

Rate of positive urine culture and double–J catheters colonization on the basis of microorganism DNA analysis

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Introduction The aim of the trial was to estimate the relationship between colonization of the Double–J catheter, and the microorganisms cultured from urine.

Material and methods 60 patients, who had Double–J catheters inserted, participated in the study. All the subjects had their midstream urine samples taken prior to the stent insertion and removal. A negative urine culture before catheterization was mandatory to participate in the study. The patients were assigned into three subgroups, according to stenting duration: 1) 20 to 30 days (18 cases); 2) 30 to 90 days (30 cases); 3) longer than 90 days (12 cases). Bacterial and fungal DNA was identified using electrophoresis in polyacrylamide gel with a denaturing gradient (PCR–DGGE). The relationship between the genetic analysis of the catheter and the urine culture was estimated.

Results Urine cultures were positive in only 8 patients, while Double–J catheter analyses were positive in all cases. In 2 cases one type of microorganism was isolated from the stent surface while the remaining 58 catheters were colonized by more than one pathogen. In three cases fungi were isolated. There were only three types of pathogens cultured from urine specimens. Urine and stent cultures were consistent in 5 cases. In 3 cases urine culture and stent analysis were not consistent.

Conclusions Double–J catheter retention in the urinary tract is associated with an extremely high risk of bacterial colonization, while the risk of urine infection is about 8–fold lower. There is a great inconsistency between urine infection and catheter colonization, indicating a low predictive value of urine culture for estimating stent colonization.

Key Words: urine culture ◊ double–J catheters ◊ DNA analysis

INTRODUCTION

Insertion of the Double–J catheter into the ureter, which facilitates drainage of the upper urinary tract, is one of the most common urological procedures. This medical procedure is generally thought of as quite easy and safe to perform, with a very low rate of severe complications. Nevertheless, as any other medical procedure, it is usually associated with some bothersome symptoms such as pain, dysuria, fever, erythrocyturia, mucose membrane injury, or ureter peristalsis disturbances, all of which have a negative impact on the patient's quality of life. Other complications include anxiety, sexual dysfunction, sleep

disturbances, and absence at work. Sporadically, stent dislocation or fragmentation and even fistulas may occur. Forgotten stents should also be mentioned as they may result in serious complications such as marked incrustation, stent fragmentation, urosepsis, or even renal failure [1–5]. It must be, however, underlined that bacterial or fungal colonization of both catheter surface and urine is the most frequent complication that is noted. It is observed especially during long–term stent retaining [6, 7]. King et al. performed a systematic review, which has disclosed that urinary catheterization was the major risk factor of healthcare–associated urinary tract infections. The authors have calculated that 79.3% of

this complication could have been prevented if catheter insertion had been avoided [8]. Many authors therefore investigate the types of pathogens isolated from catheters and urine as well as the correlation between urine and stent culture. The relationship between colonization and stenting duration, as well as some other aspects, such as age, gender, co-morbidities, reason for stenting, and the method of catheter insertion, are also found in their field of interest. Clinical trials published recently have shown great inconsistency between microbiological analysis of the stent surface and urine. It concerns both the presence of colonization and the type of pathogen cultured from the Double-J catheters and the urine sample. Available data is controversial, therefore it seems that there is a place for further studies in this field [9, 10].

The aim of our study was to estimate the relationship between bacterial colonization of the Double-J catheter, which was dissected into three separate sections, and the microorganisms isolated from urine. We have also examined the rate of urine and catheter colonization as well as the types of pathogens that were cultured. We decided to use microorganism DNA analysis while exploring the catheter colonization as this method is thought to possess the highest diagnostic sensitivity.

