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MONITORING SURVEY OF ANTIBIOTIC SENSITIVITY IN CHILD URINARY SYSTEM INFECTIOUS AGENTS (EXPERIENCE IN STAVROPOL)

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Numerous studies show that microbial inflammatory diseases in urinary system rate second among childhood infections. The relapsing course of infection in children may result in urinary tract obstruction and chronic renal failure. This makes microbial kidney issues the most common reason behind chronic renal failure in children. The latest years have witnessed an increase in the relative share of urinary tract infections (UTI) in the overall morbidity pattern in children (from 18 to 36–100 per 1.000 of child population) [2, 5, 6].

A key to success for treating UTI in children is antibiotic therapy provided started in due time and in view of the sensitivity of pathogens. Initial antibiotic treatment in most cases is administered prior to the identification of the pathogen, i.e. speculatively [9, 12], which means it is based on the knowledge of the characteristics pertaining to the most likely pathogens causing UTI, and their potential sensitivity to the medicine prescribed.

The latest decade, given the impact of various factors (accelerating mutation of microorganisms; alterations in the immunity; widespread, yet not always well grounded use of antibiotics) has seen certain changes in the structure and properties of the infectious agents causing pyelonephritis in children; a growth in the mixed infections, as well as the development of microbial flora resistance to the chemotherapeutic agents so widely used previously [1, 8, 10].

As many researches suggest, gram-negative bacteria of the Enterobacteriaceae family (80.6 %): *Escherichia coli*, *Proteus* spp., *Klebsiella* spp., etc. are the most prevalent in the spectrum of infectious agents causing UTI in children. Various authors point that the detection frequency for *E. coli* varies between 41.3 % and 83.3 % [2, 7, 8, 10]. However, there is data from local studies stating that staphylococcal microflora (32.3 %) prevails over *Escherichia* (19.4 %) [1].

The structure of other uropathogens in different parts of Russia also has some specific features [1,

2, 4, 7, 8, 10–12]. This means a need for regular regional microbiological monitoring as being aware of an up-to-date list of infectious agents behind microbial inflammatory diseases in the urinary system of children within a particular region would allow developing a timely and differentiated approach to administering an adequate empirical antibiotic therapy even before the urine culture results are available.

The purpose of this study is to investigate the specific features about the up-to-date list of infectious agents and the antibiotic sensitivity in UTI-causing pathogens in children of Stavropol (Russia).

Material and Methods. We observed 220 children aged 1 month to 5 years with acute community acquired infections of the upper and lower urinary tract, who were staying at the Nephrological Department of the Philippsky Child Clinical Hospital of Stavropol. All the children went through microbiological examination of urine, which implied determination of the degree of bacteriuria, verification of the isolated pathogen, and detection of the sensitivity to antimicrobial agents.

177 (80.5 %) out of the 220 children were girls, the rest of them – 43 (19.5 %) – being boys. All the children were divided into 3 age groups: Group I – under 1 year; Group II – 1–3 years, and Group III – 3–5 years.

The statistical analysis of the study results was performed using Microsoft Excel software whereas the statistical significance was calculated using Student's t-test; Fischer's method was employed to determine the confidence limits of shares (per cent) [3].

Results and Discussion. In Group I the boys accounted for 31.3 % of the population with the girls being in the majority – 68.7 % (boy/girl ratio – 1:2). 29 (43.3 %) children of this group were diagnosed with urinary tract infection (UTI); 26 (38.8 %) children had acute secondary obstructive pyelonephritis (PN), with another 12 (17.9 %) having acute undifferentiated PN.

In the group aged 1–3 yrs the boys/girls ratio was 1:4.5 (18.2 % vs. 81.8 %). Given the nosological structure, those with acute secondary obstructive PN (58 %) were in the majority; UTI was observed in 27 (30.7 %) children; acute undifferentiated PN – in 9 (10.2 %) children, and one of the children was

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diagnosed with acute secondary dysmetabolic PN. Group III had 59 (90.8 %) girls and 6 (9.2 %) boys, the ratio of boys vs. girls being 1:10 respectively. Acute secondary obstructive PN was on the top in the morbidity pattern in the children aged 3–5 yrs (76.9 %); children with UTI here accounted for 13.8 %, and those with acute undifferentiated PN – 9.2 % (Fig. 1).

