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İPEK AKİL

ÇINAR ÖZEN

BEYHAN CENGİZ

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Do patients with neurogenic bladder treated with clean intermittent catheterization need antibacterial prophylaxis?

İpek AKİL[1], Çınar ÖZEN[1,*], Beyhan CENGİZ[2]

[1]Department of Pediatric Nephrology, Faculty of Medicine, Celal Bayar University, Manisa, Turkey
[2]Department of Public Health, Faculty of Medicine, Celal Bayar University, Manisa, Turkey

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Background/aim: In this study, we investigated the effectiveness of antibiotic prophylaxis (ABP) with respect to the incidence of symptomatic urinary tract infections (UTIs) and evaluated the development of renal scarring in patients treated with clean intermittent catheterization (CIC).

Materials and methods: A total of 22 patients were included in the study. The patients were administered ABP in the first year (the ABP-received period) but not in the second year (the ABP-discontinued period).

Results: Twenty-eight of all cultures taken in the ABP-received period (18.2%) and 25 (16.2%) of the ABP-discontinued cultures were considered to be indicative of symptomatic UTIs (P = 0.65). The multiple antibiotic resistance rate of microorganisms in cultures taken during the ABP-discontinued period (47; 30.5%) was lower than that in those taken in the ABP-received period (62; 40.3%), (P = 0.07). There was no difference between the ABP-received and ABP-discontinued periods with respect to the development of new lesions according to dimercaptosuccinic acid results (P = 0.14).

Conclusion: Routine ABP usage is not protective against the development of symptomatic UTIs and new lesions in neurogenic bladder patients receiving CIC. Furthermore, the growth of resistant microorganisms increased in the ABP-received period.

Key words: Clean intermittent catheterization, neurogenic bladder, urinary tract infection

1. Introduction

Neurogenic bladder (NB) refers to the deterioration of bladder function and the inconvenient retention and/or discharge of urine as a result of cerebral cortex, medulla spinalis, or peripheral nervous system lesions. Although the causes of this condition are usually congenital, it may also be acquired (1).

Disruption of coordination between the detrusor and sphincter muscles leads to various pathophysiologic conditions in NB. Lack of coordination between the detrusor and sphincter muscles gives rise to high intravesical pressure and urine retention. This can be associated with the vesicoureteral reflux (VUR). The combination of high intravesical pressure, urine retention, and VUR may result in pyelonephritis and renal scar formation, which, in turn, can lead to loss of renal function (1,2).

The suggested treatment for NB patients without appropriate bladder emptying is clean intermittent catheterization (CIC), which involves emptying the bladder at regular intervals using a sterile catheter. The incidence of urinary tract infections and/or bacteriuria may be elevated in children with NB, because of contamination and inflammation resulting from catheterization and urine retention. There are various reports in the literature concerning prophylactic antibacterial treatment administration in children with NB. Despite the fact that long-term antibacterial prophylaxis (ABP) increases bacterial resistance and therefore leads to resistant infections, some groups continue to assert that this treatment is necessary (3). Multiple-drug resistance (MDR) is a condition that enables disease-causing microorganisms to resist distinct antimicrobials, first and foremost antibiotics (4).

In this study, we investigated the effectiveness of ABP with respect to the incidence of symptomatic urinary tract infections and evaluated the development of renal scarring in patients treated with CIC.

2. Materials and methods

Twenty-two patients who were admitted to the Celal Bayar University Hafsa Sultan Hospital Pediatric Nephrology Polyclinic with NB secondary to neural tube defects and

* Correspondence: ipekozunan@yahoo.com

who were being treated with CIC were included in the study. All patients were monitored for 1 year while they received ABP (prophylaxis consisting of amoxicillin for infants, trimethoprim/sulfamethoxazole, and, if resistance occurred, nitrofurantoin) and for an additional year after termination of prophylactic treatment. All symptomatic infections were treated according to routine protocols. Empirical treatment was given to patients with symptomatic reproduction (cefuroxime, ceftriaxone, ampicillin, amoxicillin clavulanate, cefixime, aminoglycoside, imipenem, etc.).

Urinary ultrasonography, dimercaptosuccinic acid (DMSA), and voiding cystourethrogram (VCUG) findings were evaluated in both the ABP-received and ABP-discontinued periods. Routine urine analysis and urinary cultures were performed at 3-month intervals. During symptomatic urinary tract infections (UTIs), urine analysis, urinary cultures, and acute-phase reactant analyses were also performed. An infection was defined as the presence of $\geq 10^5$ colonies of the same microorganism in the urine sample taken by catheter. Symptomatic infections recorded in both periods involving nausea, vomiting, abdominal pain, high fever, and cloudy and foul smelling urine were prospectively evaluated along with the resistance patterns of microorganisms. Development of new lesions was evaluated prospectively by DMSA. We obtained informed consent from all patients or their families for the study.

