

Original article

Urinary tract infections in hospital pediatrics: Many previous antibiotherapy and antibiotics resistance, including fluoroquinolones

Infections urinaires en pédiatrie hospitalière : beaucoup d'antibiothérapie préalable et d'antibiorésistance, y compris vis à vis des fluoroquinolones

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Abstract

Objective. – We studied antibiotic resistance in pediatric UTIs and we evaluated the impact of antibiotic exposure in the previous 12 months, very little French data being available for this population.

Methods. – We conducted a multicenter prospective study including children consulting for, or admitted in 2 hospitals. Prior antibiotic exposure was documented from their health record.

Results. – One hundred and ten patients (73 girls), 11 days to 12 years of age, were included in 10 months. Ninety-six percent presented with pyelonephritis, associated to uropathy for 25%. *Escherichia coli* was predominant (78%), followed by *Proteus* spp. and *Enterococcus* spp. The antibiotic resistance rate of *E. coli* was high and close to that reported for adults with complicated UTIs: amoxicillin 60%, amoxicillin-clavulanate 35%, cefotaxim 5%, trimethoprim-sulfamethoxazole 26%, nalidixic acid 9%, ciprofloxacin 7%, gentamycin 1%, nitrofurantoin and fosfomycin 0%. The antibiotic exposure in the previous 12 months involved 62 children (56%) most frequently with β -lactams (89%) for a respiratory tract infection (56%). A clear relationship between exposure and resistance was observed for amoxicillin (71% vs. 46%), first generation (65% vs. 46%) and third generation (9% vs. 3%) cephalosporins, or trimethoprim-sulfamethoxazole (36% vs. 15%). However, antibiotic exposure could not account alone for the results, as suggested by the 7% of ciprofloxacin resistance, observed without any identified previous treatment.

Conclusion. – Bacterial species and antibiotic resistance level in children are similar to those reported for adults. Antibiotic exposure in the previous 12 months increases the risk of resistance but other factors are involved (previous antibiotic therapies and fecal-oral or mother-to-child transmission).

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Keywords: Bacterial resistance; Pediatric; Urinary tract infection

Résumé

Objectifs. – Étudier l'antibiorésistance des infections urinaires en pédiatrie hospitalière et la confronter à l'exposition antibiotique dans les 12 mois antérieurs, très peu de données françaises étant disponibles pour cette population.

Patients et méthodes. – Analyse prospective des enfants consultants ou hospitalisés dans deux hôpitaux, leur exposition antibiotique étant renseignée d'après le carnet de santé.

Résultats. – Recueil en dix mois de 110 cas (73 filles), âgés de 11 jours à 12 ans, 96 % souffrant de pyélonéphrites, dont 25 % sur uropathie. Dominance d'*Escherichia coli* (78 %) devant *Proteus* et entérocoque. Antibiorésistance d'*E. coli* élevée, comparable à celle de séries d'infections

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urinaires compliquées de l'adulte : amoxicilline 60 %, amoxicilline-clavulanate 35 %, céfotaxime 5 %, cotrimoxazole 26 %, acide nalidixique 9 %, ciprofloxacine 7 %, gentamicine 1 %, nitrofurantoïne et fosfomycine 0 %. L'exposition antibiotique dans les 12 mois antérieurs concernait 62 enfants (56 %), majoritairement par β -lactamines et pour infection respiratoire (89 % et 56 % des exposés, respectivement), avec une nette corrélation entre l'exposition antibiotique et l'antibiorésistance d'*E. coli* à l'amoxicilline (71 % vs 46 %), les C1G (65 % vs 46 %), les C3G (9 % vs 3 %) et le cotrimoxazole (36 % vs 15 %). Cependant, l'exposition antibiotique n'expliquait pas tout (7 % de résistance à la ciprofloxacine sans traitement préalable identifié).

Conclusion. – Les espèces bactériennes et niveaux d'antibiorésistance chez l'enfant sont similaires à ceux actuellement observés en France chez l'adulte. L'exposition antibiotique dans les 12 mois majore le risque de résistance, mais d'autres facteurs sont en cause (rôle probable des traitements plus anciens et de la contamination oro-fécale, voire materno-fœtale pour les plus jeunes).