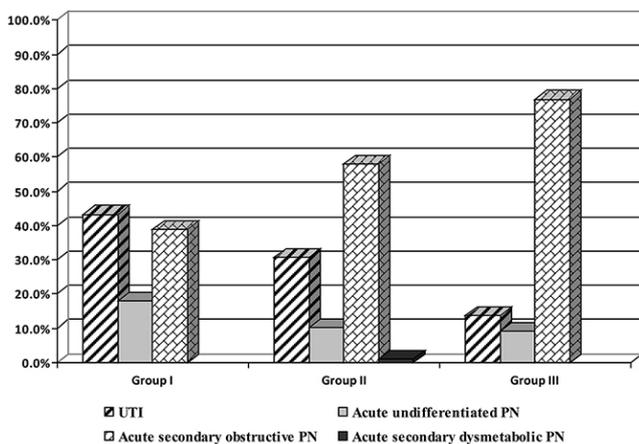


Fig. 1. Pattern of UTI morbidity depending on age

Following the data obtained, diagnostically significant bacteriuria ($\geq 10^5$ CFU/ml) was registered in 80.6 % cases in Group I, while the rest of the group's population had non-significant bacteriuria ($\leq 10^4$ CFU/ml). The children of Group II showed a high rate of bacteriuria in 59.1 % of cases, and in Group III this index was 36.9 %.

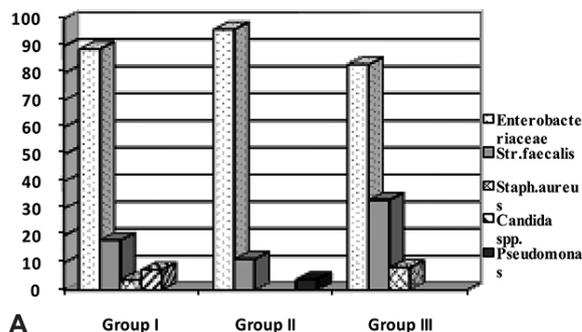
The results being negative could be largely due to the fact that the urine culture test was performed after the initiation of antibiotic therapy.

Based on the results of our study, the major causative agents for the community acquired UTI in all the groups were bacteria of the Enterobacteriaceae family, E. coli predominantly (Fig. 2a). In Group I (Fig. 2b) their share in the etiological structure was 88.9 %, including 11.1 % that had microbial associations with other pathogens (the most common association was Enterobacteriaceae + Str. faecalis association). Other uropathogens were verified much more rarely. Str. faecalis, for instance, was detected in 18.5 % of the children in the group in question, while in 14.8 % of mixed infection cases it was a second or a third microorganism.

The third most common UTI agent in children aged under 1 was Candida spp. separately and its associations with other pathogens (7.4 %). In the group aged 1–3 (Fig. 2c) the uropathogens related to the Enterobacteriaceae family were found in 96.2 %, 11.6 % of them being identified as a mixed infection. The second most common, just like in Group I, was Str. faecalis separately and its associations (11.6 %), the third most common coming Pseudomonas (3.9 %).

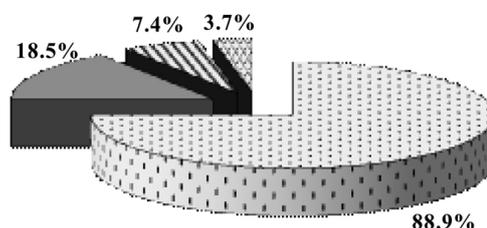
In Group III (Fig. 2d) the proportion of the Enterobacteriaceae family was somewhat lower than in the two other groups (83.4 %), while Str. faecalis was verified 1.8–2.9 times as often (33.4 %); 8.3 % children of this group were found to have Staph.aur. associated with Enterobacteriaceae и Str. faecalis.