2.1. Statistical analysis

SPSS 15.0 for Windows was used for statistical analysis. Data (numbers, percentage distributions, means, standard deviations) were evaluated using Fisher's exact test, the chi-square test for binary and multivariate data, and the Mann–Whitney U test with Spearman's correlation coefficient.

3. Results

The mean age of patients was 12.9 years (7–19 years); 15 patients were female and 7 were male. The most common uropathogen in both periods was *Escherichia coli* (in all cultures incidence of *E. coli* was 37.3%, with 26% of them extended spectrum beta-lactamase+). The other pathogens observed at decreasing frequency were *Enterobacteriaceae*, *Klebsiella*, *Pseudomonas*, etc. Colonization was observed in 48 of the routine urine cultures (54.5%) taken in the ABP-received period and in 44 cultures (50%) taken in the ABP-discontinued period (P = 0.54). Of all the urine cultures taken in the ABP-received and ABP-discontinued periods, 28 (18.2%) and 25 (16.2%) were consistent with the presence of a UTI (symptomatic), respectively. More UTIs occurred in the ABP-received period than in the ABP-discontinued period, but this difference was not statistically significant (P = 0.65, Table 1). Although the frequency of multiple antibiotic resistance in routine cultures taken in the ABP-received period (62; 40.3%) was greater than that in the ABP-discontinued period (47; 30.5%), the difference was not statistically significant (P = 0.07). Multiple-antibiotic resistance included ampicillin, amoxicillin-clavulanate, ampicillin-sulbactam, trimethoprim/sulfamethoxazole, gentamicin, nitrofurantoin, cefuroxime, cefazolin, cefoxitin, ceftazidime, and ceftriaxone (Table 2).

Six of the patients with hypoactive lesions in the baseline DMSA scan had renal scar formation after ABP (1st year). After the discontinuation of ABP, one patient's scar was regressed, and two patients had new lesions in DMSA studies. There was no difference between the DMSA findings of patients during the ABP-received and ABP-discontinued periods, as in both periods two patients developed new lesions (P = 0.14). The incidence of VUR in the study sample was 9.1% (n = 2 patients). No significant differences were found between groups with respect to the urodynamic patterns analyzed in an attempt to identify

Table 1. Symptomatic UTIs and resistance development.

In all cultures	Prophylaxis (+) (n = 66)	Prophylaxis (-) (n = 88)	P
Routine culture colonization	48 (54.5%)	44 (50.0%)	0.54
Routine culture symptomatic colonization	16 (33.3%)	16 (36.4%)	0.09
Total symptomatic colonization	28 (18.2%)	26 (16.2%)	0.65
Pyuria (+)	67 (43.5%)	67 (43.5%)	1.00
Nitrite (+)	44 (28.5%)	38 (24.6%)	0.43
Multiple-antibiotic resistance development	62 (40.4%)	47 (30.5%)	0.07

Total routine culture number in prophylaxis = 88, total routine culture number in without-prophylaxis period = 88. Total culture number in prophylaxis = 154, total culture number in without-prophylaxis period = 154. Total culture number in 2 years = 308.

factors playing a role in the development of new lesions or UTIs. Other than three patients, all patients had detrusor hyperreflexia-sphincter hyperreflexia, and three patients had detrusor areflexia-sphincter hyperreflexia.

4. Discussion

Scarring of the upper urinary tract occurs in approximately 63% of children who do not receive appropriate treatment within the first 3 years of developing NB. It has been shown that scarring can be reduced by up to 50% with appropriate early treatment (1). The most important risk factors for upper urinary tract scar formation are detrusor-sphincter dyssynergia, reduced bladder compliance, and a filling pressure exceeding 40 cmH_2O (1,2). Pyelonephritis attacks also significantly increase the risk of renal scarring. The reduction of intravesical pressure by CIC plays an important role in early phases of treatment.

The periurethral region of children treated with CIC is thought to be colonized with microorganisms arising from the gastrointestinal system. Although bacteriuria is common (30%–70%) in these cases, the UTI risk rate (20%–40%) is less than expected (1). Whereas CIC may result in contamination of the bladder with bacteria from the periurethral region, it may also reduce the risk of infection through continuous discharge of residual urine. In this sense, CIC can sterilize a chronically infected bladder (5–7). Furthermore, CIC management reduces renal scarring in children with VUR by effectively reducing intravesical pressure. Reflux incidence decreased by 30%–50% in children with NB in the 2–3 years after CIC treatment as a result of reducing bladder filling and emptying pressures (1).

