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Pathogen Prevalence and Treatment of UTI in Children after Ureter Anastomosis

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Abstract

Background: Few study has reported about the prevalence, pathogen distribution and antibiotics usage of UTI after ureter anastomosis. This study aimed to investigate the characteristics and antibiotics selection of UTI after ureter anastomosis.

Methods: Urinalysis and urine culture results of 614 patients in a single center during 2010-2015 were reviewed. Incidence, pathogen distribution, drug sensitive test result, antibiotics usage, impatient and outpatient treatment rate were summarized.

Results: Positive urinalysis rate was 72.0% (68.5-75.5%), positive urine culture rate was 30.6% (27.0-34.2%), UTI rate was 32.5% (28.8-36.2%). 198 bacteria strain was identified from 188 patients. Gram-negative bacteria accounted for 79.8% (74.2-85.4%), Gram-positive bacteria accounted for 16.7% (11.5-21.9%) and fungi accounted for 3.5% (0.9-6.1%). *E. coli, pseudomonas aeruginosa* and *klebsiella pneumoniae* were the three most common pathogens. Drug-resistant bacteria accounted for 27.8% (21.6-34.0%), opportunistic pathogens accounted for 46.0% (39.1-52.9%). The unrestricted grade antibiotics use rate was 90.6%, limited grade antibiotics use rate was 11.6% and special grade antibiotics use rate was 12.8%. Impatient treatment rate of UTI after discharge was 9.68%; outpatient treatment rate was 18.9%.

Conclusions: UTI after ureter anastomosis is complicated, with a high incidence and high proportion of drug-resistant and opportunistic pathogens. Resistance of cephalosporin is serious. It's better to choose high grade antibiotics decisively for the suspected infection and switch to sensitive antibiotic once acquire drug susceptibility results.

Keywords

UTI, Drug-resistant bacteria, Opportunistic pathogen, ESBL

Introduction

Congenital ureter diseases are the main cause of ureter anastomosis in children, including the UPJO (ureteropelvic junction obstruction), UVJO (ureterovesical junction), VUR (vesico-ureteric reflux), MU (primary megaloureter), EU (Ectopic Ureter), MUS (Middle ureteral stricture), et al. The operation methods are changeable for different primary diseases, including pyelopalsty [1], ureteral reimplantation [2] and stegnotic ureter resection with anastomosis, et al. Although some individual procedures exist, but these operations all contain ureter resection and anastomosis, so we can summarize them together. UTI (urinary tract infections) is the common complication of these operations [2,3]. For the impact of operation and Indwelling tube [4,5], the UTI is complicated and difficult to treat, increasing the length of hospital stay and costs, it's a problem worthy further study.

As the abuse of antibiotics, drug resistance bacteria are more and more popular in UTI of children [6]. The bacteria distribution in common UTI is already reported widely [7,8], but few about the prevalence, pathogen distribution and antibiotics usage of UTI after ureter anastomosis. The operation technique is routine, but the surgeon may have trouble to deal with the complicated UTI, especially for drug resistance bacterial infection. This study, urinalysis and urine culture results of 614 cases that underwent ureter anastomosis during 2010-2015 in a single center were reviewed and analyzed, aimed to investigate the characteristics of UTI and provide the guidelines for the treatment of UTI after ureter anastomosis.

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Methods

General clinical data

Data of 614 consecutive patients who underwent ureter anastomosis in a single center during 2010-2015 was retrospectively analyzed. 498 cases underwent pyeloplasty for UPJO, 108 cases underwent ureteral reimplantation for UVJO (n = 37), VUR (n = 40), MU (n = 22) and EU (n = 9), 8 cases underwent stegnotic ureter resection with anastomosis for MUS. 467 cases were male, 147 were female; The mean age was 32 ± 31 months (range 5 d-13 yrs); 375 cases occurred in left side, 189 cases right side, 50 cases double side. 526 cases underwent open operation, 88 cases underwent laparoscopic (tradition and robot assisted) operation. 357 cases indwelt double J stent for 1-6 months, 213 cases indwelt external ureteral stent for 7-12 days, and 47 cases didn't indwell ureteral stent. All patients had indwelt catheter for 1-7 days, 158 cases indwelt nephrostomy tube, 102 cases indwelt crystostomy tube, and 504 cases indwelt drainage for 1-3 days.

