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Transmission of multi-drug resistant *Pseudomonas aeruginosa* between two flexible ureteroscopes and an outbreak of urinary tract infection: the fragility of endoscope decontamination

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SUMMARY

Objectives: Flexible endoscopes are difficult to decontaminate, and endoscope-associated infections are increasing. This report describes an outbreak of multi-drug resistant *Pseudomonas aeruginosa* identified following an increase in incidence of clinical infections associated with flexible ureteroscopy at a tertiary care centre in the UK.

Methods: Clinical, laboratory and central decontamination unit (CDU) records were reviewed to determine the extent of the problem, and links to the used endoscopes. Audits of the ureteroscopy procedure, endoscopy unit and CDU were performed. Endoscopes were sampled, cultured and examined for structural integrity. All available isolates were typed.

Results: Thirteen patients developed clinical infections linked to two flexible ureteroscopes. The first ureteroscope was likely colonized from a known infected patient and the second ureteroscope after use on another patient infected by the first. Risk factors identified include surface cuts, stretching and puckering of the outer cover in both ureteroscopes, absence of bedside cleaning, overnight delay between the ureteroscopy and decontamination, inadequate drying after decontamination and non-traceability of connector valves.

Conclusions: The adequacy of flexible endoscope decontamination depends on numerous steps. With the increasing global incidence of multi-drug resistant organisms, stringent monitoring of the flexible endoscopy process by users and decontamination units is essential.

Introduction

Endoscopes are amongst the most significant advances in medicine. The simple devices of the 1960s have now evolved into multi-channel instruments with cameras and complex accessories to carry out interventions in deep internal organs.

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However, with this increase in sophistication has come increasing difficulty in decontamination [1]. Flexible endoscopes represent a particular challenge as they are not amenable to standard heat sterilization. Careful manual cleaning is a prerequisite for further cleaning and disinfection in automated endoscope washer-disinfectors. There are two steps to this cleaning: (1) a 'bedside clean' immediately after use that removes gross contamination, and (2) a fuller and more controlled manual clean prior to automated decontamination in an automated washer-disinfector. Despite multiple guidelines and protocols to ensure microbiological safety of endoscopes, there is a growing body of evidence implicating flexible endoscopes in the transmission of infections [2].

In this article, we report the investigations and outcome of an outbreak of multi-drug resistant *Pseudomonas aeruginosa* (MDRPA) urinary tract infections (UTIs) linked to flexible ureteroscopy (flex-URS) at a South London teaching hospital between October and December 2017.

Methods

Setting and identification of outbreak

Kings College Hospital (KCH) is a large tertiary care centre with approximately 1600 beds across four sites. The main hospital site also has a large outpatient service including a day-surgery unit where complex procedures such as flexible ureteroscopic procedures are routinely performed. Each year, approximately 150 flexible ureteroscopic procedures are performed on the main site mainly at the day-surgery unit (more than 90% of the cases) with only a few procedures being performed in the main theatres.

The optimum staffing level of the central decontamination unit (CDU) is 19 staff members (one manager, two senior technical and 16 junior technical staff).

In October/November 2017, three cases of MDRPA infections (patient nos 13, 27, 35, see Table I) came to the attention of the microbiology team due to difficulty in finding suitable antibiotic treatment regimens. All had similar susceptibility profiles. It was unusual for the hospital to see this number of MDRPA infections in such a short time in the urology patient population. Suspicion was raised as to possible cross-transmission and thus outbreak investigations were initiated.

Look back exercise

The laboratory database was searched for all MDRPA in the previous 6 months. This revealed an additional case (patient no. 6) of MDRPA urosepsis in July 2017 with similar antibiotic sensitivities. All these patients had a history of urological

Table I
Symptoms, case definitions, treatment and outcomes of patients identified during the outbreak