We did not find any beneficial effect of ABP in this study. Clarke et al. classified 85 cases of NB patients receiving CIC into two groups: those taking prophylactic antibiotics and those who had discontinued the use of prophylactic antibiotics. When comparing the UTI occurrence during a 4-month period, this group reported that UTI incidence was significantly higher in the group taking prophylactic antibiotics compared with that in the discontinued group. Therefore, they concluded that sustained antibiotic prophylaxis was unnecessary in patients receiving CIC (5). Schlager et al. studied the effect of nitrofurantoin prophylaxis on symptomatic UTIs and bacteriuria and found that nitrofurantoin was not effective for bacteriuria eradication in a double-blind, placebo-controlled, randomized study that included 15 children with NB treated with CIC in 1998. It was suggested that antibiotics used for prophylaxis might cause increased infection risk by increasing the antibacterial resistance of microorganisms (8). Although the incidence of UTI was higher in the ABP-received period, there was no statistically significant difference between the groups. The multiple-antibiotic resistance frequency of the ABP-discontinued period was lower than that of the ABP period, but this was not found to be statistically significant.

Infections seen in NB cases may cause upper urinary tract scarring, especially in children with VUR and/or high intravesical pressure, depending on the virulence of the microorganism involved. DMSA is an important screening method used in scanning for pyelonephritis in the acute phase and renal scarring in the chronic phase. A comparison of DMSA findings at the time of initial diagnosis, during the prophylaxis period, and after

Table 2. The antibiotic resistance patterns for each antibiotic in both periods and their statistical differences.

Antibiotics	Prophylaxis (+) (n = 66)	Prophylaxis (-) (n = 88)	P
	Resistant %	Resistant %	
Ampicillin	24.2	36.3	0.10
Ampicillin sulbactam	9.0	4.5	0.25
Amoxicillin	-	4.5	0.07
Amoxicillin clavulanate	10.6	10.2	0.93
Cefazolin	7.5	5.6	0.63
Cefuroxime	7.5	14.7	0.16
Cefaclor	3.0	2.2	0.76
Ceftriaxone	7.5	10.2	0.59
Cefotaxime	-	1.1	0.57
Ceftazidime	1.5	2.2	0.73
Gentamicin	4.5	5.6	0.75
Trimethoprim sulfamethoxazole	6.0	14.7	0.09
Nitrofurantoin	-	3.4	0.18

prophylaxis cessation found that the percentage functions were similar and no statistically significant differences were detected; however, 6 patients developed renal scarring and 2 patients developed new lesions.

In NB cases with hydronephrosis, the existence of VUR is evaluated by performing VCUG. The incidence of VUR can increase up to 50% in patients with functional bladder outlet obstruction (1). VUR incidence was found to be 9.1% (n = 2 patients) in this study.

No significant differences were found between the ABP-received and ABP-discontinued groups with respect to the urodynamic patterns analyzed in an attempt to identify factors playing a role in the development of new lesions or UTIs. The most common urodynamic pathology was observed to be detrusor sphincter dyssynergia.

Antibacterial prophylaxis for NB and VUR has become controversial in recent years, but approaches to the prevention of recurrent UTIs have changed since 2006 in response to the results of randomized controlled studies. Today, routine antibiotic prophylaxis in children with VUR is not suggested in the UTI guidelines (9,10). Six important studies showed no benefit of antibiotic prophylaxis compared with a placebo, even in high-grade VUR (11). The aim of prophylaxis in children with VUR is to prevent recurrences of symptomatic UTIs and renal scarring. A metaanalysis of 11 randomized controlled studies consisting of a total of 2046 children revealed that antibiotic prophylaxis had no effect on renal scar formation or healing, although it did reduce the recurrence of symptomatic UTIs and the rate of positive urine cultures. Furthermore, bacterial resistance and severe adverse effects were reported in many studies (12).

Another 2-year multisite, randomized, placebo-controlled study evaluating 607 children with VUR and a first or second febrile UTI examined the effect of trimethoprim/sulfamethoxazole prophylaxis for preventing UTI recurrence, renal scar formation, treatment failure, and antimicrobial resistance. At the end of study, no difference was seen between groups with respect to renal scar formation, but the recurrence rate was reduced in response to antibiotic prophylaxis (13). Although the frequency with which multiple-antibiotic resistance was observed in all cultures taken in the antibiotic-discontinuation period was lower than that in the prophylaxis period, this difference was not statistically significant. According to the DMSA data, there were no significant differences between the two periods with respect to the formation of new lesions. Our study did not include a sufficient number of cases of NB with VUR to permit observations regarding this matter.

In this study, we revealed that routine ABP usage in NB cases treated with CIC has no protective effect on the development of symptomatic UTIs and new lesions according to DMSA results. Furthermore, more resistant colonies were observed in the ABP-received period. A limiting aspect of this study was the small number of patients. However, we would like to conclude that routine ABP usage is not necessary under these circumstances.

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