Examined urinalysis and urine culture preoperatively and postoperatively: Those patients with positive urinalysis or UTI symptoms (e.g. fever, lumbago, turbid urine, frequent micturition, urgent urination, odynuria) should reexamine urine culture. This study defines positive urine leukocyte and (or) positive granulocyte esterase, bacteria strain as positive urinalysis. According to the Prescription right administration in china, the antibiotics was divided into Unrestricted (the first and second generation cephalosporin), restricted (the third generation cephalosporin) and special (the fourth generation cephalosporin, vancomycin, linezolid, carbapenems, anti-fungals, et al.) grade antibiotics, we adopted this grade classification method in this study.

Urine specimens collection methods: 1. Take clean midstream urine specimen if conveniently 2. Take urine specimen by aseptic catheterization if hard to collect or during catheter indwelling.

Urine bacteria culture and drug sensitive test: Strain identification was strictly in accordance with the national inspection procedures. Drug sensitive test complied with standard procedure recommended by the National committee for clinical laboratory (NCCLS) and were performed by Kirby - Bauer method.

UTI diagnostic criteria: 2015 Chinese expert consensus version.

Observation indicators: UTI rate, pathogen distribution and drug susceptibility results, antibiotics usage, impatient and outpatient treatment rate.

Statistic analysis

Use excel to record data, spss17.0 software for statistical analysis. Measurement data was expressed with ($\bar{x}$ ± s). 95% CI of rate was calculated by Normal approximation method. Inspection levels was set at α = 0.05.

Results

Prevalence of postoperative UTI

442 cases was positive in postoperative urinalysis more than one time, the positive urinalysis rate was 72.0% (68.5-75.5%). 188 cases is positive in urinalysis and urine culture with more than a kind of pathogen was identified in each patient, the positive urine culture rate was 30.6% (27.0-34.2%). 12 patients whose urinalysis was positive in with UTI symptoms were also diagnosed with UTI. The UTI rate was 32.5% (28.8-36.2%). 39.5% (35.6-43.4%) patients with positive urinalysis and negative urine culture, and the urinalysis turned negative quickly with the use of low-grade antibiotics, were not diagnosed as UTI. The positive urinalysis and urine culture rate between different operation methods and diseases had no significant difference (showed in Table 1).

Pathogen distribution and sensitive antibiotics

198 bacteria strain was identified from188 patients with positive urine culture. The pathogen distribution and sensitive antibiotics (quinolone, aminoglycoside, levomycetin, tetracycline, et al. hasn't listed for prohibited use in children) are listed in Table 2. Gram-negative bacteria accounted for 79.8% (74.2-85.4%), Gram-positive bacteria accounted for 16.7% (11.5-21.9%) and fungi accounted for 3.5% (0.9-6.1%). *E. coli* (89/198), *pseudomonas aeruginosa* (27/198) and *klebsiella pneumoniae* (19/150) is the three most common postoperative UTI pathogens. Except the normal *E. coli* and *Staphylococcus aureus* is still sensitive to the first and second -generation cephalosporins, other pathogens all need to use restricted and special grade antibiotics. Resistance to antibiotics increased obviously once the bacteria produce ESBL (Table 3), it had better choose the third and fourth-generation cephalosporins or carbapenems as early as possible.

The prevalence of drug-resistant bacteria and opportunistic pathogens

ESBL E. coli (41/198), *ESBL klebsiella pneumoniae* (6/198), *MRSA* (5/198), *MDR pseudomonas aeruginosa* (3/198) was found prevalent in UTI after ureter anastomosis in this study. The other bacteria hadn't appeared resistant pattern. Drug-resistant bacteria accounted for 27.8% (21.6-34.0%). Opportunistic pathogens was found in *acinetobacter*

Table 1: Positive urinalysis and urine culture rate of different operation methods and diseases.

Positive rate	Pyeloplasty	Ureteral reimplantation				Resection	P (operation)	P (disease)
	UPJO	VUR	UVJO	MU	EU	MUS		
Urinalysis	354/498	34/40	22/37	17/22	9/9	6/8	< 0.586	0.068
Urine culture	150/498	16/40	11/37	8/22	3/9	0/8	0.098	0.344

Table 2: Pathogen distribution and sensitive antibiotics after ureter anastomosis.