Patient no.	Ureteroscope ID	Age/sex	Case definition	Indication for ureteroscopy	Samples positive for MDRPA	Clinical presentation	Treatment	Outcome
6	A	38/F	C/PR	Nephrolithiasis	Urine and Blood culture	U	Colistin	Recovered
11	A	50/M	C/PR	Nephrolithiasis	Urine	LUTI	Nitrofurantoin	No further presentations
13*	A	69/M	P	Nephrolithiasis	Nil	U	Ceftriaxone	Recurrence
16	A	45/F	P	Nephrolithiasis	Nil	U	Ciprofloxacin	Presented to GP with mild s/s UTI, then no further presentations
13*	B	69/M	C/PR	Nephrolithiasis	Urine	U	Ceftriaxone+ Ciprofloxacin	Recovered
27	A	42/M	C/PR	Nephrolithiasis	Urine	U	Colistin	Recovered
28	B	36/M	C/PR	Nephrolithiasis	Urine	LUTI	Amoxicillin	Asymptomatic by the time culture results available
29	A	46/F	C/PR	Nephrolithiasis	Urine	LUTI	Nitrofurantoin	No further presentations
32	A	65/M	P	Renoscopy	Nil	U	Ciprofloxacin	No further presentations
33	B	20/F	C/PR	Nephrolithiasis	Urine	LUTI	Trimethoprim	Recovered
35	B	35/M	C/PR	Ureterocoele + nephrolithiasis	Urine	U	Colistin	Recovered
15	A	66/M	C/PR	Renoscopy	Blood culture	U	Piperacillin-tazobactam	No further presentations
38	A	79/M	C/PR	Renoscopy	Urine	LUTI	Ciprofloxacin	Asymptomatic by the time culture results available
39	A	25/F	P	Renoscopy	Nil	LUTI	Nitrofurantoin	No further presentations

C, confirmed case; LUTI, lower UTI; MDRPA, multi-drug resistant *Pseudomonas aeruginosa*; P, possible case; PR, probable case; U, urosepsis.
* Two episodes in the same patient.

intervention and had presented with UTI within seven days following the procedure. A full investigation for a potential outbreak was initiated in November 2017. An ambidirectional methodology was followed.

As all the initial patients had flex-URS, further investigations were performed to determine whether any one endoscope was linked to the transmission or if there was a wider problem. The CDU scans each endoscope identity code and the patient identity code and links it together in an electronic database. In addition, a sticker with the endoscope barcode is attached to the patient's paper records. These records were extracted for this investigation. All of the hospital's flexible ureteroscopes ($N = 3$) were included in the initial investigation and a list of patients on whom they had been used from June 1st, 2017 to December 10th, 2017 was reviewed. This information was compared with the patient list in the theatre records for accuracy. Ureteroscopes A and B were used in the day-surgery unit only, whereas ureteroscope C was used only in the main theatre. Both ureteroscopes A and B were brought in as new and were first used on July 5th, 2017 (A) and July 6th, 2017 (B). Neither had been sent for servicing or repairs since their introduction into practice.

Hospital clinical records of each patient who had a flex-URS were interrogated to check whether any had an MDRPA reported before or after their procedures and for evidence of clinical signs and symptoms compatible with a post ureteroscopy infection. Records of general practitioners (GPs) and other hospitals (in case of hospital transfers) for each patient were also interrogated to determine whether they had presented elsewhere with an illness compatible with a post-ureteroscopy infection and microbiological results were retrieved where necessary.

While investigating, a CDU staff shortage was detected as no manager was in post, and the department was operated by only two senior technical and 11 junior technical staff.

Case definitions

The following case definitions were used in this outbreak investigation.

Confirmed case: A patient who had flex-URS at KCH from July 2017 onwards with a clinical illness compatible with post-ureteroscopy infection from whom *P. aeruginosa* was isolated from urine or blood culture and typing results identical to isolates from the initial cases.

Probable case: A patient who had flex-URS at KCH from July 2017 onwards with a clinical illness compatible with post-ureteroscopy infection from whom *P. aeruginosa* was isolated from urine or blood culture with similar resistance profile but no typing results available.

Possible case: A patient who had flex-URS at KCH from July 2017 onwards with a clinical illness compatible with post-ureteroscopy infection from whom no organism was isolated.

Patients who had symptoms compatible with a post flex-URS infection but yielded another organism were excluded from the above definitions.

For the purpose of analysis, reporting and duty of candour for confirmed and probable cases were combined.

Decontamination reviews

Prior to June 2017, flexible ureteroscopes were decontaminated in the day-surgery unit by an automated washer disinfector but this was reaching the end of its useful life and updated versions were available on the market. It was condemned on June 8th, 2017 and subsequently all flexible ureteroscopes were decontaminated at the CDU located on the same hospital site but in a separate building from the day-surgery unit.

