Short Communication

Infection Control Following an Outbreak of Extended-Spectrum Beta-Lactamase-Producing *Klebsiella pneumoniae* Isolated from Catheter-Associated Urinary Tract Infection

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SUMMARY: We present our experience with controlling an outbreak of extended-spectrum beta-lactamase (ESBL)-producing bacteria in catheter-associated urinary tract infection and the measures taken to prevent future outbreaks. In June 2015, 9 out of 44 hospitalized patients in the same ward tested positive for antibiotic-resistant bacteria in urine cultures, including ESBL-producing *Klebsiella pneumoniae*. Since these bacteria belonged to the same cluster, we concluded this was a localized outbreak. Seven out of 10 environmental tests detected resistant strains at 1,000 colony forming units/cm² or more. After an outbreak, we undertook periodic monitoring by active surveillance culture (ASC) every 2 months, along with environmental wipe testing. Cleaning regimen was performed through alcohol disinfection 5 or 7 times a day, then changed to complex-type chlorine-based disinfectant cleaner once a day that includes potassium peroxymonosulfate. ASC revealed only one positive case of antibiotic-resistant strain after incorporating new infection controls. Only a few environmental tests were positive for the bacteria after the new cleaning regimen, suggesting this cleaner might be effective for inhibiting outbreaks. Our control measures successfully prevented further outbreak and inhibited the recurrence.

Spinal cord injury (SCI) patients often urinate through clean intermittent catheterization (CIC), cystostomy, or urethral catheter. Urinary tract catheters are managed not only by the patients themselves but also by medical staff (1–3). Therefore, the risk of healthcare-associated infection is possible. Particularly, extended-spectrum beta-lactamase (ESBL) and carbapenem-resistant *Enterobacteriaceae* can cause severely problematic nosocomial infection outbreaks. Infection control needs to include urinary tract device management, such as cleaning, proper standard precautions and disinfection, and staff education (4,5). One important measure is active surveillance culture (ASC) for all hospitalized patients in the same wards to quickly identify potential outbreaks caused by ESBL-producing bacteria (6,7).

In June 2015, antibiotic-resistant strains were isolated from the urine of 9 patients in the same ward, including ESBL-producing *Escherichia coli* or *Klebsiella*

pneumoniae and 2 patients with pre-multidrug resistant *Pseudomonas aeruginosa* (MDRP), which was resistant to 2 of carbapenems, amikacin, or fluoroquinolones. This was considered to be an outbreak (Fig. 1). We speculated the reasons for origin of the outbreak as follows: i) Those patients with antibiotic-resistant strains were not from the same room but several different rooms; ii) There was no correspondence between nurses, doctors, or therapists taking care of those patients during outbreak period; iii) There was no common device use among those patients; and iv) ACS demonstrated that multiple antibiotic-resistant bacteria were isolated from the environment such as chairs in shower room. For these reasons, we consider the outbreak was caused by infection through the environment, so we have mainly undertaken infection control measures of environment disinfection. Analyses by random amplified polymorphic DNA PCR (RAPD-PCR) showed that 3 patients had the same or a similar cluster of *K. pneumoniae* which confirmed occurrence of an outbreak. Two isolates also had a similar antibiotic-resistance pattern (Fig. 1 and Table 1). The Infection Control Team (ICT) then intervened by investigating the outbreak along with infection control and prevention measures.

This study was approved by the institutional review board of Hyogo Prefectural Central Rehabilitation Hospital (No. 1521) and performed in accordance with the ethical standards of the institutional research committee

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ESBLs Outbreak in SCI Patients

Fig. 1. ESBLs-producing bacteria (*K. pneumoniae* and *E. coli*) isolation history in the 10 patients involved in this outbreak. In the handicapped patient wards, 36 positive antibiotic-resistant strains were isolated from the urine of 10 patients in this study period. Especially, in June 2015, the 9 patients had ESBL-producing *E. coli* or *K. pneumoniae*, and 2 patients had pre-MDRP, suggesting occurrence of outbreak. The period when ESBL-positive bacteria and pre-MDRP were detected was highlighted in gray.

Fig. 1. (Continued) Genetic analysis of ESBL-producing *K. pneumoniae* causing the outbreak. RAPD-PCR showed 3 patients (Pt A, B, and C; enclosed with white circle) with the same or similar cluster of ESBL-producing *K. pneumoniae*, confirming an outbreak. Leftmost and rightmost lanes: DNA size marker; ATCC KPC (+), ATCC standard control *K. pneumoniae* carbapenemase production-positive; ATCC KPC (-): ATCC standard control *K. pneumoniae* carbapenemase production-negative.

and the 1964 Helsinki declaration.

For the RAPD-PCR, DNA extraction was performed using a Cica Geneus DNA Extraction Kit (Kanto Chemical, Tokyo, Japan). RAPD-PCR was performed with extracted DNA and ERIC2 primer: 5'-AAG TAA GTG ACT GGG GTG AGC G-3' in the presence of Taq DNA polymerase. PCR conditions were as follows: denaturation at 95°C for 5 min, 35 cycles of 94°C for 1 min, 35°C for 1 min and 72°C for 1 min, and incubation at 72°C for 10 min.