Pathogen	Proportion	Sensitive antibiotics
Gram-negative	158/198	-
Normal *E. coli*	48/198	First, second-generation cephalosporins
ESBL *E. coli*	41/198	Third, fourth-generation cephalosporins, carbopenems
Acinetobacter baumannii	14/198	Third, fourth-generation cephalosporins, carbopenems
klebsiella pneumoniae	13/198	Third, fourth-generation cephalosporins, carbopenems
ESBL *klebsiella pneumoniae*	6/198	Carbopenems
Pseudomonas aeruginosa	24/198	Third, fourth-generation cephalosporins, carbopenems
MDR *Pseudomonas aeruginosa*	3/198	Carbopenems
Enterobacter cloacae	4/198	Third, fourth-generation cephalosporins, carbopenems
Others	5/198	-
Gram-positive	33/198	-
MRSA	5/198	Vancomycin, linezolid
Staphylococcus aureus	4/198	First-generation cephalosporins
Staphylococcus epidermidis	3/198	Third, fourth-generation cephalosporins, Vancomycin, linezolid
Enterococcus faecium	7/198	Vancomycin, linezolid
Enterococcus faecalis	10/198	Third, fourth-generation cephalosporins, vancomycin, linezolid
Others	4/198	-
Fungi	7/198	Anti-fungals

Table 3: Drug susceptibility results of ESBL *E. coli*.

Antibiotics	KB (mm)	MIC (ug/ml)	Sensibility
Amikacin	22	≤ 2	Sensitive
Ampicillin	-	≥ 32	Resistant
Ampicillin sulbactam	-	16	Medial
Aztreonam	19	4	Sensitive
Cefazolin	-	≥ 64	Resistant
Cefepime	20	≤ 1	Sensitive
Cefoperazone sulbactam	25	≤ 2	Sensitive
Cefotetan	18	≤ 4	Sensitive
Ceftazidime	20	≤ 1	Sensitive
Cefatriaxone	-	≥ 64	Resistant
Ciprofloxacin	-	≥ 4	Resistant
Ertapenem	28	≤ 0.05	Sensitive
Gentamicin	-	≥ 16	Resistant
Imipenem	28	≤ 1	Sensitive
Levofloxacin	-	≥ 8	Resistant
Furadantin	-	32	Resistant
Panipenem	29	≤ 0.05	Sensitive
Piperacillin tazobactam	20	≤ 4	Sensitive
Tobramycin	-	8	Medial
SMZ-TMP	-	≥ 320	Resistant

baumannii, *pseudomonas aeruginosa*, *staphylococcus epidermidis*, *enterococcus faecium*, *enterococcus faecalis* and *fungi*, accounted for 46.0% (39.1-52.9%). These two type of bacteria are resistant to the first and second-generation cephalosporins and penicillin.

Postoperative antibiotics usage

Antibiotics was used in all patients of this study for UTI prevention or treatment. The unrestricted grade antibiotics use rate was 90.6%, applied to patients with preoperative negative urine culture for 1-5 days. High-grade antibiotics were used if drug-resistant and opportunistic bacteria were positive or poor control of infection. The restricted grade antibiotics use rate was 11.6%, special grade antibiotics use rate was 12.8%. The impatient treatment rate of UTI after discharge was 9.68% and the outpatient oral antibiotic treatment rate was 18.9%.

Discussion

UTI is the common complication of ureter anastomosis. UTI of patient in this study with a high incidence of 32.5%, significantly higher than the other case report studies result [3,5,9], may because the urine culture rate in our study was higher and the follow-up time was longer than other study, which increased the diagnosis rate of UTI. The UTI after ureter anastomosis is hospital acquired and complicated, it has its individual risk factors below: 1. Operation factors: Ureter can directly contact the outside bacteria during operation. 2. Tube factors: indwelling several tubes postoperatively, such as ureteral stent, drainage tube, nephrostomy tube, crystostomy tube, catheter, et al. And the indwelling time is long (e.g. the double J stent is indwelt for 1-6 months and the external ureteral stent is indwelt for 7-12 days). It causes the retrograde bacterial infection along the indwelling tube. Multiple Studies [10-12] showed positive culture