The standard procedure for all flexible endoscopes was that they should be externally wiped, and fluid drawn through the suction/biopsy channel immediately after use (the 'bedside clean'). They would then be transported to the CDU where subsequent decontamination would comprise: manual leak test, manual wash including brushing the suction/biopsy lumen, automated cleaning and chemical disinfection (peracetic acid (AperlanPoka Yoke)) in the automated endoscope washer disinfector (Lancer ED Flow) including an automated leak test. Then endoscopes were placed in baskets as per the automated endoscope washer disinfector's manufacturer's validated process and further kept in same basket thus limiting staff handling. Procedures following this were variable. Endoscopes were either used within 3 h or stored in a system which used inert gases to preserve non-dried endoscopes (Getinge Sentinel) or stored in an endoscope drying cabinet (Lancer FD8) and packaged using the Getinge Sentinel system. No alcohol was used at any stage of endoscope reprocessing.

The automated endoscope washer disinfector final rinse water was tested weekly for total viable count by an external company. Additional tests for *P. aeruginosa* and mycobacteria were conducted on rinse water at the quarterly and annual tests. There were two sets of reusable endoscope valves owned by the hospital and these were used interchangeably with all three flexible ureteroscopes. Cameras attached to endoscopes were covered with a single-use sheath which was discarded immediately after use.

Once the incident was identified, all three flexible ureteroscopes were removed from use. Ureteroscopes (A and B), implicated in the outbreak, were sent to the manufacturers to check for damage that may have impaired cleaning and disinfection. In addition to the regular audit of the endoscopy process, there was more specific scrutiny of the endoscope journey along the decontamination processes.

Microbiological investigations

Urine and blood cultures were tested according to standard laboratory methods and identification and sensitivity were performed by Vitek (Version 7.01, Biomerieux). Five isolates had been stored and hence were available for epidemiological typing (variable number tandem repeat (VNTR) performed at Healthcare Associated Infection and Antimicrobial Resistance Division, Public Health England).

Tap water from the CDU was cultured for *P. aeruginosa* (by an external laboratory).

All three flexible ureteroscopes (A, B and C) used in the hospital were tested for bacterial contamination. Ten millilitres of BHI broth (Oxoid) was passed through the suction/biopsy lumen and collected into a sterile container and the same fluid was then flushed two more times through the lumen and collected. Aliquots of this fluid (10 μl and 50 μl) were cultured directly on blood agar (Oxoid) and MacConkey agar (Oxoid) and incubated overnight for enrichment culture the next day. The valves were soaked in a wide-mouthed container with 20 mL BHI broth for 10 min and gently agitated. This fluid

was also cultured as above. Sterile cotton-tipped swabs were moistened with saline and used to sample exposed parts of the cameras and other external parts of the scopes. These were cultured directly onto blood agar and MacConkey agar.

Results

Patients and procedures

All four initial cases (patient nos 6, 13, 27, 35; see Table I) had urinary calculi and had developed UTI with MDRPA following flex-URS. Many patients also had cystoscopes used during their treatment but laboratory records of sequential patients on whom each cystoscope was used did not show any evidence of subsequent MDRPA infection. The only common factor between all MDRPA-culture-positive patients was either flexible ureteroscope A or flexible ureteroscope B. Both ureteroscopes A and B were first introduced as new in July 2017, were used only in the day-surgery unit and by the same urological team. A review of the timeline did not show common wards or other shared procedures and the sequence of infected cases suggested a point source (see Figure 1). Therefore, we focused the investigation on flexible ureteroscopes A and B and investigated in detail the patients who had procedures using these endoscopes from July 2017 onwards.

The initial patient (patient no. 6) had a history of repeated hospital admissions for UTI complicated by urinary calculi, had been exposed to multiple antibiotics and MDRPA had been isolated from the patient's urine before the flex-URS. This patient developed urosepsis with MDRPA one day after the flex-URS. Since MDRPA was identified in this patient even before this ureteroscope was used, this patient was considered the index case. The pre-ureteroscopy urine isolate was not available for typing and hence this cannot be proved, however, the suspicion was high due to similar antibiotic resistance profile. The subsequent MDRPA was typed and found to be identical to the other confirmed cases.

The other three initial cases (patient nos 13, 27, 35) did not have a history of previous MDRPA infection.

