

Installation or exchange of double-J ureteral stent is a risk factor of febrile urinary tract infection in a compromised host

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Research article

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Abstract

Background : To study the predictors of febrile urinary tract infections (febrile UTI) after the placement of Indwelling double-J ureteral stent (DJS), and effective prophylactic antimicrobial agent. **Methods :** Installation or exchange of 298 double-J stents (DJS) (66 men and 232 women, median age 67 years, range 42–86) were examined. 258 patients had been given prophylactic antibiotic therapy after the placement of stents, 40 patients with no prophylactic antibiotic therapy. **Results :** 14 patients (4.2%) had febrile UTI after the placement of the stent. The pathogens was identified from the pelvic urine culture of 9 patients with febrile UTI. Enterococcus faecalis was the most common pathogen, it accounted for 25.0% of all pathogens. Compromised host was potential risk factors for the febrile UTI in patients with DJS. 1.1% of patients who received with fluoroquinolones or 4.7% of patients with cephalosporin developed a febrile UTI. **Conclusions :** Indwelling DJS is a risk factor of febrile UTI in a compromised host, fluoroquinolones may be effective for preventing febrile UTI after placement of DJS.

Background

Placement of indwelling double-J ureteral stent (DJS) are common procedure in an urology department. This procedure is performed for disease to complicated hydronephrosis and relief of obstruction, prevention of stricture formation, treatment of urinary tract leaks. However, with accumulated experience, we know that patients with indwelling DJS experience some effects such as lower abdominal pain, urinary frequency, hematuria, dysuria and febrile UTI.

The reported rates for bacterial colonization in adults within several weeks of double-J stent insertion range from 28% to 90%, and rates for UTI range from 7% to 34%^{1,2}. Because pathogens responsible for febrile UTI caused by ureteral stenting and effective prophylactic antibiotics remain unknown, it is not clear that guidelines for infection control with transurethral ureteral stenting have been issued. We sought to identify predictors of the occurrence of febrile UTI following transurethral double-J ureteral stenting and responsible pathogens, with the ultimate aim of selecting the most appropriate prophylactic antibiotics.

Methods

The study was approved by the Ethics Committee of Hiroshima University (E–23, Hiroshima, Japan).

The patients enrolled in this study underwent the DJS installation or exchange from January 2014 to December 2015.

298 cases of an indwelling DJS placement for 45 patients were investigated in this study.

□Prophylactic Antimicrobial administration□

We used levofloxacin (LVFX), sitafloxacin (STFX), cefcapen pivoxil (CFPN-PI), cefdinir (CFDN), ampicillin (ABPC), faropenem (FRPM), timetoprim / sulphametazole (ST) as prophylactic antibiotics before urological procedures. The patients that no prophylactic antibiotics were used in enrolled in the study.

□Infectious Complication□

A febrile infectious complications including pyelonephritis, prostatitis and epididymitis were defined as an infection with fever ($>38^{\circ}\text{C}$) occurring within 30 days of follow-up and bacteriuria as $\geq 10^3$ colony forming units (CFU)/ml³. Additionally we investigated risk factors such as age, sex, stent placement on one side or both side, installation at first time or exchange, causative disease (benign or malignancy), presence of pyuria, urinary dysfunction (neurogenic bladder, benign prostate hyperplasia, bladder output obstruction) renal failure (GFR $< 60\text{ml} / \text{min}$), malnutrition (serum Albin $< 3.7 \text{ g} / \text{dl}$), compromised host (steroid user, diabetes mellitus, still on using anticancer drug), administration of prophylactic antibiotics before and after the procedure, the choice of fluoroquinolone for prophylactic antibiotics.

□statistical analysis□

Chi-square test was used to analyze the association of bacterial stent colonization with events of UTI, patient backgrounds. Logistic-regression analysis was used to analyzed the risk factors of febrile UTI. In all statistical analysis, a pvalue of <0.05 was considered to indicate statistically significant differences. All statistical analyses were performed using JMP v10.0 software (SAS Institute, Cary, NC, USA).

Results

□Infectious Complication□

Patient' characteristics are shown in Table 1.

There were 14 febrile UTI (4.2%) after the placement or exchange of DJS.

