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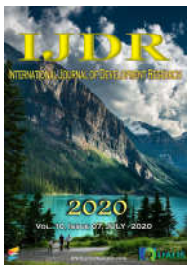

RESEARCH ARTICLE OPEN ACCESS

ETIOLOGICAL STRUCTURE OF URINARY TRACT INFECTIONIN PREMATURE NEWBORNS

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ABSTRACT

We studied the etiological structure of urinary tract infection (UTI) in 51 preterm infants and the etiology of asymptomatic bacteriuria in 60 preterm infants with body weight at birth from 780 g to 3000 g and gestational age from 27 to 37 weeks. Urine culture was carried out by Gould quantitative method from 3 to 6 times in the dynamics of observation. Most UTI pathogens are represented by gram negative microorganisms. Most often (48-50%) bacteria of the Enterobacteriaceae are found among them. Gram positive cocci (Staphylococcus spp., Enterococcus faecalis) were found in 3-27% of infants. Candida spp. was found in 7-40% of infants. The etiology of UTIs in infants with a birth weight of less than 1500 g was characterized by a high frequency of bacterial and Candida spp associations. Asymptomatic bacteriuria was represented by the same spectrum of microorganisms as UTI pathogens.

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INTRODUCTION

Urinary tract infection (UTI) in newborns, especially in premature infants, remains an urgent problem. The frequency of UTI in the structure of diseases of the urinary system in newborns is 37, 3% (ChugunovaetDumova, 2010).The UTI frequency among preterm infants with pneumonia is 14%, and full-term with pneumonia is 10% according to our clinic.According to the literature data, inflammatory changes in the clinical analysis of urine were observed in 25% of newborns in the intensive care unit and in the postresuscitativecare (Chugunova et Dumova, 2010, Chugunova et Shumikhina, 2015). The cause of severe chronic kidney disease and disability is often UTI in newborns (Campanella et Kara, 2007, Chugunova et Shumikhina, 2015, Makovetskaya et al., 2012; Kuppermann et al., 2019). Currently, the term UTI includes infectious and inflammatory diseases in any part of the urinary system such as pyelonephritis, cystitis, urethritis. It is connected with the fact that it is difficult to differentiate in infants the urinary system, where inflammation developed (Chugunova et Shumikhina, 2015, Yuryeva et Dlin, 2020).

Timely diagnosis and treatment of UTI helps prevent the development of severe chronic pathology of the urinary system (Dlin et Osmanov, 2017).The effectiveness of UTI treatment largely depends on knowledge of modern etiology and adequate antibiotic therapy (Campanella et Kara, 2007; Chugunova et Shumikhina, 2015).

Purposeof the study: determine the etiological structure of urinary tract infections in premature newborns and the sensitivity of pathogens to antibiotics.

MATERIAL AND METHODS

The study was conducted in Moscow (Russia) in the City Clinical Hospital №13 from November 2013 to December 2015. Urine cultures were performed in 117 preterm infants. Among them UTI were diagnosed in 51 infants, and asymptomatic bacteriuria were shown in 66 infants. The examined infants were divided into 4 groups. The 1st group included the following: 30 premature infants with UTI and body weight at birth ≤1500 g, average body weight at birth - 1080 ± 31 g (from 780 to 1450 g), average gestational age of