MATERIAL AND METHODS

The study sample comprised 60 patients (25 women and 35 men, aged 34 to 67 years) who had Double-J polyurethane catheters (Balton®) inserted. The participants of the trial were recruited from the 2nd Department of Urology of the Medical University of Lodz between January 2011 and June 2012. Indications for ureteral catheter insertion were the following: urinary tract lithiasis, hydronephrosis due to ureteropelvic junction stricture, ureter stricture, tumors, and the presence of additional blood vessels. The patients were divided for further analysis into three subgroups, according to stenting duration: 1) subjects with their stents kept for 20 to 30 days (18 cases); 2) participants with the catheters retained longer than 30 but shorter than 90 days (30 cases); 3) patients with their catheters kept for the period longer than 90 days (12 cases). There were no statistical differences in age and gender distributions between the three subgroups. All the participants had their midstream urine samples taken prior to the stent insertion and removal. A negative urine culture before catheterization was mandatory to participate in the study.

Double-J stents were inserted via an open or endoscopic manner (9 and 51 cases, respectively). All

the subjects included in our study were given fluoroquinolone prophylaxis after catheterization. In our trial, 500 mg of ciprofloxacin twice daily, was administered orally for five days. No episodes of urinary tract infection symptoms were noted in our subjects during the observation period.

A second urine culture was performed before catheter removal. Significant bacteriuria or funguria was defined as a bacterial or fungal count of more than 10⁵ CFU/ml. Double-J stents were then removed and immediately sent for genetic analysis. After initial analysis of the whole stent it was further divided, under aseptic conditions, into three sections: pelvic, ureteral, and vesicular, which were analyzed separately. Bacterial and fungal DNA was identified using electrophoresis in polyacrylamide gel with a denaturing gradient (PCR-DGGE).

The trial protocol was approved by the local ethics committee of the Medical University of Lodz. All the participants have given written informed consent after a complete description of the study. Appropriate tests for statistical analysis were used and *P* values <0.05 were considered statistically significant.

RESULTS

Double-J catheter DNA analyses were positive in all cases. In 2 cases one type of microorganism was isolated from the stent surface. The remaining 58 catheters were colonized by more than one pathogen, including 12 stents with two species and 46 stents with three types of pathogens.

Each of three sections of Double-J catheters was analyzed separately. 32 stents were colonized by the same pathogens on all three sections. In 6 cases, stent analyses have shown two types of microorganisms isolated from the different parts, while the remaining 22 catheters were colonized by three different bacteria or fungi species. Bacteria species that were most frequently isolated from the catheter surface were the following: *Staphylococcus aureus*, *Enterococcus faecalis*, *Pseudomonas aeruginosa* and *Escherichia coli*. The whole microorganism spectrum isolated from the stents is presented in Table 1. DNA analysis revealed fungi in three cases.

Urine cultures were positive in only 8 patients before the catheter removal. Only three bacteria species were isolated from the urine specimens: *Escherichia coli*, *Pseudomonas aeruginosa*, and *Klebsiella oxytoca*. No fungi were cultured from urine samples. The number of bacteria species isolated from urine specimens is shown in Table 2.

Urine and catheter cultures were consistent in 5 cases. In 3 cases urine culture and stent analyses have shown different bacteria species.

Table 1. Types of pathogens isolated from the respective Double-J catheter sections

| Pathogen species | Pelvic section | Ureteral section | Vesicular section |
|-----------------------------------|----------------|------------------|-------------------|
| <i>Staphylococcus aureus</i> | 20 | 13 | 8 |
| <i>Enterococcus faecalis</i> | 8 | 21 | 25 |
| <i>Pseudomonas aeruginosa</i> | 20 | 16 | 14 |
| <i>Escherichia coli</i> | 11 | 16 | 19 |
| <i>Staphylococcus epidermidis</i> | 0 | 3 | 5 |
| <i>Hafnia alvei</i> | 3 | 3 | 5 |
| <i>Citrobacter freundii</i> | 1 | 3 | 1 |
| <i>Proteus mirabilis</i> | 11 | 10 | 8 |
| <i>Lactobacillus</i> | 0 | 2 | 10 |
| <i>Providencia stuartii</i> | 7 | 7 | 7 |
| <i>Morganella morgani</i> | 3 | 1 | 0 |
| <i>Enterobacter cloacae</i> | 1 | 3 | 3 |
| <i>Streptococcus agalactiae</i> | 1 | 1 | 0 |
| <i>Klebsiella pneumoniae</i> | 8 | 6 | 2 |
| <i>Serratia marcescans</i> | 10 | 4 | 0 |
| <i>Trichomonas vaginalis</i> | 0 | 1 | 1 |
| <i>Burkholderia cepacia</i> | 0 | 3 | 2 |
| <i>Gardnerella vaginalis</i> | 0 | 2 | 8 |
| <i>Prevotella bivia</i> | 0 | 1 | 1 |