We compared the patient' characteristics between a group that developed UTIs and a group that didn't developed UTIs, there are many compromised hosts significantly in the group that developed UTIs, and numbers of patients administered fluoroquinolone agents as prophylactic antibiotics is less significantly in the group that developed UTIs.

□Pathogens cultured from urine□

Table 2 shows pathogens identified from urine cultures.

Of these 14 patients with febrile UTI, pathogens cultured from ureteropelvic urine were isolated in 9 patients. Because other 5 patients were admitted to other hospitals, culture test was not enforced. Half of the pathogens were gram-negative rods.

Of the 284 patients who had no onset of febrile UTI, 63 urine sampling for monitoring of UTI were cultured. Pathogens cultured from urine were isolated in 38 patients (60.3%). Gram-negative rods accounted for 47.9% (23 / 48 isolets) of all the pathogens. There were more bacteria that tend to resistant antibiotics such extended-spectrum β -lactamase producing *E. coli* and *P. aeruginosa* in surveillance group than in febrile UTI group.

□Risk factors of infectious complication□

Compromised host was potential risk factors for the febrile UTI in patients with DJS ($p = 0.0098$, odds = 4.35, Table3). The incidence of febrile UTI (1 / 92, 1.1%) in patients with fluoroquinolones is lower than the incidence with cephalosporin (10 / 131, 7.6%), but administration of fluoroquinolones was not independent predictor that prevented febrile UTI.

Discussion

To the best of our knowledge, this study is the first report to clarify that compromised host is a risk factor for febrile UTI onset.

The placement of DJS is associated with some complications while the use of indwelling DJS is one of the indispensable techniques in urological surgeons.

Early complications include low abdominal pain, hematuria, urinary urgency, frequency.

Stone formation, infection are late complications.⁴⁻⁹⁾ Bacteremia secondary to urological procedures has an incidence of around 30% in adults,¹⁰⁾ but the relationship between the placement of DJS and febrile UTI is not clear. In addition, there is no guidance on using antibiotic prophylaxis in the placement of DJS¹¹⁾. In our study, the incidence of febrile UTI in the patients with DJS was 4.7%, this was consistent with the results of previous studies which reported that the rate of febrile UTI onset due to ureteral stent placement regardless of antibiotic treatment was 6–7%¹²⁾. When we placed the ureteral stent, we sampled the ureteropelvic urine of the 63 patients to perform bacteriologic tests and found that 38 patients had bacteriuria. Riedl et al.¹³⁾ and Farsi et al.¹⁴⁾ reported that bacteriuria associated with stent placement in 45% and 30% of patients, respectively. The positive rate at our hospital was 60.3%, which is higher than those reported by the other authors. However, the median duration of placement in this study was approximately 2 years, and patients who had been undergoing ureteral stent exchange continuously for 5 or more years have been included. In the surveillance cultures of ureteropelvic urine, *Enterococcus faecalis* was the most common bacterial species, and it was also the most common pathogen of febrile urinary tract infections occurring in our hospital. But in the surveillance cultures, there are drug resistance *pseudomonas aeruginosa* and drug resistance enterobacteriaceae. Careful attention must be paid to select antibiotics with the onset of febrile urinary tract infection.

In the present study, there were 21% of patients who did not receive antibiotics before and after treatments. However compromised host was only potential risk factor for febrile UTI in patients with DJS

regardless of whether antibiotics were administered. There were few reports that considered predictors of febrile UTI in patients with DJS, Moltzahn et al.¹²⁾ reported that urinary sediment threshold of leucocytes / HPF or nitrite reaction was't be useful to predict febrile UTI. In many of previous studies, the duration of administration, and the choice of antibiotics for prophylaxis in the placement of DJS is not clear. In the study to compare the efficacy of single dose oral ciprofloxacin (500mg) with intravenous cefazolin (1g) as a antibiotic prophylaxis in patients undergoing endourologic procedures for outpatients including stent placement or exchange, retrograde pyelogram, diagnostic or therapeutic ureteroscopy, collagen injection, internal urethrotomy, cystoscopy, bladder biopsy, a single oral dose ciprofloxacin in the patients undergoing outpatient endourology surgery was equally effective as cefazolin¹⁵⁾. In our study, the rate of onset of febrile urinary tract infection was significantly decreased in the fluoroquinolone using group compared to the cephalosporin group. While cephalosporin antibiotics were administered orally to 131 patients, cefazolin was administered intravenously to 16 patients This indicates the possibility that the oral cephalosporin antibiotics are not effective against febrile UTI. One of the reason why there are more febrile UTI in cephalosporin using group than in fluoroquinolone using group is that cephalosporin is not effectiveness against *Enterococcus faecalis* which is common pathogen of febrile UTI. Our data suggested that optimal choice for prophylactic antibiotics was required based on the procedures.

