Antibiotic Sensitivity of Uropathogens in Acute Pyelonephritis Children

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ABSTRACT

Acute pyelonephritis (APN) is a common childhood infection, which localizes in the upper urinary tract. Our aim in this study was to investigate the most common uropathogens in APN children and their antibiotic sensitivity patterns. Urine samples were taken from 65 children who were diagnosed with APN, from which uropathogens were isolated and identified by selective culture media and biochemical tests, and antibiotic sensitivity trends were evaluated on Muller Hington agar by disk diffusion method. E.coli was the leading isolate (66.7%) followed by Klebsiella pneumonia (13.98%), Proteus mirabilis (7.53%), Pseudomonas aeruginosa (4.3%), Staphylococcus aureus (4.3%) and Enterococcus faecalis (3.2%). The highest sensitivity rates were against imipenem, nalidixic acid, nitrofurantoin and amikacin (97.8%, 84.9%, 82.8% and 78.5% respectively), whereas the least were against augmentin and amoxicillin (30% and 4.3% respectively). Children younger than one year old had higher resistance rates than older ones. Imipenem, nalidixic acid, nitrofurantoin and amikacin were the most effective antibiotics, and higher resistance rates were found in younger children, who were suffering from more frequently recurrent infections.

Keywords: Acute pyelonephritis, Antibiotic, Children, Sensitivity, Uropathogens.

INTRODUCTION

Acute pyelonephritis (APN) is an urinary tract infection in which bacteria usually reach the kidney by ascending from lower urinary tract. The incidence of APN in children is difficult to ascertain, but it has been demonstrated that it is a common problem and the cause of 5-7% of their febrile episodes. Vesicoureteral reflux (VUR) is one of the most urinary tract abnormality associated with APN diagnosed children. In this reflex, the valve mechanism normally prevent back ward flow of bladder urine into the ureter and kidney is not working properly, which increases their recurrent infections. APN is associated with severe complications like permanent renal scarring and renal failure, which can be reduced by prompt and proper treatment. However, the resistance to antibiotics is increasing nowadays, due to the careless and irregular use of antibiotics especially in children with recurrent urinary tract infections. So our aim in this study was to investigate the most common uropathogens that can lead to APN in children and their antibiotic resistance patterns for later use of this information in proper antibiotic treatment.

MATERIALS AND METHODS

Urine samples were collected from 65 children with APN, who were admitted to Children Hospital in Damascus, Syria, between July 2012 and September 2013. The patients ages were between 1 month to 12 years. We obtained samples either by midstream clean catch method from urination controlled children, or by urethral catheters from urination uncontrolled ones. Children who had another infection or receiving antibiotic had been excluded from the study. Isolation of urine microorganisms was made on nutrient agar and next identification depended on gram staining, colonies characters on MacConkey, EMB and blood agar, in addition to biochemical tests like indole, methyl red-Voges Proskauer, Simmon’s citrate, urease broth, oxidase, catalase and coagulase tests. We investigated the microorganism’s resistance rates against amoxicillin, augmentin, trimethoprim and sulfamethaxazole, cefoxitine, cefazoline, nitrofurantoin, ceftriaxone, Gentamicin, amikacin, ceftaxime, ceftazidime, nalidixic acid and imipenem on Muller Hington agar by disk diffusion method.

Statistical analysis

SPSS program and Chi square test were used to analyze the results, which were presented as percentage rates (%). A P value less than 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

65 patients had been classified into 3 groups according to their age, Group I: children under one year (27 patients, 41.5%), Group II: children between one and four years (31 patients, 47.7%) and Group III: older children (7 patients, 10.8%). By reviewing patient files we found that 18.2% of boys were uncircumcised (100% in first group), and 33.8% of children had VUR (72.7% in the first group and 27.3% in the second group), as it is described in figure 1. Both VUR and uncircumcision are considered to be important infection risk factors, while the former is the most frequent APN associated abnormality, in which the urine reflux promotes the ascending of infection into the kidneys, the latter increases the risk by 10-12 folds.
The girls (43, 66.2%) were twice the number of boys (22, 33.8%), but 70% of Group I was only boys and girls increased after this age (95%), (P value<0.001). This can be explained by increasing boys risk factors at this age, because 21% of boys younger than a year old were uncircumcised and 72.7% had VUR. Most of boys were also at younger ages in Huang et al6 and Peng et al7 studies, but not in Czaja et al7 one, in which girls were predominant in all ages.