Of 18 urine specimens taken from the subjects with the shortest period of the stent retaining, only 1 was infected (5.5%). In case of catheters left in the urinary tract for the period of longer than 30 days but shorter than 90 days, 3 of 30 urine samples were infected (10%). Urine specimens taken from the patients with catheters retained for longer than 90 days were infected in 6 of 12 cases (50%). Statistical analysis revealed significant correlation between urine culture and Double-J stenting duration ($p < 0.05$). Gender, reason for catheter insertion, and the method of stenting were not related to variables such as urine culture and the number of pathogens isolated from the stent surface.

DISCUSSION

Our present findings show 100% risk for catheter colonization. They are consistent with our previous observations, where we noted that 64 of 65 stents were colonized [7]. Also Riedl et al. have found a 100% risk for colonization while retaining stents long-term [11]. Similarly, Farsi et al. have observed a 67.9% rate of stent colonization [9]. On the other hand, the results of other authors have shown a markedly lower rate of colonization. Lifshitz et

Table 2. Microorganisms cultured from urine specimens

| Bacteria species | Number of patients |
|-------------------------------|--------------------|
| <i>Escherichia coli</i> | 6 |
| <i>Pseudomonas aeruginosa</i> | 1 |
| <i>Klebsiella oxytoca</i> | 1 |

al., as well as Paick et al., point to a nearly 44% risk of catheter colonization [12, 13], and Kehinde et al. of nearly 42% [14]. Urine culture was positive in 8 of 60 patients in our study, which accounts to about 13%. This is a relatively low incidence comparing to other studies. Riedl et al. have noted a 45% risk of urine infection during short-term stenting and 100% during long-term stenting [11]. Akay et al. have observed a 24% risk of infection [15]. Similarly, our previous results also indicate a 26% rate of urine infection [7]. A possible explanation for such differences in the rate of stent colonization and urine infection may be the sample of patients (number, age, sex, concomitant diseases), type of catheter, use of prophylactic antibiotic therapy, or different methodology of colonization estimation (culture, DNA analysis).

The results of many trials show that the rate of catheter colonization is much higher than the rate of urine infection. Farsi et al. noted in their study that urine cultures were positive in 29.9% while catheter colonization was found in 67.9% [9]. Observations made by Kehinde et al. point to more than 2.5-fold higher risk of catheter colonization (42%) than urine infection (17%) [14]. Similarly, Riedl et al. have noted that short-term catheterization is accompanied with catheter colonization in 69% and urine infection in 45% [11]. Our previous study has shown that urine infection was detected in 17 of 65 cases while stent colonization was observed in 64 of 65 cases, so the risk for catheter colonization was 4-fold higher [7]. All these observations stay in agreement with our present results. We have noted that the rate of stent colonization was 100%, and was 8-fold higher than the incidence of urine infection.

Available data indicate, similarly to our present observation, that the species most frequently isolated from urine is *Escherichia coli* [7, 14, 16]. Among others, are included *Staphylococcus sp.*, *Enterococcus sp.*, *Proteus sp.*, *Klebsiella sp.*, and *Pseudomonas sp.* [7, 16]. Urine specimens were colonized by only 3 bacteria species, while no fungi were observed. However, other authors point to other species as being the most common. Kehinde et al. have noted that *Staphylococcus* was isolated most frequently from urine samples [17]. Findings of Lifshitz et al.,

as well as Farsi et al., show that *Pseudomonas sp.* is the most common bacteria species isolated from urine [9, 12]. It must be stressed, however, that no antibiotic prophylaxis was administered in these patients, which could have had a significant impact on obtained results. In our study we have noted one such sample.