During the look back exercise, it was found that patient no. 15 who underwent ureteroscopy at KCH (ureteroscope A) during the risk period had developed urosepsis (identified at a different hospital site) with MDRPA isolated from blood and urine cultures. The isolates from these five patients were identical by VNTR (11, 3, 2, —, 3, 1, 9, 3, 8) corresponding to sequence type ST654. This VNTR profile was reported once before at KCH in 2015 (not related to urology patients). The MDRPA isolates were uniformly resistant to ciprofloxacin, gentamicin, amikacin, ceftazidime and showed variable resistance to meropenem and piperacillin–tazobactam, perhaps because the method of testing varied at external labs. OprD porin loss, upregulated efflux and extended spectrum beta-lactamase (ESBL) activity were inferred by the susceptibility testing and no carbapenemase genes were detected.

A total of 40 patients had a flex-URS from July to December 2017 by either ureteroscope A or B (42 procedures). In addition to the five confirmed cases, five probable cases (patient nos 11, 28, 29, 33, 38) and six possible episodes (patient nos 3, 8, 13, 16, 32, 39) were found on retrospective active case finding. However, two of the possible cases (patient nos 3 and 8) are unlikely to be related to the MDRPA outbreak as they predate the index case and no bacterium was isolated from their urine. Five patients had symptoms of lower UTI whereas the remaining had features of urosepsis. All patients received IV gentamicin as perioperative prophylaxis. Demographics, post-procedure infections, treatment given and outcomes are listed in Table I. Five of the 15 procedures which subsequently led to infections had been by endoscopes dried for less than 3 h before storage.

A letter of candour was sent to all confirmed and probable cases. All other patients who had been exposed to the implicated endoscopes were sent inform and advice letters inviting them to present directly to the urology department should they develop any symptoms suggestive of a post-procedure infection. Their GPs were also alerted for a possibility of MDRPA UTI not susceptible to oral antibiotics.

Endoscope

No technical defect or malfunction of ureteroscope A or B was reported by the surgical team or during decontamination checks while the transmission was ongoing. Ureteroscope A was last used on December 4th, 2017, after which it was removed from use pending outbreak investigations and had no evidence of a failed leak test. Endoscope B failed a leak test on October 25th, 2017, and was removed from use. Both scopes were sent

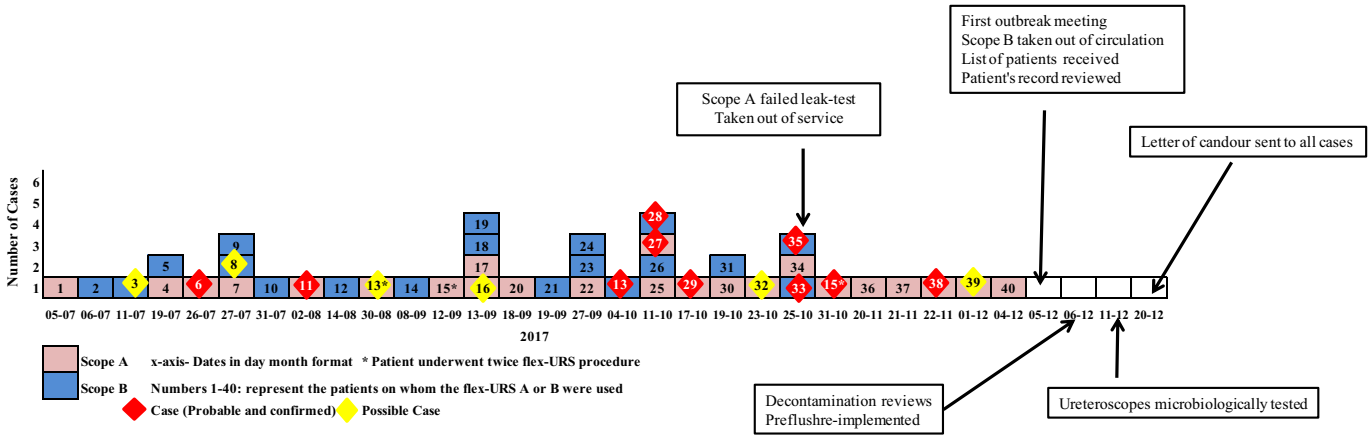

Figure 1. Timeline of cases and events during the outbreak.

to the manufacturers for technical examination. The reports showed that there were partial depth cuts in the outer cover in both endoscopes. Endoscope B had laser damage to the interior surface and a flap of material could be seen projecting into the lumen.