Conclusion

Our data showed that compromised host to be significant risk factors to the procedures for febrile UTI and fluoroquinolone prevented febrile UTI. But if patients are receiving an indwelling DJS for the first time or exchanging an indwelling DJS, it is not clear which patient are giving prophylactic antibiotic therapy using fluoroquinolone or cephalosporin. It seems that future studies are needed in order to reveal appropriate prophylactic antibiotics before installation or exchange of DJS.

Abbreviations

febrile UTI: febrile urinary tract infections

DJS: double-J ureteral stent

LVFX: levofloxacin, STFX: sitafloxacin, CFPN-PI: cefcapen pivoxil, CFDN: cefdinir, ABPC: ampicillin, FRPM: faropenem, ST: timetoprim / sulphametazole

Declarations

Competing Interests

There are no potential sources of conflicts for this study.

Ethics approval and consent to participate

There is no human participants and animals. This is retrospective study.

The study was approved by the Ethics Committee of Hiroshima University (E-23, Hiroshima, Japan).

'Author's Contribution' statement

H Kitano: Protocol/project development, Data collection, Data analysis, Manuscript writing. J Teishima: Date analysis, Manuscript writing, H Ohge: Manuscript editing, A Matsubara: Manuscript editing

all authors have read and approved the manuscript

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Tables

Table 1. Patient background

	Febrile UTI (n=14)	No febrile UTI (n=284)	p value
Median age, (years old range)	65.5 (43~81)	67 (42~86)	0.55
Sex			0.65
male	4	66	
female	10	218	
Disease			0.30
Benign	4	120	
malignancy	10	164	
Stent placement			0.42
On one side	10	229	
On both side	4	55	
Stent installation			0.15
first time	2	12	
exchange	12	272	
Pyuria	12 (85.7)	255 (89.8)	0.64
Dysuria	3 (21.4)	69 (24.3)	0.80
Renal Dysfunction	10 (71.4)	166 (58.4)	0.33
Malnutrition	8 (57.1)	144 (50.7)	0.64
Compromised Host	10 (71.4)	116 (58.5)	0.024
Antibiotic Prophylaxis	11 (78.6)	247 (87.0)	0.399
Administration of fluoroquinolone for prophylaxis	1 (7.1)	92 (32.4)	0.025

Table 2. Pathogens of pelvic urine cultures

	Pelvic urine cultures in 14 febrile UTI patients	Monitoring pelvic urine cultures in 63 patients
Positive urine culture	9 patients	38 patients
Pathogens (strain)	11 <u>isollets</u> (7 strain)	48 <u>isollets</u> (12 strains)
Gram Negative Rod		
<i>Klebsiella pneumoniae</i>	1	4
<i>Proteus mirabilis</i>	2	1
<i>Enterobacter cloacae</i>	0	2
<i>Pseudomonas aeruginosa</i>	0	2
<i>E.coli</i>	0	5
<i>Bacteroides</i> spp	0	5
ESBL <i>E.coli</i>	1	3
ESBL <i>Proteus mirabilis</i>	1	0
Multidrug-resistant <i>P. aeruginosa</i>	0	1
Gram Positive Cocci		
<i>Enterococcus faecalis</i>	3	12
<i>Streptococcus</i> spp	1	5
Coagulase-negative <i>staphylococci</i>	0	3
Gram Positive Rod		
<i>Corynebacterium</i> spp	2	5

Table 3. Risk factors of Febrile UTI after Transurethral Placement of DJS

	Univariate analysis	Multivariate analysis		
	P value	Odds ratio	95%CI	P value
Compromised Host	0.024	4.354	1.41–16.22	0.0098
Administration of fluoroquinolone for prophylaxis	0.025	1.66	0.435–5.295	0.428