Among 65 urine sample, 93 bacterial isolates were found. In most of the samples we isolated one bacterial type (66.24%), but also more than one were isolated (33.76%). 77% of infections with more than one bacterial type were in the Group I, whereas 76% of one bacterial type infections were in older children, (P value=0.001). Increase the isolates in children younger than a year old is explained by their weak immune response,8 and higher rates of VUR and being uncircumcized, which increase the number of opportunistic bacteria reaching the kidneys.

E.coli was the leading isolate in our study (66.7%), because of its ability to form biofilm against the immune response,9 in addition to its high virulence, which helps it ascend along ureters to the kidneys, in spite of opposite urine flow and defending immune response.9 These results are similar to those in previous studies in Turkey,10 Iran,10 Serbia,15 India,11 Iraq12 and Saudi Arabia.13 Klebsiella pneumonia was the second isolate in the study (13.98%), that it is opportunistic bacteria and a common isolate in nosocomial infections.14 We also isolated Proteus mirabilis (7.53%), Pseudomonas aeruginosa (4.3%), Staphylococcus aureus (4.3%) and Enterococcus faecalis (3.2%), as it is described in the figure 2.

E.coli was predominant in all age groups, while 80% of non E.coli isolates were found in Group I, which are described in figure 3.

This can be explained by the highest rate of VUR founded in Group I, which is also seen in Johanson et al15 and Park et al16 whom submitted the increase of infection with non E.coli bacteria in VUR children. In addition Cascio et al17 found increase of these bacterial concentration around preputial sac of VUR children, in whom urine reflux push them into the kidneys. Non E.coli isolates were similarly predominant in newborns in some previous study,4,18 but Ipek et al19 concluded differently that there wasn’t age-bacterial type correlation.

Although hospital isolates are considered highly resistance, we investigated high sensitivity against imipenem, nalidixic acid, nitrofurantoin and amikacin (97.8%, 84.9%, 82.8% and 78.5% respectively), as they are described in figure 4, which may explained by their limited and medically controlled uses in our country. Nitrofurantoin spread poorly into infected renal tissues, so it is not used in the treatment.20 However, its high efficacy promotes its use in prophylaxis of APN in VUR and other high risk children, as it produces an antibacterial urine environment without affecting intestinal micro flora.21 Similar high sensitivities against imipenem, nalidixic acid and nitrofurantoin were reported in previous study,2,19,22 while lower sensitivities were found in others.10,13,23,24 Although high amikacin sensitivity had been demonstrated in our study (78.5%), the Gentamicin sensitivity was much lower (43%) and lower than that reported in AL-Omar study in our country in 2008 (78%)25 and in other regional studies (>60%).5,12,19,20,26 This may be related to increase gentamicin use, which develop bacterial resistance and its tendency to prevent its intracellular accumulation up to the level.27

Similar sensitivity decreasing was found against cephalosporins, that was intermediate against
ceftriaxone, ceftazidime (53.8%, 44.1% respectively), while was lower against cefotaxime, cefoxitin and cefazolin (38.7%, 37.6%, 35.5% respectively). Higher cephalosporins sensitivities were reported in AL-Omar study in 2008 (67-70%)\textsuperscript{25} and in other regional ones (60-80%).\textsuperscript{5,19,22,26} Decreased cephalosporins sensitivity may be resulted from the development of resistance strains that produce extended spectrum β-lactamases (ESBLs),\textsuperscript{27} especially after the increase of their use in the treatment of nosocomial and even community-acquired bacterial infections. The resistance rates against cefotaxime and cefazolin were even higher than that of other examined cephalosporins, because of their oral dosage forms which are more commonly used in children.