MDRPA of identical VNTR profile to that from the patients was isolated from ureteroscope A in both 10-μl and 50-μl aliquots, whereas the samples from endoscopes B and C and all valves were microbiologically clear. The audit of the decontamination procedure in the CDU reported no non-compliances. However, audit of the live flex-URS procedure at the day-surgery unit identified the absence of a bedside clean. Further investigation revealed that since the (now decommissioned) automated endoscope washer disinfector was located in the day-surgery unit itself, all flexible ureteroscopes were decontaminated immediately after use and hence bedside clean was not thought necessary as per local tradition. However, this practice inadvertently continued even after the more remote CDU took over the decontamination process. Ureteroscope C had always had a bedside clean as was the practice in the main theatre which had always sent their instruments to CDU only. Some procedures involving the flexible endoscope were carried out after working hours in the day-surgery unit and the ureteroscope would remain in the day-surgery unit overnight (having not had a bedside clean), before transport to the CDU on the next day. Records showed that on 7/40 (17.5%) occasions the endoscopes has been stored overnight before being received by CDU for decontamination.

Automated endoscope washer disinfector final rinse water cultures did not detect total viable counts above the acceptable 10 colony forming units limit nor was *P. aeruginosa* isolated on any occasion. The tap water cultures from the unit were also within normal limits.

Discussion

MDRPA was known to be present in patient no. 6 prior to ureteroscopy and it is probable that this was the source of endoscope colonization (ureteroscope A). Patient 13 was exposed to ureteroscope A on August 30th, 2017, and developed pyelonephritis after the procedure. However, his urine culture revealed heavy mixed growth at first. He was treated with broad-spectrum antibiotics (meropenem followed by ceftriaxone) and made a symptomatic recovery. He then underwent laser treatment for kidney stones with ureteroscope B on October 4th, 2017 and his pre-procedure cultures grew MDRPA. It is possible there was residual MDRPA in his urine due to partial treatment with ineffective antibiotics when ureteroscope B was used on him. It is hence likely that ureteroscope B then became colonized with the organism as a result of this procedure and transmitted infection onwards (two probable and one confirmed case).

The external structural damage reported on both endoscopes could lead to inaccessible niches that might compromise cleaning and disinfection. Although the elongated outer cover could have been stretched to eliminate the fold and enable efficient manual cleaning, there was no evidence that this was carried out, perhaps because these are fragile instruments which are handled delicately.

As ureteroscope B subsequently failed a leak test there may have been a stage when there was enough internal damage to allow internal colonization to persist. Endoscope A, however, had no leak-test failures. The outer damage does not explain why the internal channels of ureteroscope A were found to be colonized with the MDRPA and this remains a gap in our knowledge.

There was no method to pair the valves to individual endoscopes and hence there was no assurance on the traceability of these parts (two sets of valves for three endoscopes). It remains possible that if valves are not traceable with the endoscopes, there may be a mix up of used and unused. It is good practice to ensure traceability or to use disposable valves.

Another finding of significance was the missing bedside clean in the day-surgery unit, particularly when there was an overnight delay before the decontamination process started. This may have led to development of *P. aeruginosa* growth in biofilms which are highly resistant to antimicrobial compounds [3]. The adherence characteristics of biofilms [4] could have made it difficult to remove them, particularly from irregular surfaces. An additional relevant observation is that use of ureteroscope C was confined to the main theatres where it always had a bedside clean and, notably, this endoscope was not linked to the outbreak.

Furthermore, not all endoscopes were being dried before reuse. Whether the endoscope had been used wet or after drying did not seem to be correlated with transmission of infection to the patient it was next used on, but it is feasible that a proportion of patients did not present with clinical features even though bacteria were transferred. As a result of this finding, all reusable ureteroscopes are now dried for a minimum of 3 h before storage.

We hypothesize that automated endoscope washer disinfector final rinse water cultures did not yield abnormal results because this sampling would only detect residual microbial contamination in the machines' rinse circuits which weekly sampling is unlikely to pick up, even if some biofilm-embedded cells escaped the ureteroscopes into rinse water.

Following the outbreak, the staffing levels of the department have been addressed and the full complement have been appointed. Flexible endoscope decontamination is a manually intensive job which requires a high level of vigilance. It is possible that when there was a shortage, staff members were not giving enough time to individual endoscopes and this may have contributed to the development of biofilm.

