risque significatif (analyse univariée). Trois facteurs de risque de résistance à l'acide nalidixique et l'ofloxacine étaient indépendants (analyse multivariée): consommation de fluoroquinolone dans les 3 mois précédents, hospitalisation dans les 6 mois précédents et institutionnalisation. En présence d'au moins une de ces caractéristiques, le taux de résistance à l'ofloxacine s'élevait à 30,6 %. En leur absence, il s'abaissait à 9 %.

Conclusions. – Ces considérations invitent à revoir les référentiels locaux concernant le traitement probabiliste d'une PNA. Les limites méthodologiques de notre travail obligent à conforter ces résultats par des études prospectives multicentriques qui pourraient aboutir à de nouvelles recommandations nationales.

Mots clés : *Escherichia coli* ; Facteurs de risque ; Pyélonéphrite ; Résistance aux quinolones

1. Introduction

Bacteria resistant or even multiresistant, nosocomial and community-acquired, have been worryingly emerging and spreading, due to the selection pressure of antibiotics used in human and veterinarian medicine [1]. Understanding the bacterial epidemiology and the individual risk factors (RF) for resistance is mandatory to adapt recommendations for the prescription of antibiotic therapy.

The potential severity of acute pyelonephritis (APN), especially in fragile populations (immunodepression, etc.) [2], requires a quick initiation of antibiotherapy before obtaining the results of susceptibility testing (antibiogram) of the isolated bacterium. The French Agency for the safety of Health Products (French acronym AFSSAPS) recommendations for the empirical treatment of community-acquired APN were based on the susceptibility of *Escherichia coli*, the predominant bacterium in APN [3]. A fluoroquinolone or a third generation cephalosporin (3GC) IV, combined with an aminoside in case of severe APN, are indicated [3]. Nevertheless, the rate of community-acquired urinary quinolone resistant *E. coli* isolates in France increased from 9 to 21% for nalidixic acid (NA) and from 4.2 to 15.3% for the ciprofloxacin, between 2000 and 2010 [4]. Several authors have reported an increase of morbidity and mortality if APN or bacteremia, due to quinolone resistant *E. coli*, was treated with fluoroquinolones in monotherapy (inappropriate antibiotherapy) [2,5]. Furthermore, the Infectious Diseases Society of America and the European Society of Clinical Microbiology and Infectious Diseases published a guide for the antibiotherapy of uncomplicated APN in 2010, recommending the use of an alternative treatment if the local rate of enterobacteriaceae resistance to fluoroquinolones was superior to 10% [6]. The AFSSAPS mentioned that only fluoroquinolone intake in the previous 6 months could restrict their use in first intention [3]. But other risk factors for urinary quinolones resistant *E. coli* isolates have been reported [5,7–14].

We tried to determine which of these risk factors, especially complicated APN, could be proved in the specific context of APN.

2. Patients and method

2.1. Patient selection

We conducted our study in 2 emergency departments (ED) for adult patients, in the Loire region, from January 1, 2011 to February 29, 2012. The Roanne general hospital (GH) admitted 28,383 patients in 2011, for a city population of 80,678 individuals. The Saint-Etienne Teaching Hospital admitted 44,793 patients in 2011, for a city population of 371,728 individuals (population also concerned by other GH).

The inclusion criteria of patients were: female gender, 18 years of age or more, and clinical and microbiological diagnosis of *E. coli* APN [3,15,16]. This latter was defined by:

- urinalysis performed in the 24 hours after admission: leukocyturia ≥ 104/mL and *E. coli* bacteriuria ≥ 104 CFU/mL;
- clinical signs: temperature ≥ 38°C and/or biological inflammatory syndrome (CRP ≥ 40 mg/L), and/or acute lumbar pain spontaneous and on palpation.

The non-inclusion criteria were: other diagnosis explaining the clinical and biological symptoms, on-going pregnancy, redundant *E. coli* strain during the same hospital stay, contaminated urinalysis (≥ 3 bacteria).

The exclusion criterion was lack of documented history and/or usual treatments.

The population sample size was calculated with CDC Epi-InfoTM version 6.04d.fr (WHO) for a study power of 80% and a CI at 95%, in the hypothesis of 2 uncomplicated APN for 1 complicated APN; with 5% of fluoroquinolone-resistant *E. coli* in uncomplicated APN and 15% in complicated APN [10]: 339 patients were needed.