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ORIGINAL RESEARCH

Analysis of Characteristics, Pathogens and Drug Resistance of Urinary Tract Infection Associated with Long-Term Indwelling Double-J Stent

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Objective: To investigate the characteristics, pathogens and drug resistance of urinary tract infection (UTI) associated with long-term indwelling double-J stent.

Methods: The clinical data of 102 patients with urinary tract infection associated with long-term indwelling double-J stent in University-Town Hospital of Chongqing Medical University and Chongqing Traditional Chinese Medicine Hospital from September 2010 to July 2022 were collected retrospectively, and the difference between etiological characteristics were analyzed. Urine and double-J stent samples of patients were collected for pathogen identification and drug sensitivity test.

Results: A total of 102 patients, 39 (38.23%) males and 63 (61.77%) females, aged 24–72 years, with a median age of 48 years, were included in this study. Urinary calculi (40.20%) and ureteral stricture (24.50%) were the main causes of urinary tract infection associated with long-term indwelling double-J stent. Among the patients with urinary tract infection caused by double-J stent, female patients were higher than male patients (61.77% vs 38.23%). In terms of positive rate of pathogenic bacteria culture, the rate of double-J stent was higher than that of urine (67.65% vs 35.29%). The main pathogenic bacteria in urine were Escherichia coli (30.55%) of Gram negative bacteria, while the main pathogenic bacteria in double-J stent were enterococcus faecalis (27.53%) of Gram positive bacteria. The resistance rate of Gram positive bacteria in double-J stent to vancomycin, ciprofloxacin, meropenem and piperacillin/tazobactam was significantly higher than that in urine ($P<0.05$). The resistance rate of Gram negative bacteria in double-J stent to imipenem, cefepime, piperacillin/tazobactam, meropenem and cefoperazone/sulbactam was significantly higher than that in urine ($P<0.05$).

Conclusion: Double-J stent associated urinary tract infection is more common in women than in men. Escherichia coli and Enterococcus faecalis are the main pathogens, and the pathogens show strong drug resistance.

Keywords: double-J stent, biofilm, pathogens, urinary tract infection, drug resistance, drug resistant bacteria, infection

Introduction

Nowadays, healthcare-associated infection is one of the most important public health problems in the world, and the use of double-J tube increases the risk of urinary tract infection.[1] In the treatment of urological diseases, double-J stent has dual functions of support and drainage.[2–4] Therefore, it is widely used in urological surgery, such as kidney stone, ureteral stone, hydronephrosis, kidney transplantation, ureteral stenosis, etc.[1–4] However, in actual clinical work, double-J stent indwelling can cause pain, bladder irritation, hematuria, fever and other conditions.[4–7] In severe cases, it can induce retrograde systemic inflammatory response syndrome and urinary sepsis, endangering the life safety of patients.[4–7] Therefore, exploring the clinical characteristics of double-J stent associated infection and the characteristics of pathogenic bacteria is the core of treating double J stent associated infection.

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Current research suggests that the repeated urinary tract infection caused by indwelling double-J stent is mainly caused by bacterial biofilm on the surface of double-J stent.[8–10] Bacteria can produce polysaccharide protein complexes, such as fibrin, lipoprotein and polysaccharide matrix on the surface of double-J stent to form a biofilm, which is called bacterial biofilm. The formation of bacterial biofilm is a defense reaction for bacteria to adapt to the external environment.[8–10] Bacterial biofilm can prevent bacteria from killing by antibacterial agents and promote bacteria to develop drug resistance.[8–10] Bacterial biofilm and bacterial colony formation are important factors for the recurrence and treatment difficulty of double-J stent associated infection.[8–11] In view of the refractory and high recurrence of double-J stent-associated infection, it is important to explore the clinical characteristics and pathogenic characteristics of double-J stent-associated infection for the treatment of double-J stent-associated infection. Accordingly, this study analyzed the characteristics of urinary tract infection caused by long-term indwelling double-J stent, and explored the bacterial species and sensitive drugs related to double-J stent infection, so as to provide reference for clinical intervention and treatment.