29.3 ± 0.46 weeks (from 27 to 32 weeks). The 2nd group included the following: 21 premature infants with UTI and body weight more than 1500 g. The average body weight was 2340 ± 55 g (from 1580 to 3000 g), the average gestational age was 34.2 ± 1.3 weeks (from 32 to 37 weeks). The 3rd group consisted of 46 preterm infants with asymptomatic bacteriuria and body weight at birth ≤1500 g. The average body weight at birth was 1120 ± 38 g (from 795 to 1480 g), the average gestational age was 29.0 ± 0.64 weeks (from 27 to 32 weeks).The 4th group included 14 infants with asymptomatic bacteriuria and weighing more than 1500 g. The average body weight was 2350 ± 64 g (from 1520 to 2990 g), the average gestational age was 34.8 ± 3.3 weeks (from 32 to 37 weeks). Urine cultures were performed in 106 preterm infants. Microbiological examination of urine was conducted in the dynamics of observation of infants at least 3 times (3-6 times) during the neonatal period by the generally accepted quantitative Gould method (Menshikov et Dolgov, 2013).The principle of the method is as follows: urine culture is done with a loop of urine (2 mm diameter) on solid medium (agar, blood agar) in a standard Petri dish into 4 sectors. Bacterial colonies are counted in each sector after growing microorganisms, and the number of microorganisms in 1 ml of urine is determined from the table. Diagnostically significant is the number of microorganisms in the urine of more than 10^5 colony forming units in 1 ml (CFU / ml) (Menshikov et Dolgov, 2013).The number of fungi $\geq 10^3$ CFU / ml was considered to be diagnostically significant for fungi of the genus Candida (Buslaeva et Samsygina, 2004). The antibiotic sensitivity of the selected strains of microorganisms was determined by the disk diffusion method on Mueller Hinton agar using standard commercial NITSF test systems (Russia) and ATV pse 5 test systems (BioMerieux) (Vandepitte et al, 1991; . MUK, 2004). Statistical analysis of the results was performed using Biostat, Ver .3.03 application package. The frequency of occurrence of the trait was determined in the percentage (%). The percentage of small numbers was given for comparison between groups. Comparison of the indicators within the studied groups and between groups was performed by Pearson criterion (χ^2 - criterion).

well as an increase in the physiological frequency of urination, the presence of diaper rash and hyperemia in the external genital area. Among 13 out of 51 infants had atony, somnolence, and loss of appetite. Bacteriuria in the urine with the content of conditionally pathogenic microorganisms in the amount of lg6 - lg8 CFU / ml was detected in all infants. Moreover, this infection process was isolated in a quarter of the examined newborns, both in the 1st and 2nd groups, and the resthad it in combination with an infection of the respiratory tract (pneumonia, tracheobronchitis), omphalitis, meningitis, and gut dysfunctions (rapid bowel movement with more mucus production, undigested lumps, vomiting), methiorism, disruption of the intestinalmicrobiome. The results of the study of the UTI etiological structure are presented in table 1. As it is seen from table 1, most often bacteria of the Enterobacteriaceae were dischargedfrom urine: in 15 infants of the 1st group (50%) and in 10 infants (48%) in the 2nd group. Gram positive cocci were less common. They were discharged from urine in 11 infants of the 1st group (37%) and in 5 infants of the 2nd group (24%). It should be noted that Candida albicans and E. coli were 2 times more common and Enterococcus faecalis was 2.8 times more commonin infants of the 1st group. Bacteriuria was combined with candiduria 14 infants (46.7%) and only bacteria were found in the urine in 14 infants (46.7%) in the 1st group. As a rule, associations of bacteria and Candida spp. were found in repeated studies. Apparently, this was due to the development of candidiasis on the background of antibiotic therapy (Buslaeva et Samsygina, 2004). Only Candida spp was found in the urine of 2 infants (6.7%). Only Candida albicans without bacteriuria was found in the urine of 3 infants (14.3%) in the 2nd group which was 2.1 times more often than it was in the 1st group. One infant (4.8%) had a combination of Candida albican with Enterococcus faecalis, and only 17 bacteria were found in 17 infants (81%). Thus, monoinfection and associations of microorganisms were found with some equal frequency in the 1st group, while monoinfection was 4.3 times more likely than associations ($p < 0.05$) in the 2nd group. Associations of fungi and bacteria in infants of the 1st group were found 9.7 times more often than in the 2nd group.

Table 1. Etiological structure of urinary tract infection in premature infants

N	Pathogen	Group 1 (infants with body weight ≤1500 g, n=30)		Group 2 (infants with body weight more than 1500 g, n=21)	
		n_1	%	n_1	%
1	Proteus vulgaris*	1	3,3	2	9,5
2	Enterobacter cloacae	0	0	3	14
3	Citrobacter spp	1	3,3	0	0
4	E.coli	8	27	3	14
5	Klebsiella pneumoniae	5	17	2	9,5
6	Staphylococcu sepidermidis (h+)	2	6,7	2	9,5
7	Staphylococcus haemoliticus	0	0	1	4,8
6	Staphylococcus aureus	1	3,3	0	0
8	Pseudomonas aeruginosa	2	6,7	2	9,5
9	Candidakrusei	2	6,7	0	0
10	Candida albicans*	12	40	4	19
11	Enterococcus faecalis*	8	27	2	9,5
12	Stenotrophomon as maltophilia	0	0	1	4,8

Tables notes 1 and 2. 1. n – the number of infants in the group, n_1 - the number of infantsin whom strain is isolated.
2. * – significance of differences between the groups, p<0,05.