The procedure of CIC was as follows: i) hand hygiene by alcohol; ii) clean wiping around outer urethral orifice (0.025%, benzalkonium chloride or 10 times-diluted 10 % povidone-iodine); iii) catheter insertion with lubricating jelly; iv) hand hygiene through alcohol disinfection

Table 1. Antimicrobial susceptibilities of ESBL-producing *K. pneumoniae* in the patients

Antimicrobial agent	Pt A	Pt B	Pt C
ampicillin	> 16 ¹⁾	> 16	> 16
piperacillin	> 64	> 64	> 64
cefazolin	> 16	> 16	> 16
cefotiam	> 16	> 16	> 16
cefotaxime	> 2	> 2	> 2
ceftriaxone	> 2	> 2	> 2
ceftazidime	> 8	> 8	> 8
cefpirome	> 16	> 16	> 16
cefaclor	> 16	> 16	> 16
cefcape	> 1	> 1	> 1
cefmetazole	≤ 8	≤ 8	≤ 8
flomoxef	≤ 8	≤ 8	≤ 8
imipenem	≤ 1	≤ 1	≤ 1
meropenem	≤ 1	≤ 1	≤ 1
aztreonam	> 8	> 8	> 8
ampicillin/sulbactam	> 16/8	> 16/8	> 16/8
cefoperazone/sulbactam	≤ 16/8	≤ 16/8	≤ 16/8
piperacillin/tazobactam	≤ 16	≤ 16	≤ 16
gentamicin	> 8	> 8	> 8
amikacin	8	8	8
minocycline	8	4	8
levofloxacin	2	1	0.5
sulfamethoxazole/trimethoprim	> 2/38	> 2/38	> 2/38

¹⁾ MIC, minimal inhibitory concentration (μg/ml).

again after confirmation drainage of urine; and v) shelving urinals with collected urine for a couple of hours, then handling by nurses and carrying to a dirty utility room for disposal. Periodical surveillance of urine cultures for the catheterized patients were performed every

2 months after this outbreak. In addition, ASC was performed for patients 1 month after the outbreak. Environmental cultures were obtained once a week to estimate the factors responsible for transmission of the outbreak based on bacterial identification results and follow up. For outbreak control and prevention of recurrence, the shelf for transient storage of CIC catheters in the sanitary room was removed, and inspection by wiping for environmental smear tests was performed periodically and monitored. Cleaning procedures for the sanitary room were reviewed, and the number of routine cleanings for the utility room was increased to once a day using a complex-type chlorine-based disinfectant cleaner (RUBYSTA; Kyorin Pharmaceutical, Tokyo, Japan) with potassium peroxydisulfate. Regarding the selection of disinfectant cleaners in this case, Doidge et al. reported that a complex-type chlorine-based disinfectant cleaner was effective for inhibiting outbreaks caused by antibiotic-resistant strains, and that usual disinfection by alcohol could not prevent such kind of outbreak (8).

Outer sheaths of CIC catheters were cleaned by sterile cross. Sanitary room walls and the circumferences around the spaces (about 30 cm²) where bacteria had been detected were prioritized to be cleaned. This included the hanger for urine catheters, shelf for urine catheters, lever of steam sterilization, toilet lever, toilet, rack for urine bag, and the automatic electronic cock. These materials were wiped with such a complex-type chlorine-based disinfectant cleaner. Use of this new cleaner for routine cleaning continued as mentioned above. Nurses working in wards were educated on infection control in study meetings with the ICT. In par-

ticular, the significance of contact precautions and hand hygiene was reinforced and explained every morning.

All patients with positive urine culture for antibiotic-resistant strains such as ESBL-producing bacteria and pre-MDRP (resistant to 2 of carbapenems, amikacin, or fluoroquinolones) underwent periodical urine culture tests. Of 10 patients in this category, 3 had ESBL-producing *K. pneumoniae* (Fig. 1), showing the same cluster patterns. The likely explanation for this was horizontal infection with very similar antibiotic-susceptibilities (Table 1). Table 2 shows the results from 5 rounds of tests after the outbreak. The 1st round of environment inspection was just after the outbreak, the 2nd round followed the increase of the number of cleanings, the 3rd round followed the use of a complex-type chlorine-based disinfectant cleaner mentioned above, the 4th round followed daily use of this cleaner, and the 5th was a snap inspection at 6 months after the initiation of the new cleaning regimen. The 1st inspection reflected the usual periodical cleaning and showed positive bacterial isolation in 8 out of 10 areas tested. After the measures recommended by the ICT, including more frequent cleaning and change of disinfectant, we had a significant decrease of bacterial isolation (Table 2).