Pattern of UTI agents depending on age of the children



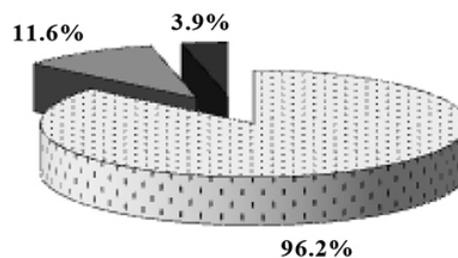
A

Pattern of UTI agents in children aged under 1



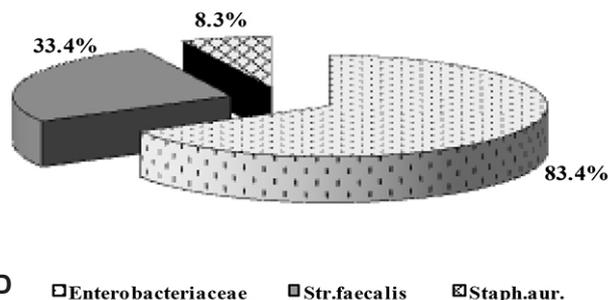
B

Pattern of UTI agents in children aged 1-3



C

Pattern of UTI agents in children aged 3-5



D

Fig. 2. Pattern of UTI agents depending on age

In the group of children aged below 1 (Table), the pathogens of the Enterobacteriaceae family revealed the highest sensitivity to Ciprofloxacin (83.3%), Ceftazidime (79.2%), Cefotaxime (70.8%), Cefoperazone (70.8%), Cefepime (70.8%), Amoxiclav (66.7%), Meropenem (66.7%), Furadonin (66.7%), and Gentamicin (62.5%). At the same time 70.8% of them proved resistant to Ampicillin, 50.0% – to Amoxicillin, 45.8% – to Oxacillin, 37.5% – to Cefazolin and Laevomycetin, 33.3% – to Gentamicin, Biseptol, Vancomycin and Palin.

(40.0%), and Palin (40.0%) was also present.

The children aged 3–5 demonstrated high sensitivity of Enterobacteriaceae to Ceftazidime (100.0%), Ciprofloxacin (100.0%), Cefuroxime (80.0%), Cefotaxime (80.0%), Cefoperazone (80.0%), Cefepime (80.0%), Gentamicin (80.0%), Sulperazone (70.0%), Imipenem (70.0%), Amikacin (70.0%), Amoxiclav (60.0%), Cefazolin (60.0%), Meropenem (60.0%), Ofloxacin (60.0%), and Furadonin (60.0%). Yet, to Ampicillin (80.0%), Oxacillin (50.0%), Amoxicillin (40.0%), Furadonin (40.0%), and Laevomycetin (40.0%) the isolated strains of the Enterobacteriaceae family were highly resistant, which prevented them from being used as initial antibiotics.

An analysis of the sensitivity shown by *Str. faecalis* to various antibiotics in Group I reveals a high number of strains susceptible to Cefoperazone (100%), Ciprofloxacin (100%), Furadonin (100%), Ampicillin (80%), Amoxiclav (80%), and Sulperazone (80%). However, *Str. faecalis* was found to be highly resistant to other cephalosporins and aminoglycosides.

In Group II, Ampicillin, Cefoperazone, Ciprofloxacin, and Furadonin revealed a high level of activity towards all isolated strains of *Str. faecalis*; high resistance being registered to cephalosporins and aminoglycosides, though. The group aged 3 to 5 yrs showed a sensitivity spectrum of *Str. faecalis* similar to that in the group of children under 1 year of age.

Conclusion. Therefore, the main pathogens for the community acquired UTI in children within their first 5 years are represented by the Enterobacteriaceae family, *E. coli* predominantly. The specific features of the UTI infectious agents in children (in Stavropol, Russia) included more frequent isolation of *Str. faecalis*, which rated second in all the groups, while in the children aged 3 to 5 it was identified 1.8–2.9 times as often. The third most common was *Candida* spp. in the children under 1 year, *Pseudomonas* – in those aged 1–3, and *Staph. aur.* – in the group aged 3–5 yrs.

In view of the leading etiological significance of Enterobacteriaceae as well as of the obtained data on the pathogens susceptibility towards antibiotics, Amoxiclav, Cefotaxime, Cefoperazone, Ceftazidime, Cefepime, and Meropenem make a reasonable choice as empiric therapy for treating community acquired UTI in children up to 5. The penicillins (Ampicillin, Amoxicillin, Oxacillin) and Laevomycetin should not be administered for empiric treatment due to the high-level resistance Enterobacteriaceae showed towards them.

Table

Antibiotic sensitivity in the major UTI pathogens depending on children's age (% of sensitive strains)

Drugs	Group I		Group II		Group III	
	Enterobacteriaceae n=48	Str. faecalis n=10	Enterobacteriaceae n=50	Str. faecalis n=6	Enterobacteriaceae n=20	Str. faecalis n=8
Ampicillin	16.7	80.0	20.0	100.0	20.0	75.0
Amoxicillin	29.2	60.0	48.0	66.7	40.0	75.0
Amoxiclav	66.7	80.0	64.0	66.7	60.0	50.0
Cefalexin	41.7	-	48.0	-	40.0	-
Cefazolin	50.0	-	64.0	-	60.0	-
Cefuroxime	58.3	-	64.0	-	80.0	-
Cefotaxime	70.8	-	80.0	-	80.0	-
Cefoperazone	70.8	100.0	76.0	100.0	80.0	75.0
Ceftazidime	79.2	-	80.0	-	100.0	25.0
Sulperazone	41.7	80.0	60.0	66.7	70.0	50.0
Cefepime	70.8	-	76.0	-	80.0	25.0
Imipenem	41.7	20.0	52.0	33.3	70.0	50.0
Meropenem	66.7	60.0	80.0	33.3	60.0	75.0
Gentamicin	62.5	-	80.0	-	80.0	25.0
Amikacin	50.0	-	68.0	-	70.0	-
Ciprofloxacin	83.3	100.0	88.0	100.0	100.0	75.0
Ofloxacin	45.8	60.0	52.0	66.7	60.0	75.0
Furadonin	66.7	100.0	44.0	100.0	60.0	75.0
Laevomycetin	58.3	60.0	48.0	66.7	50.0	50.0
Biseptol	33.3	60.0	48.0	66.7	40.0	25.0
Vancomycin	-	-	-	-	-	25.0
Nitroxolin	4.2	-	-	-	10.0	-