In case of the Double-J catheters, the most common species isolated were *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Enterococcus fecalis*, and *Escherichia coli*. It is worth mentioning that species such as *Staphylococcus aureus*, *Enterococcus fecalis* were not isolated from any urine specimen. *Escherichia coli* – the most common cause of urine infection – was also among bacteria most frequently cultured from catheter surface in other observations [12].

Bacterial colonization seems to depend on the use of antibiotic prophylaxis. In the previously mentioned study of Farsi et al., in patients not given any antibiotic prophylaxis *Pseudomonas aeruginosa* was the most common pathogen found on the stent surface and cultured from urine [9]. Daniel et al. have found that colonization of Foley catheters was more frequent in patients not receiving systemic fluoroquinolones. He has also quite often observed polymicrobial colonization, with both Gram-positive and Gram-negative species [18]. The above findings remain in agreement with our results, as in almost all of our cases (58/60) we have isolated more than one pathogen. In our previous study, 22 of 65 stents were colonized by more than one species [7]. This is a very important issue as it points to the need for use of a quite broad spectrum of antibiotics in post-procedure prophylaxis.

There is a constant discussion concerning the possibilities of reducing the catheter related complications. This issue is of great importance, as urinary stenting is the procedure most commonly carried out in urology and also because of accompanying complications, especially high rates of urinary tract infections. The current strategies comprise either stent modifications or additional medical interventions – both non-pharmacologic and pharmacologic. Catheter modification may concern its durometer (“soft” or “firm” stents), design (distant coil stents vs. loop stents), diameter, or type of material that the stent is made of. Modifications of stent surface such as silver coating, diamond-like coating, hydrophobicity change, or antimicrobial activity molecules (heparin, triclosan) have been created, to inhibit or maybe even in the future to prevent, stent colonization and biofilm formation [19]. Use of antibiotic-releasing biomaterials has additional advantages, as they deliver the drug to

target tissues and have a positive impact on both effectiveness (influencing directly the biofilm that is often resistant to systemic antibiotic therapy) and lowering the risk of systemic side effects. Additionally, it is suggested that increase in patient’s fluid intake, augmentation of urine pH value (via citrate consumption), analgesics, anticholinergics, alpha-blockers, and/or prophylactic antibiotic therapy may decrease the rate of complications or minimize the complaints [5]. Unfortunately, none of the above-described strategies has the power to fully prevent catheter colonization, so there is a need for further investigations and technological innovations in this field.

It is well known that there are certain groups of patients who are extremely predisposed to this complication. The risk factors include age, sex, lower urinary tract obstruction, co-morbidities such as diabetes, chronic renal failure, or impairment of the immune system. Therefore, the indications for stenting in these groups of patients should be thoroughly considered. Marigliano et al. have achieved a significant reduction of the rate of catheterization thanks to educational intervention that was implemented in a teaching hospital in central Italy [20]. Stenting duration is thought to be a strong risk factor for urine and/or stent colonization [9, 13, 17]. Akay et al. observed the relationship between long-term stenting and catheter colonization, but not urine infection [15]. In light of these observations it seems that removal of the catheter should be performed as early as possible. On the contrary, in the group of patients presented in our study, no relationship between the duration of urinary stenting and catheter colonization could be observed, as all stents were colonized regardless of the duration. Similarly, in our previous study almost all (64 of 65) Double-J catheters were colonized [7]. These results point to a rule that stent insertion practically means it will be colonized.

CONCLUSIONS

Double-J catheter retention in the urinary tract is associated with an extremely high risk of bacterial colonization, while the associated risk of urine infection is about 8-fold lower. There is a great inconsistency between urine infection and catheter colonization, indicating a low predictive value of urine culture for estimating stent colonization. There is also a great heterogeneity of microorganisms colonizing Double-J catheters, while there were only three bacteria species isolated from urine specimens.

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