Materials and Methods

Data Collection

The clinical data of 102 patients with urinary tract infection associated with long-term indwelling double-J stent in University-Town Hospital of Chongqing Medical University and Chongqing Traditional Chinese Medicine Hospital from September 2010 to July 2022 were collected retrospectively, and the etiology and characteristics of urinary tract infection were analyzed. Double-J stent is made by American Bud Company, and the size is 4.7F. Double-J stent is placed during operation. The retention time of double-J stent is 1–3 months. The position of the support tube before taking out the support tube is normal, without double J tube displacement. As previously reported, the diagnostic criteria for double-J stent associated urinary tract infection are: (1) the patient's fever is higher than 37.5°C; (2) The number of white blood cells in urine is greater than 5/HPF; (3) The number of bacteria cultured in the middle urine is more than 10^5/mL, and there are obvious urinary tract irritation symptoms, such as frequent urination and discomfort.[12,13] Urine and double-J stent bladder samples were collected for bacterial culture, identification and drug sensitivity test. This study was conducted with the approval of the ethics committee of the University-Town Hospital of Chongqing Medical University and Chongqing Traditional Chinese Medicine Hospital. All participants gave written informed consent. All research studies on humans (individuals, samples or data) have been performed in accordance with the principles stated in the Declaration of Helsinki.

Urine and Double J Tube Sample Acquisition

After cleaning the vulva, the urine was collected, and the middle part of the clean urine was left in the designated sterile container, and sent it to the laboratory for analysis within 30 minutes. The patient pulled out the double-J stent under the ureteroscope in hospital, and the double-J stent bladder segment was selected on the aseptic operation platform and placed in the aseptic inoculation bottle, and was quickly sent to the laboratory for analysis.

Bacterial Culture, Identification and Drug Sensitivity Test

Bacterial culture, identification and drug sensitivity tests were completed with the assistance of the Laboratory Department of Chongqing Traditional Chinese Medicine Hospital. The full automatic bacterial identification system (France BioMerier Company) was used to isolate and identify the strains.[14–16] The K-B disk diffusion method was used to conduct drug sensitivity test on the obtained pathogenic bacteria, and the results were judged according to the relevant standards of the Clinical and Laboratory Standards Institute (CLSI) in the United States.[14–16] The drug sensitivity of Gram positive bacteria was tested on MH medium with Tekoplanin, minocycline, cefoperazone/sulbactam, erythromycin, gentamicin, vancomycin, linezolidine, ciprofloxacin, compound sulfamethoxazole, imipenem, meropenem and piperacillin/tazobactam. The drug sensitivity of Gram negative bacteria was tested on MH medium with gentamicin, ampicillin/sulbactam, ciprofloxacin, compound sulfamethoxazole, ceftazidime, cefepime, levofloxacin, aztreonam, Piperacillin/tazobactam, Cefazolin, Cefotaxime, Amikacin, Meropenem, imipenem and Cefoperazone/sulbactam.

Statistical Analysis

SPSS 22.0 software (IBM Corp, USA) was used for data analysis. The measurement data conforming to the normal distribution is expressed by mean ± SD. The comparison between the two groups of independent, normal and homogeneous data is performed by *t* test. The nonparametric numerical data were expressed as median (range) and analyzed using Kruskal–Wallis test. Counting data are expressed by number of cases or percentages, and categorical data were analyzed by Pearson's chi-squared test and Fisher's test. $P<0.05$ means the difference is statistically significant.

Results

Etiological Analysis of Urinary Tract Infection Associated with Long-Term Indwelling Double-J Stent

As shown in Table 1, a total of 102 patients, aged 24–72 years, with a median age of 48 years, were included in this study. The main causes of urinary tract infection associated with long-term indwelling double-J stent were urinary calculi (40.20%) and ureteral stricture (24.50%). Among the patients with urinary tract infection associated with long-term indwelling double-J stent, female patients were higher than male patients (61.77% vs 38.23%). In terms of positive rate of pathogenic bacteria culture, the rate of double-J stent was higher than that of urine (67.65% vs 35.29%).

Distribution of Pathogens in Urine and Double-J Stent

As shown in Table 2, the main Gram negative pathogens in the urine of patients with urinary tract infection related to long-term double-J stent indwelling are *Escherichia coli* (30.55%), *Klebsiella pneumoniae* (16.66%) *Staphylococcus aureus* and *Pseudomonas aeruginosa* (11.11%), while the Gram positive pathogens are *Enterococcus faecalis* (13.89%)

Table 1 Etiological Analysis of Urinary Tract Infection Associated with Long-Term Indwelling Double-J Stent

Parameter		Composition Ratio (%)
Urolithiasis		41/102 (40.20%)
Ureteral stenosis		25/102 (24.50%)
Pyeloureteroplasty		13/102 (12.75%)
Tumor hydronephrosis		15/102 (14.70%)
Ureteral injury		8/102 (7.85%)
Gender	Male	39/102 (38.23%)
	Female	63/102 (61.77%)
Culture positive rate	Urine	36/102 (35.29%)
	Double-J stent	69/102 (67.65%)