RESULTS

UTI was diagnosed in 51 infants (30 infants in the 1st group and 21 infants in the 2nd group). The clinical manifestations of UTI were characterized by changes in the clinical analysis of urine in the form of detection of protein in the amount of 0.03-0.12 gram/litre, leukocytosis, erythrocytosis, bacteriuria, as

This was due to the longer antibiotic therapy and weaker anti-infective protection in very premature infants compared to more mature babies (Shabalov, 2004). Asymptomatic bacteriuria was detected among 66 newborns (in 46 infants of the 3rd group and 20 infants of the 4th group). These infants did not have the characteristic clinical manifestations of UTI. So, the clinical analysis of urine and the physiological

Table 2. The spectrum of microorganisms in the urine with asymptomatic bacteriuria in premature infants

N	Pathogen	Group 3 (infants with body weight ≤1500 r, n=46)		Group 4 (infants with body weight 1500 r, n=20)	
		n_1	%	n_1	%
1	Enterococcus faecalis*	4	9	8	40
2	Staphylococcu sepidermidis (h-)	1	2	0	0
3	Staphylococcu sepidermidis (h+)	4	9	1	5
4	Proteus mirabilis	1	2	0	0
5	Enterobactercloacae	2	4	0	0
6	E.coli	13	28	7	35
7	Klebsiella pneumoniae	3	7	1	5
8	Enterobacter aerogenes	2	4	0	0
9	Candidakrusei	3	7	0	0
10	Candida albicans	17	37	7	35
11	Pseudomonas aeruginosa	2	4	0	0
12	Stenotrophomonas maltophilia	1	2	0	0

frequency of urination were normal, there was no diaper rash and hyperemia in the external genital area. Bacteriuria developed against the background of IID outside the organs of the urinary systemin 40 (87%) among infants of the 3rd group; 6 infants of the 3rd group (13%) were conditionally healthy. Infectious and inflammatory diseases were diagnosed in 18 infants (90%) in the 4th group, and2 infants were conditionally healthy (10%). IID in infants of the 3rd and 4th groups were represented by an infection of the respiratory system (pneumonia, tracheobronchitis), intestinal dysfunctions, omphalitis (4 in each group).Asymptomatic bacteriuria in infants of the groups 3 and 4 was characterized by the content in the urine of conditionally pathogenic microorganisms in the amount of lg6 - lg7 CFU / ml. The spectrum of microorganisms excreted from urine with asymptomatic bacteriuria is presented in table 2. As itisseen from table 2, the microorganisms with bacteriuria did not differ in species composition from UTI agents presented in table 1. Bacteriuria maintained the same ratio between microorganisms of various groups as it is with UTI in premature infants. Gram-positive cocci, gram-negative bacilli and fungi were found at approximately the same frequency (0.45 -0.4 and 0.35, p> 0.05) in more mature infants. Enterococcus faecalis was found 4.4 times less often in deeply premature babies (group 3) than in more mature babies (group 4), which had the opposite direction in frequency of occurrence in comparison with infants with UTI. Among the most of infants asymptomatic bacteriuria was caused by one microorganism (74% - in 34 deeply preterm infants; and 80% - in 16 more mature infants). Colonization with two strains was met rarely (26% and 20%, respectively).

Thus, the frequency of monoculture and microbial associations was not different between groups of infants with different gestational age and body weight at birth with asymptomatic bacteriuria. Massive colonization of Candida spp. (more than 1000 CFU / ml of urine) of the urinary system was observed only with antibiotic therapy in premature infants with asymptomatic bacteriuria and UTI. The following regularity was noted: the fungus titer was generally lg3-4in infants who was receiving 3 antibiotics, and the titer was lg5-lg8 among those who was treated with 4-8 antibiotics, regardless of the degree of maturation of the newborn. The content of Candida spp. in infants who was receiving 1-2 antibiotics was generally less than lg3. Generally asymptomatic bacteriuria in premature infants was stopped during antibiotic therapy of the main infectious and inflammatory disease that was connected with the sensitivity of the strains isolated from urine to the used antibiotics.