Sensitivities to trimethoprim and sulfamethoxazole, augmentin and amoxicillin were low (38.7%, 30% and 4.3% respectively), and they are not effective any more in the APN treatment similarly to what demonstrated in many previous studies.\textsuperscript{5,10,23,26} Amoxicillin and augmentin are rapidly excreted and the duration of their significant urine concentration is short,\textsuperscript{28} in addition the bacterial resistance against them like that against trimethoprim and sulfamethoxazole is constantly increasing, because of the increase use without prescriptions in the treatment of bacterial infections or even the common cold. Haward et al\textsuperscript{29} submitted that there is linked resistance between cephalosporins, trimethoprim and sulfamethoxazole, augmentin and amoxicillin, which may describe their associated resistance increasing in our study.

Figure 4: Percentages of isolates sensitivities against examined antibiotics.


The resistance against nalidixic acid, nitrofurantoin and gentamicin were higher in children younger than one year old in statistically significant manner (P value<0.05), and against amikacin and cephalosporins in statistically insignificant manner (P value>0.05), which are documented in the table 1.

Haward et al\textsuperscript{29} and Peco-Antić et al\textsuperscript{4} indicated that bacterial resistance was higher in newborns and neonates, because of their weak immune responses which lead to increase their recurrence infections and so treatment rates. In addition, Valavi et al\textsuperscript{26} and Taneja et al\textsuperscript{30} submitted that bacterial resistance was higher in children with urinary tract abnormality, because of their higher recurrence and treatment rates. Similarly the resistance in our study was higher in first group children, in whom the immune system was weak and the rates of VUR, uncircumcision and antibiotic treatment were higher. Differently from our study Caraciolo et al\textsuperscript{16} found bacterial resistance was similar in all children ages.

Table 1: antibiotic resistance in children younger than one year old and older ones

| Antibiotics | Number and percentage of resistance isolates | | | | | P value |
|-------------|---------------------------------------------|--------|--------|--------|--------|
|             | Younger than 1 year (n = 27) | Older than 1 year (n = 38) | total (n = 65) | |
| IMP         | 2 (2.1%) | 0 (0%) | 2 (2.1%) | - |
| NAL         | 13 (14.1%) | 1 (1.1%) | 14 (15.2%) | 0.005 |
| NIT         | 14 (15.1%) | 2 (2.1%) | 16 (17.2%) | 0.003 |
| AMK         | 15 (16.1%) | 5 (5.4%) | 20 (21.5%) | > 0.05 |
| GEN         | 33 (35.5%) | 20 (21.5%) | 53 (57%) | 0.049 |
| CTR         | 24 (25.8%) | 19 (20.4%) | 43 (46.2%) | > 0.05 |
| CFX         | 32 (34.4%) | 25 (26.9%) | 57 (61.3%) | > 0.05 |
| CAZ         | 31 (33.3%) | 21 (22.6%) | 52 (55.9%) | > 0.05 |
| FOX         | 32 (34.4%) | 26 (28%) | 58 (62.4%) | > 0.05 |
| CZ          | 34 (36.5%) | 26 (28%) | 60 (64.5%) | > 0.05 |

CONCLUSION

E.coli was the most common uropathogen that lead to APN in children. High sensitivity was found against imipenem, nalidixic acid, nitrofurantoin and amikacin, which promote imipenem, nalidixic acid and amikacin usage in the treatment of APN and nitrofurantoin usage in the prophylaxis in children suffering from recurrent infections. On the other hand, the highest resistance was found against cefazolin, cefoxitin, trimethoprim and sulfamethoxazole, augmentin and amoxicillin which are frequently prescribed for treatment in children. Therefore these information should be considered while prescribing antibiotics for treatment and further studies are needed to follow the development of antibiotic resistance with time.
REFERENCES


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