Table 2 Distribution of Pathogenic Bacteria in Urine and Double-J Stent

Mycobacterium	Bacterial Name	Urine (n=36)	Double-J Stent (n=69)
Gram positive bacteria	Enterococcus faecalis	5 (13.89%)	19 (27.53%)
	Enterococcus faecium	1 (2.78%)	5 (7.24%)
	Staphylococcus epidermidis	3 (8.33%)	8 (11.59%)
	Staphylococcus epidermidis	2 (5.55%)	3 (4.35)
	Staphylococcus hominis	1 (2.78%)	4 (5.79%)
	Staphylococcus aureus	-	3 (4.35%)
Gram negative bacteria	Escherichia coli	11 (30.55%)	13 (18.84%)
	Pseudomonas aeruginosa	4 (11.11%)	5 (7.24%)
	Klebsiella pneumoniae	6 (16.66%)	6 (8.69%)
	Acinetobacter baumannii	2 (5.55%)	2 (2.89%)
Fungi		1 (2.78%)	1 (1.44%)

and *Staphylococcus epidermidis* (8.33%). The main Gram negative pathogens in double-J stent associated with urinary tract infection were *Enterococcus faecalis* (18.84%), *Klebsiella pneumoniae* (8.69%) and *Pseudomonas aeruginosa* (7.24%), while the Gram positive pathogens were *Enterococcus faecalis* (27.53%) and *Staphylococcus epidermidis* (11.59%). According to the research results, the main pathogenic bacteria in the urine is *Escherichia coli*, while the main pathogenic bacteria in the double-J stent is *Enterococcus faecalis*.

Analysis of Drug Resistance of Pathogenic Bacteria in Urine and Double-J Stent

As shown in Table 3, Gram positive bacteria in urine and double-J stent showed strong resistance to minocycline, erythromycin, gentamicin and compound sulfamethoxazole, and relatively low resistance to teicoplanin, vancomycin, linezolidine, imipenem, meropenem and piperacillin/tazobactam. However, the resistance rate of Gram positive bacteria in double-J stent to vancomycin, ciprofloxacin, meropenem and piperacillin/tazobactam was significantly higher than that in urine ($P<0.05$). As shown in Table 4, Gram negative bacteria in urine and double-J stent showed strong resistance to

Table 3 Drug Sensitivity Analysis of Gram Positive Bacteria

Antibiotics	Drug Resistance Rate of Urine Samples	Drug Resistance Rate of Double J Tube	*P* value
Tekoplanin	1/12 (8.33%)	9/42 (21.43%)	0.303
Minocycline	5/12 (41.67%)	28/42 (66.67%)	0.117
Cefoperazone/sulbactam	3/12 (25.00%)	16/42 (38.09%)	0.579
Erythromycin	8/12 (66.67%)	33/42 (78.57%)	0.395
Gentamicin	9/12 (75.00%)	38/42 (90.47%)	0.159
Vancomycin	0/12 (0%)	12/42 (28.57%)	0.036*
Linezolidine	0/12 (0%)	6/42 (14.28%)	0.165
Ciprofloxacin	4/12 (33.33%)	30/42 (71.42%)	0.016*
Compound sulfamethoxazole	11/12 (91.66%)	40/42 (95.24%)	0.634
Imipenem	0/12 (0%)	5/42 (11.90%)	0.201
Meropenem	0/12 (0%)	11/42 (26.19%)	0.047*
Piperacillin/tazobactam	1/12 (8.33%)	17/42 (40.47%)	0.037*

Note: *$P<0.05$.