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Mots clés : Infection urinaire ; Pédiatrie ; Résistances bactériennes

1. Introduction

Therapeutic recommendations depend on the surveillance of antibiotic resistance, especially for the empirical treatment of severe infections.

The epidemiological variations, sometimes important from one country to another, including within Europe (www.ecdc.org), justify obtaining national statistics. But, in the domain of urinary tract infection (UTI), the French National Observatory for Epidemiology of Bacterial Resistance to Antimicrobials (French acronym ONERBA) (www.onerba.org) does not specify any pediatric particularity. It is nevertheless one of the most frequent bacterial infections in children that, without an optimal treatment, exposes to the risk of a renal scarring and nephron loss [1,2].

The antibiotic exposure of children, a large source of antibiotic resistance, a fortiori for UTIs induced by bacteria of digestive flora, is significantly different from that of adults, more important in volume in the first years of life (because of the frequency of respiratory infections), but sparing some antibiotics classes such as fluoroquinolones and in a lesser way aminoglycosides [3]. In France, this exposure to antibiotics is much easier to analyze in children, using the healthcare record globally well documented both in community and in hospital practice, thanks to the vigilance of parents and healthcare personnel, whereas this tool is missing for adults [4].

The objective of this pilot study conducted in 2 Normandy hospital centers was to assess the antibiotic resistance of isolates from UTIs in children, and to compare it to exposure to antibiotics in the previous 12 months as documented in the healthcare record. The results were compared to antibiotic resistance data of adult UTI isolates collected in the same region thanks to 2 other concomitant studies [5,6].

2. Material and methods

2.1. Study population

Children 0 to 15 years of age, consulting or hospitalized at the Rouen teaching hospital (TH) or at the Evreux general hospital (CH) for an UTI, were included in a prospective study from January 1st to October 30th, 2011. The diagnosis of UTI (cystitis or pyelonephritis) had been made for each child, by a physician of the ward, because of a combination of suggestive

clinical signs (functional urinary signs, altered global health status, abdominal pains, etc.) and positive urine microscopy and culture (UMC). Fever ($>38^{\circ}\text{C}$) and a biological inflammatory syndrome ($\text{CRP}>5$) were also required to diagnose a pyelonephritis.

2.2. Urinalysis

Urine was collected after careful disinfection of the meatus with sodium hypochlorite (Dakin solution[®]) by healthcare personnel (nurse or child care assistant). The urine was collected at mid-stream in all children with voluntary urination; for infants, it was performed with collection bags (placed for less than 1 hour). In some rare cases, urine was collected by a 2-way vesical catheter. UMC was performed in the bacteriology laboratories of the Rouen TH and of the Evreux GH, on centrifuged urine. The positivity threshold were those define by the French Agency for the safety of Health Product (French acronym Afssaps) for children, i.e. leukocyturia $\geq 10^4/\text{ml}$ and bacteriuria $> 10^4$ UFC/ml [7]. The antibiograms were analyzed according to recommendations issued by the Antibiogram Committee of the French Microbiology Society (CA-SFM, www.sfm-microbiology.org).

2.3. Patient history and previous antibiotic treatment

We documented the following history for each child included: any previous episodes of UTI or of a known underlying uropathy (vesical ureteral reflux, mega ureter, dilatation of pyelocalyceal cavities, hydronephrosis, ureteral duplication, etc.), exposure to antibiotics in the 12 months before the UTI was also documented, specifying the name of the administered antibiotic and the reason for its prescription. This data was collected during an interview with the parents with, whenever it was possible, study of the child's healthcare record. The data was documented with a standardized questionnaire by the physician managing the child.

2.4. Statistical analysis

The statistical analysis assessing the risk of antibiotic resistance according to exposure to antibiotics in the previous focused on *Escherichia coli*, by grouping intermediately resistant and resistant strains. The rate of antibiotic resistance in the group of children exposed to antibiotics was compared to that of children not exposed, with the Chi^2 test for populations > 5 and Fischer's

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