The detection of Candida spp. in the urine required additional prescription of antifungal therapy or an increase in the doses of prophylactic antifungal drugs used and, if necessary, the replacement of one drug with another. As a rule the infectious agent of urinary tract were sensitive to antibiotics directed against the respective groups of microorganisms.Bacteria of the Enterobacteriaceae were sensitive to Imipenem / cilastatin, Meropenem, Amicacyn, Ceftazidime, Cefotaxime, Cefoperazone, Piperacillin + Tasobactam. E. coli strains were also sensitive to Gentamycin and Ciprofloxacin (18 strains each), Netilmycinum (12 strains), Ampicillin + Sulbactam (15 strains), Rifampicin (14 strains), Azlocillin (16 strains), Chloramphenicol (12 strains). All strains of Pseudomonas aeruginosa (6) were sensitive to Colistin, Imipenem / cilastatin, Meropenem, Amicacyn. Three (3) strains were sensitive to Ceftazidime and 3 strains were resistant to Ceftazidime. The last three strains of Pseudomonas aeruginosa strains were hospital strains. Stenotrophomonas maltophilia were sensitive to Ticarcillin + clavulanate, Co-trimoxazole, sulfamethoxazole + trimethoprim. Enterococcus faecalis was sensitive to Vancomycin, Linezolid, (all strains), to Imipenem / cilastatin and Meropenem (12 strains), to Cefazolin (8 strains), moderately resistant to Ampicillin (8 strains). Hemolytic staphylococcus epidermidis (h +) was sensitive to Vancomycin, Linezolid, Cefazolin, Ceftazidime, Ciprofloxacin, (all strains), Erythromycin, Lincomycin and Chloramphenicol (3 strains each). The Staphylococcus aureus strain was sensitive to Vancomycin, Linezolid, Erythromycin, Lincomycin, Benzylpenicillin, Oxacillin, Ampicillin + Sulbactam, Amoxicillin / clavulanic acid, Cefazolin, Ceftazidime, Amicacyn, Gentamycin, Rifampicin, Fusidinum-natrium, Ciprofloxacin.

DISCUSSION

The formation of UTI in newborns depends on the massiveness of bacteriuria, the properties of microorganisms and the state of the macroorganism (Schmidt et Copp, 2015). High colonization of the newborn by the microflora of the mother during childbirth and the microflora of the surrounding hospital environment in conditions of reduced anti-infective protection of the infant can be the cause of bacteriuria. Conducting daily sanitary treatment of the external genitalia and urinary system prevents their ascending infection (Raimund Steinaet el., 2015; Dlin et Osmanov, 2017). Currently, the authors emphasize uropathogenic strains of microorganisms. These microbes have the property of good adhesion (adherence) to the epithelium of the urinary tract. Uropathogenic strains are characterized by high rates of

colonization and growth (Shabalov, 2004; Schmidt etCopp, 2015).A certain contribution to the development of UTIs is made by hospital strains of bacteria that have pathogenicity factors: this is a high adhesive ability, the ability to synthesize bacterial toxins (coagulase, phospholipase, DNAse and others) and antibiotic resistance (Agyepong et al., 2018; Ignatova, 2011). A hospital strain of Pseudomonas aeruginosa was isolated in three infants with UTI during our study. It should be noted that antibiotic therapy of infectious and inflammatory diseases with localization outside the urinary tract (pneumonia, tracheobronchitis, omphalitis, meningitis and others) can significantly reduce the rate of bacteriuria. This can prevent the development of urinary infection and to reverse it, on the one hand, or make it difficult to diagnose UTI with a pathogen determination, on the other hand (Ignatova, 2011; Chugunova et Shumikhina, 2015). Disorders of the intestinal microbiome with an increase in the conditionally pathogenic microflora is one of the proven mechanisms of infection of the urinary tract in infants (Campanella et Kara, 2007; Dlin et Osmanov, 2017; Yuryeva et Dlin, 2020). Features of the macroorganism also affect the development of UTI in infants. These are small and large congenital abnormalities of the organs of the urinary system, impaired urodynamics, a decrease in local and systemic anti-infection protection (Dlin et Osmanov, 2017; Kuppermann et al., 2019; Yuryeva et Dlin, 2020).

Conclusion

The etiological structure of UTI in preterm infants is very diverse. Most pathogens are represented by grams negative microorganisms. Most often (48-50%) the bacteria of the Enterobacteriaceae are found among them.Gram positive cocci (Staphylococcus spp., Enterococcus faecalis) were found in 3-27% of infants. Candida spp. was found in 7-40% of infants. The etiology of UTIs in infants with a birth weight of less than 1500 g was characterized by a high frequency of bacterial and Candida spp associations. Asymptomatic bacteriuria was represented by the same spectrum of microorganisms as UTI pathogens.