Table 4 Drug Sensitivity Analysis of Gram Negative Bacteria

Antibiotics	Drug Resistance Rate of Urine Samples	Drug Resistance Rate of Double J Tube	*P* value
Gentamicin	16/23 (69.56%)	22/27 (81.48%)	0.325
Ampicillin/sulbactam	13/23 (56.52%)	18/27 (66.67%)	0.461
Ciprofloxacin	10/23 (43.47%)	12/27 (44.44%)	0.945
Compound sulfamethoxazole	17/23 (73.91%)	25/27 (92.59%)	0.127
Imipenem	0/23 (0%)	5/27 (18.52%)	0.030*
Ceftazidime	7/23 (30.43%)	14/27 (51.85%)	0.203
Cefepime	11/23 (52.17%)	21/27 (77.78%)	0.028*
Levofloxacin	19/23 (82.60%)	26/27 (96.29%)	0.108
Aztreonam	14/23 (60.87%)	17/27 (62.96%)	0.879
Piperacillin/tazobactam	2/23 (8.69%)	9/27 (33.33%)	0.036*
Cefazolin	16/23 (69.56%)	23/27 (85.18%)	0.305
Cefotaxime	12/23 (52.17%)	19/27 (70.37%)	0.186
Amikacin	9/23 (39.13%)	16/27 (59.25%)	0.156
Meropenem	1/23 (4.34%)	8/27 (29.62%)	0.020*
Cefoperazone/sulbactam	5/23 (21.73%)	16/27 (59.26%)	0.042*

Note: *$P<0.05$.

gentamicin, ampicillin/sulbactam, ciprofloxacin, compound sulfamethoxazole, cefepime, levofloxacin, aztreonam, cefazolin and cefotaxime, and relatively low resistance to imipenem, piperacillin/tazobactam, amikacin, meropenem, tegacycline and cefoperazone/sulbactam. However, the drug resistance rate of Gram negative bacteria in double-J stent to imipenem, cefepime, piperacillin/tazobactam, meropenem and cefoperazone/sulbactam was significantly higher than that of Gram negative bacteria in urine ($P<0.05$).

Discussion

Double-J stent is the most commonly used medical implant in urological surgery. It is widely used in clinic because it can relieve urinary obstruction, drain urine and protect renal function.[17,18] In recent years, the rapid development of endourological technology has greatly increased the indication and application range of double-J stent implantation.[17–20] Clinically, the duration of double-J stent indwelling is generally 2 to 6 weeks, but due to the complexity of patients' conditions, the duration of double-J stent indwelling in some patients can be as long as half a year to one year. However, prolonged double-J stent indwelling will cause patients pain, bladder irritation, hematuria, fever, etc. Among them, double-J stent-related infection is a common complication of double-J stent indwelling, which can lead to retrograde urogenic sepsis and endanger the life safety of patients in severe cases.[17–20]

The colonization of bacteria on ureteral stent is an important problem. Bacteria can interact and adhere to the surface of bare double-J tube. After bacteria adhere to the surface of double-J tube, they can produce polysaccharide protein complex such as fibrin, lipoprotein, polysaccharide matrix on the surface of double-J tube to form a biofilm, which is called bacterial biofilm.[8–10] The bacterial biofilm on the double-J tube has extremely strong drug resistance and immune evasion, which is the main reason for repeated and refractory clinical infection.[8–10] Previous studies have shown that long-term indwelling of double-J stent is an important risk factor for recurrent urinary tract infection.[21] In addition, the increase of double-J stent retention time significantly increases the risk of gross hematuria, pain, bladder irritation, urinary tract infection and fever.[22] However, there are few reports on the etiology of urinary tract infection caused by long-term (1–3 months) double-J stent indwelling, as well as the characteristics of pathogenic bacteria and drug resistance in urine and double-J stent. Therefore, this study explored the etiological characteristics of 102 cases of urinary tract infection associated with long-term indwelling of double-J stent, and analyzed the characteristics of pathogenic bacteria and drug resistance in urine and double-J stent. In this study, we found that the most common causes of urinary tract infection associated with long-term indwelling double-J stent were urinary calculi (40.20%) and ureteral stenosis (24.50%). In infected patients, we found that female patients were significantly higher than male patients (61.77% vs 38.23%). Studies have shown that women are more than men in patients with urinary sepsis, and perimenopausal women are more likely to develop urinary sepsis than women of other ages.[23–25] The female urethra is shorter than the male urethra. At the same time, the external orifice of the urethra is adjacent to the rectum and vagina, and the mucosa is more vulnerable to the influence of venous circulation, so female is prone to infection. Animal experiments show that the immune function and organ response ability of ovariectomized and aging animals will be inhibited under stress.[26] The integrity of female urinary system needs estrogen to maintain.[27] The decline of estrogen will cause atrophy of urinary system mucosa, increase the susceptibility of urethral epithelium and mucosa to local pathogens, and thus cause urinary tract infection.[27] These factors may be the reason why the urinary tract infection caused by double-J stent is higher in women than in men.