One month later in July 2015, follow up ASC culture test showed reduction of multiple antibiotic-resistant strain cross infections to 1 strain of ESBL-producing *E. coli* (Pt J in Fig. 1). Following this episode, we did not have any cross infection. Use of the new cleaner in routine cleaning continued for 6 months, and then unannounced environmental cleaning tests

Table 2. Environmental smear culture tests: wiping and follow up¹⁾

Environmental facility	1st: July 2, 2015 regular cleaning		2nd: July 15, 2015 7 times/day		3rd: July 22, 2015 RUBYSTA 7 times/day		4th: August 6, 2015 RUBYSTA once/day		5th: January 26, 2016 RUBYSTA once/day	
	<i>n</i> (CFU/cm ²)	Bacteria	<i>n</i>	Bacteria	<i>n</i>	Bacteria	<i>n</i>	Bacteria	<i>n</i>	Bacteria
Hanger for urine catheter	> 1,000	<i>S. marcescens</i>	0	-	0	-	0	-	0	-
Shelf for urine catheter	> 1,000	<i>S. marcescens</i> MRSA <i>E. coli</i>	0	-	0	-	0	-	0	-
Lever of steam sterilization	0	-	0	-	0	-	0	-	0	-
Lever of toilet	0	-	0	-	0	-	0	-	0	-
Toilet	> 1,000	<i>S. marcescens</i> <i>A. baumannii</i> MRCNS	> 100	<i>E. coli</i> <i>S. marcescens</i>	0	-	0	-	0	-
Rack for urine bag	> 10	<i>P. oryzae</i>	0	-	0	-	0	-	N/A	N/A
Shower chair	> 1,000	<i>K. pneumoniae</i> ESBL CNS	> 10	<i>E. coli</i> ESBL <i>K. pneumoniae</i> ESBL	4	CNS	5	CNS	0	-
Keyboard and mouse	> 1,000	<i>Candida</i> spp.	0	-	0	-	0	-	0	-
Sink for nurse	> 1,000	<i>P. aeruginosa</i> <i>C. freundii</i>	0	-	0	-	0	-	0	-
Sink for patient	> 1,000	<i>C. indologenes</i>	> 10	<i>C. meningi</i>	6	CNS	7	CNS	2	<i>Candida</i> spp.

¹⁾ Environmental inspections were performed 5 times after outbreak. After frequent cleaning and introduction of a complex-type chlorine-based disinfectant cleaner (RUBYSTA), positive cultures decreased periodically. CFU, colony forming unit; MRSA, methicillin-resistant *Staphylococcus aureus*; MRCNS, methicillin-resistant coagulase-negative *Staphylococcus*; N/A, not applicable; ESBL, extended-spectrum beta-lactamase; CNS, coagulase-negative *Staphylococcus*; *S. marcescens*, *Serratia marcescens*; *A. baumannii*, *Acinetobacter baumannii*; *P. oryzae*, *Pseudomonas oryzae*; *C. freundii*, *Citrobacter freundii* complex; *C. indologenes*, *Chryseobacterium indologenes*; *C. meningi*, *Chryseobacterium meningoseptica*.

were performed. This resulted in maintaining a clean environment for January 2016 (Table 2).

This study emphasizes 3 points: i) A complex-type chlorine-based disinfectant cleaner is highly effective; ii) ASC is useful; and iii) Assessing environmental factors as possible sources of transmission is significant in determining horizontal infection. Through studying ESBL-producing bacteria in these catheterized patients, we took the following measures for infection control and prevention of the recurrence:

- ① The shelf for CIC catheter storage was removed, and the environmental cleaning method changed to include a complex-type chlorine-based disinfectant cleaner.
- ② Nursing staff education emphasized the significance of contact precautions and hand hygiene every morning.
- ③ The frequency of utility room cleaning decreased to once a day due to use of a complex-type chlorine-based disinfectant cleaner.
- ④ Periodical surveillance culture was changed to ASC for strict observation of potential recurrence.

Measures for preventing outbreaks emphasize i) education for medical staff, patients, and their families; ii) hand hygiene; iii) contact precautions and/or gloving; iv) isolation precaution; v) cohorting; vi) dedicated infection control staff; vii) change in antibiotics; viii) screening cultures for patients, equipment, and environment; ix) increased cleaning; and x) closing suspicious wards and limiting new hospitalizations. Center for Disease Control and Prevention guidelines stress the significance of i) checking the supporting system in terms of financial management; ii) education; iii) antimicrobial stewardship; iv) surveillance; v) infection control (contact and standard precautions); and vi) environmental measures (9–11).

The ICT has an educational role for nursing staff regarding reinforcement of hand hygiene or wearing gloves during any outbreak of ESBL-producing bacteria in addition to ASC (12,13). Self-protection by personal equipment and hand hygiene should be emphasized as well as increasing general knowledge of how infection outbreaks spread (14).

We would like to emphasize the study limitation. Regarding RAPD-PCR data, we showed only those from 3 patients since some samples were missing. Further prospective-relates studies need to be performed in the near future.

In summary, our ICT measures for controlling an outbreak of ESBL-producing bacteria and pre-MDRP isolates possibly helped to prevent the spread of the outbreak and control the infection, suggesting the efficacy of active ASC and new environment cleaning products. These may decrease the number of cleanings without outbreak recurrence and keep a low number of isolated bacteria in the environment.

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