Initial antibacterial therapy with cephalosporins III in children with upper urinary tract infections: is this choice rational?



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Abstract

Empirical therapy with cephalosporins III in children with pyelonephritis was not microbiologically justified in 85% of cases (n=100). In 22% of cases (n=26) isolated bacteria were resistant to cephalosporins III, these were enteroccoci and E.coli isolates, resistant to cephalosporins III and sensitive to aminoglycosides. In 63% of cases (n=74) bacterial isolates were sensitive to cephalosporins III (gram-negative pathogens), but were also sensitive to cephalosporins II, aminopenicillins and/or their combinations with beta-lactamase inhibitors. Comparison of immediate clinical and laboratory outcomes of antibiotic treatment options of pyelonephritis in children revealed equal efficacy of aminopenicillins (including their combinations with beta-lactamase inhibitors), cephalosporins III and aminoglycosides.

Introduction



Among childhood infections urinary tract infections (UTI) are the second most prevalent cause of morbidity after acute respiratory tract infections, and are the second most common cause for prescription of antibiotics [1-2]. Antimicrobial therapy of UTI is most often empirical: antibiotic choice aims at targeting the most probable causal pathogens [3]. Due to growing antibacterial resistance of uropathogens prescribing of cephalosporins III to children with UTI, including pyelonephritis, becomes widespread.

Hypothesis/Problem Addressed

Our study focuses on the problem of significant increase in the use of cephalosporins III in children with community-acquired UTI, which can lead to increased antibiotic resistance of uropathogens.

The objective of our study was to analyze whether the use of cephalosporins III as initial therapy in children with acute and chronic pyelonephritis was microbiologically/causally and clinically sound.

Method

- Retrospective analysis of 118 medical charts of hospitalized patients aged 1 month – 18 years in whom cephalosporins III were used on admission, was carried out in parallel with analysis of 118 results of their urine bacteriology tests. Children were not treated with antibiotics prior to hospital admission. Urinary samples were collected prior to any antibiotic prescription. We excluded cases with negative bacteriology tests.
- Analysis of clinical and laboratory outcomes of different modes of antibiotic therapy of active phase of pyelonephritis in hospitalized children (497 prescriptions of antibiotics in 397 patients).
- 3) Statistics: Revman 5.00.11 (Cochrane collaboration); SPSS 11.5.

Results

118 hospitalized children with upper UTI (pyelonephritis)

<u>Comparative clinical and laboratory efficacy of antibacterial therapy</u>

1) Aminopenicillins (AMP) and their combination with beta-lactamase

Sampling of urine samples prior of antibacterial therapy

Initial therapy of cephalosporins III

(cefotaxime, ceftriaxone, cefoperazone, cefixime)

Results of urine culture

63% (n=74) – isolates were sensitive to cephalosporins III, but were also sensitive to cephalosporins II, aminopenicillins and/or their combinations with beta-lactamase inhibitors

22% (n=26) – isolates were resistant to cephalosporins III (*enterococcus spp.* and resistant strains of *E.coli*)

15% (n=18) - isolates (Gram-negative
bacteria) were sensitive to cephalosporins III
and resistant to aminopenicillins and/or their
combinations with beta-lactamase inhibitors



Empirical therapy with cephalosporins III was not microbiologically justified!



inhibitors (AMP+BLI) vs cephalosporins III

	AMP and AMP+BLI		cephalosporins III		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
UTI1	68	75	336	366	100.0%	0.99 [0.91, 1.07]	
Total (95% CI)		75		366	100.0%	0.99 [0.91, 1.07]	•
Total events	68		336				
Heterogeneity: Not ap Test for overall effect:					0.2 0.5 1 2 5 cephalosporins III AMP and AMP+BLI		

2) Combinations of aminopenicillins with beta-lactamase inhibitors (AMP+BLI) vs cephalosporins III

	Aminopenicillins+BLI		Cephalosporins III		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
UTI1	51	57	58	64	100.0%	0.99 [0.88, 1.11]	
Total (95% Cl)		57		64	100.0%	0.99 [0.88, 1.11]	•
Total events Heterogeneity: Not ap Test for overall effect:	l events 51 rogeneity: Not applicable for overall effect: Z = 0.21 (P = 0.83)						0.1 0.2 0.5 1 2 5 10 Cephalosporins III Aminopenicillins+BLI

3) Aminoglycosides vs cephalosporins III

	Aminoglycosides		Cephalosporins III		Risk Ratio		Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixe	ed, 95% Cl	
UTI1	32	36	336	366	100.0%	0.97 [0.86, 1.09]			
Total (95% Cl)		36		366	100.0%	0.97 [0.86, 1.09]	•		
Total events	32		336						
Heterogeneity: Not ap Test for overall effect:	plicable Z = 0.53 (P =		0.2 0.5 Cephalosporins III	1 2 Aminoglyc	5 osides				

Conclusion

Empirical use of cephalosporins III was not microbiologically justified in the majority of cases and posed additional risks to public health in terms of selection of resistant bacterial strains. Aminopenicillins (including their combinations with beta-lactamase inhibitors), cephalosporins II and aminoglycosides could be used alternatively.

Policy relevance

The results of this study can be used to inform and improve clinical practice guidelines for the treatment of UTI in children and contribute to policy changes for antibiotic use in hospital settings.

Key references

1. American academy of pediatrics. Practice Parameter: The Diagnosis, Treatment, and Evaluation of the Initial Urinary Tract Infection in Febrile Infants and Young Children //Pediatrics. – 1999. – V. 103 (4). – P. 843-852

2. Watson A.R. Management of urinary tract infection in children / A.R. Watson //BMJ. – 2007. – V.335. – P.356-357

3. Cincinnati Children's Hospital Medical Center. Evidence-based care guideline for medical management of first urinary tract infection in children 12 years of age or less. Cincinnati (OH): Cincinnati Children's Hospital Medical Center; 2006. - 23 p.