This study showed that the culture rates of pathogenic bacteria in bladder, ureter, pelvis and urine of double-J stent were 85.0%, 42.9%, 67.3% and 24.3% respectively, and the positive culture rate of double-J stent bladder was high.[10] Therefore, we chose the bladder segment of double-J stent as the object of bacterial culture and detection. Previous studies have suggested that the pathogens of double-J stent-related infections mainly include *Escherichia coli, Pseudomonas aeruginosa, Enterococcus faecalis and Klebsiella pneumoniae*.[12,21,28] In this study, we found that under the condition of double-J stent associated urinary tract infection, the pathogenic bacteria culture rate of double-J stent was significantly higher than that of urine (67.65% vs 35.29%). In addition, we also found that the main pathogenic bacteria in the urine were *Escherichia coli* (30.55%) from Gram negative bacteria, while the main pathogenic bacteria in double-J stent were *Enterococcus faecalis* from Gram positive bacteria (27.53%). The Gram positive bacteria in urine and double-J stent showed strong resistance to minocycline, erythromycin, gentamicin and compound sulfamethoxazole, and the resistance rate of Gram

positive bacteria in double-J stent to vancomycin, ciprofloxacin, meropenem and piperacillin/tazobactam was significantly higher than that of Gram positive bacteria in urine (P<0.05). Gram negative bacteria in urine and double-J stent showed strong resistance to gentamicin, ampicillin/sulbactam, ciprofloxacin, compound sulfamethoxazole, cefepime, levofloxacin, aztreonam, cefazolin and cefotaxime. In addition, the drug resistance rate of Gram negative bacteria in double-J stent to imipenem, cefepime, piperacillin/tazobactam, meropenem and cefoperazone/sulbactam was significantly higher than that of Gram negative bacteria in urine (P<0.05). The results of this study are similar to those of other scholars. It is found that Escherichia coli is the main pathogenic bacteria, and the pathogenic bacteria have strong drug resistance.[29,30] These results suggest that the drug resistance of Gram negative and Gram positive bacteria in double-J stent is significantly higher than that in urine. The increase of bacterial resistance in the double-J stent may be related to the biofilm formed by bacteria gathering on the surface of the double-J stent.[8–10] Previous studies suggest that bacteria colonized on the double-J stent can form microbiota by secreting polysaccharide, fibrin, lipopolysaccharide and other polysaccharide compounds, and further differentiate and mature to form a biofilm on the surface of the double-J stent.[31,32] Under the protection of biofilm, bacteria can escape the body's phagocytosis and the killing of antibacterial drugs, and the resistance of biofilm bacteria to antibacterial drugs can be increased by 10 to 1000 times, which is difficult to be completely eliminated by drugs. With the passage of time, these bacteria have formed strong resistance.[31–34] The formation of biofilm causes repeated infection of the patient's urinary system and the whole body, which ultimately leads to the forced removal of the double J tube, which cannot play its due therapeutic role.[31–34] Based on the findings of this study, we suggest that the urinary tract infection associated with double J tube should be conducted with simultaneous bacterial culture and drug sensitivity test on the urine and bladder segment of double-J stent. At the same time, considering the strong drug resistance of urinary tract infection bacteria associated with double J tubes, we suggest that before drug sensitivity test, empirical antibiotics, such as piperacillin/tazobactam, meropenem, tegacyclin, cefoperazone/sulbactam, teicoplanin, imipenem and vancomycin with relatively low drug resistance rates can be used.

Limitation of the Study

Although there are some findings in this study, this study still has the following limitations: First, the sample size of this study is small, and the research results have certain limitations. Second, this study is a single center, retrospective study, which has some limitations. Third, due to the differences in testing methods and equipment, the results of this study have certain limitations. Fourth, because of the differences in age, race and living environment, the research results only reflect the characteristics of the population in the center. Fifth, in this study, the phenotype of bacteria and molecular phenotype of bacteria has not been described in detail, and further research and exploration are needed in the future.

Conclusion

In this study, we found that double-J stent associated urinary tract infection is more common in women than in men. Escherichia coli and Enterococcus faecalis are the main pathogens, and the pathogens show strong drug resistance, in which the resistance of double-J tube pathogenic bacteria is significantly stronger than that of urine pathogenic bacteria.

Data Sharing Statement

The datasets are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

This study was conducted with the approval of the ethics committee of the University-Town Hospital of Chongqing Medical University and Chongqing Traditional Chinese Medicine Hospital. All participants gave written informed consent. All research studies on humans (individuals, samples or data) have been performed in accordance with the principles stated in the Declaration of Helsinki.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically

reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests in this work.

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