Analyzing the antibiotic sensitivity of the Enterobacteriaceae in Group II, mention should be made of the dominating role of Ciprofloxacin (88.0%), Cefotaxime (80.0%), Ceftazidime (80.0%), Meropenem (80.0%), Gentamicin (80.0%), Cefoperazone (76.0%), Cefepime (76.0%), and Amikacin (68.0%). However resistance to Ampicillin (80.0%), Laevomycetin (52.0%), Oxacillin (52.0%), Amoxicillin (40.0%), Furadonin (40.0%), Vancomycin

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The population subject to the study included 220 children aged 1 month – 5 years, with acute community acquired infections of the upper and lower urinary tract. As the data obtained showed, the major agents causing community acquired UTI in the first 5 years of age were bacteria belonging to the Enterobacteriaceae family, *E. coli* predominantly. The major features in the structure of the agents responsible for UTI development in the children of Stavropol (Russia) were higher detection frequency of *Str. faecalis*, which was the second most common in all the groups examined, while the children aged 3–5 had it 1.8–2.9 times as often.

In view of the leading etiological significance of Enterobacteriaceae as well as taking into account the obtained data on the pathogens susceptibility towards antibiotics, Amoxiclav, Cefotaxime, Cefoperazone, Ceftazidime, Cefepime, and Meropenem make a reasonable choice as empiric therapy for treating community acquired UTI in children aged up to 5. The penicillin antibiotics (Ampicillin, Amoxicillin, Oxacillin) and Laevomycetin should not be administered for empiric treatment due to the high-level resistance Enterobacteriaceae revealed towards them.

Key words: children, urinary tract infection, sensitivity, antibiotic drugs

МОНИТОРИНГ ЧУВСТВИТЕЛЬНОСТИ ВОЗБУДИТЕЛЕЙ ИНФЕКЦИЙ МОЧЕВОЙ СИСТЕМЫ У ДЕТЕЙ Г. СТАВРОПОЛЯ

А. Н. МЕДВЕДЕВА, А. С. КАЛМЫКОВА

Было обследовано 220 детей в возрасте от 1 месяца до 5 лет с острыми внебольничными инфекциями верхних и нижних мочевых путей. Установлено, что основными возбудителями внебольничных ИМС у детей первых 5 лет жизни являются представители семейства Enterobacteriaceae, главным образом *E. coli*. Основными особенностями структуры возбудителей ИМС детей г. Ставрополя являлось более частое выделение *Str. faecalis*, занимавшего второе место в структуре во всех группах, причем у детей с 3 до 5 лет он обнаруживался в 1,8–2,9 раза чаще.

Учитывая ведущую этиологическую роль Enterobacteriaceae и полученные результаты чувствительности, для эмпирической терапии внебольничной ИМС у детей до 5 лет целесообразно использовать амоксилав, цефотаксим, цефоперазон, цефтазидим, цефепим, меропенем. Антибиотики из группы пенициллинов (ампициллин, амоксициллин, оксациллин) и левомицетин не следует назначать для эмпирической терапии в связи с высоким уровнем резистентности к ним Enterobacteriaceae.

Ключевые слова: дети, инфекция мочевой системы, чувствительность, антибиотики

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DURATION OF LATENT PERIOD AND IRON DEFICIENCY DEVELOPMENT IN CHILDREN WITH CELIAC DISEASE

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Celiac disease in children is mostly associated with the development of a typical malabsorption syndrome, the nevitabile parts of the latter being polyhypomicroelementosis and polyhypovitaminosis [3, 4, 15]. Obviously, the age at the onset of the disease typically depending on the time gluten was introduced into the diet, as well as the period prior to the verification of diagnosis (i.e. latent period), do have an impact on the patient body's iron supply [8]. In view of the high lability and vulnerability typical of iron metabolism in children, any disturbances in its