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REFERENCES

Agyepong N, Govinden U, Owusu-Ofori A, Essack SY (2018). Multidrug-resistant gram-negative bacterial infections in a teaching hospital in Ghana. Antimicrob Resist Infect Control. 2018; 7:37. doi: 10.1186/s13756-018-0324-2. eCollection,.

Buslaeva GN, Samsygina GA (2004). Candidiasis of newborns (diagnosis, prevention, treatment).A guide to pharmacotherapy in pediatrics and pediatric surgery. Volume 4. Neonatology. Under the general editorship of A.D. Tsaregorodtsev and V.A. Tabolin. Chapter 9. Moscow.Medpraktika-M,pp 108-115. (inrus).

Campanella S, Kara T (. 2007.). Urinary tract infection. Starship Children's Health Clinical Guidelin: 11:.1—6.

Chugunova OL, Dumova S V (2010). Features of diseases of the urinary system in young children. In: Pharmacotherapy of children's diseases. Guide . Edited by A. D. Tsaregorodtsev. Moscow: Medical information Agency,pp704-734.

Chugunova OL, Shumikhina MV (2015). Urinary tract infection in children. Effective pharmacotherapy. Pediatrics. 94:3: 10-20 (in rus). https://umedp.ru/articles/infektsiya_mochevoy_sistemy_u_detey_aktualnye_voprosy.html

Clinical laboratory diagnosis. National manual in 2 volumes.(, 2013). Volume 2. edited by VV Menshikov and VV Dolgov, in 2 volumes, Moscow. Ed. GEOTAR-Media Group, 808 pp.

Control methods. Biological and microbiological factors. Determination of sensitivity of microorganisms to antibacterial preparations. Methodical instructions. MUK 4.2.1890-04.(2004.). Moscow. Medicine, 64p.https://www.rospotrebnadzor.ru/documents/details.php?ELEMENT_ID=4957

Dlin VV, Osmanov IM (2017). Infections of the urinary system in children. Moscow.Overlay, 422 pp. (in rus). https://www.libex.ru/detail/book914975.html .

Ignatova MS (2011). Children's nephrology. A guide for doctors. 3rd edition, revised. and add. Moscow. MIA:,696 p. (in rus). https://www.booksmed.com/pediatriya/2520-detskaya-nefrologiya-ignatova.html .

Kuppermann N, Dayan PS, Levine DA, Vitale M. et al. (2019). A Clinical Prediction Rule to Identify Febrile Infants 60 Days and Younger at Low Risk for Serious Bacterial Infections. JAMA Pediatr: 173:4: 342-351. doi: 10.1001/jamapediatrics.2018.5501.

Makovetskaya GA, Borisova OV, Mazur LI, Gasilina EC (2012). Predicting the development of kidney disease associated with an infection onset. Pediatriya, 91:6: 12-17. (inrus). https://pediatriajournal.ru /files/upload/mags/326/2012_6_3538.pdf

Raimund Steina, Hasan S Dogan, Piet Hoebeke, RadimKocˇvara et al. (2015). Urinary Tract Infections in Children: EAU/ESPU Guidelines. European urology, 67: 546–558.

Schmidt B, Copp HL (2015). Work-up of Pediatric Urinary Tract Infection. UrolClin North Am, 42:4::519-26. doi: 10.1016/j.ucl.2015.05.011. Epub, 2015 Aug 4.

Shabalov NP (2004). Antibiotic therapy in the neonatal period. A guide to pharmacotherapy in pediatrics and pediatric surgery. Volume 4. Neonatology. Under the general editorship of A.D. Tsaregorodtsev and V.A. Tabolin. Chapter 9. Moscow.Medpraktika-M, pp69-83; (in rus).

Vandepitte J, EngbaeK K, Piot P et all. (1991). Basic laboratory procedures in clinical bacteriology. Geneva: World Health Organization; pp43-51, 117-118.

Yuryeva EA, Dlin VV (2020). Guidelines for the clinical and laboratory diagnosis of kidney disease in children. 2nd Edition, supplemented and revised. Moscow. Ed. Overlay, 244 p.

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