Notably, only three of the infected patients were treated with appropriate antibiotics as per antimicrobial sensitivities. One patient developed two episodes of infection (after two procedures, respectively) but the others all appeared to recover after a brief period of illness. According to local antibiotic guidelines, all patients undergoing ureteroscopic procedures routinely receive gentamicin prophylaxis [5]. Hence, as seen in this report, it is more likely that gentamicin-resistant organisms transferred by ureteroscopy would become apparent in clinical samples.

There has been greater awareness of flexible endoscopes as a route of transmission of multi-drug resistant organisms including carbapenemase-producing Enterobacteriaceae, but instances specific to flexible ureteoscopes are few in the literature. An outbreak of *P. aeruginosa* associated with flexible cystoscopes reported in the past was brought under control by stringent implementation of the cleaning protocol [6]. Conversely, during a previous outbreak of *Enterobacter cloacae* UTI due to a contaminated flexible ureteroscope [7], further

infections were reported even after revised decontamination procedures were introduced, achieving control when a weekly ethylene oxide sterilization protocol was introduced. However, ethylene oxide has associated safety concerns and endoscopes would need to be sent to external specialist centres, greatly increasing turnaround times. In the present outbreak, effective control was achieved by enhancing cleaning procedures and vigilance.

After removing the two implicated ureteroscopes, we did not identify any more cases of MDRPA following ureteroscopy. Single-use flexible ureteroscopes are used in the hospital at the time of writing this report. Moreover, only one reusable flexible ureteroscope is available for the cases with complex lower pole kidney stones. Disadvantages of some single-use flexible ureteroscopes have been reported and include fragility and a higher degree of deflection loss on instrumentation [8], which may lead some surgeons to prefer reusable endoscopes. However recent studies comparing single use flexible ureteroscopes with flexible reusable ureteroscopes for treating renal calculi found no significant differences in outcomes including procedure duration, stone size, stone clearance and complication rates [9]. Furthermore disposable ureteroscopes may also offer a cost advantage in some settings when repair and maintenance and cleaning of reusable ureteroscopes are factored in [10]. Single-use ureteroscopes cost approximately GBP 600—700 each.

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References

[1] Herve RC. Endoscopy in the twenty-first century: minimally invasive state-of-the-art medical technology or a future main vector of hospital-acquired infections? J Hosp Infect 2017;97 4:329—30.
[2] Kenters N, Huijskens EG, Meier C, Voss A. Infectious diseases linked to cross-contamination of flexible endoscopes. Endosc Int Open 2015;3 4:E259—65.
[3] Tolker-Nielsen T. Pseudomonas aeruginosa biofilm infections: from molecular biofilm biology to new treatment possibilities. APMIS Suppl 2014;138:1—51.
[4] Donlan RM, Costerton JW. Biofilms: survival mechanisms of clinically relevant microorganisms. Clin Microbiol Rev 2002;15 2:167—93.
[5] Wolf Jr JS, Bennett CJ, Dmochowski RR, Hollenbeck BK, Pearle MS, Schaeffer AJ. Best practice policy statement on urologic surgery antimicrobial prophylaxis. J Urol 2008;179 4:1379—90.
[6] Wendelboe AM, Baumbach J, Blossom DB, Frank P, Srinivasan A, Sewell CM. Outbreak of cystoscopy related infections with Pseudomonas aeruginosa: New Mexico, 2007. J Urol 2008;180 2:588—92. discussion 92.
[7] Chang CL, Su LH, Lu CM, Tai FT, Huang YC, Chang KK. Outbreak of ertapenem-resistant Enterobacter cloacae urinary tract infections due to a contaminated ureteroscope. J Hosp Infect 2013;85 2:118—24.
[8] Emiliani E, Traxer O. Single use and disposable flexible ureteroscopes. Curr Opin Urol 2017;27 2:176—81.
[9] Davis NF, Quinlan MR, Browne C, Bhatt NR, Manecksha RP, D'Arcy FT, et al. Single-use flexible ureteropyeloscopy: a systematic review. World J Urol 2018;36 4:529—36.
[10] Hennessey DB, Fojecki GL, Papa NP, Lawrentschuk N, Bolton D. Single-use disposable digital flexible ureteroscopes: an ex vivo assessment and cost analysis. BJU Int 2018;121(Suppl 3):55—61.