rate of removed double J stent was high (29.4%, 58.9%, 42.9%), which can explain why UTI lasted after discharge. 3. Obstruction factors: the stent blocking or anastomosis stricture or obstruction can cause the bad urine drainage which is baneful for bacteria excretion. 4. Nursing factors: stool and urine is easy polluting the indwelling tube, incision and urethral orifice, which can explain why *enterococcus faecium* and *enterococcus faecalis* infection is not rare. These factors associate with the occurrence and treatment of UTI. If infection occurs, we must deal with these factors followed antimicrobial therapy, e.g. emergent stent removal and nephrostomy. It had better decrease the indwelling tubes and shorten the indwelling time, keep the indwelling tubes and urethral orifice clean in order to reduce the risk of UTI. In this study, we hasn't found the impact of primary diseases and operation methods on UTI after ureter anastomosis, it may because these diseases and operation methods have similar risk factors, recommends than we can adopt the similar treat strategy for UTI after ureter anastomosis.

Compared with common UTI, UTI after ureter anastomosis have the following characteristics: 1. Pathogenic bacteria spectrum has big difference: higher percentage of resistant bacteria, opportunistic pathogens and cocci (e.g. *staphylococcus aureus*, *staphylococcus epidermidis*, *enterococcus faecium* and *enterococcus faecalis*), which is different with community acquired UTI [13,14] whose main pathogen is common *E. coli.* 2. Few effective antibiotics can be selected: Quinolone, aminoglycoside, levomycetin and tetracycline can't be used in children generally. Most bacteria is resistant to low grade antibiotics and often need use high grade antibiotics, high grade antibiotics use rate of patients in this study was as high as 24.4%. However, for the community acquired UTI sensitive rate of first and second-generation cephalosporins is as high as 95% [15]. 3. Infection is more difficult to control, easy to relapse, infections still exists after discharge. In view of this, we should fully understand the characteristics of UTI after ureter anastomosis and the difference with common UTI, and make different empirical antibiotic use strategy.

Antibiotics usage strategy is worth further discussion. Although the clinical antibiotics use indications is strict than former and a classification of antibiotics according to prescription right is provided, but for worry of postoperative UTI, prophylactic antibiotics (the first or second-generation cephalosporins) use rate is still very high (90.2%) in this study. Urine culture is hard to implement in community and primary hospital, empirical antibiotic use is general and lack of effective antibiotics, these factors cause antibiotics abuse phenomenon is still very serious. Several studies have showed the increasing popularity of *ESBL E. coli* year by year [6,14,16] in community. Above mentioned phenomenon Combined with operation, indwelling tube, obstruction and nursing factors cause *ESBL E. coli*, *ESBL klebsiella pneumoniae*, *MDR pseudomonas aeruginosa* and *MRSA* in the popularity of postoperative UTI after ureter anastomosis, which should be taken more attention [17]. Antimicrobial resistance information influences the selection of antibiotics for management of UTI [18]. This research also showed the bacteria cultured in postoperative UTI are mostly resistant to the first and second-generation cephalosporins. The carbapenems is still sensitive to bacteria that produce ESBL and be recommended to use as early as possible [19]. Situation of simple positive urinalysis without UTI is common (39.3%) may is due to anastomotic bleeding and aseptic inflammation reaction, which should be differentiated from UTI and can be cured without antibiotics. Ferroni MC, et al. have found that prophylactic antibiotics after minimally invasive pyeloplasty with ureteral stent placement are useless and meaningless [20]. In conclusion, we recommend that the prophylactic antibiotics after ureter anastomosis should be avoided, but for the suspected infection and those with multiple risk factors of infection, we should choose high grade antibiotics decisively, then switch to sensitive antibiotic when drug susceptibility results come out, thus can quickly, effectively and thoroughly kill pathogenic bacteria, shorten the treatment time and also reduce the prevalence of drug-resistant bacteria.

Conclusions

UTI after ureter anastomosis is complicated, with a high incidence and high proportion of drug-resistant and opportunistic pathogens. Resistance of cephalosporin is serious. The prophylactic antibiotic usage is meaningless. It's better to choose high grade antibiotics decisively for the suspected infection and switch to sensitive antibiotic once acquire drug susceptibility results.

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Compliance with Ethical Standards

Conflict of Interest

The authors declare that they have no conflict of interest. This study has acquired the permission of The First Affiliated Hospital of SunYat-sen University.

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